

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.

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

29

30 **Ethical Approval**

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

36

37 **Methods**

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

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

54

55 **Results**

56 Fifty-four people met the inclusion criteria and were included in the study; no patients
57 were excluded from the study. Participant characteristics are shown in Table 1. Twenty-six
58 (48.1%) patients had previously documented hypertension: the mean blood pressure for these
59 patients was 122/65 mm Hg (SD 17.0/10.5), while for the normotensive patients it was
60 122/73 (SD 21.0/11.6). Standing blood pressure was taken in 11 patients: for patients
61 previously documented with hypertension the mean standing blood pressure reading was
62 95/55 mm Hg (SD 27.5/12.1), while for the normotensive patients, the mean was 125/70 mm
63 Hg (30.8/16.0). Thirteen (24.1%) patients had documented symptoms of postural
64 hypotension (5 of which had a diagnosis of hypertension). All of the patients with previously
65 diagnosed hypertension were taking at least one antihypertensive medication: 19 were using
66 1; 4 were using 2; and, 3 patients were using three medications.

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

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

82

83 **Discussion**

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

99 We would urge policy-makers to build on this and produce clear practical guidance
100 outlining blood pressure thresholds in order to facilitate the appropriate and safe use of
101 antihypertensive medication. Indeed, a set of recommendations have recently been published
102 that outline approaches to the deprescribing of medication in diminished life expectancy [8],
103 while Scott and colleagues have provided a step-wise protocol to the deprescribing process
104 [9]: these works could be applied to antihypertensive medication, but fall short of explaining
105 when medication should actually be discontinued.

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

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

123

124 **Conclusion**

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

131

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134

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137 or not-for-profit sectors.

138

139 **Conflicts of interest**

140 None

141

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Table 1. Study participant information

Characteristic	Frequency (%)
Gender	
Male	24 (44.4)
Female	30 (55.5)
Age	
<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%)
Primary Diagnosis	
Non-malignant disease	14 (25.9)
Malignant disease	40 (74.1)
Antihypertensive agents	
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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