

## **ABSTRACT**

### **Background**

Systematic reviews and guidelines are available to guide management of cough in lung cancer, but evidence for intervention efficacy is limited, and little research has yet described current practice.

### **Aim**

To canvass the experiences and perspectives of Australian health professionals with regard to the clinical importance and current management of cough in people with lung cancer.

### **Methods**

An open, online, cross-sectional survey was conducted in 2018. Health professionals of all disciplines were eligible, and recruitment was by direct approach to lung cancer multidisciplinary teams, professional listservs and conferences.

### **Findings**

Fifty-eight people completed the survey, of whom 26 (45%) were medical practitioners, 21 (36%) registered nurses, and 10 (17%) allied health practitioners. Nearly all (>90%) considered cough to be of clinical concern and welcomed efforts to improve management. In most services,  $\leq 25\%$  of patients with clinically concerning cough receive management. Opiates were perceived to be the most consistently effective pharmacological strategy, with  $\geq 50\%$  participants indicating minimal or variable effectiveness for all others. The few participants who had experience of non-pharmacological strategies perceived these to be only somewhat or variably effective.

### **Discussion**

Results from this study identified variability in the management of cough associated with lung cancer, and suggest this problem may be under-treated in most services. Unmet needs identified by this study are likely under-estimated due to the volunteer effect associated with open surveys.

### **Conclusion**

Further efforts are needed to raise awareness about the importance of managing cough and provide evidence-based strategies for this population.

### **Keywords**

Cough, lung neoplasms, surveys and questionnaires

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## **MANUSCRIPT**

### **Problem or issue**

Cough is a common problem for people with lung cancer associated with reductions in quality of life.

### **What is already known**

Clinical practice guidelines are available, but there is limited evidence for both pharmacological and non-pharmacological strategies. Little is known about how cough is managed in practice.

### **What this paper adds**

We report a survey of current practice, which suggests that cough associated with lung cancer may be under-treated in most Australian services. Health professionals lack confidence in the efficacy of recommended strategies and would welcome new efforts to support management.

### **Background**

Lung cancer kills more Australians each year than any other cancer, accounting for 17.4% of referrals to specialist palliative care in 2015 (Palliative Care Outcomes Collaborative, 2015). Cough occurs in more than half of people with lung cancer and is associated with reduced quality of life (Amélie S. M. Harle et al., 2019; Amélie Sylvia Mary Harle et al., 2014; Molassiotis, Lowe, Blackhall, & Lorigan, 2011). Systematic reviews and guidelines are available to guide management but have highlighted a paucity of evidence-based therapies (Molassiotis, Bailey, Caress, & Tan, 2015; Molassiotis, Bryan, Caress, Bailey, & Smith, 2010; Alex Molassiotis et al., 2010; Molassiotis et al., 2017). Guidelines recommend using non-pharmacological management strategies such as cough suppression exercises and endobronchial brachytherapy as first-line therapies, followed by a 'step-up' approach to pharmacological strategies starting with demulcents then moving to opioids, peripherally acting antitussives and anaesthetics, if required (Alex Molassiotis et al., 2010; Molassiotis et al., 2017).

Given the lack of evidence-based strategies, it seems likely that health professionals may be prescribing off-label and/or recommending non-pharmacological strategies based on clinical experience, with variation in practice. A UK survey of health professionals (N=27) found morphine to be the most widely used strategy (n=10), followed by codeine linctus (n=8), simple linctus (=6), hydration (n=6) and steroids (n=5) (Wagland & Molassiotis, 2011). This study did not elicit health professionals' perceptions regarding the clinical importance of cough, how well cough was managed or whether further management strategies might be welcomed.

The current study set out to canvass the experiences and perspectives of Australian health professionals with regard to: the clinical importance of cough in people with lung cancer; the use and efficacy of pharmacological and non-pharmacological management practices; and the need for new interventions to better manage cough in this population.

## **Methods**

### Design

A cross-sectional survey design was used. The study was assessed as negligible risk and exempt from review by the Human Research Ethics Committee at the University of Technology Sydney. To maintain anonymity and reduce social desirability bias, completion of the survey was assumed sufficient evidence of consent to participate rather than using a formal informed consent procedure.

### Participants

To be eligible, participants needed to be Australian registered health professionals of any discipline and specialty with experience of caring for patients with lung cancer in any setting.

The study used a non-probability approach to sampling. A direct approach using email and/or telephone was made to lung cancer multi-disciplinary teams across Australia identified through a directory available on the Lung Foundation Australia's website (Lung Foundation Australia, 2018).

Invitations to participate were also circulated through conferences and email listservs of peak bodies with a special interest in lung cancer (Lung Foundation Australia, Australasian Lung Cancer Trials Group, Australia and New Zealand Lung Cancer Nurses Forum, Thoracic Society of Australia and New Zealand) and palliative care (Palliative Care Nurses Australia, Australian Allied Health in Palliative Care, Palliative Care Clinical Studies Collaborative).

#### Data collection

Data were collected through an anonymous, open, online survey administered using the SurveyMonkey© platform from January to December 2018. Open surveys are considered vulnerable to selection bias due to a volunteer effect wherein people with a special interest in the phenomenon under study are more likely to respond. In this case, a volunteer effect was considered to support rather than undermine the study's aim to obtain a snapshot of relatively expert best practice.

In the absence of any validated precedent, the researchers developed an ad hoc survey. The survey was developed with input from a multidisciplinary team including palliative care physicians (DC, MA) and nurses (JP, AM) and a social scientist with experience in survey design (TL). No further testing of face or content validity occurred, and the survey was not subjected to pilot testing. For scoring, items were kept separate rather than aggregated into scales to facilitate interpretation in the absence of psychometric testing. Questions were concerned with participants' professional characteristics and experience of managing cough in lung cancer, as well as views on the clinical importance of cough, perceived efficacy of various management approaches, and the need for developing further management strategies. Participants were asked 'for what proportion of the patients with lung cancer you have seen clinically over the past 6 months has cough been of clinical concern?' and 'at its most serious, how clinically important have you observed cough in lung cancer to be?' Perceived importance was rated using a three point scale as 'not important or minimally so', 'somewhat important' or 'extremely important'. For these questions, participants were invited to define clinical concern/importance in whatever way they thought best, and then asked in a separate

question to rank five factors from 1 (most important) to 5 (least important) regarding their role in increasing clinical concern, namely: interrupts sleep; impacts on respiratory function; impacts on physical function; associated with haemoptysis; and/or symptom-related distress. Participants were also asked whether they perceived the importance of cough to be under-estimated in clinical practice, and whether cough was more common in non-small cell versus small cell lung cancer or in late versus early stage disease. Participants were asked to rate their perceptions of the efficacy of non-pharmacological and pharmacological strategies selected from the most recent guidelines on managing cough in lung cancer (Molassiotis et al., 2017) as: 'very effective'; 'somewhat effective'; 'not effective or minimally so'; or 'highly variable'. Participants were also given the option of indicating 'my experience is insufficient to comment' and to identify any other strategies they had known to be effective or had been reported by patients as effective (whether or not recommended by a health professional). Finally, participants were asked whether they would welcome efforts to improve existing or identify new strategies for managing cough in lung cancer, and to add any additional comments. A copy of the survey is available on request.

## **Analysis**

Responses on quantitative items were analysed using summary statistics. Mean ranks were estimated for the question asking participants to rank importance of reasons for the clinical importance of cough. Textual responses to open questions asking participants to identify factors increasing clinical concern about cough and management strategies other than those mentioned in the guidelines were grouped by one researcher (TL). Analyses were undertaken in Excel 2016 (Microsoft) and SPSS Statistics v25 (IBM).

## **Results**

Seventy two health professionals responded to the survey, of whom 58 (81%) completed all questions and formed the focus for analysis. Just over two thirds were women (n=40, 69%) or aged

over 40 years (n=40, 69%). Twenty three (40%) were from New South Wales, 14 (24%) Queensland, 13 (22%) Victoria, 6 (10%) Western Australia, and 2 (3%) Australian Capital Territory. Just under half (n=26, 45%) were medical practitioners, and most (n=37, 64%) worked in the public health system. Professional characteristics are summarised in Table 1.

*Table 1 about here*

Medical participants were most commonly respiratory physicians (n=14), followed by medical oncologists (n=8), three palliative care physicians, two radiation oncologists and one surgical oncologist; two medical participants specified more than one specialty. Nurses most commonly worked in cancer care (n=10), followed by palliative care (n=7), respiratory (n=3), liaison (n=2), and cardiothoracic (N=1); two nursing participants specified more than one specialty. Allied health professionals were mostly physiotherapists (n=7), with just one each from social work, nutrition/dietetics and speech pathology.

### **Perceived clinical importance and seriousness of cough in people with lung cancer**

Participants' perceptions of the frequency and seriousness cough in lung cancer are summarised in Table 2.

*Table 2 about here*

Reasons for heightened clinical concern in relation to cough in lung cancer received the following mean ranks out of 5: symptom distress (ranked score 3.72), impact on physical functioning (3.03), interrupting sleep (2.88), impact on respiratory function (2.81), associated with haemoptysis (2.55).

Other causes of concern identified by participants included family/carer distress, interference with eating, stress incontinence, risk of aspiration and vomiting.

### **Current practice in managing cough in lung cancer**

Current practice in management of cough in lung cancer reported by participants is summarised in Table 3.

*Table 3 about here*

Perceptions of the effectiveness of different pharmacological and non-pharmacological strategies are summarised in Figure 1.

*Figure 1 about here*

Non-pharmacological management strategies not listed in the cough guidelines but that were reported to be effective by one participant each included hand-held fan, saline nebuliser, radiotherapy laser, and airway clearance techniques. Non-guideline listed pharmacological strategies that were identified as effective by one participant each included gabapentin, mucolytics, anticholinergics and thalidomide.

When asked what strategies patients had reported as helpful (regardless of whether these had been recommended by a health professional), participants most commonly identified humidified air (e.g. steam inhalation) and inhalers/nebulisers (sometimes specified as bronchodilators or steroids), as well as less frequently positioning and relaxation.

Ninety-five percent (n=55) of participants indicated that they would welcome efforts both to improve existing strategies and also to develop new strategies for managing cough in lung cancer.

Participants' comments emphasised the need for detailed assessment given variability in cough between patients with regard to aetiology, quality (e.g. productive versus dry) and psychosocial impact.

## **Discussion**

The results of this Australian survey of current practice identified variability in the management of cough associated with lung cancer, and suggest this problem may be under-treated in most services.



Nearly all (>90%) health professionals who responded considered cough to be of potential clinical concern and said they would welcome efforts to improve management. In the majority of workplaces, a quarter or less of patients for whom cough was of clinical concern received help with management. Relatively few participants had experience of non-pharmacological strategies, but those who did perceived these to be only somewhat or variably effective. Opiates were reported to be the most consistently effective pharmacological management strategy, with at least half of participants indicating minimal effectiveness or variability in effectiveness for all other strategies. These findings are all the more worrying given that the poor prognosis typically associated with lung cancer makes symptom control a priority for this patient group.

Participants' perceptions of the clinical importance of cough and effectiveness of management should be considered within the context of their varying estimates regarding the proportions of patients for whom cough might be of clinical concern and its association with lung cancer of different types and stages. The most reliable estimates to date come from two UK studies at one outpatient unit, which found that 37% and 57% of lung cancer patients respectively had a cough, of whom 52% and 62% felt that it warranted treatment; results did not vary according to stage of disease (Amélie S. M. Harle et al., 2019; Amelie Sylvia Mary Harle et al., 2014). These prevalence estimates suggest that the proportion of patients for whom cough is a clinical concern may have been either under- or over-estimated by a substantial minority of survey participants.

The unmet need for management among patients with cough of clinical concern identified by our study is, if anything, likely to be an underestimate due to the volunteer bias associated with open surveys. Non-pharmacological management in particular was rarely used, even among health professionals who can be assumed to have a greater-than-average interest in managing cough in lung cancer. Guidelines recommend non-pharmacological strategies as first-line treatment for cough, although evidence for effectiveness in this population is limited (Alex Molassiotis et al., 2010; Molassiotis et al., 2017). Results from our survey suggest further testing is needed to inform

recommendations, but also caution that clinical trial sampling should enable subgroup analyses regarding coughs of varying aetiologies and qualities. In the meantime, humidified air, positioning and relaxation were reported by participants as receiving positive feedback from patients, and have negligible cost and adverse effects.

Participants' perception that opiates are more effective than demulcents or antitussives is of interest in the context of similar evidence for each of these, graded 2C in the most recent guidelines (Molassiotis et al., 2017). This may reflect the variable contents and pharmacology in antitussives, with those containing codeine perhaps being more effective. Participants' mixed perceptions of the effectiveness of local anaesthetics and diazepam broadly accords with guideline consensus recommendations that these options can be tried where other strategies have failed but should not be first choice treatments. While gabapentin and thalidomide fall within the same category of recommendations, other pharmacological strategies reported to be effective do not feature in the guidelines (mucolytics, anticholinergics, thalidomide and steroids for pneumonitis), and no participants reported having tried other consensus medications (carbamazepine, baclofen and amitriptyline). Many participants reported that patients told them they benefitted from use of inhalers/nebulisers, in some cases specified as bronchodilators and steroids. There is limited evidence that these are effective either in lung cancer or chronic cough (Speich et al., 2018). However, these medications are effective for chronic obstructive pulmonary disease (COPD), which is associated with lung cancer (Durham & Adcock, 2015).

#### Limitations

As noted above, the generalisability of our results is limited by the volunteer effect that is inevitably encountered with open surveys. While our recruitment approaches do not enable a response rate to be estimated, there is likely that the sample included less than 10% of those who received an invitation to participate. The sample size was small, especially when broken down into disciplines/specialties, and did not enable inferential statistics aimed at exploring associations

between different variables. Readers should also keep in mind the subjective nature of the data and risk of recall and other cognitive biases among participants when reporting current practice and perceived effectiveness. Most notably, participants were asked to bring their own interpretations to the constructs of clinical importance, seriousness and impact, and no attempt was made to explore variability. Nor did we explore whether relatively few patients received management for cough because it was not deemed a priority or management strategies were deemed too ineffective to offer.

## Conclusion

This study suggests that cough may remain a refractory problem for most people with lung cancer for whom management is warranted. Health professionals lack confidence in pharmacological strategies recommended by current guidelines, and may not accord the recommended precedence to non-pharmacological over pharmacological management. Survey results are likely to underestimate limitations in current practice due to a likely volunteer effect from our sampling method. Further efforts are needed to raise awareness about the importance of managing cough and provide evidence-based strategies for this population.

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## References

- Durham, A. L., & Adcock, I. M. (2015). The relationship between COPD and lung cancer. *Lung Cancer, 90*(2), 121-127. doi:10.1016/j.lungcan.2015.08.017
- Harle, A. S. M., Blackhall, F. H., Molassiotis, A., Yorke, J., Dockry, R., Holt, K. J., . . . Smith, J. A. (2019). Cough in Patients With Lung Cancer: A Longitudinal Observational Study of Characterization and Clinical Associations. *Chest, 155*(1), 103-113. doi:10.1016/j.chest.2018.10.003
- Harle, A. S. M., Buffin, O., Burnham, J., Molassiotis, A., Blackhall, F. H., & Smith, J. A. (2014). The prevalence of cough in lung cancer: Its characteristics and predictors. *Journal of Clinical Oncology, 32*(31\_suppl), 162-162. doi:10.1200/jco.2014.32.31\_suppl.162

- Lung Foundation Australia. (2018). Multidisciplinary teams. Retrieved from <https://lungfoundation.com.au/health-professionals/networks/multidisciplinary-teams/>
- Molassiotis, A., Bailey, C., Caress, A., & Tan, J. Y. (2015). Interventions for cough in cancer. *Cochrane Database Syst Rev*, 5, Cd007881. doi:10.1002/14651858.CD007881.pub3
- Molassiotis, A., Bryan, G., Caress, A., Bailey, C., & Smith, J. (2010). Pharmacological and non-pharmacological interventions for cough in adults with respiratory and non-respiratory diseases: A systematic review of the literature. *Respiratory Medicine*, 104(7), 934-944. doi:10.1016/j.rmed.2010.02.010
- Molassiotis, A., Lowe, M., Blackhall, F., & Lorigan, P. (2011). A qualitative exploration of a respiratory distress symptom cluster in lung cancer: cough, breathlessness and fatigue. *Lung Cancer*, 71(1), 94-102. doi:10.1016/j.lungcan.2010.04.002
- Molassiotis, A., Smith, J. A., Bennett, M. I., Blackhall, F., Taylor, D., Zavery, B., . . . Morice, A. H. (2010). Clinical expert guidelines for the management of cough in lung cancer: report of a UK task group on cough. *Cough (London, England)*, 6, 9-9. doi:10.1186/1745-9974-6-9
- Molassiotis, A., Smith, J. A., Mazzone, P., Blackhall, F., Irwin, R. S., & Panel, C. E. C. (2017). Symptomatic Treatment of Cough Among Adult Patients With Lung Cancer: CHEST Guideline and Expert Panel Report. *Chest*, 151(4), 861-874. doi:<https://dx.doi.org/10.1016/j.chest.2016.12.028>
- Palliative Care Outcomes Collaborative. (2015). *National Report on Patient Outcomes in Palliative Care in Australia, January - June 2015*. Retrieved from Wollongong:
- Speich, B., Thomer, A., Aghlmandi, S., Ewald, H., Zeller, A., & Hemkens, L. G. (2018). Treatments for subacute cough in primary care: systematic review and meta-analyses of randomised clinical trials. *British Journal of General Practice*, 68(675), e694-e702. doi:10.3399/bjgp18X698885
- Wagland, R., & Molassiotis, A. (2011). How standard is 'standard care' in the symptom management of patients with lung cancer? The example of the 'respiratory distress' symptom cluster. *European Journal of Oncology Nursing*, 15(1), 1-2. doi:<https://doi.org/10.1016/j.ejon.2010.12.001>

**Table 1. Professional characteristics of health professionals responding to the survey on cough in lung cancer (N=58)**

Characteristic	n (%)
<i>Primary role</i>	
Medical practitioner	26 (45%)
Registered nurse	21 (36%)
Allied health practitioner	10 (17%)
Clinical trial manager	1 (2%)
<i>Number of years in current role</i>	

1-5	12 (21%)
>5	46 (79%)

*Sector/setting(s)\**

Public hospital	37 (64%)
Public practice	24 (41%)
Private practice	11 (19%)
Private hospital	9 (16%)
Community care	6 (10%)
Residential aged care	1 (3%)

*Metropolitan/regional/rural/remote status\**

Metropolitan	47 (81%)
Regional	16 (28%)
Rural	10 (17%)
Remote	1 (2%)

*Number of newly referred lung cancer patients seen over past 6 months*

0-10	11 (19%)
11-50	31 (53%)
51-100	13 (22%)
101+	3 (5%)

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\* Some participants selected more than one response option

**Table 2. Australian health professionals' experiences and perceptions concerning cough in lung cancer (N=58)**

Perceptions	n	(%)
<i>% patients with lung cancer seen over past 6 months for whom cough was of clinical concern</i>		
10% or less	10	(17%)
11-25%	19	(33%)
26-50%	15	(26%)
51-75%	10	(17%)
76%+	4	(7%)
<i>Clinical importance cough in lung cancer at its most serious</i>		
Extremely important	33	(57%)
Somewhat important	20	(34%)
Not important or minimally so	5	(9%)
<i>The seriousness of cough for people with lung cancer is often under-estimated in clinical practice</i>		
Agree	32	(55%)
Neither agree not disagree / unsure	21	(36%)
Disagree	5	(9%)
<i>Perceptions that cough is more common or serious in different types of lung cancer</i>		
Not more common/serious in different types	46	(79%)
More common/serious in small cell	3	(5%)
More common/serious in non-small cell	9	(15%)
<i>Perceptions that cough is more common or serious in different stages of lung cancer</i>		
Not more common/serious at any stage	23	(40%)
More common/serious in early stage	6	(10%)
More common/serious in late stage	29	(50%)

**Table 3. Frequency with which cough in lung cancer is managed and the disciplines involved, as reported by Australian health professionals (N=58)**

Perceptions	n	(%)
<i>% patients with clinically concerning cough who received management from a health professional</i>		
10% or less	13	(22%)
11-25%	16	(28%)
26-50%	12	(21%)
51-75%	4	(7%)
76%+	13	(22%)
<i>Disciplines usually involved in managing cough in lung cancer</i>		
Medical	51	(88)%
Nursing	26	(45)%
Allied health or other	25	(43)%

Author

**Figure 1. Percentages of health professionals perceiving different levels of effectiveness for pharmacological and non-pharmacological management strategies for cough in lung cancer**

**Note:** The number of health professionals reporting themselves sufficiently experienced to judge effectiveness of each strategy was: 44 (demulcents such as simple or glycerin-based linctus), 49 (opiates), 28 (peripherally acting antitussives), 26 (local anesthetics), 32 (diazepam), 20 (cough suppression exercises) and 5 (endobronchial brachytherapy)

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