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Patients' and caregivers' experiences of driving with chronic breathlessness before and after regular low-dose sustained-release morphine: A qualitative study

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Abstract:	Background: Chronic breathlessness is a disabling syndrome that profoundly impacts patients' and caregivers' lives. Driving is important for most people, including those with advanced disease. Regular, low dose, sustained-release morphine safely reduces breathlessness, but little is known about its impact on driving. Aim: To understand patients' and caregivers' (i) perspectives and experiences of driving with chronic breathlessness; and (ii) perceived impact of regular, low-dose, sustained-release morphine on driving. Design: A qualitative study embedded in a pragmatic, phase III, randomised, placebo-controlled trial (RCT) of low-dose, sustained-release morphine (≤32mg/24 hours) for chronic breathlessness. Semi-structured interviews were conducted immediately after participants withdrew or completed the RCT. Informed by grounded theory, a constant comparative approach to analysis was adopted. Setting/participants: Participants were recruited from an outpatients palliative-care service in Adelaide, Australia. Participants included: patients (n=13) with severe breathlessness associated with chronic obstructive pulmonary disease; and their caregivers (n=9). Results: Participants were interviewed at home. Eleven received morphine 8-32mg. Three themes emerged: i) independence; ii)

	breathlessness' impact on driving; and iii) driving while taking regular, low-dose, sustained-release morphine. Conclusions: Driving contributed to a sense of identity and independence. Being able to drive increased the physical and social space available to patients and caregivers, their social engagement and well-being. Patients reported breathlessness at rest may impair driving skills, while the introduction of sustained-release morphine seemed to have no self-reported impact on driving. Investigating this last perception objectively, especially in terms of safety, is the subject of ongoing work.

Patients' and caregivers' experiences of driving with chronic breathlessness before and after regular low-dose sustained-release morphine: A qualitative study

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ABSTRACT

Background: Chronic breathlessness is a disabling syndrome that profoundly impacts patients' and caregivers' lives. Driving is important for most people, including those with advanced disease. Regular, low dose, sustained-release morphine safely reduces breathlessness, but little is known about its impact on driving.

Aim: To understand patients' and caregivers' (i) perspectives and experiences of driving with chronic breathlessness; and (ii) perceived impact of regular, low-dose, sustained-release morphine on driving.

Design: A qualitative study embedded in a pragmatic, phase III, randomised, placebo-controlled trial (RCT) of low-dose, sustained-release morphine (≤32mg/24 hours) for chronic breathlessness. Semi-structured interviews were conducted immediately after participants withdrew or completed the RCT. Informed by grounded theory, a constant comparative approach to analysis was adopted.

Setting/participants: Participants were recruited from an outpatients palliative-care service in Adelaide, Australia. Participants included: patients (n=13) with severe breathlessness associated with chronic obstructive pulmonary disease; and their caregivers (n=9).

Results: Participants were interviewed at home. Eleven received morphine 8-32mg. Three themes emerged: i) independence; ii) breathlessness' impact on driving; and iii) driving while taking regular, low-dose, sustained-release morphine.

Conclusions: Driving contributed to a sense of identity and independence. Being able to drive increased the physical and social space available to patients and caregivers, their social engagement and well-being. Patients reported breathlessness at rest may impair driving skills, while the introduction of sustained-release morphine seemed to have no self-reported impact on driving. Investigating this last perception objectively, especially in terms of safety, is the subject of ongoing work.

Keywords

Driving, opioids, morphine, breathlessness, dyspnea, caregivers, patients

What is already known about the topic?

- Chronic breathlessness is a debilitating syndrome, which can be ameliorated by small doses of regular, low-dose, sustained-release morphine in some people.
- Driving is important for most adults, including the ones with life-limiting illnesses associated with chronic breathlessness.
- Despite growing concerns about the impact of opioids on driving ability, there are no studies investigating people's experiences of driving with chronic breathlessness before or after initiating treatment with regular, low-dose, sustained-release morphine.

What this paper adds?

- Being able to drive is important for people with chronic breathlessness and their caregivers because it provides them with a continuing sense of self-worth, independence, pleasure and widening life space.
- Episodes of intense breathlessness can impact on patients' perceived ability to drive, which is not easily perceived by caregivers.
- Although people have fears surrounding driving while taking morphine, regular, low-dose sustained-release morphine does not seem to impact on patients' self-perceived driving ability.

Implications for practice, theory and policy

- In clinical practice, it is important to enquire about peoples' perceived ability to drive with chronic breathlessness and the medications that they are prescribed.
- Clinical research should focus on investigating whether oral, low-dose sustained-release morphine impacts on patients' driving ability, particularly during initiating therapy and any subsequent dose increases.
- Understanding the impact of low-dose, sustained release morphine on people's driving ability is essential to inform guideline development about who is able to drive safely and who is not.

INTRODUCTION

Chronic breathlessness persists and is disabling despite optimal treatment of the underlying disease(s). [1] Chronic breathlessness affects almost 10% of adults and 17% of those ≥65 years. [2] Patients with chronic obstructive pulmonary disease (COPD) are particularly affected, with >90% reporting breathlessness at some stage. [3] Chronic breathlessness is physically and psychologically debilitating, [4] leading to increasing dependence, social isolation, and worse health-related and mortality outcomes. [5, 6] Loss of independence is also profoundly distressing for caregivers, who struggle seeing their loved ones' decline. [7, 8]

Driving provides a sense of freedom, independence, identity and hope. [9] Not driving worsens social isolation and is associated with worse health-related outcomes. [10, 11] One quarter of people with life-limiting illnesses continue driving. [12] Although there is ample evidence that chronic breathlessness severely restricts people's everyday lives, the effect of chronic breathlessness on people's driving ability has not been explored.

Regular, low-dose (≤30mg/day), [13] sustained-release morphine safely reduces chronic breathlessness in people with COPD. [14, 15] Recently, low-dose, sustained-release morphine has been approved by regulatory bodies in Australia for the treatment of chronic breathlessness. [16] This is the first world approval of any medication for the symptomatic reduction of chronic breathlessness, likely increasing prescriptions for this indication. Simultaneously, there are concerns about safe driving while taking psychoactive substances, including prescribed opioids. [17] While high dose opioids can impair driving, it is unknown whether regular, low dose, sustained-release morphine impacts on patients' ability to drive, particularly when initiating therapy and up-titration. [18]

This aim of this qualitative study was to elicit patients' and caregivers' perceptions about

driving with chronic breathlessness and to understand their perceptions about driving as regular, low dose, sustained release morphine was introduced.

METHODS

Design

A qualitative study embedded in a pragmatic, phase III, randomised, placebo-controlled trial (RCT) evaluating the effectiveness of sustained-release morphine for people with chronic breathlessness and COPD (BEAMS trial). [19] The RCT had a parallel-arm, dose increment design. Participants were randomised to placebo, 8mg or 16mg of once-daily sustained-release morphine for one week, with possible additional blinded up-titrations, of 8 or 16mg in weeks 2 and 3. Maximum daily doses of morphine by the end of the randomisation period ranged from 0mg (placebo) to 32mg (0, 8, 16, 24 or 32mg), with chances of being on placebo after randomisation being 1:12. The trial primary outcome measure was change in intensity of "worst breathlessness" in the previous 24 hours, measured with a 0-10 numerical rating scale after one week of therapy. The pragmatic design ensured that participants included in the RCT were a close reflection of the population of interest. [20,21]

Setting and Participants

Participants were recruited from the metropolitan region serviced be the Southern Adelaide Palliative Services, Australia. Participants included: patients who had ceased their participation in the BEAMS trial [19] either by completion or withdrawal; and 'the person closest to the patient' ('caregiver'), if present. [22] This sampling provided a broad range of perspectives. All patients had COPD and chronic breathlessness; a modified Medical Research Council (mMRC) breathlessness score of 3 or 4 corresponding to "stops for breath after walking about 100 meters or stops after a few minutes walking on the level" and "too breathlessness to leave the house or breathlessness when dressing or undressing",

respectively. [23,24] Participants were active drivers or people who had recently stopped driving and were still able to recall their experience of driving with severe chronic breathlessness. The latter group's perceptions contributed to expand the understanding of the experience of driving with this disabling syndrome, but were not questioned about their experiences of driving after initiating sustained-release morphine.

Research Team

The interviewer (D.F.) has a medical background and was a full-time doctoral student with training in qualitative research. J.B. is Senior Clinical Lecturer and Honorary Consultant in Palliative Medicine with a medical and research background. A.H. is a university researcher with background in data collection and people-centred research. S.K. is a university researcher with a linguistics background. J.P. is a senior researcher with a background in palliative care nursing and qualitative research. D.C. is a researcher with expertise in chronic breathlessness.

Recruitment

Using convenience sampling, the trial nurses approached potential participants by telephone. If interested, they were then phoned by the interviewer (D.F.), with whom they had no previous contact. The interviewer explained the study's objectives and scheduled a face-to-face meeting with potential participants to answer questions and obtain written consent.

Data collection

Face-to-face, semi-structured interviews were conducted separately with patients and their caregivers at a location of their choice (July 2017- November 2018), providing participants with safe and private settings to express freely any concerns or emotions. [25,26] Interviews evaluated the overall impact of chronic breathlessness in people's daily lives and perceived

changes after initiating study drug. [19] Given the lack of evidence examining experiences of driving in people with chronic breathlessness, the interviews included three questions about driving, analysed in a separate sub-study (Box 1).

Participants' responses were recorded and transcribed verbatim (D.F.). Field notes were collected and the researcher kept a reflexive journal with impressions about each participant-researcher interaction. Interview transcripts were not reviewed by participants to minimise burden on people already debilitated due to chronic breathlessness, given minimal advantages from doing this. [27] Potential misinterpretations were minimised by having a second researcher (A.H.) listen to interviews' recordings, checking transcriptions for accuracy. Participants were only contacted again if there were disagreements between these researchers. Data were collected until saturation (i.e. no new concepts were emerging), as agreed between all researchers.

Data Analysis

NVivo (V 11.4.0 for Mac) was used. The analysis was driven by the principles of grounded theory, using a constant comparative approach. [28,29,30] Given the lack of qualitative studies exploring people's experiences of driving with chronic breathlessness, an inductive approach to analysis was adopted. [31] The constant comparative approach helped identify new concepts emerging from the data that could be explored in subsequent interviews. [30] Two researchers independently conducted open coding (D.F., A.H.) of all transcripts, which were grouped into themes (D.F.); each theme was illustrated with several quotes to confirm coding validity (D.F., J.B., S.K., J.P.). Patients' and caregivers' viewpoints were then compared and contrasted.

Ethical considerations

The BEAMS trial was approved by relevant Human Research Ethics Committees (15/12/16/3.06) and was registered (NCT02720822). All participants provided written informed consent.

The COREQ framework is used to report this study. [32]

RESULTS

Fifteen patients and 11 matched caregivers were invited to this study: two patients declined (so their caregivers were excluded); 13 patients and 9 caregivers were interviewed. Interviews took 20-55 minutes. Patients had a median age of 76 years (interquartile range [IQR] 68-78), nine of whom were men, living with their partners. All were still mobile outside their homes, but were severely restricted in their daily activities due to breathlessness (Table 1).

Eight of 13 patients were regularly driving and one drove occasionally. Only two of nine men had stopped driving, while two of four women had stopped driving. The four participants who had stopped driving had all driven regularly until recently (Table 2). Eleven patients took sustained-release morphine during the study (Table 3): 8mg (n=4), 16mg (n=3), 24mg (n=3) and 32mg (n=1).

Three major themes described the experience of driving for patients with chronic breathlessness and their caregivers: 1) independence, 2) breathlessness' impact on driving, 3) driving while taking regular low-dose sustained-release morphine (Table 4).

Theme 1 - Independence

Being able to drive helped patients keep their sense of self and feeling useful. This was more noticeable in patients experiencing severe functional limitations due to breathlessness.

> *"Well, I suppose it's something that I don't do every day (driving) and you know, and I am doing something! Maybe that's the reason why… Well I've always enjoyed driving actually but more so now, more so now, yeah… Probably because it's something different in my life now, you know? I can do something! Whereas usually, I am just sitting."* [Patient 8]

Most patients reported that driving was one of the few activities that brought them a sense of joy and pleasure. Even those patients not required to drive (i.e. because their caregiver drove), still felt the need to drive at times for pure enjoyment.

> *"We have got the van and I drive the van. I love getting out in the country and driving."* [Patient 12]

For caregivers, seeing their partners enjoy themselves was particularly importantly. They acknowledged the role of driving in widening the physical space available to both the patients and themselves, a space that had been severely reduced by breathlessness in most cases.

> *"Well, driving is important… There are certain things… When we go on holiday because he is not bothered about walking out on the streets, you know? (…) But we went to Barossa Valley last week, and I don't know if you have been there, but we went to Mengler's Hill to the look out. He got up there, well we drove up there of course, we got out of the car and we walked down a little bit to the picnic area there and he stayed there while I walked around and looked at it because walking down and up and down… [meaning it was tiresome for him]. So things like that you know?"* [Caregiver 11]

For some patients, driving was their most important activity. One patient without a caregiver explained that driving was key to maintaining relationships and roles, whilst also providing a sense of purpose:

> *"I get my adult daughter every Saturday for a while, she is profoundly autistic, she just had her 26th birthday yesterday and it is very important to her. So I have got to drive to go get her, drive to bring her back. So it's a very important thing, making sure*

I can still drive. (…) And that's the main reason, apart from that, it is just to get to the shop and the doctor which are a kilometer away. That's the only big one." [Patient 3]

Another patient explained that driving was the only out-of-home activity he was still able to do independently and that losing it would be extremely disturbing.

"Well, I think the most important thing to be able to do at the moment is to be able to drive because physically there is nothing I can do, I can't do anything". [Patient 8]

Overall, people who were still driving expressed fear about not being able to drive in the future. Driving was seen as an important marker of independence and there was fear over any loss and its consequences.

"I couldn't give up driving, I couldn't do that [disturbed facial expression]. I think it's your independence, you know? And once that is taken away you're reliant on somebody else…" [Patient 9]

For the four patients who had stopped driving, only one (male) reported that driving was important to maintain his independence. The other three patients (one male, two females) reported driving was not overly important because their caregivers could drive when needed.

"It gives me a lot more freedom to have the car. I don't do things that I would normally do… If I had the car and I felt like KFC for lunch, I can go and get it (laughing)… or if I wanted to go out for dinner with someone, I could just go and do it. Whereas now, for me to walk to the bus stop to get a bus somewhere, it's just too hard…" [Patient 10]

"I don't miss driving. B. (husband) does everything. We are together all the time anyway." [Patient 1]

Breathlessness' impact on driving

In general, patients and caregivers considered that breathlessness did not reduce patients' driving skills because it did not require over-exertion.

"Normally, I am fine. I don't get tired driving." [Patient 7]

Some patients reported they had situations in which they felt breathlessness at rest. When present, they felt their driving ability was affected. Strategies to overcome this limitation included not driving at all or using oxygen while driving. Interestingly, the use of oxygen in the car raised some concerns about its safety and legality.

"There were a couple of times in which I have been buggered a bit. I haven't had the oxygen the night before, so I will put the oxygen on the car and I will have the oxygen running while I am driving. Whether that's legal or not I don't know." [Patient 11]

One patient experiencing breathlessness at rest explained that breathlessness impacted on his concentration and hence ability to drive. When he drove, he felt anxious and concerned about his and other people's safety.

"For me it is not so much driving, but the concentration level about what is going on around. Stuff I used to take for granted, so I automatically did it before. Now, I have to make sure I do it. And it depends on the concentration because if it is concentrating on something that could end in a disaster, is a bit different to concentrating on something that might just a non-event anyway." [Patient 13]

Overall, caregivers' views matched patients' views. Most caregivers confirmed that patients drove safely despite their breathlessness. For the only patient who stated that driving was stressful (previous quote, patient 13), the caregiver thought he could still drive safely.

> *"Yes, usually when we go stay with our son at Wallaroo, he drives there. So he can. And he is quite good, I think. I don't notice any diminishing of his driving skills. I feel quite relaxed when he is driving."* [Caregiver 13]

Driving while taking regular, low-dose sustained-release morphine

Participants' views on driving were quite uniform, irrespectively of the drug (i.e. morphine or placebo) and dose. Most patients and caregivers perceived that the study drug did not have any perceived adverse impact on patients' ability to drive, irrespectively of the study drug/dose.

> *"No, no problems (to drive while taking the study drug)."* [Patient 7 - maximum morphine dose 32mg]

> *"No, no, not at all. I don't think driving was affected (by morphine)".* [Caregiver 2 – maximum morphine dose 16mg]

Despite not perceiving any impact on driving with the study drug, a small number of participants were still concerned about the potential effects of morphine on driving. Most believed that the trial dose (up to 32mg sustained-release morphine a day) could impair driving. One caregiver did not want the patient to continue with morphine because she believed morphine could lead to driving cessation. One patient took action to minimise any negative impact of morphine on his driving skills.

"I was concerned about… If he does take it, I think he wouldn't be able to drive (…) and I don't really want him to go on that because he loves driving and I think if he took it, that would be the end. I want him to be around for a few more years yet." [Caregiver 8 – maximum morphine dose 8mg]

"I have a friend coming here and he will sit with me (while I drive) and tells me what is going on with the driving. (…) I know they say if I am taking a quite powerful opioid drug that driving while under the immediate influence is probably not that smart. I would not be inclined to do it unless it was an emergency." [Patient 3 – maximum morphine dose 8mg]

DISCUSSION

Main findings

This is the first study reporting patients' and caregivers' perspectives and experiences of driving with chronic breathlessness. Additionally, the study was set in a study to compare before-and-after taking regular, low dose, oral sustained-release morphine. Findings suggest that driving is crucial in helping patients with chronic breathlessness keep a sense of identity, purpose, independence and connection to the outside world, while also being a source of joy and comfort for both patients and caregivers. According to patients, breathlessness at rest can reduce their driving skills but the study drug (i.e. morphine/placebo) had no perceived impact on their ability to drive.

Similar to healthy individuals, owning and driving a private vehicle is perceived as an amenity offering people freedom of movement. [33] However, participants' reflections highlight that the ability to drive is particularly important for people experiencing severe functional limitations in other aspects of life due to chronic breathlessness and their caregivers. For these patients, driving is associated with a sense of identity and feeling

useful. Similar findings were reported by a previous qualitative study of three focus groups: i) low disability/broad life space, ii) high disability/broad life space, iii) high or low disability/constricted life space. Although all groups considered driving an important activity, the third group was the most affected by driving cessation which was perceived by them as devastating. [34] Importantly, the present study also shows that driving widens both patients' and caregivers' life space (i.e. the physical space in which they move and socially interact). [35,36] Previous evidence suggests that as patients become more restricted by chronic breathlessness, caregivers tend to adjust by slowing their life rhythm, also becoming more restricted. [37] Thus, it is likely that any strategies supporting patients' function (such as driving) may also positively affect caregivers. [35] Functional decline is one of the major contributors to driving cessation in older age. [11] Older adults who stop driving have twice the risk of depressive symptoms compared to those who continue driving. [11] Importantly, there is a significant association between the well-being of these patients and their caregivers. [38] Thus, risks and benefits for patients and caregivers need to be weighed carefully before advising patients not to drive.

Most patients considered that their chronic breathlessness did not impact on their driving primarily because driving was sedentary and did not trigger breathlessness. Patients who had experienced or were experiencing breathlessness at rest explained that breathlessness affected their concentration when driving. Previous research has highlighted potential effects of uncontrolled symptoms on people's driving skills. [39] Worsening breathlessness scores are associated with worsening performance in neuropsychological assessments but any relationship with driving performance is unknown. [40] Worsening breathlessness scores are associated with increased chances of experiencing breathlessness at rest. [23] Thus, it is possible that patients with worse breathlessness are particularly at risk of having some degree of psychomotor impairment that could affect driving. Interestingly, caregivers did not seem to notice any changes in patients' ability to drive. This may result from patients' adaptation to breathlessness, including development of driving strategies that are not

evident to caregivers (e.g. increased attention, driving slightly slower). Reportedly, the use of oxygen while driving may be one of these strategies. Using oxygen while driving is legal in most countries but patients need to ensure oxygen tanks are adequately secured and respect specific state/country requirements. Given that driving cessation is also emotionally challenging for caregivers, caregivers may overlook changes in patients' driving ability in order to keep them driving. [41]

All participants agreed that their study drug/dose did not affect their perceived driving skills. Previous research had suggested that regular therapeutic opioid-agonists are unlikely to affect driving-related skills. [18] This study raises the hypothesis that low-doses of sustained-release morphine may have no impact on driving even during therapy initiation and careful upward titration. This is in line with previous studies showing that uncontrolled symptoms are more likely to have an impact on driving than therapeutic opioids. [39] Despite that, both patients and caregivers were still concerned about potential side effects of sustained-release morphine that could affect their driving. Concerns about opioids are common amongst patients, caregivers and clinicians. [42,43] Interestingly, while patients' concerns were focused on safety for themselves and others, caregivers' were more concerned with patients' deterioration if they were to stop driving. Chronic breathlessness affects both patients and caregivers, involving both in symptom management and again reinforcing the patient-caregiver unit as the unit of care. [44]

This study suggests that initiating morphine for chronic breathlessness may raise concerns about driving for patients and caregivers, and those concerns need to be proactively addressed with both. Frequently, clinicians advise patients not to drive immediately after taking opioids. [45] There is a need for further research to understand if patients taking regular, low-dose, sustained-release morphine are able to drive safely given the different pharmacokinetic profile they have to immediate-release oral morphine solutions. [46] The relation between breathlessness and driving performance whist on opioids must also be

explored as current legal morphine limits for driving (where imposed) are far higher than the doses used in this study. [13]

Strengths and Limitations

This is the first qualitative study reporting on people's experiences of driving with chronic breathlessness and the perceived effects of regular, low-dose sustained-release morphine on driving ability. The inclusion of people taking different doses of morphine and placebo provided a range of different perspectives that could be compared and contrasted. The qualitative design limits generalisability, but findings point to important questions and future research directions, particularly in the context of growing concerns about drug-affected drivers. This study is limited by looking at self-reported effects on driving. People tend to overestimate their own driving performance. [47] Most studies conducted in this field asked participants to rate their driving ability compared with the "average driver", rather than assessing aspects of their own driving. [48] The latter has been shown to more accurately reflect driving performance, and is closer to the approach used in this study. [48,49] Similarly, caregivers' perception is not an optimal reflection of patients' driving skills, but their assessment of specific driving aspects correlates with on-the-road performance. [50] Opioids may affect cognitive function, which may affect self-perception. [51] However, it is less likely that would be the case with small doses of morphine. [52]

A strength of this study is that participants were recruited from a phase III RCT that allowed COPD-status and morphine-dose transparency. While the participants may not be representative of the overall population with severe breathlessness associated with COPD, the RCT had a pragmatic design to ensure high external validity. [20,21] Due to the main trial dose-increment design, people were more likely to be taking morphine than placebo after the randomisation period (11:12 chance). This reduced the number of perspectives from people

taking placebo, but increased the number of people who could provide useful information about morphine.

What this study adds

This study highlights that driving is important for people living with chronic breathlessness and their caregivers. It also suggests that regular, low-dose, sustained-release morphine does not impact on patients' perceived ability to drive. Based on these findings, there is a need to objectively evaluate the impact of chronic breathlessness on patients' driving ability. Previous studies focused on objective measures of disease severity but not on the symptom itself. [53] It is also important to understand if people are safe to drive with low-doses of sustained-release morphine, particularly during therapy initiation and upward titration. Equally, the impact of uncontrolled symptoms such as chronic breathlessness on driving performance needs to be researched. There is a common assumption in the clinical setting that people should refrain from driving in the first hours or days after initiating any opioid. There are no published RCTs to confirm this should be the case with low-dose sustained-release morphine. Due to lack of evidence to support decision-making, clinicians may advise people taking low dose sustained-release morphine to stop driving, but be aware that this may have severe implications for people's well-being and social functioning.

Author contributions

DF, JP, DC contributed to the study design; DF contributed to the acquisition of data; DF, JB, AH, JP, DC contributed to data analysis; DF drafted the article; all authors have critically revised the articles and have approved the manuscript version to be published.

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Declaration of conflicting interests

David C. Currow is an unpaid advisory board member for Helsinn Pharmaceuticals. He is a paid consultant and receives payment for intellectual property with Mayne Pharma and is a consultant with Specialised Therapeutics Australia Pty. Ltd. Diana H. Ferreira, Jason Boland, Aaron Honson, Slavica Kochovska and Jane Phillips disclose no competing interests relevant for this work.

Ethical approval and informed consent

Ethics approval was obtained from relevant Health Human Research Ethics Committees, and the trial was registered (Registration No. NCT02720822) before recruitment commenced. All participants gave informed written consent.

Data sharing

The study databases are available from the corresponding author on reasonable request.

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Table 1 - Patients Characteristics (n=13)

Median age [IQR]	76 [68 – 78]
Gender	
Female	4
Ethnicity	
Oceanian (Australia or New Zealand)	11
North-West European	2
Usual language spoken at home	
English	13
Residence	
Living in a private residence	13
Marital status	
Married or de facto	9
Separated or divorced	2
Widowed	2
Highest level of education	
Did not complete high school	4
Completed high school	4
Completed a trade certificate	3
University Degree	2
mMRC score at baseline	
3	13
NRS Wost breathlessness (24 hours)	
4	2
6	3
7	4
8	3
9	1
10	1
AKPS	
50	3
60	6
70	3
80	1

IQR – Interquartile range; mMRC – modified Medical Research Council Scale; NRS – Numerical Rating Scale; AKPS – Australian Karnofsky Performance Status

Table 2 – Driving status for participants on trial (n=13)

Patient	Gender	Caregiver	Driving status	Reasons to stop driving
1	Female	Husband	Not currently driving	Deemed unfit to drive
2	Male	Wife	Active driver	-
3	Male	-	Active driver	-
4	Female	Son	Not currently driving	Sold the car after husband died
5	Male	Wife	Not currently driving	Deemed unfit to drive
6	Male	Wife	Active driver	-
7	Female	-	Active driver	-
8	Male	Wife	Active driver	-
9	Male	-	Active driver	-
10	Male	-	Not currently driving	Sold the car due to financial issues
11	Male	Wife	Active driver	-
12	Female	Husband	Active driver	-
13	Male	Wife	Active driver (occasionally)	

Table 3 – Maximum morphine doses patients took while on the BEAMS trial (n=13)

Participant	Doses of morphine on trial					Cessation time-point
	Week 1	Week 2	Week 3	End of randomisation stage	Extension	
1	Placebo	8mg	16mg		16mg	Completed the study
2	16 mg	16 mg	16 mg		16 mg	Completed the study
3	Placebo	Placebo	8 mg		8 mg	Completed the study
4	Placebo	Placebo	Placebo		-	Withdrew after week 3
5	16mg	16mg	24mg		24mg	Withdrew during extension
6	8 mg	16 mg	24 mg		24 mg	Completed the study
7	16 mg	24 mg	32 mg		-	Withdrew after week 3
8	8 mg	8 mg	8 mg		8 mg	Completed the study
9	Placebo	8 mg	8 mg		8 mg	Withdrew during extension
10	8 mg	8 mg	8 mg		8 mg	Completed the study
11	Placebo	Placebo	Placebo		Placebo	Withdrew during extension
12	8 mg	16 mg	24 mg		24 mg	Completed the study
13	Placebo	8 mg	16 mg		16 mg	Completed the study

Table 4 - Comparative analysis of findings from patients and caregivers

Patients & Caregivers	Patient	Caregiver
1. Independence Driving widens the "living-space" for both patient and caregiver	• Doing something • Being useful • Enjoyment and pleasure • Fear of losing their ability to drive • The most important activity	• Happy to see patients enjoy themselves • More independence if the patient is able to drive • Fear that patients lose their ability to drive
2. Breathlessness impact on driving Breathlessness does not impact on perceived driving	• Overall, breathlessness does not impact on driving • Breathlessness at rest can affect concentration and the ability to drive	• Breathlessness does not affect the patients' ability to drive safely • More confident about patients' driving skills than the patients themselves
3. Driving while taking low-dose sustained-release morphine Sustained-release morphine does not impact on perceived driving	• Did not perceive any changes in driving ability with the study drug • Fears associated with low-dose morphine - putting others at risk	• Did not perceived any changes in patients' driving ability with the study drug • Fears associated with low-dose morphine – patients' decline

Box 1 - Interview guide used for patients and caregivers

Questions asked to patients 1. How important is driving to you? 2. Before the study, was your breathlessness impacting your ability to drive? 3. Were there any changes in your ability to drive after initiating the study medication?
Questions asked to caregivers 1. How important is it for you that [*patient*] is able to drive? 2. Before the study, was [*patient's*] breathlessness impacting on his/her ability to drive? 3. Were there any changes in [*patient's*] ability to drive after initiating the study medication?

ABSTRACT

Background: Chronic breathlessness is a disabling syndrome that profoundly impacts patients' and caregivers' lives. Driving is important for most people, including those with advanced disease. Regular, low dose, sustained-release morphine safely reduces breathlessness, but little is known about its impact on driving.

Aim: To understand patients' and caregivers' (i) perspectives and experiences of driving with chronic breathlessness; and (ii) perceived impact of regular, low-dose, sustained-release morphine on driving.

Design: A qualitative study embedded in a pragmatic, phase III, randomised, placebo-controlled trial (RCT) of low-dose, sustained-release morphine (≤32mg/24 hours) for chronic breathlessness. Semi-structured interviews were conducted immediately after participants withdrew or completed the RCT. Informed by grounded theory, a constant comparative approach to analysis was adopted.

Setting/participants: Participants were recruited from an outpatients palliative-care service in Adelaide, Australia. Participants included: patients (n=13) with severe breathlessness associated with chronic obstructive pulmonary disease; and their caregivers (n=9).

Results: Participants were interviewed at home. Eleven received morphine 8-32mg. Three themes emerged: i) independence; ii) breathlessness' impact on driving; and iii) driving while taking regular, low-dose, sustained-release morphine.

Conclusions: Driving contributed to a sense of identity and independence. Being able to drive increased the physical and social space available to patients and caregivers, their social engagement and well-being. Patients reported breathlessness at rest may impair driving skills, while the introduction of sustained-release morphine seemed to have no self-reported impact on driving. Investigating this last perception objectively, especially in terms of safety, is the subject of ongoing work.

Keywords

Driving, opioids, morphine, breathlessness, dyspnea, caregivers, patients

What is already known about the topic?

- Chronic breathlessness is a debilitating syndrome, which can be ameliorated by small doses of regular, low-dose, sustained-release morphine in some people.
- Driving is important for most adults, including the ones with life-limiting illnesses associated with chronic breathlessness.
- Despite growing concerns about the impact of opioids on driving ability, there are no studies investigating people's experiences of driving with chronic breathlessness before or after initiating treatment with regular, low-dose, sustained-release morphine.

What this paper adds?

- Being able to drive is important for people with chronic breathlessness and their caregivers because it provides them with a continuing sense of self-worth, independence, pleasure and widening life space.
- Episodes of intense breathlessness can impact on patients' perceived ability to drive, which is not easily perceived by caregivers.
- Although people have fears surrounding driving while taking morphine, regular, low-dose sustained-release morphine does not seem to impact on patients' self-perceived driving ability.

Implications for practice, theory and policy

- In clinical practice, it is important to enquire about peoples' perceived ability to drive with chronic breathlessness and the medications that they are prescribed.
- Clinical research should focus on investigating whether oral, low-dose sustained-release morphine impacts on patients' driving ability, particularly during initiating therapy and any subsequent dose increases.
- Understanding the impact of low-dose, sustained release morphine on people's driving ability is essential to inform guideline development about who is able to drive safely and who is not.

INTRODUCTION

Chronic breathlessness persists and is disabling despite optimal treatment of the underlying disease(s). [1] Chronic breathlessness affects almost 10% of adults and 17% of those ≥65 years. [2] Patients with chronic obstructive pulmonary disease (COPD) are particularly affected, with >90% reporting breathlessness at some stage. [3] Chronic breathlessness is physically and psychologically debilitating, [4] leading to increasing dependence, social isolation, and worse health-related and mortality outcomes. [5, 6] Loss of independence is also profoundly distressing for caregivers, who struggle seeing their loved ones' decline. [7, 8]

Driving provides a sense of freedom, independence, identity and hope. [9] Not driving worsens social isolation and is associated with worse health-related outcomes. [10, 11] One quarter of people with life-limiting illnesses continue driving. [12] Although there is ample evidence that chronic breathlessness severely restricts people's everyday lives, the effect of chronic breathlessness on people's driving ability has not been explored.

Regular, low-dose (≤30mg/day), [13] sustained-release morphine safely reduces chronic breathlessness in people with COPD. [14, 15] Recently, low-dose, sustained-release morphine has been approved by regulatory bodies in Australia for the treatment of chronic breathlessness. [16] This is the first world approval of any medication for the symptomatic reduction of chronic breathlessness, likely increasing prescriptions for this indication. Simultaneously, there are concerns about safe driving while taking psychoactive substances, including prescribed opioids. [17] While high dose opioids can impair driving, it is unknown whether regular, low dose, sustained-release morphine impacts on patients' ability to drive, particularly when initiating therapy and up-titration. [18]

This aim of this qualitative study was to elicit patients' and caregivers' perceptions about

driving with chronic breathlessness and to understand their perceptions about driving as regular, low dose, sustained release morphine was introduced.

METHODS

Design

A qualitative study embedded in a pragmatic, phase III, randomised, placebo-controlled trial (RCT) evaluating the effectiveness of sustained-release morphine for people with chronic breathlessness and COPD (BEAMS trial). [19] The RCT had a parallel-arm, dose increment design. Participants were randomised to placebo, 8mg or 16mg of once-daily sustained-release morphine for one week, with possible additional blinded up-titrations, of 8 or 16mg in weeks 2 and 3. Maximum daily doses of morphine by the end of the randomisation period ranged from 0mg (placebo) to 32mg (0, 8, 16, 24 or 32mg), with chances of being on placebo after randomisation being 1:12. The trial primary outcome measure was change in intensity of "worst breathlessness" in the previous 24 hours, measured with a 0-10 numerical rating scale after one week of therapy. The pragmatic design ensured that participants included in the RCT were a close reflection of the population of interest. [20,21]

Setting and Participants

Participants were recruited from the metropolitan region serviced be the Southern Adelaide Palliative Services, Australia. Participants included: patients who had ceased their participation in the BEAMS trial [19] either by completion or withdrawal; and 'the person closest to the patient' ('caregiver'), if present. [22] This sampling provided a broad range of perspectives. All patients had COPD and chronic breathlessness; a modified Medical Research Council (mMRC) breathlessness score of 3 or 4 corresponding to "stops for breath after walking about 100 meters or stops after a few minutes walking on the level" and "too breathlessness to leave the house or breathlessness when dressing or undressing",

respectively. [23,24] Participants were active drivers or people who had recently stopped driving and were still able to recall their experience of driving with severe chronic breathlessness. The latter group's perceptions contributed to expand the understanding of the experience of driving with this disabling syndrome, but were not questioned about their experiences of driving after initiating sustained-release morphine.

Research Team

The interviewer (D.F.) has a medical background and was a full-time doctoral student with training in qualitative research. J.B. is Senior Clinical Lecturer and Honorary Consultant in Palliative Medicine with a medical and research background. A.H. is a university researcher with background in data collection and people-centred research. S.K. is a university researcher with a linguistics background. J.P. is a senior researcher with a background in palliative care nursing and qualitative research. D.C. is a researcher with expertise in chronic breathlessness.

Recruitment

Using convenience sampling, the trial nurses approached potential participants by telephone. If interested, they were then phoned by the interviewer (D.F.), with whom they had no previous contact. The interviewer explained the study's objectives and scheduled a face-to-face meeting with potential participants to answer questions and obtain written consent.

Data collection

Face-to-face, semi-structured interviews were conducted separately with patients and their caregivers at a location of their choice (July 2017- November 2018), providing participants with safe and private settings to express freely any concerns or emotions. [25,26] Interviews evaluated the overall impact of chronic breathlessness in people's daily lives and perceived

changes after initiating study drug. [19] Given the lack of evidence examining experiences of driving in people with chronic breathlessness, the interviews included three questions about driving, analysed in a separate sub-study (Box 1).

Participants' responses were recorded and transcribed verbatim (D.F.). Field notes were collected and the researcher kept a reflexive journal with impressions about each participant-researcher interaction. Interview transcripts were not reviewed by participants to minimise burden on people already debilitated due to chronic breathlessness, given minimal advantages from doing this. [27] Potential misinterpretations were minimised by having a second researcher (A.H.) listen to interviews' recordings, checking transcriptions for accuracy. Participants were only contacted again if there were disagreements between these researchers. Data were collected until saturation (i.e. no new concepts were emerging), as agreed between all researchers.

Data Analysis

NVivo (V 11.4.0 for Mac) was used. The analysis was driven by the principles of grounded theory, using a constant comparative approach. [28,29,30] Given the lack of qualitative studies exploring people's experiences of driving with chronic breathlessness, an inductive approach to analysis was adopted. [31] The constant comparative approach helped identify new concepts emerging from the data that could be explored in subsequent interviews. [30] Two researchers independently conducted open coding (D.F., A.H.) of all transcripts, which were grouped into themes (D.F.); each theme was illustrated with several quotes to confirm coding validity (D.F., J.B., S.K., J.P.). Patients' and caregivers' viewpoints were then compared and contrasted.

Ethical considerations

The BEAMS trial was approved by relevant Human Research Ethics Committees (15/12/16/3.06) and was registered (NCT02720822). All participants provided written informed consent.

The COREQ framework is used to report this study. [32]

RESULTS

Fifteen patients and 11 matched caregivers were invited to this study: two patients declined (so their caregivers were excluded); 13 patients and 9 caregivers were interviewed. Interviews took 20-55 minutes. Patients had a median age of 76 years (interquartile range [IQR] 68-78), nine of whom were men, living with their partners. All were still mobile outside their homes, but were severely restricted in their daily activities due to breathlessness (Table 1).

Eight of 13 patients were regularly driving and one drove occasionally. Only two of nine men had stopped driving, while two of four women had stopped driving. The four participants who had stopped driving had all driven regularly until recently (Table 2). Eleven patients took sustained-release morphine during the study (Table 3): 8mg (n=4), 16mg (n=3), 24mg (n=3) and 32mg (n=1).

Three major themes described the experience of driving for patients with chronic breathlessness and their caregivers: 1) independence, 2) breathlessness' impact on driving, 3) driving while taking regular low-dose sustained-release morphine (Table 4).

Theme 1 - Independence

Being able to drive helped patients keep their sense of self and feeling useful. This was more noticeable in patients experiencing severe functional limitations due to breathlessness.

> *"Well, I suppose it's something that I don't do every day (driving) and you know, and I am doing something! Maybe that's the reason why… Well I've always enjoyed driving actually but more so now, more so now, yeah… Probably because it's something different in my life now, you know? I can do something! Whereas usually, I am just sitting."* [Patient 8]

Most patients reported that driving was one of the few activities that brought them a sense of joy and pleasure. Even those patients not required to drive (i.e. because their caregiver drove), still felt the need to drive at times for pure enjoyment.

> *"We have got the van and I drive the van. I love getting out in the country and driving."* [Patient 12]

For caregivers, seeing their partners enjoy themselves was particularly importantly. They acknowledged the role of driving in widening the physical space available to both the patients and themselves, a space that had been severely reduced by breathlessness in most cases.

> *"Well, driving is important… There are certain things… When we go on holiday because he is not bothered about walking out on the streets, you know? (…) But we went to Barossa Valley last week, and I don't know if you have been there, but we went to Mengler's Hill to the look out. He got up there, well we drove up there of course, we got out of the car and we walked down a little bit to the picnic area there and he stayed there while I walked around and looked at it because walking down and up and down… [meaning it was tiresome for him]. So things like that you know?"* [Caregiver 11]

For some patients, driving was their most important activity. One patient without a caregiver explained that driving was key to maintaining relationships and roles, whilst also providing a sense of purpose:

> *"I get my adult daughter every Saturday for a while, she is profoundly autistic, she just had her 26th birthday yesterday and it is very important to her. So I have got to drive to go get her, drive to bring her back. So it's a very important thing, making sure*

I can still drive. (…) And that's the main reason, apart from that, it is just to get to the shop and the doctor which are a kilometer away. That's the only big one." [Patient 3]

Another patient explained that driving was the only out-of-home activity he was still able to do independently and that losing it would be extremely disturbing.

"Well, I think the most important thing to be able to do at the moment is to be able to drive because physically there is nothing I can do, I can't do anything". [Patient 8]

Overall, people who were still driving expressed fear about not being able to drive in the future. Driving was seen as an important marker of independence and there was fear over any loss and its consequences.

"I couldn't give up driving, I couldn't do that [disturbed facial expression]. I think it's your independence, you know? And once that is taken away you're reliant on somebody else…" [Patient 9]

For the four patients who had stopped driving, only one (male) reported that driving was important to maintain his independence. The other three patients (one male, two females) reported driving was not overly important because their caregivers could drive when needed.

"It gives me a lot more freedom to have the car. I don't do things that I would normally do… If I had the car and I felt like KFC for lunch, I can go and get it (laughing)… or if I wanted to go out for dinner with someone, I could just go and do it. Whereas now, for me to walk to the bus stop to get a bus somewhere, it's just too hard…" [Patient 10]

"I don't miss driving. B. (husband) does everything. We are together all the time anyway." [Patient 1]

Breathlessness' impact on driving

In general, patients and caregivers considered that breathlessness did not reduce patients' driving skills because it did not require over-exertion.

"Normally, I am fine. I don't get tired driving." [Patient 7]

Some patients reported they had situations in which they felt breathlessness at rest. When present, they felt their driving ability was affected. Strategies to overcome this limitation included not driving at all or using oxygen while driving. Interestingly, the use of oxygen in the car raised some concerns about its safety and legality.

"There were a couple of times in which I have been buggered a bit. I haven't had the oxygen the night before, so I will put the oxygen on the car and I will have the oxygen running while I am driving. Whether that's legal or not I don't know." [Patient 11]

One patient experiencing breathlessness at rest explained that breathlessness impacted on his concentration and hence ability to drive. When he drove, he felt anxious and concerned about his and other people's safety.

"For me it is not so much driving, but the concentration level about what is going on around. Stuff I used to take for granted, so I automatically did it before. Now, I have to make sure I do it. And it depends on the concentration because if it is concentrating on something that could end in a disaster, is a bit different to concentrating on something that might just a non-event anyway." [Patient 13]

Overall, caregivers' views matched patients' views. Most caregivers confirmed that patients drove safely despite their breathlessness. For the only patient who stated that driving was stressful (previous quote, patient 13), the caregiver thought he could still drive safely.

> *"Yes, usually when we go stay with our son at Wallaroo, he drives there. So he can. And he is quite good, I think. I don't notice any diminishing of his driving skills. I feel quite relaxed when he is driving."* [Caregiver 13]

Driving while taking regular, low-dose sustained-release morphine

Participants' views on driving were quite uniform, irrespectively of the drug (i.e. morphine or placebo) and dose. Most patients and caregivers perceived that the study drug did not have any perceived adverse impact on patients' ability to drive, irrespectively of the study drug/dose.

> *"No, no problems (to drive while taking the study drug)."* [Patient 7 - maximum morphine dose 32mg]

> *"No, no, not at all. I don't think driving was affected (by morphine)".* [Caregiver 2 – maximum morphine dose 16mg]

Despite not perceiving any impact on driving with the study drug, a small number of participants were still concerned about the potential effects of morphine on driving. Most believed that the trial dose (up to 32mg sustained-release morphine a day) could impair driving. One caregiver did not want the patient to continue with morphine because she believed morphine could lead to driving cessation. One patient took action to minimise any negative impact of morphine on his driving skills.

"I was concerned about… If he does take it, I think he wouldn't be able to drive (…) and I don't really want him to go on that because he loves driving and I think if he took it, that would be the end. I want him to be around for a few more years yet." [Caregiver 8 – maximum morphine dose 8mg]

"I have a friend coming here and he will sit with me (while I drive) and tells me what is going on with the driving. (…) I know they say if I am taking a quite powerful opioid drug that driving while under the immediate influence is probably not that smart. I would not be inclined to do it unless it was an emergency." [Patient 3 – maximum morphine dose 8mg]

DISCUSSION

Main findings

This is the first study reporting patients' and caregivers' perspectives and experiences of driving with chronic breathlessness. Additionally, the study was set in a study to compare before-and-after taking regular, low dose, oral sustained-release morphine. Findings suggest that driving is crucial in helping patients with chronic breathlessness keep a sense of identity, purpose, independence and connection to the outside world, while also being a source of joy and comfort for both patients and caregivers. According to patients, breathlessness at rest can reduce their driving skills but the study drug (i.e. morphine/placebo) had no perceived impact on their ability to drive.

Similar to healthy individuals, owning and driving a private vehicle is perceived as an amenity offering people freedom of movement. [33] However, participants' reflections highlight that the ability to drive is particularly important for people experiencing severe functional limitations in other aspects of life due to chronic breathlessness and their caregivers. For these patients, driving is associated with a sense of identity and feeling

useful. Similar findings were reported by a previous qualitative study of three focus groups: i) low disability/broad life space, ii) high disability/broad life space, iii) high or low disability/constricted life space. Although all groups considered driving an important activity, the third group was the most affected by driving cessation which was perceived by them as devastating. [34] Importantly, the present study also shows that driving widens both patients' and caregivers' life space (i.e. the physical space in which they move and socially interact). [35,36] Previous evidence suggests that as patients become more restricted by chronic breathlessness, caregivers tend to adjust by slowing their life rhythm, also becoming more restricted. [37] Thus, it is likely that any strategies supporting patients' function (such as driving) may also positively affect caregivers. [35] Functional decline is one of the major contributors to driving cessation in older age. [11] Older adults who stop driving have twice the risk of depressive symptoms compared to those who continue driving. [11] Importantly, there is a significant association between the well-being of these patients and their caregivers. [38] Thus, risks and benefits for patients and caregivers need to be weighed carefully before advising patients not to drive.

Most patients considered that their chronic breathlessness did not impact on their driving primarily because driving was sedentary and did not trigger breathlessness. Patients who had experienced or were experiencing breathlessness at rest explained that breathlessness affected their concentration when driving. Previous research has highlighted potential effects of uncontrolled symptoms on people's driving skills. [39] Worsening breathlessness scores are associated with worsening performance in neuropsychological assessments but any relationship with driving performance is unknown. [40] Worsening breathlessness scores are associated with increased chances of experiencing breathlessness at rest. [23] Thus, it is possible that patients with worse breathlessness are particularly at risk of having some degree of psychomotor impairment that could affect driving. Interestingly, caregivers did not seem to notice any changes in patients' ability to drive. This may result from patients' adaptation to breathlessness, including development of driving strategies that are not

evident to caregivers (e.g. increased attention, driving slightly slower). Reportedly, the use of oxygen while driving may be one of these strategies. Using oxygen while driving is legal in most countries but patients need to ensure oxygen tanks are adequately secured and respect specific state/country requirements. Given that driving cessation is also emotionally challenging for caregivers, caregivers may overlook changes in patients' driving ability in order to keep them driving. [41]

All participants agreed that their study drug/dose did not affect their perceived driving skills. Previous research had suggested that regular therapeutic opioid-agonists are unlikely to affect driving-related skills. [18] This study raises the hypothesis that low-doses of sustained-release morphine may have no impact on driving even during therapy initiation and careful upward titration. This is in line with previous studies showing that uncontrolled symptoms are more likely to have an impact on driving than therapeutic opioids. [39] Despite that, both patients and caregivers were still concerned about potential side effects of sustained-release morphine that could affect their driving. Concerns about opioids are common amongst patients, caregivers and clinicians. [42,43] Interestingly, while patients' concerns were focused on safety for themselves and others, caregivers' were more concerned with patients' deterioration if they were to stop driving. Chronic breathlessness affects both patients and caregivers, involving both in symptom management and again reinforcing the patient-caregiver unit as the unit of care. [44]

This study suggests that initiating morphine for chronic breathlessness may raise concerns about driving for patients and caregivers, and those concerns need to be proactively addressed with both. Frequently, clinicians advise patients not to drive immediately after taking opioids. [45] There is a need for further research to understand if patients taking regular, low-dose, sustained-release morphine are able to drive safely given the different pharmacokinetic profile they have to immediate-release oral morphine solutions. [46] The relation between breathlessness and driving performance whist on opioids must also be

explored as current legal morphine limits for driving (where imposed) are far higher than the doses used in this study. [13]

Strengths and Limitations

This is the first qualitative study reporting on people's experiences of driving with chronic breathlessness and the perceived effects of regular, low-dose sustained-release morphine on driving ability. The inclusion of people taking different doses of morphine and placebo provided a range of different perspectives that could be compared and contrasted. The qualitative design limits generalisability, but findings point to important questions and future research directions, particularly in the context of growing concerns about drug-affected drivers. This study is limited by looking at self-reported effects on driving. People tend to overestimate their own driving performance. [47] Most studies conducted in this field asked participants to rate their driving ability compared with the "average driver", rather than assessing aspects of their own driving. [48] The latter has been shown to more accurately reflect driving performance, and is closer to the approach used in this study. [48,49] Similarly, caregivers' perception is not an optimal reflection of patients' driving skills, but their assessment of specific driving aspects correlates with on-the-road performance. [50] Opioids may affect cognitive function, which may affect self-perception. [51] However, it is less likely that would be the case with small doses of morphine. [52]

A strength of this study is that participants were recruited from a phase III RCT that allowed COPD-status and morphine-dose transparency. While the participants may not be representative of the overall population with severe breathlessness associated with COPD, the RCT had a pragmatic design to ensure high external validity. [20,21] Due to the main trial dose-increment design, people were more likely to be taking morphine than placebo after the randomisation period (11:12 chance). This reduced the number of perspectives from people

taking placebo, but increased the number of people who could provide useful information about morphine.

What this study adds

This study highlights that driving is important for people living with chronic breathlessness and their caregivers. It also suggests that regular, low-dose, sustained-release morphine does not impact on patients' perceived ability to drive. Based on these findings, there is a need to objectively evaluate the impact of chronic breathlessness on patients' driving ability. Previous studies focused on objective measures of disease severity but not on the symptom itself. [53] It is also important to understand if people are safe to drive with low-doses of sustained-release morphine, particularly during therapy initiation and upward titration. Equally, the impact of uncontrolled symptoms such as chronic breathlessness on driving performance needs to be researched. There is a common assumption in the clinical setting that people should refrain from driving in the first hours or days after initiating any opioid. There are no published RCTs to confirm this should be the case with low-dose sustained-release morphine. Due to lack of evidence to support decision-making, clinicians may advise people taking low dose sustained-release morphine to stop driving, but be aware that this may have severe implications for people's well-being and social functioning.

Author contributions

DF, JP, DC contributed to the study design; DF contributed to the acquisition of data; DF, JB, AH, JP, DC contributed to data analysis; DF drafted the article; all authors have critically revised the articles and have approved the manuscript version to be published.

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Declaration of conflicting interests

David C. Currow is an unpaid advisory board member for Helsinn Pharmaceuticals. He is a paid consultant and receives payment for intellectual property with Mayne Pharma and is a consultant with Specialised Therapeutics Australia Pty. Ltd. Diana H. Ferreira, Jason Boland, Aaron Honson, Slavica Kochovska and Jane Phillips disclose no competing interests relevant for this work.

Ethical approval and informed consent

Ethics approval was obtained from relevant Health Human Research Ethics Committees, and the trial was registered (Registration No. NCT02720822) before recruitment commenced. All participants gave informed written consent.

Data sharing

The study databases are available from the corresponding author on reasonable request.

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PALLIATIVE MEDICINE AUTHOR SUBMISSION CHECKLIST

Please complete this checklist for all papers submitted. Please indicate, very briefly, how this has been addressed. This checklist is a mandatory upload on submission.

Item	Explanation	How this has been addressed (briefly, a sentence will suffice)
Article title	***WHY: Because we want readers to find your work.*** Have you followed our guidelines on writing a good title that will be found by search engines? (E.g. with methods in the title, use of common words for the issue addressed, no country names, and possibly indicating findings). If your study has an acronym is it included in the title?	The title reports this is a qualitative study of patients' and caregivers' living with chronic breathlessness
Abstract	***WHY: Because structured abstracts have more detail for readers and search engines.*** Have you followed our guidelines on writing your structured abstract? Please remember we have separate abstract structures for original research, different types of reviews and case reports/series. There should be **no** abbreviations in the abstract, EXCEPT a study acronym which should be included if you have one. If a trial (or other design formally registered with a database) have you included your registration details?	Yes, the guidelines of Palliative Medicine for original research studies were followed.
Key statements	***WHY: Because readers want to understand your paper quickly.*** Have you included our key statements within the body of your paper (after abstract and before the main text is a good place!) and followed our guidelines for how these are to be written? There are three main headings required, and each may have 1-3 separate **bullet** points. Please use clear, succinct, single sentence separate bullet points rather than complex or multiple sentences.	Yes, the key statements are provided according to the guidelines.
Keywords	***WHY: Because MeSH headings mean it is properly indexed.*** Have you given keywords for your study? We ask that these are current **MeSH** headings unless there is no suitable heading for use (please give explanation in cover letter). https://meshb.nlm.nih.gov/search	Yes, were possible, MeSH headings were used in the keywords.
International relevance	***WHY: We have readers from around the world who are interested in your work.*** Have you contextualised your work for an international audience and explained how your work contributes to an international knowledge base? Avoid drawing from policy from one context only, think	Yes, we explain the relevance of the study to all patients with chronic breathlessness and COPD.

	how your work could be relevant more widely. Do define terms clearly e.g. hospice has a different meaning in many countries.	
Publishing guidelines	***WHY: Because clear and robust reporting helps people interpret your work accurately*** Have you submitted a completed checklist for a relevant publishing guideline as a supplementary file? http://www.equator-network.org/ These include CONSORT, PRISMA, COREQ checklists, but others may be more relevant for your type of manuscript. If no published checklist exists please create one as a table from the list of requirements in your chosen guideline. If your study design does not have a relevant publishing guideline please review closest matches and use the most appropriate with an explanation.	We followed the COREQ checklist for reporting of qualitative studies (this will be uploaded as a separate file).
Word count	***WHY: Because readers want to find the core information quickly.*** Does your paper adhere to our word count for your article type? Please insert number of words in the box to the right. Remember that tables, figures, qualitative data extracts and references are not included in the word count.	Word count: 2974
Figures and tables and/or quotations	***WHY: Because readers want to find the core information quickly.*** Have you adhered to our guidelines on the number of tables and figures for your article type? Data (e.g. quotations) for qualitative studies are not included in the word count, and we prefer that they are integrated into the text (e.g. not in a separate table).	Yes, guidelines were followed. We have less than 6 tables. Example of quotes are integrated in the text.
Study registration	***WHY: Because this means readers understand how you planned your study*** Where appropriate have you included details (including reference number, date of registration and URL) of study registration on a database e.g. trials or review database. If your study has a published protocol, is this referenced within the paper?	The main trial registration details are included with dates and URL. The main trial protocol is referenced in the text.
Other study publications?	***WHY: So readers can understand the full context of your study*** If there are other publications from this study are these referenced within the body of the paper? Please do not reference papers in preparation or submitted, but in-press publications are acceptable.	Only the main trial protocol is published at this stage, as the protocol is referenced in the text.
Scales, measures or questionnaires	***WHY: So readers can understand your paper in the context of this information*** If your study primarily reports the development or testing of scales/measures or questionnaires have you included a copy of the instrument as a supplementary file?	Yes, a copy of the interview guides is supplied.

Abbreviations	***WHY: Because abbreviations make a paper hard to read, and are easily misunderstood*** Have you removed **all** abbreviations from the text except for extremely well known, standard abbreviations (e.g. SI units), which should be spelt out in full first? We do not allow abbreviations for core concepts such as palliative or end of life care.	Yes, only known abbreviations are included and are spelt out in full first.
Research ethics and governance approvals for research involving human subjects	***WHY: We will only publish ethically conducted research, approved by relevant bodies*** Have you given full details of ethics/governance/data protection approvals with reference numbers, full name of the committee(s) giving approval and the date of approval? If such approvals are not required have you made it explicit within the paper why they were not required. Are details of consent procedures clear in the paper?	Yes, Ethics approval details are provided. Consent procedures are clear in the text.
Date(s) of data collection	***WHY: So readers understand the context within which data were collected*** Have you given the dates of data collection for your study within the body of your text? If your data are over 5 years old you will need to articulate clearly why they are still relevant and important to current practice.	Yes. This is provided in the Data collection section.
Structured discussion	***WHY: So readers can find key information quickly*** Papers should have a structured discussion, with sub headings, summarising the main findings, addressing strengths and limitations, articulating what this study adds with reference to existing international literature, and presenting the implications for practice.	The discussion is structured and includes a summary of the main findings, articulation with current literature and highlights limitations and implications for clinical practice.
Case reports & Case Series Practice Reviews	***WHY: So that participants are protected, and its importance made clear*** If your study is a case report, series or practice review have you followed our clear structure and detailed author instructions, including highlighting what research is needed to address the issue raised? Have you made clear what consent was required or given for the publication of the case report? Have you provided evidence of such consent as a supplementary file to the editor? Is your practice review formatted with the requisite 'Do's, Don'ts and Don't knows'?	Not applicable
Acknowledgements and declarations	***WHY: So readers understand the context of the research***	Yes. The required information is included in the last sections of the manuscript.

	Have you included a funding declaration according to the SAGE format? Are there acknowledgements to be made? Have you stated where data from the study are deposited and how they may be available to others? Have you conflicts of interest to declare?	
Supplementary data and materials	***WHY: So the context is clear, but the main paper succinct for the reader*** Is there any content which could be provided as supplementary data which would appear only in the online version of accepted papers? This could include large tables, full search strategies for reviews, additional data etc.	Interview guides are provided as appendixes.
References	***WHY: So people can easily find work you have referenced*** Are your references provided in SAGE Vancouver style? You can download this style within Endnote and other referencing software.	Yes, Vancouver style was used.
Ownership of work.	Can you assert that you are submitting your original work, that you have the rights in the work, that you are submitting the work for first publication in the Journal and that it is not being considered for publication elsewhere and has not already been published elsewhere, and that you have obtained and can supply all necessary permissions for the reproduction of any copyright works not owned by you.	Yes, this is my original work that is being submitted for publications for the first time and that is not being considered for publication elsewhere. There is no copyright work that is not owned by the authors.

Item	Guide questions/description	Location in manuscript
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	See 'research team'
2. Credentials	What were the researcher's credentials?	See 'research team
3. Occupation	What was their occupation at the time of the study?	See 'research team'
4. Gender	Was the researcher male or female?	See 'research team
5. Experience and training	What experience or training did the researcher have?	See 'research team
6. Relationship established	Was a relationship established prior to study commencement?	See 'recruitment'
7. Participant knowledge of the interviewer	What did the participants know about the researcher?	See 'recruitment'
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator?	See 'recruitment'
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study?	See 'design'
10. Sampling	How were participants selected?	See 'participants and setting'
11. Method of approach	How were participants approached?	See 'recruitment'
12. Sample size	How many participants were in the study?	See 'results'
13. Non-participation	How many people refused to participate or dropped out? Reasons?	See 'results'
14. Setting of data collection	Where was the data collected?	See 'results'
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	See 'data collection'
16. Description of sample	What are the important characteristics of the sample?	See 'findings' and Table 1
17. Interview guide	Were questions, prompts, guides provided by the authors?	See 'data collection'
18. Repeat interviews	Were repeat interviews carried out?	See 'data collection'
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	See 'data collection'
20. Field notes	Were field notes made during and/or after the interview or focus group?	See 'data collection'
21. Duration	What was the duration of the interviews or focus group?	See 'results'
22. Data saturation	Was data saturation discussed?	See 'data collection'
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	See 'data collection'
24. Number of data coders	How many data coders coded the data?	See 'data analysis'
25. Description of the coding tree	Did authors provide a description of the coding tree?	See 'results' and Table 4
26. Derivation of themes	Were themes identified in advance or derived from the data?	See 'data analysis'
27. Software	What software, if applicable, was used to manage the data?	See 'data analysis'
28. Participant checking	Did participants provide feedback on the findings?	See 'data collection'
29. Quotations presented	Were participant quotations presented to illustrate the themes / findings?	See 'results'
30. Data and findings consistent	Was there consistency between the data presented and the findings?	See 'results' and Table 4
31. Clarity of major themes	Were major themes clearly presented in the findings?	See 'results' and Table 4
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	See 'findings'

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