

# Life-Threatening and Non-Life-Threatening Complications Associated With Coughing

## A Scoping Review



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**BACKGROUND:** This is an update of the section on complications that are associated with coughing in the 2006 CHEST cough guidelines that addresses two aims: (1) to systematically identify and thematically categorize the diverse complications of cough by providing a guide for future studies and (2) to identify gaps in the literature for future research.

**RESEARCH QUESTION:** What are the potential complications that are associated with the act of coughing that have been reported in infants, children, adolescents, and adults?

**STUDY DESIGN AND METHODS:** A scoping review was performed with the use of PubMed and SCOPUS databases that were searched from their beginning until September 6, 2019.

**RESULTS:** Two hundred forty-seven publications met our inclusion criteria. To these, we added 38 articles from the 2006 complications paper that were not identified in the literature search plus the paper itself for a final total of 286 publications that formed the basis of this review. Since 2006, three new categories of complications have been reported: ear, nose and throat; disease transmission; and laboratory testing. Multiple additional complications that fall outside of these three categories have also been identified and included in the following categories: cardiovascular, constitutional symptoms, dermatologic, GI, genitourinary, musculoskeletal, neurologic, ophthalmologic, psychosocial/quality of life, and respiratory. Not previously highlighted is that some of the complications led to serious morbidity that included death, especially in patients with comorbid conditions, and potentially resulted in harm to others when cough resulted in a motor vehicle accident.

**INTERPRETATION:** Our work identified a large number of cough complications that we thematically categorized primarily by organ system so that future studies of each system or each complication can be conducted. The gap in the literature that future studies should address is to identify the frequency of the complications and the strength of their association with cough. Only then will one be able to describe the findings in a manner that allows specific recommendations for avoiding these complications. In the meantime, patients with cough should be evaluated and treated according to evidence-based guidelines to mitigate or prevent the myriad of potential complications that are associated with coughing.

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**KEY WORDS:** complication; cough; organ system

FOR EDITORIAL COMMENT, SEE PAGE 1818

**ABBREVIATIONS:** CQLQ = cough quality of life questionnaire

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This review provides an update to our article on the topic of complications associated with coughing in the 2006 American College of Chest Physicians Clinical Practice Guidelines on the Diagnosis and Management of Cough.<sup>1,2</sup>

As previously stated in 2006,<sup>1</sup> complications that are associated with coughing stem from physiologic events that teleologically seem to be designed to allow cough to carry out its two main protective functions: to prevent foreign material from entering the lower respiratory tract and to clear foreign material and excessive secretions from the lower respiratory tract. During the physiologic phases of coughing (ie, inspiratory, compressive, and expiratory), sufficiently high expiratory velocities are generated to carry out the aforementioned functions. The potentially injurious nature of these physical forces is recognized; for example, during vigorous coughing, intrathoracic pressures can reach 300 mm Hg<sup>3</sup> that help to generate expiratory velocities up to 500 miles per hour<sup>4</sup> (ie, 85% of the speed of sound).

From a cardiovascular standpoint, the physiologic effects of coughing can be a two-edged sword. Because intrathoracic pressures generated during coughing may hemodynamically compare favorably with chest compressions, cough CPR can be successfully used in a controlled environment.<sup>5</sup> Because vigorous coughing can also generate intrathoracic energies up to 25 J,<sup>6</sup> cardiologists, in a monitored in-hospital cardiac catheterization laboratory, often instruct patients, before the procedure begins, to vigorously cough when instructed to do so, if and when awake patients

experience ventricular tachycardia and asystole during cardiac catheterization procedures. Because coughing can also be associated with a reflex increase in vagal tone, coughing can interrupt aberrant conduction of atrioventricular junctional tachycardia.<sup>7</sup> On the other hand, coughing can also lead to atrioventricular block<sup>8</sup> and other arrhythmias (Table 1).

As noted in 2006,<sup>1</sup> although the pressures, velocities, and energy described earlier, particularly those that relate to the effects on the cardiovascular system, allow coughing to be an effective way of protecting the lungs from near aspiration and aspiration and of providing CPR and arrhythmia control, they can also cause a variety of complications that can be categorized as cardiovascular, constitutional, dermatologic, GI, genitourinary, health-related quality of life, musculoskeletal, neurologic, ophthalmologic, psychosocial, and respiratory.

In planning this update, we followed current *CHEST* guideline methods<sup>9</sup> that emphasizes that guidelines should be based on high-quality systematic reviews to address clearly formulated key clinical questions. Because our question was broad and the literature had not been reviewed comprehensively, we chose to conduct a scoping review. A scoping review is based on similar established methods to a systematic review with the intent to clarify working definitions, to identify key concepts, and to establish conceptual boundaries by examining the extent and nature of the evidence.<sup>10,11</sup> Our specific aims were to (1) systematically identify and thematically categorize the diverse complications of cough providing a guide for future studies and (2) identify gaps in the literature for future research.

## Methods

To begin our literature search, we asked the following key clinical question: What are the potential complications associated with the act of coughing that have been reported in infants, children, adolescents and adults? A complication was defined as “a morbid process or event that occurs during the course of a disease that is not an essential part of that disease, although it may result from it or from independent causes.”<sup>12</sup> We considered death to be associated with a complication when the authors of the case report or case series described the death as following the complication of cough and it did not appear to be due to another event. To guide the search of our scoping review, we sought the following elements: population (infants, children, adolescents, and adults), concept (does the study report on the complications as defined earlier secondary to the act of coughing), and context (cough of any duration in patients who are either ambulatory or in the hospital). Inclusion criteria were limited to the English language, cough of any duration, and any study design such as systematic reviews with or without a metaanalysis, diagnostic cohort, case-control study, cross-sectional

study, letter to the editor, case reports/series, other reports. Exclusion criterion was a report of an adverse event rather than a complication, unless cough initiated the event. An adverse event was defined as “an incident in which harm resulted to a person receiving health care.”<sup>13</sup>

### Search Strategy

A systematic review of the literature was performed. Studies published in PubMed and SCOPUS databases were identified from the beginning of the database to September 6, 2019. Because cough and complication retrieved 13,750 citations in PubMed alone, the search was limited to subject heading. The search strings can be found in e-Appendix 1.

### Data Screening and Extraction

Two authors (C. L. F. and R. S. I.) independently analyzed the titles and content of the abstracts to assess inclusion criteria. From the selected titles and abstracts, full reports about potentially relevant studies were obtained, and two authors (C. L. F., N. D., or R. S. I.)

**TABLE 1 ] Cough-Associated Complications**

System Category	Complication
Cardiovascular	<b>Aortic dissection</b> <sup>14</sup>
	Arterial hypotension <sup>3,15-19</sup>
	Arrhythmia
	• Bradyarrhythmias with or without heartblock with and without dizziness and syncope <sup>8,20-27</sup>
	• Tachyarrhythmias, atrial, or ventricular <sup>28-30</sup>
	<b>Coronary artery dissection</b> <sup>31,32</sup>
	<b>Cardiac luxation after pneumonectomy</b> <sup>33</sup>
	<b>Stress cardiomyopathy</b> <sup>34</sup>
	<b>Dislodgement/malfunctioning of intravascular catheters or other intravascular devices</b> <sup>35-40</sup>
	Loss of consciousness <sup>3,15</sup>
Constitutional symptoms	<b>Pneumopericardium during coronary angiography</b> <sup>41</sup>
Dermatologic	Excessive sweating, anorexia, exhaustion, temperature elevation (various combinations), vomiting <sup>42</sup>
Ear, nose, and throat	Petechiae and purpura <sup>43</sup>
	Disruption of surgical wounds (sternal and abdominal) <sup>44-46</sup>
	<b>Subcutaneous hematoma not anticoagulated</b> <sup>47-50</sup>
GI	<b>Subcutaneous hematoma receiving anticoagulation therapy</b> <sup>51,52</sup>
	<b>Arytenoid subluxation with or without obliteration of cricoarytenoid space</b> <sup>53,54</sup>
	<b>Hemotympanum</b> <sup>55</sup>
GI	<b>Thyroid cartilage fracture with phlegmon</b> <sup>56</sup>
	<b>Esophageal rupture</b> <sup>57</sup>
	<b>Gastroduodenal artery pseudoaneurysm rupture</b> <sup>58</sup>
	Gastroesophageal reflux events <sup>59</sup>
	Gastric hemorrhage after percutaneous endoscopic gastrostomy <sup>60</sup>
	Gastric perforation after upper endoscopy <sup>61</sup>
	Hepatic cyst rupture <sup>62</sup>
	<b>Laceration of stomach and spleen</b> <sup>63</sup>
	Malfunction of gastrostomy button <sup>64</sup>
	Mallory-Weiss tear <sup>65,66</sup>
	Rectal prolapse with rupture of distal colon and evisceration of small intestine through anus and death in an infant <sup>67</sup>
	Small bowel herniation through laparoscopic trocar site <sup>68</sup>
	Splenic rupture <sup>69-73</sup>
	<b>Spontaneous retroperitoneal bleed with hematoma</b> <sup>74</sup>
	<b>Inguinal or femoral or umbilical or lumbar or abdominal wall hernia</b> <sup>75-81</sup>
Genitourinary	Inversion of bladder through urethra <sup>82</sup>
	Urinary incontinence <sup>77,83-87</sup>
	<b>Vaginal cuff dehiscence with evisceration of ileal loops</b> <sup>88</sup>
Musculoskeletal	<b>Avulsion of lesser trochanter of femur</b> <sup>89</sup>
	From asymptomatic elevations of serum creatinine phosphokinase to rupture of rectus abdominus muscles with and without hematoma <sup>51,90-103</sup>
	<b>Diaphragmatic rupture with abdominal content herniation (small bowel and omentum)</b> <sup>104-106</sup>
	<b>False-positive PET scan uptake in muscle related to cough</b> <sup>107</sup>
	<b>Intercostal muscle rupture with lung herniation</b> <sup>108-110</sup>

(Continued)

TABLE 1 ] (Continued)

System Category	Complication
	<b>Lung herniation through rib separations</b> <sup>49,111</sup>
	<b>Lung herniation through previous incision</b> <sup>112</sup>
	<b>Liver, colon, small bowel, omentum, and lung herniation through transdiaphragmatic intercostal separation</b> <sup>113</sup>
	<b>Intercostal artery rupture and hematoma with or without hemothorax with or without rib fracture</b> <sup>47,114-116</sup>
	<b>Internal oblique muscle tear with hematoma</b> <sup>117,118</sup>
	<b>Osteophytes of the ribs</b> <sup>119</sup>
	Rib fractures <sup>47,78,120-140</sup>
	<ul style="list-style-type: none"> <li>• <b>Costal margin separation with or without rib fracture and diaphragmatic rupture with abdominal visceral herniation into thoracic cavity or abdomen and/or subcutaneously</b><sup>141-148</sup></li> <li>• <b>Rib fracture with pseudo hernia of abdominal contents</b><sup>149</sup></li> <li>• <b>Rib fracture with lung herniation with or without pleural effusion</b><sup>150-154</sup></li> </ul>
	<b>Scapula fracture</b> <sup>155</sup>
Neurologic	Acute cervical radiculopathy and disc herniation <sup>156</sup>
	<b>Carotid artery dissection and pseudoaneurysm</b> <sup>157</sup>
	<b>Carotid artery dissection with stroke</b> <sup>158</sup>
	<b>Cerebral air embolism causing stroke with and without death</b> <sup>159-162</sup>
	Cerebral spinal fluid rhinorrhea <sup>163,164</sup>
	<b>Cervicobrachial pain</b> <sup>165</sup>
	Cervical epidural hematoma associated with oral anticoagulation <sup>166</sup>
	Cough syncope <sup>17,167-206</sup>
	<b>Cough syncope causing car crash with injuries</b> <sup>187</sup>
	<b>Cough syncope causing traffic accident</b> <sup>191</sup>
	<b>Cough syncope causing traffic accident with death of pedestrians</b> <sup>190</sup>
	<b>Cough-induced anoxic cerebral injury in child</b> <sup>207</sup>
	<b>Cough-induced cluster headache</b> <sup>208</sup>
	<b>Cough-induced transient ischemic attack</b> <sup>209</sup>
	<b>Cough-induced nystagmus</b> <sup>210</sup>
	<b>Cough-induced recurrence of spinal anesthesia</b> <sup>211</sup>
	<b>Cough-induced vertigo</b> <sup>192</sup>
	Cough headache <sup>77,212-225</sup>
	<b>Cough headache presenting as toothache</b> <sup>226</sup>
	<b>Cough-induced hemiparesis</b> <sup>227</sup>
	<b>Cough-induced hemiplegic migraine</b> <sup>228</sup>
	<b>Cough-induced myxoma embolism causing paraplegia</b> <sup>229</sup>
	Dizziness <sup>230</sup>
	Cough-induced seizures <sup>172,176,185,201,231</sup>
	Malfunctioning ventriculoatrial shunts <sup>232</sup>
	<b>Pneumocephalus</b> <sup>233</sup>
	<b>Pneumorrhachis</b> <sup>233-236</sup>
	<b>Spontaneous dissection of cerebral arteries</b> <sup>237</sup>
	Stroke due to vertebral artery dissection <sup>238-240</sup>
	<b>Stroke due to bilateral carotid artery thrombus formation</b> <sup>241</sup>
Ophthalmologic	<b>Extrusion of ocular contents during surgery</b> <sup>242</sup>

(Continued)

TABLE 1 ] (Continued)

System Category	Complication
	Spontaneous compressive orbital emphysema of rhinogenic origin <sup>243</sup>
	<b>Orbital emphysema compressing the eyeball and the optic nerve</b> <sup>243</sup>
	<b>Periorbital ecchymosis (Panda sign)</b> <sup>244,245</sup>
	<b>Subconjunctival hemorrhages</b> <sup>77,180,245,246</sup>
	<b>Retinal detachment</b> <sup>247</sup>
	<b>Subhyaloid hemorrhage</b> <sup>248</sup>
	<b>Suprachoroidal hemorrhage</b> <sup>249,250</sup>
	<b>Transient blindness</b> <sup>251</sup>
	<b>Postoperative Trabeculectomy bleb leak</b> <sup>252</sup>
Psychosocial/quality of life	Fear of serious disease <sup>230,253,254</sup>
	Lifestyle changes <sup>230,254,255</sup>
	Self-consciousness <sup>230,254,255</sup>
	<b>Adverse effects on quality of life</b> <sup>87,254-264</sup>
Respiratory	<b>Apical lung herniation with tracheal displacement</b> <sup>265</sup>
	<b>Chylothorax</b> <sup>266</sup>
	<b>Diaphragmatic rupture with herniation of small intestine or stomach into chest</b> <sup>63,267</sup>
	Exacerbation of asthma <sup>268</sup>
	<b>Hemothorax</b> <sup>116,144</sup>
	Herniations of the lung (eg, intercostal and supraclavicular) with and without incarceration <sup>269-273</sup>
	Hydrothorax in peritoneal dialysis <sup>274</sup>
	<b>Hydropneumothorax and tension pneumothorax</b> <sup>57</sup>
	Laryngeal trauma (eg, laryngeal edema and hoarseness) <sup>230,254,255,275,276</sup>
	Pulmonary interstitial emphysema, with one or more of pneumatosis intestinalis, pneumomediastinum, pneumoperitoneum, pneumopericardium, pneumoretroperitoneum, pneumorrhachis, pneumothorax, subcutaneous emphysema, retropharyngeal, paraesophageal air <sup>49,111,161,233-235,271,277-293</sup>
	<b>Rupture of bronchus during bronchoscopy with or without pneumothorax</b> <sup>294,295</sup>
	<b>Rupture of trachea</b> <sup>287,296</sup>
	Tracheobronchial trauma (eg, bronchitis and bronchial rupture) <sup>233,297</sup>
	<b>Transmission of infectious disease</b> <sup>298,299</sup>
Disease transmission	<b>Transmission of infectious disease</b> <sup>298,299</sup>
Laboratory testing	<b>False-positive PET scan uptake in muscle related to cough</b> <sup>107</sup>

Modified from Table 1 in Irwin RS. Complications of cough: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(suppl1):54S-58S.<sup>1</sup> Complications that are new since 2006 are given in bold italic type.

independently assessed the eligibility of the studies and completed data extraction. Disagreements were discussed and resolved by consensus. A third author was available to help resolve disagreements if necessary. Even though the screening focused on publications not published in

the 2006 guideline, all the articles cited in the 2006 review were reanalyzed. During this re-review of the articles published in the 2006 review, we came across 38 articles that did not appear in the current search.

## Results

### Literature Study Selection

The process of study selection is outlined in Figure 1, which shows that there were an initial 3,202 unique articles identified by our search string. After being

screened, 2,858 abstracts and titles were excluded based on the inclusion and exclusion criteria, which left 344 that underwent full text review. Full text review resulted in the inclusion of 247 articles plus 38 additional citations from the 2006 guideline that were not identified by our search string. The 2006

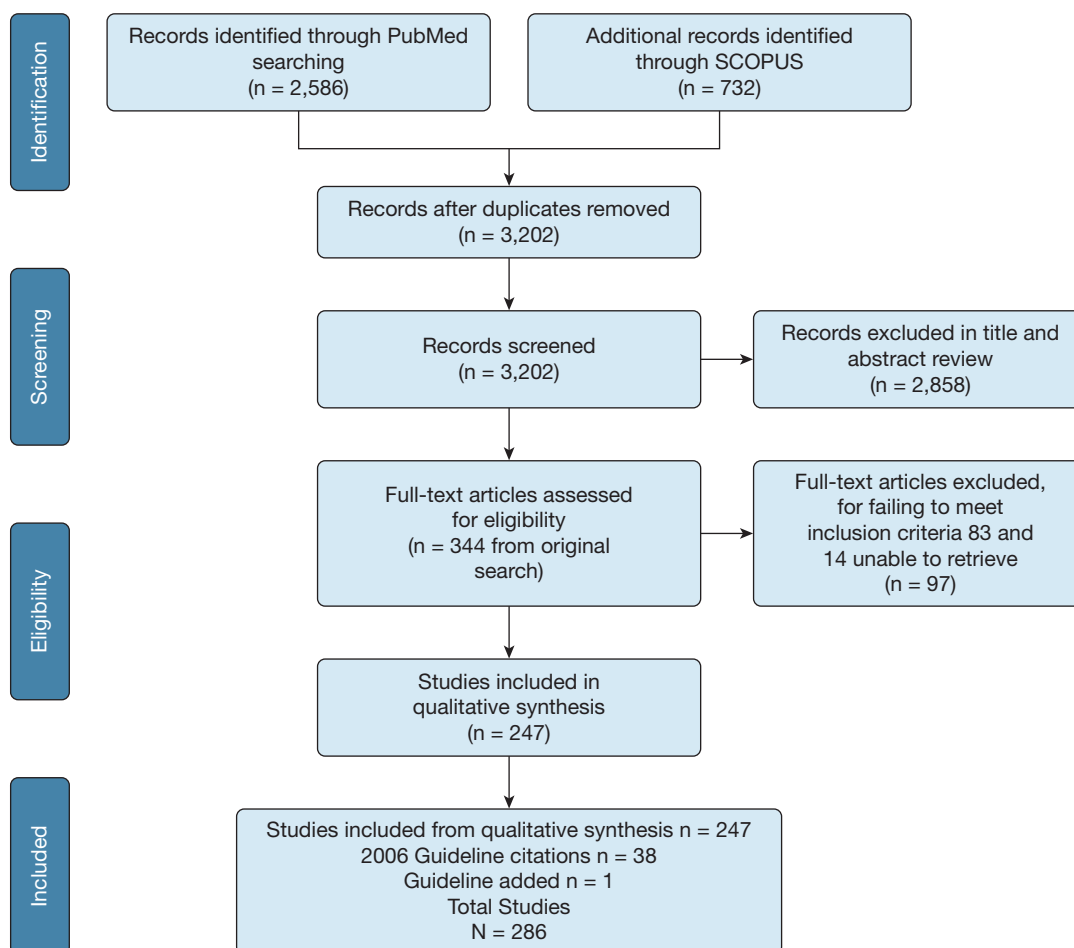


Figure 1 – Flow diagram of preferred reporting items for study selection. From Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 2009;6(7):e1000097. For more information, visit [www.consort-statement.org](http://www.consort-statement.org).

guideline was also included, which resulted in 286 articles.

### Complications

The complications associated with cough, as identified by the scoping review, are summarized in [Tables 1 and 2](#). The spectra of complications that are associated with coughing are listed in [Table 1](#) in categories that are primarily organ system based and have been modified only minimally from that previously reported in 2006. The new complications, which were identified by the review, that have been added to the original table are included. Since 2006, three new categories of complications have been identified: ear, nose and throat; disease transmission; and laboratory testing. Those complications that were reported as leading to death are listed in [Table 2](#). A data table ([e-Table 1](#)) shows more detail about the complications in the articles from the

new search that are categorized and summarized in [Tables 1 and 2](#).

### Discussion

Reviews of complications of cough have appeared periodically in the medical literature for many years. Prior to and even after 1991, these publications primarily focused on complications of a physical nature.<sup>42,300-302</sup> In 1991, we published a prospective study that involved 108 consecutive and unselected patients who were referred to our Cough Clinic with chronic cough that included the results of qualitative interviews that identified reasons for which these patients sought medical attention.<sup>230</sup> The reasons all related to cough-associated complications; some were physical, and others were of a psychosocial nature such as fearing that something is wrong, exhaustion, life style change, self-consciousness, and/or fearing cancer, AIDS,

**TABLE 2 ] Cough-Associated Complications That Lead to Death**

Cough-Associated Complication	Age/Sex	Comorbid Illness	Comment
<b>Death to self and others</b>			
Cough syncope in heavy goods-vehicle drivers causing serious traffic accidents resulting in death of two drivers and two pedestrians <sup>190</sup>	UA, UA	UA	Cough syncope can lead to death for the drivers and others.
<b>Death to self</b>			
Cough associated with spontaneous arterial gas embolism in patient with chronic necrotizing pneumonia, bullae, and brain infarct with death from complications <sup>160</sup>	78 y, M	COPD, smoker, chronic <i>Enterobacter cloacae</i> pneumonia, hypertension, atrial fibrillation, type 2 diabetes mellitus, hypothyroidism, dyslipidemia	Spontaneous arterial gas embolism resulted in brain infarcts and air in the cavernous sinuses, which led to death precipitated by coughing in a patient with preexisting chronic necrotizing pneumonia, blebs, and bullae. Proposed mechanism is likely weakened parenchyma that led to bleb rupture with entrainment of air into the pulmonary veins and left heart.
Paroxysms of cough followed by fainting in patients with asthma (four deaths in the series) <sup>173</sup>	UA, M (n = 281); F (n = 9) (N = 290)	Case series included patients with emphysema, bronchitis, TB, asthma, laryngitis, bronchiectasis, pneumoconiosis, sarcoidosis	Death reported as unequivocal cause after post-tussive syncope in four cases, which accounted for 1% mortality rate in the collective series included two in the literature and two personal cases
Fatal rectus sheath hematoma <sup>102</sup>	82 y, F	Polymyositis and related collagen disorders, well controlled with long-term corticosteroids (prednisone 5 mg daily), occult coronary artery disease	Rectus sheath hematoma in one of three patients reported may have been attributed to coughing associated with pneumonia. She was also on thromboprophylaxis with heparin and prednisone for polymyositis. Her course was complicated by a large hematoma, hypotension, and ultimately death.
Cough-induced lung intercostal (8th space) hernia with large abdominal hematoma in patient with COPD exacerbation and death <sup>49</sup>	73 y, M	COPD, total laryngectomy for laryngeal cancer with tracheostomy	Cough-induced intercostal muscle rupture with lung hernia associated with hematoma of the left chest and abdomen, massive subcutaneous emphysema of the left chest and lumbar region in a patient presenting with an exacerbation of COPD that was improving before the coughing insult, which ultimately resulted in death.
Fatal gas cerebral embolism after heavy coughing while using noninvasive ventilation (bilevel positive airway pressure) for fibrotic lung disease <sup>162</sup>	78 y, M	Severe restrictive lung disease due to fibrotic remodeling due to TB, MALT lymphoma	Cerebral air embolism precipitated by episodes of severe coughing that led to catastrophic stroke in a patient presenting with hemoptysis treated with left bronchial artery embolization, on noninvasive positive pressure ventilation and ultimately death due to intractable treatment of resistant cough.
Pneumomediastinum in children with cough with a death <sup>286</sup>	4 y, M	Measles and pneumonia	In a case series of five patients with severe cough, one patient had refractory cough due to measles, bronchopneumonia that resulted in

(Continued)



**TABLE 2 ] (Continued)**

Cough-Associated Complication	Age/Sex	Comorbid Illness	Comment
			extensive subcutaneous emphysema, pneumomediastinum that ultimately led to progressive decline and death.
Pneumomediastinum secondary to coughing in an elderly patient with emphysema with death due to complications <sup>288</sup>	96 y, M	Under custodial care in the geriatrics division	In this case series of three patients, the current patient experienced extensive subcutaneous emphysema and pneumomediastinum after an episode of coughing that resulted in progressive decline and death.
Prolapse of the rectum with spontaneous rupture of the distal colon and evisceration of the small intestine through the anus in an infant after a bout of coughing and death due to complications <sup>67</sup>	4 Mo, F	Low birthweight	Severe bout of coughing putatively resulted in increased abdominal pressure that caused rectal prolapse, spontaneous rupture of visceral colon, and evisceration of the small bowel.
Cough-induced syncope that resulted in death in the setting of cor pulmonale and obstructive lung disease <sup>198</sup>	61 y, M	Anthracosilicosis, COPD, cor pulmonale, right ventricle myocardial infarction	Cough exacerbated the existing pulmonary hypertension and cor pulmonale as measured by right heart catheterization which led to hypotension, syncope, and ultimately death due to cardiac arrest.

F = female; M = male; MALT = mucosal associated lymphoid tissue; UA = unavailable.

or TB (Table 3).<sup>230</sup> These results broadened our understanding of the reasons that patients with chronic cough were seeking care and led to the development of our Adverse Cough Outcome Survey<sup>254</sup> that eventually led to our development of the first cough quality of life questionnaire, the CQLQ.<sup>255</sup> The importance of the development of validated and reliable cough quality of life patient reported outcome questionnaires in the new millennium has now allowed us to assess not only for and quantify the common physical but also for psychosocial complications as summarized in this review.<sup>255,264,303,304</sup>

This scoping review has confirmed the psychosocial complications mentioned earlier as well as more broadly identifying physical complications compared with our 2006 report. The physical complications that have been identified, while primarily drawn from case reports and small case series, suggest that coughing can lead to a variety of complications from the relatively minor to those that can be life-threatening or even lead to death. Although the physiologic forces generated by coughing can result in acute and serious injury to an otherwise healthy individual, their effects may be magnified in patients in the following situations, especially when

coughing is sustained: compromised by comorbid illnesses or extremes of age; undergoing surgery (eg, ocular) or procedures (eg, bronchoscopy, upper GI endoscopy); recovering from surgery (eg, cardiac or abdominal); and risk from the side-effects of medications (eg, corticosteroids or anticoagulants). Until definitive studies show the way forward, we speculate that it makes physiologic sense that, whenever possible, attempts to control coughing should be made before surgery to avoid wound dehiscence (eg, sternal or abdominal) or extrusion of ocular contents during eye surgery. This review also raises awareness of potential injury to self and others from uncontrolled coughing during automobile driving.

Our study was a scoping review and not a full systematic review; as such, we were able to identify a multitude of complications of cough and to categorize them for future study. The gap in the literature that this review identified is that we do not know how frequent all the complications are or the strength of their association with cough. However, until future research prospectively provides us with the answer, we are left to speculate about the frequency of some of the more common and/or most troublesome complications of chronic cough in those



**TABLE 3 ] Reasons That Patients With Chronic Cough Seek Medical Attention**

Reason	Frequency, %	Most Troublesome, %
Something's wrong	98	12
Exhaustion	57	17
Self-conscious	55	10
Insomnia	45	4
Lifestyle change	45	12
Musculoskeletal pain <sup>a</sup>	44	3
Hoarseness	43	2
Excessive perspiration	42	1
Urinary incontinence <sup>b</sup>	39	9
Dizziness	38	0
Fear of cancer	33	11
Headache	32	3
Fear of AIDS or TB	28	11
Retching	21	4
Vomiting	18	1
Nausea	16	0
Anorexia	15	0
Syncope or near syncope	5	0

<sup>a</sup>Musculoskeletal pain was documented by chest radiography to be due to rib fracture in only one patient.

<sup>b</sup>Urinary incontinence complicated by cough only in women and two men who had undergone prior transurethral prostatectomy. Reprinted from Irwin RS, Curley FJ. The treatment of cough: a comprehensive review. *Chest*. 1991;99(6):1477-1484.<sup>230</sup> With permission from Elsevier.

who presented to a Cough Clinic. For example, in our 1991 prospective study that was cited earlier, the frequency of different categories of complications were tabulated (Table 3).<sup>230</sup> This table suggested that musculoskeletal adverse events that included rib fracture occurred in 44%, syncopal or near-syncopal events in 5%, and urinary incontinence, primarily in women, in 39%. It is interesting to note that another prospective study of ours, published 26 years later in 2017,<sup>87</sup> with the use of the CQLQ, replicated the urinary incontinence finding of the 1991 study in that urinary incontinence, primarily in women, was cough-associated in 38.8% of subjects. Because of the importance of urinary incontinence in women, and especially women with cough,<sup>305</sup> it is important to know that the CQLQ is the only commonly used cough quality of life instrument in research studies that specifically asks about this complication.<sup>306</sup>

### Methodologic Considerations

As noted in the Methods section, our initial literature search returned 13,750 citations in PubMed alone. In

reviewing the titles and abstracts of this large volume of literature, we noted a complex and heterogeneous nature of the data (eg, variety of complications, diversity of system affected, diversity of nature of evidence, and a diverse origin of the publications by specialty and country). Based on these findings, it was our opinion that the medical community and patients would be best served by our conducting a scoping review, with the intention of clarifying the conceptual boundaries for the next step of study of complications of cough. This was accomplished by identifying key concepts (actual complications) within the research area and by thematically categorizing them to clarify the working definition of complications of cough. Although this review has identified a multitude of potential complications of cough, we were not attempting to quantify the findings or to make recommendations that go beyond facilitating clinician awareness of the multitude and potential serious nature of the various complications and the importance of following the best available evidence for controlling cough. Because most of the complications were gleaned from case reports and small case series, it is possible that some of the complications occurred coincidentally with cough rather than being caused by coughing. That is the reason that we have used the term, associated with coughing, throughout this review. By thematically categorizing the large number of cough complications, we have provided an outline so that future studies of each system or each complication can be conducted. Only then will one be able to describe the findings in a manner that allows specific recommendations for avoiding these complications.

Although ours is not the only recent review of the complications that are associated with cough,<sup>307</sup> it is the only one that has followed current established methods,<sup>10,11</sup> which is similar to a systemic review because it is transparent, systematic, and replicable.<sup>308</sup> This methodologic rigor makes our review different from both our 2006 publication<sup>1</sup> and the more recent review.<sup>307</sup>

In summary, clinicians should not underestimate the impact of coughing to patients due to the potential for serious and life-threatening complications to themselves or to others and the adverse effect on quality of life. It is not an inconsequential problem or concern and should not be trivialized. As noted by Banyai and Joannides,<sup>301</sup> in their 1956 seminal review that addressed cough hazards, “the assessment of cough can be made only in light of its possible advantages and harmful implications” and “obviously,

there is an urgent need for greater awareness of the potential damage of cough so as to accomplish its satisfactory treatment as well as to prevent its serious sequelae.” Therefore, patients with cough should be evaluated and treated according to evidence-based guidelines to mitigate or prevent the myriad of potential complications associated with coughing.<sup>309,310</sup>

Additionally, clinicians should also make sure that patients are made aware of the potential unintended consequences of not following recommendations that are intended to ameliorate cough. The myriad complications that can occur from cough indicate the need both for further study and for aggressive treatment of cough when it occurs.

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