

## 1 Introduction

2 Patients with life limiting illness may experience significant symptom burden  
3 associated with their disease necessitating the need for the addition of complex  
4 pharmacotherapy.[1] This is often complicated by established medications used to treat co-  
5 morbid conditions, or prevent adverse consequences of these conditions. One such example  
6 is using medications to treat hypertension in life limiting illness. Indeed, the prevalence of  
7 hypertension is strongly associated with age – with more than 50 per cent of those aged 60  
8 years of age having a diagnosis of high blood pressure.[2] Given that the majority of people  
9 with a life limiting illness are over 60 years of age, the use of antihypertensive medication in  
10 this patient population is common. Previous studies have shown that reducing blood  
11 pressure significantly decreases the probability of developing ischaemic heart disease and  
12 stroke, although the time till benefit of this is several years.[3] This is problematic in the  
13 context of diminished life expectancy, as the time till benefit of the medication can often  
14 outweigh the remaining life expectancy of the patient, raising questions over the risk benefit  
15 ratio of treatment. This is further complicated by the fact that some patients with life  
16 limiting illness experience symptoms of cachexia, early satiety and thus lose significant  
17 amounts of body weight. Whilst this can have a negative impact on quality of life, the weight  
18 loss can also reduce a patient's blood pressure, thus negating the need to use antihypertensive  
19 medication. It is important, therefore, to review antihypertensive medication in the context of  
20 remaining life expectancy whilst monitoring blood pressure vigilantly, to ensure that the  
21 medication is used safely and appropriately. While previous studies have assessed the  
22 appropriateness of medication in the context of diminished life expectancy, there is no work  
23 specifically exploring blood pressure control and the use of antihypertensive medication in  
24 this patient population.

The objectives of this study were, therefore, to: (1) assess the prevalence of previously documented hypertension and associated blood pressure in a cohort of patients with life limiting illness; and, (2) assess the appropriateness of antihypertensive medication in this patient group.

## **Ethical Approval**

Full NHS ethical approval was not required for this work, as it was considered a service improvement study. As such, the study was registered with, and approved by South Tyneside NHS Foundation Trust (approval number CA6178), UK. All data was managed in accordance with the Data Protection Act and the requirements of the Caldicott guardian were met.

## **Methods**

Patients were included in the study if they were registered as part of the specialist palliative care day service at St Benedict's Hospice, based in the North of England, on the 4th August 2015, and had been attending the service for at least one week. Participants were excluded from the study if they were not part of the day service and attended another part of the hospice (e.g. the inpatient unit). The average the life expectancy of patients attending day services was approximately 18 months. To meet the study objectives, patient electronic hospital records were reviewed and data relating to patient gender, age, diagnosis, standing blood pressure (where available) and sitting blood pressure were extracted. Medication data were also extracted from the electronic record, which included medication type, dose and formulation; medication data were classified according to British National Formulary (BNF) category. The appropriateness of the antihypertensive medication was assessed by the

clinical team, which included a palliative medicine consultant and a clinical pharmacist, using a framework, as proposed by Holmes et al., that considered the following factors: remaining life expectancy of the patient, time until benefit of the treatment, goals of care and treatment targets.[4] Any patient that was assessed to be using antihypertensive medication inappropriately was referred to the wider clinical team for further investigation.

## Results

Fifty-four people met the inclusion criteria and were included in the study; no patients were excluded from the study. Participant characteristics are shown in Table 1. Twenty-six (48.1%) patients had previously documented hypertension: the mean blood pressure for these patients was 122/65 mm Hg (SD 17.0/10.5), while for the normotensive patients it was 122/73 (SD 21.0/11.6). Standing blood pressure was taken in 11 patients: for patients previously documented with hypertension the mean standing blood pressure reading was 95/55 mm Hg (SD 27.5/12.1), while for the normotensive patients, the mean was 125/70 mm Hg (30.8/16.0). Thirteen (24.1%) patients had documented symptoms of postural hypotension (5 of which had a diagnosis of hypertension). All of the patients with previously diagnosed hypertension were taking at least one antihypertensive medication: 19 were using 1; 4 were using 2; and, 3 patients were using three medications.

Of the 26 patients using antihypertensive medication, the clinical team (a palliative medicine consultant and clinical pharmacist) accessed that 25 were using the medication inappropriately; this could have resulted in clinical intervention to reduce or stop these medications. These medications were considered inappropriate given the current blood pressure readings and the remaining life expectancy of the patient. The patient who was accessed as using their antihypertensive medication appropriately also had heart failure; they were an ACE inhibitor and a beta-blocker to manage their symptoms.

In terms of other medication with the potential to affect blood pressure control, 15 patients were using at least one anticholinergic medication: tri-cyclic antidepressants were the most common, while other medication included nefopam and drugs used to treat urinary urgency/frequency (oxybutynin, tropsium, solifenacin, fesoterodine and tolterodine). Only five patients with hypertension were using anticholinergic drugs, compared to ten normotensive patients. Loop diuretics were used in 8 patients, while potassium sparing diuretics were used in 3 patients: all of these patients had a previous diagnoses of hypertension.

## **Discussion**

The main findings of this study showed the majority of patients attending a specialist palliative care day service were inappropriately using their antihypertensive medication. Indeed, many patients had low blood pressure – with some having symptoms of postural hypotension or large differences between sitting and standing blood pressure. Given the association with postural hypertension and the risk of falls, this potentially has implication for patient safety.[5] Previous studies have shown that patients with life limiting illness commonly use preventative medication inappropriately in the context of their remaining life expectancy.[6] Our study, however, is the first to assess and report patients' blood pressure and shows that many patients with previously diagnosed hypertension have low blood pressure with an average value of 122/65 mm Hg (SD 17.0/10.5). This finding is timely given that, for patients with limited life expectancy, a recent Canadian consensus guideline recommends a target systolic blood pressure of 160 to 190 mm Hg[7], while NICE currently state that, for patients with hypertension, the blood pressure target should be below 140/90 mm Hg if aged under 80 years, or below 150/90 mm Hg if aged over 80 years, although we note there is no specific reference to patients with limited life expectancy.[2]

We would urge policy-makers to build on this and produce clear practical guidance outlining blood pressure thresholds in order to facilitate the appropriate and safe use of antihypertensive medication. Indeed, a set of recommendations have recently been published that outline approaches to the deprescribing of medication in diminished life expectancy [8], while Scott and colleagues have provided a step-wise protocol to the deprescribing process [9]: these works could be applied to antihypertensive medication, but fall short of explaining when medication should actually be discontinued.

In terms of the wider literature, it is not known how discontinuing antihypertensive medication in life limiting illness affects blood pressure or patient outcome in terms of mortality. A recent study, by Moonen and colleagues, has shown that discontinuing antihypertensive medication in older people with mild cognitive deficits did not improve cognitive, psychological or general daily functioning, although systolic and diastolic blood pressures increased by an average of 7.36 and 2.63 respectively.[10] This is significant progress, but given our work shows that antihypertensives are used inappropriately in patients with life limiting illness, it would be prudent to focus future trials in this area to establish evidence-based approaches to deprescribing medication.

While we believe our results are important and have potential implications around developing deprescribing approaches for antihypertensive medication, we acknowledge the main limitation of this study is that retrospective data, recorded in patients' medical notes, was used. There could therefore, in theory, be errors in the blood pressure data, as the blood pressure recording process was not quality assured. We also acknowledge that only patients from one centre were sampled and sample size was relatively small; it would be prudent for future studies to extend the number of participants by including other palliative care centres. Our results should, therefore, be interpreted with this in mind.

## **Conclusion**

The blood pressure for patients with previously documented hypertension who access specialist palliative care day services is commonly below the NICE target threshold of 140/90 mm Hg (150/90 mm Hg for patients aged over 80 years). The majority of these patients are prescribed antihypertensive medications inappropriately and should have their antihypertensive medications reviewed in the context of their original therapeutic goals taking into account their current blood pressure control.

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## **Conflicts of interest**

None

**Table 1.** Study participant information

<b>Characteristic</b>	<b>Frequency (%)</b>
<b>Gender</b>	
Male	24 (44.4)
Female	30 (55.5)
<b>Age</b>	
<51 years	5 (9.3%)
51-60 years	10 (18.5%)
61-70 years	8 (14.8)
71-80 years	16 (29.6%)
81-90 years	13 (24.1%)
>90 years	2 (3.7%)
<b>Primary Diagnosis</b>	
Non-malignant disease	14 (25.9)
Malignant disease	40 (74.1)
<b>Antihypertensive agents</b>	
ACE inhibitors	9 (16.7)
Angiotensin II receptor antagonists	5 (9.3)
Beta-blockers	16 (30.0)
Calcium channel blockers	3 (5.6)
Thiazide diuretics	3 (5.6)

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