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Estimated cost savings from dose banding guidance: a case study using treatments for Stage IV melanoma

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Objectives

In 2016/2017, the National Health Service England (NHSE) spent approximately £1.7 billion on routinely commissioned chemotherapy.[1] Drug costs were the largest proportion of this spend (80%) and are increasing at a high rate.[1]

Chemotherapy drugs, also known as systemic anti-cancer therapies, are commonly dosed variably, according to patient weight or body surface area. This can lead to wastage as large volumes of drug are left over in vials. It is often not possible to use left-over drug product for other patients due to practical, logistical or regulatory reasons.

To improve value and increase efficiency, recent NHSE guidance encourages hospitals to use dose banding, whereby individualised doses are rounded up or down to predetermined standard doses.[1, 2] The exact, individualised dose is first calculated, which will fall into a range (or band) of doses corresponding to a single dose, permitting doses to be rounded down or up. Doses can also be made up in advance. Therefore, dose banding is expected to lead to efficiencies by reducing both drug wastage and administration time, while providing doses that do not affect efficacy or toxicity.[3]

The National Institute for Health and Care Excellence (NICE) has released a position statement supporting the approach,[3] although how to apply dose banding in economic evaluations to inform NICE Health Technology Assessment (HTA) decisions remains unclear. As drug costs are invariably a key driver of results, it is important to acknowledge the potential impact of dose banding.

This study aimed to estimate annual drug and administration costs per patient, using the example of variably dosed Stage IV melanoma treatments for which dose-banding guidance is available. Annual per-patient drug and administration costs were compared between dose-banding and non-dose-banding scenarios.

Methods

Drug costs

Dose banding guidance is available for three systemic anti-cancer therapies for Stage IV melanoma: dacarbazine, ipilimumab and pembrolizumab. Dacarbazine is available in 100mg and 200mg vial sizes and was assumed to be administered at a dose of 850mg/m^2 based on NICE TA319.[4] Dacarbazine 200mg vials are cheaper per mg than 100mg vials, so it was assumed that clinicians would choose one 200mg vial over two 100mg vials where possible. Ipilimumab was assumed to be administered at 3mg/kg, and pembrolizumab at 2mg/kg, as specified in their Summaries of Product Characteristics (SPCs).[5, 6] As ipilimumab and pembrolizumab vials are divisible and linearly priced, the smallest vial size was used in the analysis for simplicity. Preparation strengths, pack sizes and costs were taken from the electronic Market Information Toot (eMIT) and the Monthly Index of Medical Specialities (MIMS).[7, 8] List prices were used for all drugs. **Table 1** summarises the drug costs used in the analysis.

Table 1: Stage IV melanoma treatments, posology and costs

Drug	Strength	Pack size	mg per pack	Cost*	Cost per mg	Cost per unit	Source
Dacarbazine 100mg powder for solution for injection vials	10mg/ml	10	1000	£46.15	£0.046	£4.62	eMIT[7]
Dacarbazine 200mg powder for solution for injection vials	10mg/ml	10	2000	£86.65	£0.043	£8.67	eMIT[7]
Ipilimumab 5mg/ml concentrate for solution for infusion in vial, 10ml (50mg)	5mg/ml	1	50	£3,750.00	£75.00	£3,750.00	MIMS[8]
Pembrolizumab 50mg powder for concentrate for solution for infusion in vial	25mg/ml	1	50	£1,315.00	£26.30	£1,315.00	MIMS[8]

Key: eMIT, electronic Market Information Tool; MIMS, Monthly Index of Medical Specialities.
Notes: *List prices used for drug costs.

Administration costs

Administration regimens were taken from the SPCs,[5, 6, 9] and costed using NHS reference costs 2015 to 2016.[10] Dacarbazine and pembrolizumab were assumed to need simple parenteral regimens whereas ipilimumab was assumed to need a more complex regimen based on the extended infusion time required.[11] **Table 2** summarises the administration costs used in the analysis.

Table 2: Stage IV melanoma treatments, administration costs

Drug	Route	Frequency	HRG description	HRG code	Cost
Dacarbazine	Intravenous injection or infusion over 15–30 minutes	On day 1 and then once every 3 weeks as intravenous infusion	Deliver simple parenteral chemotherapy	SB12Z	£253.00
Ipilimumab	Intravenous over a 90-minute period	Every 3 weeks	Deliver more complex parenteral chemotherapy	SB13Z	£337.00
Pembrolizumab	Intravenous infusion over 30 minutes	Every 3 weeks	Deliver simple parenteral chemotherapy	SB12Z	£253.00

Key: HRG, Healthcare Resource Group.

Due to a lack of literature on the topic, assumptions were made about the reduction in administration time due to dose banding. It was assumed that the complex regimen for ipilimumab would become a simple one leading to a cost saving of 24.9% (calculated from **Table 2**), and that the simple regimens for dacarbazine and pembrolizumab would be associated with proportionate cost savings though reduced administration time.*

Treatment duration

Data on treatment duration were taken from NICE TA319, TA268 and TA366 for dacarbazine, ipilimumab and pembrolizumab.[4, 12, 13] Average numbers of administrations per year were 4.49, 3.63 and 7.19, respectively.

Weight data

As proxies for weight and body surface area of patients with Stage IV melanoma, general population data from the Health Survey for England were used. Porter and colleagues fitted log normal distributions to these data (**Table 3**).[14] Parameters were used to inform the average cost of treatment.

Costing methods

Three drug costing methods were explored and compared: (1) non-banded dosing assuming individual preparation, (2) banded dosing assuming individual preparation and (3) non-banded exact dosing, assuming no drug wastage due to preparation for the population. For the methods assuming individual preparation (i.e. Methods 1 and 2), the moments of the distributions of patient weight (ipilimumab and pembrolizumab) and body surface area (dacarbazine) shown in **Table 3** were used to determine the proportion of patients requiring each vial size or falling into each dose band. For Method 3, mean weight was multiplied by the required doses, assuming no wastage during preparation.

Table 3: Log normal distribution of weight and body surface area, fitted to Health Survey for England data

	Mu	Theta
Weight	4.344	0.211
BSA	0.622	0.116

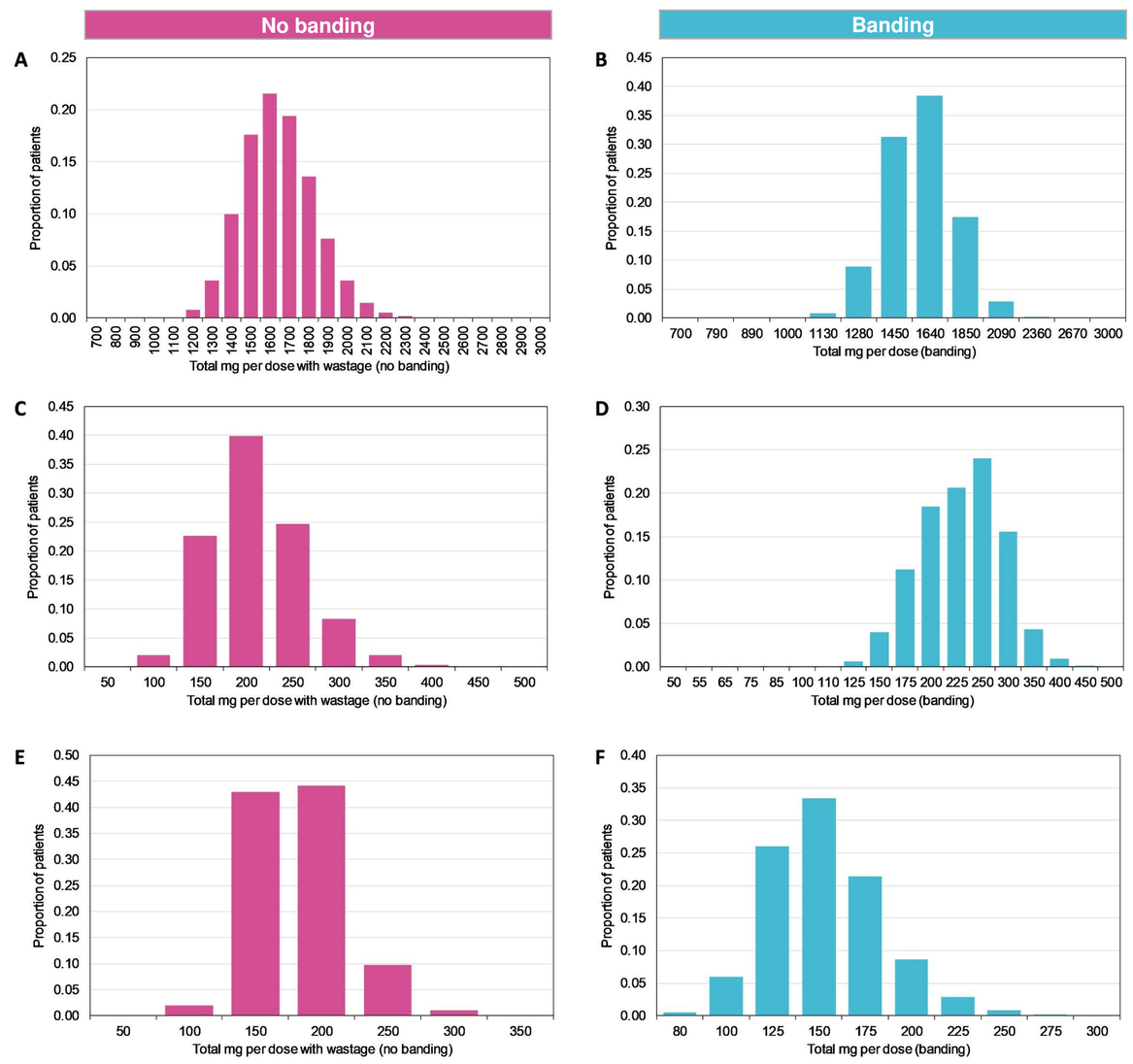
Key: BSA, body surface area.

Results

Distributions for total mg per dose for (1) non-banded dosing and (2) banded dosing assuming individual preparation are presented in **Figure 1**.

For ipilimumab and pembrolizumab, Method 2 (dose banding assuming individual preparation) resulted in per-patient, annual drug cost savings of 6.4% (£4,581) and 9.1% (£3,143), respectively, versus Method 1 (non-banded dosing assuming individual preparation). For dacarbazine, this method led to a 0.3% increase in annual drug costs (+£0.88). Method 3 (exact dose and no wastage due to preparation for the population) led to savings of between 3.9% and 15.6% compared with Method 1. Estimated annual cost savings due to reduced administration time ranged from £283 to £453. Results are summarised in **Tables 4 and 5**.

Figure 1: Total milligrams per dose for all treatments based on a log normal fit to Health Survey for England data



Notes: A and B: dacarbazine; C and D: ipilimumab; E and F: pembrolizumab.

Table 4: Estimated annual drug cost savings from adopting dose banding for Stage IV melanoma treatments

	Annual drug cost per patient (£)			Annual cost savings compared with no banding, individual prep (Method 1)	
	Method 1: No banding, individual preparation	Method 2: Banding, individual preparation	Method 3: Exact dose, no wastage, population preparation	Method 2: Banding, individual preparation cost saving (£,%)	Method 3: Exact dose, no wastage, population preparation cost saving (£,%)
Dacarbazine	£320	£321	£308	−£0.88, −0.3%	£12, 3.9%
Ipilimumab	£71,124	£66,544	£62,902	£4,581, 6.4%	£8,222, 11.6%
Pembrolizumab	£34,503	£31,360	£29,127	£3,143, 9.1%	£5,377, 15.6%

Table 5: Estimated annual administration cost savings from adopting dose banding for Stage IV melanoma treatments

	Annual administration cost per patient: no banding	Annual administration cost per patient: banding	Annual cost savings of banding compared with no banding cost saving (£,%)
Dacarbazine	£1,135	£852	£283, 24.9%
Ipilimumab	£1,223	£918	£305, 24.9%
Pembrolizumab	£1,819	£1,366	£453, 24.9%

Conclusions

Assuming no wastage, as in Method 3, may be unrealistic due to drug instability when stored, or an orphan drug's use in a rare cancer posing logistical barriers to preparation for the population. However, the results of this analysis demonstrate the potential cost savings of dose banding, due to similar or lower drug costs and reduced administration time.

Limitations of the analysis include the lack of patient-level weight data for Stage IV melanoma. Weight in practice may differ from that of the general population due to illness or increased age. Additionally, of all melanoma diagnoses, 10% of males are diagnosed with Stage IV disease compared with 7% females.[15] General population weight data could be adjusted to account for these differences.

Economic evaluations incorporating the costs of systemic anti-cancer therapies should include scenarios with dose banding where relevant. Further guidance on the methods for doing so may help standardise and proliferate such practices.

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Further information is available on request. Please visit BresMed at Stand 605.

*In the submitted abstract, this figure was estimated to be 29%. Since acceptance of the abstract, this value was found to be describing an incorrect cost saving related to the implementation of dose banding. Therefore, the analysis was updated to use 24.9% as described in the poster text. Consequently, some of the results included within the Results section are different to those in the submitted abstract. The authors apologise for any confusion caused.

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