

# Health professional attitudes and perceptions of prehabilitation and nutrition before haematopoietic cell transplantation

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## Abstract

**Background:** Nutritional prehabilitation may improve haematopoietic cell transplantation (HCT) outcomes, although little evidence exists. The present study aimed to understand healthcare professional (HCP) perceptions of prehabilitation and nutritional care pre-HCT in UK centres.

**Methods:** An anonymous online survey (developed and refined via content experts and piloting) was administered via email to multidisciplinary HCPs in 39 UK adult centres, between July 2021 and June 2022. Data are presented as proportions of responses. Routine provision denotes that care was provided >70% of time.

**Results:** Seventy-seven percent ( $n = 66$ ) of HCPs, representing 61.5% ( $n = 24$ ) of UK adult HCT centres, responded. All HCPs supported prehabilitation, proposing feasible implementation between induction chemotherapy (60.4%;  $n = 40$ ) and first HCT clinic (83.3%;  $n = 55$ ). Only 12.5% ( $n = 3$ ) of centres had a dedicated prehabilitation service. Nutrition (87.9%;  $n = 58$ ), emotional wellbeing (92.4%;  $n = 61$ ) and exercise (81.8%;  $n = 54$ ) were considered very important constituents. HCPs within half of the HCT centres ( $n = 12$  centres) reported routine use of nutrition screening pre-HCT with a validated tool; 66.7% of HCPs ( $n = 36$ ) reported using the malnutrition universal screening tool (MUST). Sixty-two percent ( $n = 41$ ) of HCPs reported those at risk, received nutritional assessments, predominantly by dietitians (91.6%;  $n = 22$ ) using the dietetic care process (58.3%;  $n = 14$ ). Body mass index (BMI) was the most frequently reported body composition measure used by HCPs (70.2%,  $n = 33$ ). Of 59 respondents, non-dietitians most routinely provided dietary advice pre-HCT (82.4%;  $n = 28$  vs. 68%;  $n = 17$ ,  $p = 0.2$ ); including high-energy/protein/fat and neutropenic diet advice. Prophylactic enteral feeding pre-HCT was rare, indicated by low BMI and significant unintentional weight loss. Just under half ( $n = 25$  of 59, 42.4%) HCPs reported exercise advice was given routinely pre-HCT.

**Conclusions:** Nutrition and prehabilitation pre-HCT are considered important and deliverable by HCPs, but current provision in UK centres is limited and inconsistent.

## KEYWORDS

diet, haematopoietic cell transplantation, malnutrition, nutrition, prehabilitation, rehabilitation

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### Key Points

- Prehabilitation was considered important in the context of haematopoietic stem cell transplantation care by all health care professionals (HCPs), although only 12.5% of centres had a dedicated prehabilitation service.
- There are inequities in nutritional care provision prior to haematopoietic cell transplantation (HCT) between transplantation centres.
- Lack of nutrition screening and systematic approaches to body composition assessments may limit the potential to identify and optimise nutritional and functional health prior to HCT.
- Non-dietitians most frequently provided dietary advice pre-HCT. Dietary advice focused on total energy intake (71.1%,  $n = 32$ ) over protein (46.7%,  $n = 21$ ), fat (44.4%,  $n = 20$ ) and fibre (24.4%,  $n = 11$ ).

## INTRODUCTION

Haematopoietic cell transplantation (HCT) is a procedure used to treat malignant and non-malignant haematological disorders. In 2019, primary indications for HCT in centres reporting to the European Society of Blood and Marrow Transplantation (EBMT) were haematological malignancies (88.7%,  $n = 38,659$ ), followed by non-malignant haematological conditions (3.9%,  $n = 1691$ ), solid tumours (3.6%,  $n = 1576$ ), immunological disorders (3.0%,  $n = 1292$ ) and ‘other’ indications (0.8%,  $n = 363$ ).<sup>1</sup> For those recipients with a cancer diagnosis, most will have received numerous cycles of varying intensity chemotherapy regimens prior to HCT to control disease, which may result in an associated risk of deconditioning events.

The HCT process itself is physically and emotionally demanding, negatively impacting the nutritional,<sup>2,3</sup> functional<sup>4</sup> and psychological status<sup>5</sup> of recipients. Patients are treated with high dose cytotoxic therapy (chemotherapy  $\pm$  total body irradiation) with the aim of destroying diseased cells. An infusion of stem cells is then given, which engraft and differentiate into mature functioning cells of the blood and immune system, such that the disease indication enters remission and is potentially cured. The type of HCT depends on whether the infused stem cells are collected from the individual (autologous transplant) or from a donor (allogeneic transplant). Allogeneic transplants are associated with greater complications and longer recovery than autologous transplantation.<sup>6</sup>

Nutritional sequelae such as obesity, malnutrition and sarcopenia impact and predict HCT outcomes. Obesity pre-HCT is increasingly prevalent<sup>7</sup> negatively predicting 100-day readmission, nonrelapse mortality<sup>8,9</sup> and Graft-versus-Host Disease (GvHD) rates.<sup>8</sup> Malnutrition, defined as undernutrition in this context, impacts treatment outcome, length of admissions, infectious complications,<sup>9</sup> fatigue and quality of life.<sup>10</sup> Additionally, secondary sarcopenia, a loss of skeletal muscle mass associated with cancer related inflammation and nutritional deficiencies,<sup>11</sup> is an independent negative prognostic indicator for HCT outcomes.<sup>12</sup>

These nutritional sequelae both precede and transcend the HCT process, exacerbated by previous treatments, side-effects and complications of HCT such as nutrition impact symptoms and GvHD. Following HCT, there is also an increased risk of further nutrition related comorbidities such as metabolic syndrome and diabetes,<sup>6,13</sup> which can develop as a late effect.<sup>14,15</sup>

Despite the potential impact of nutrition sequelae on HCT outcomes, a survey of European HCT centres<sup>16</sup> showed nutrition practices were inconsistent and failed to meet international guidelines.<sup>17</sup> Alongside this, although international accreditation standards for HCT in the USA and Europe recommend having access to some allied services, they do not stipulate definitive need for dietetic support of patients.<sup>18</sup>

Intervening early with proactive nutritional care may help mitigate some of these risks and contribute to improved HCT outcomes. The UK National Health Service (NHS) long-term plan calls for personalised<sup>19</sup> proactive<sup>20</sup> interventions that enable self-management.<sup>21</sup> Prehabilitation is a package of proactive interventions aiming to optimise physical (including nutritional) and emotional wellbeing before treatment, through the identification of deficits and delivery of personalised intervention(s).<sup>22</sup> There are numerous population specific definitions for prehabilitation, such as the definition by Silver and Baima<sup>22</sup> for cancer: “a process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment including assessment of baseline function, identification of impairments, and provision of interventions that promote health in order to reduce the incidence and/or severity of future impairments”. These definitions can help to characterise programme aims, context and constituents, informing research, policy and clinical service delivery.

Surgical prehabilitation programmes have been shown to reduce hospital length of stay, infection rates and improve quality of life.<sup>23</sup> This has led to

increasing interest in its potential role in haematological settings; however, few studies of prehabilitation in HCT exist.<sup>24</sup> Additionally, nutrition interventions within prehabilitation studies have been shown to vary, lack detailed description and are often poorly evaluated.<sup>25</sup> Despite the expansion of prehabilitation services to HCT settings, the prehabilitation services currently being delivered in the UK, nutrition practices pre-HCT and the feasibility of nutritional prehabilitation in this context are all poorly understood.

The present study aimed to explore the current provision and healthcare professional (HCP) perceptions of prehabilitation and nutritional care pre-HCT within UK and Republic of Ireland HCT centres. Definitions of prehabilitation in the context of HCT, perceptions on its implementation, and nutrition practices such as screening, assessment and intervention delivery were also investigated.

## METHODS

### Questionnaire development and piloting

The questionnaire was developed by six content experts covering nutrition and metabolism, prehabilitation and HCT. Questionnaire contents were informed by prehabilitation guidelines,<sup>26</sup> nutrition practices in HCT<sup>3,17</sup> and similar studies in other cohorts.<sup>16</sup> Question and answer constructs were reviewed by experts and rationale for both questions and wording was discussed.<sup>27</sup> Amendments were made and the full questionnaire piloted by five HCPs for feedback, which was then incorporated into a definitive version. A range of question types including five-point Likert scale, multiple response and open-ended questions were included. Participants were also presented with the definition of prehabilitation by Silver and Baima<sup>22</sup> to consider its relevance for the context of prehabilitation in HCT.

### Dissemination and data collection

The survey was imported onto REDCap Cloud, version 1.4 (<https://www.redcapcloud.com>) and distributed via email by the British Society of Blood and Marrow Transplantation and Cellular Therapy to clinical leads at 39 adult HCT centres between August 2020 and February 2022. The questionnaire was also disseminated via email to dietetic departments within centres. Invitation emails included a summary of the study and the participant information sheet. No data or precedents on sample size were available; therefore, a pragmatic multidisciplinary recruitment target of one nurse, dietitian and doctor from each centre was determined. Three email reminders were sent in September 2020, July 2021 and

January 2022. Online consent was taken as part of the questionnaire, and all responses were anonymous.

### Data analysis

Responses were downloaded from REDCap cloud to Excel 365, version 2312 (Microsoft Corp.). Incomplete and duplicate entries were removed. Quantitative data were imported to SPSS, version 29 (IBM Corp.) for analysis. Proportions of respondents for each item were reported (%), (*n*). When reporting prehabilitation or nutritional practices within a centre the average response for all HCPs within a centre were used. Provider of dietary advice delivered was dichotomised into dietitians and non-dietitians to review differences in advice by HCPs. Because of the small sample, size correlations were not considered. Thematic analysis<sup>28</sup> was used for qualitative free text question data, initial analyses were conducted by one of the investigators (LJM) and reviewed by another (DG) with discrepancies reviewed, discussed and agreed.

### Ethical statement

The study was registered with the Health Research Authority who confirmed that ethics approval was not required. All local governance and GDPR processes were followed. [Clinicaltrials.gov](https://clinicaltrials.gov): NCT05352789.

## RESULTS

### Respondent characteristics

Ninety-nine responses were received, 23 were excluded as a result of no parts of the consent or survey being completed. This left 66 unique respondents, from 24 transplant centres, with responding centres covering Great Britain and Republic of Ireland, and no Northern Irish centres responding. Most respondents were dietitians (39.4%, *n* = 26) (84.6%, *n* = 22; haematology specialist dietitians), followed by haematologists (21.2%, *n* = 14) and nurses (25.8%, *n* = 17). Other staff included physiotherapist (6.1%, *n* = 4), occupational therapist (3%, *n* = 2), HCT coordinators (3%, *n* = 2) and one clinical psychologist (1.5%). Most respondents (80.3%, *n* = 53) reported they delivered clinical care pre-HCT.

Responses were received from HCPs in 24 HCT centres (61.5% of target), 75% (*n* = 18) of centres represented by the HCP respondents delivered both autologous and allogeneic HCT with an average of 152 (72–240) transplants per year, and 25% (*n* = 6) delivered autologous only, with an average of 39 (12–70) transplants per year. Respondent and centre characteristics are provided in Table 1.

**TABLE 1** Respondent characteristics and that of their associated transplant centres.

Healthcare professional (HCP) ( <i>N</i> = 66)	<i>N</i> (%)
<b>Profession</b>	
Dietitian ( <i>N</i> = 26; 39.4)	
Haematology specialist	22 (33.3)
Nonspecialist	4 (6.1)
Nurse ( <i>N</i> = 17; 25.7)	
Clinical nurse specialist	14 (21.2)
Nurse (other)	3 (4.5)
Doctor ( <i>N</i> = 14; 21.2)	
Haematologist (consultant)	14 (21.2)
Haematology (doctor other)	0
Allied health professional ( <i>N</i> = 7; 10.6)	
Physiotherapist	4 (6.1)
Occupational therapist	2 (3)
Psychologist	1 (1.5)
Bone marrow transplant coordinator	2 (3)
Proportion delivering clinical care pre-HCT	53 (80.3)
<b>Haematopoietic cell transplant centre (<i>N</i> = 23)</b>	
<b>Treated populations in adult centres</b>	
≥18 years	15 (65.2)
≥16 years	8 (34.8)
Combined adult/paediatric unit	7 (30.4)
Combined adult/teenage and young adults' unit	9 (39.1)
<b>Locality of centres</b>	
Northern England	4 (17.4)
Midlands	4 (17.4)
Eastern England	1 (4.3)
Southern England	5 (21.7)
London	4 (17.4)
Scotland	2 (8.7)
Wales	1 (4.3)
Northern Ireland	0
Republic of Ireland	2 (8.7)
<b>JACIE accredited centres</b>	
Initial accreditation	2 (8.7)
Re-accredited	12 (52.2)
Not accredited	9 (39.1)

Abbreviation: JACIE, Joint Accreditation Committee ISCT-Europe & EBMT.

## HCT prehabilitation provision

HCPs within only three centres (12.5%) showed agreement on the provision of a dedicated multidisciplinary prehabilitation service for HCT in their centre. In some centres, there was disagreement between HCPs on whether dedicated prehabilitation was provided or not (16.7%,  $n = 4$ ), with 4.2% ( $n = 1$ ) reporting that they were unsure. Potential reported explanations for this included nurse led prehabilitation with option to refer into support services such as dietetics, but no dedicated prehabilitation capacity.

## Defining prehabilitation in the context of HCT

When asked to consider the definition of prehabilitation by Silver and Baima<sup>22</sup> in the context of HCT, 57.6% ( $n = 38$ ) of HCPs felt the current definition could be applied to HCT without modification. However, 21.2% ( $n = 14$ ) felt modifications were required and 18.2% ( $n = 12$ ) were unsure; 50% ( $n = 6$ ) of which went on to suggest modifications. Further details of HCP suggested changes are provided in Table 2. Themes derived from these suggestions were then used to inform a HCT-specific refinement of the definition by Silver and Baima.<sup>22</sup>

## Proposed definition of prehabilitation in HCT by Miller et al.

“Prehabilitation is part of a proactive multiphasic rehabilitation continuum, involving early assessment of baseline function (screening), identification of impairments (assessment), and provision of interventions that promote physical and psychological wellbeing prior to HCT. It is a personalised holistic process that empowers recipients and families via multidisciplinary expert guidance with the aim of reducing the incidence and/or severity of future impairments”.

## Implementation of prehabilitation in HCT

### Timing

All respondents felt prehabilitation should be considered as part of future HCT services. Most (83.3%,  $n = 55$ ) felt this could be implemented in the pre-HCT assessment clinic; for example, end of consolidation chemotherapy or other treatment. However, 60.6% ( $n = 40$ ) felt prehabilitation could be delivered either during or at the end of induction chemotherapy before consolidation chemotherapy, with 10.6% ( $n = 7$ ) suggesting delivery at the point of diagnosis. Figure 1 shows prehabilitation timing perspectives of dietitians' and non-dietitians.

**TABLE 2** Template analysis of proposed definition modifications for haematopoietic cell transplantation (HCT) relevance.

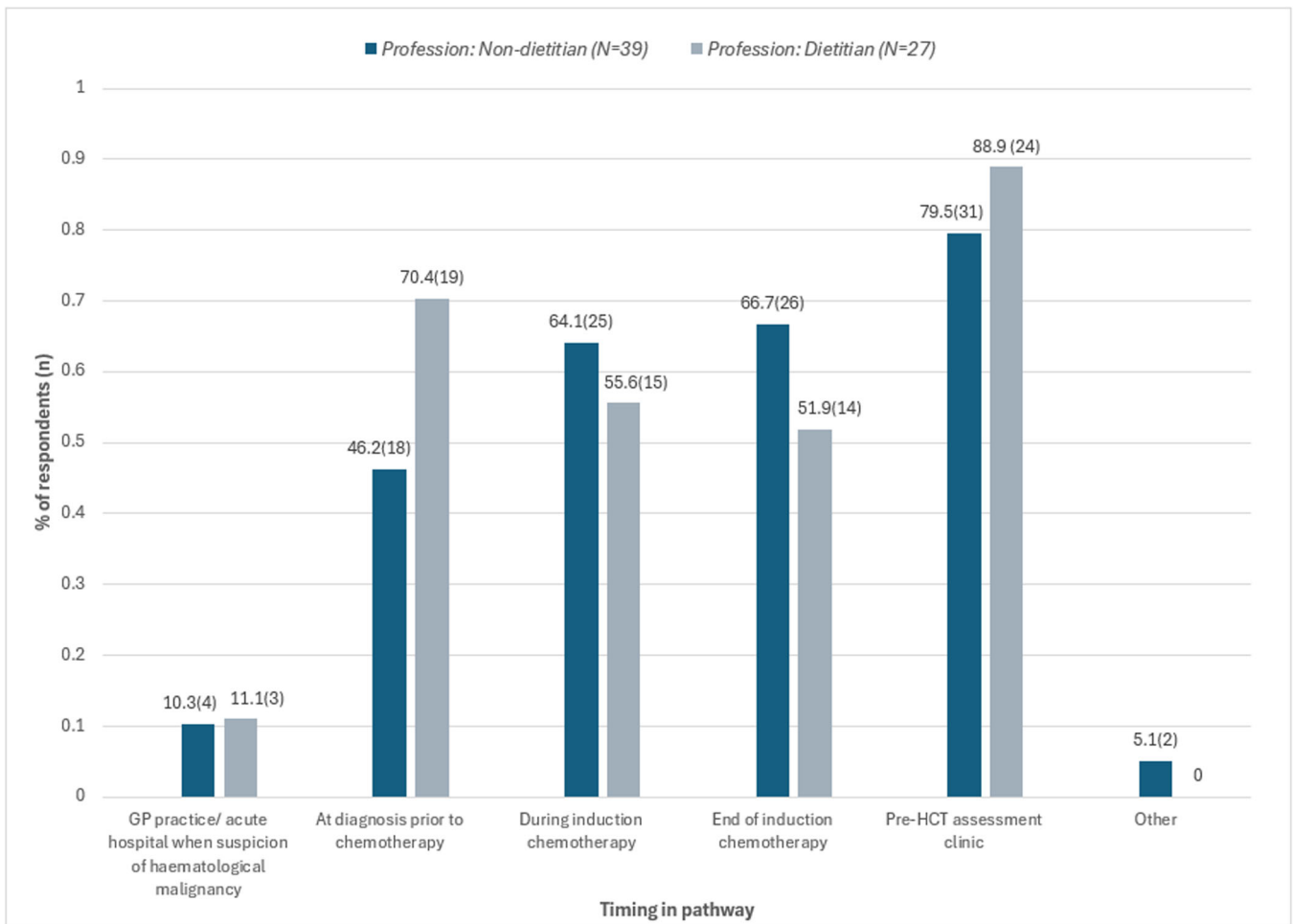
Theme	Subtheme	Total number of respondents <sup>a</sup> (N = 20)	Selection of exemplar quotes <sup>b</sup>	Respondent (identifier)
Timing	Acute episode	10	“There is very little time between diagnosis and treatment for acute haematology patients – would be better to undertake prehab during induction chemo and prior to HCT”	Nurse (7)
			“Patient prehab for BMT are often already on active/acute treatment (chemo) so the definition should be amended to incorporate this, for example time of decision for a BMT and admission for BMT”	Dietitian (9)
			“In case of urgent treatment it may not always be possible to intervene before first line treatment so it may be able mitigating losses than optimisation”	Dietitian (16)
	Multiphasic treatment	6	“There are multiple acute phases of treatment in cancer treatment over a life course”	Dietitian (1)
			“assessment on a continuum”	Nurse (15)
			“Needs change in relation to the fact that there is no real time between diagnosis and treatment so needs to be assessed on treatment then again Pre Tx”	Dietitian (13)
“timing of intervention can be different depending on previous acute treatment”	Physiotherapist (18)			
Population	Inclusivity	3	“Does not account for transplant in non-malignant conditions, that is MS, sickle cell disease, aplastic anaemia”	Nurse (17)
			“Some HCT patients do not have a cancer diagnosis”	Physiotherapist (12)
			“It is a very good definition, but it does not support the idea of utilising in patient selection for transplant”	Nurse (3)
Delivery	MDT	3	“May not be a plan for HCT at the time of diagnosis”	Dietitian (8)
			“Add in how it is the job of the whole MDT to provide prehabilitation, an opportunity for specialists to contribute”	Dietitian (5)
			“physical and psychological”	Nurse (4)
Programme constituents	4	4	“It is aspirational but doesn't define what should be implemented”	Consultant (6)
			“it is important to outline within prehab expectations, goals and what alternative methods are needed to reach these”	Dietitian (11)

Abbreviations: BMT, bone marrow transplant; HCT, haematopoietic cell transplantation; MDT, multidisciplinary team; MS, multiple sclerosis; Prehab, prehabilitation; Tx, treatment.

<sup>a</sup>The total number of respondents relates to the number of contributing comments related to the theme;

<sup>b</sup>The exemplar statements provided are indicative of the comments provided by the participants relevant to the theme but do not include all responses.





**FIGURE 1** When in the haematopoietic cell transplantation (HCT) pathway do you think a prehabilitation service could be introduced? In the context of those with a malignancy.

## Prehabilitation components

Emotional wellbeing (92.4%,  $n = 61$ ), nutrition (87.9%,  $n = 58$ ) and physical activity (81.8%,  $n = 54$ ) in prehabilitation were considered very important. Additional constituents proposed in free text responses, included social and financial advice, fatigue management, medication optimisation, and the incorporation of family and friends in prehabilitation delivery.

## Barriers and facilitators

Just under half of respondents (45.5%,  $n = 30$ ) felt there were no barriers to prehabilitation delivery in HCT. Where barriers were identified (54.5%,  $n = 36$ ), the most common were staffing (61.1%,  $n = 22$ ) and funding (41.7%,  $n = 15$ ). Table 3 provides themes of barriers and facilitators taken from free text quotes by HCP respondents.

## Nutritional care pre-HCT

### Nutrition screening

Respondents identified that 50% ( $n = 12$ ) of the 24 centres nutritionally screened recipients using a validated tool >70% of the time pre-HCT. Barriers to nutritional screening were reported by 61 respondents (92.4%). This included available time (50%,  $n = 33$ ), training (34.8%,  $n = 23$ ), staffing (54.5%,  $n = 36$ ), anthropometric measuring equipment (12.1%,  $n = 8$ ), information communications technology (i.e., ICT) equipment (12.1%,  $n = 8$ ) and clinic space (31.8%,  $n = 21$ ). Of those HCPs reporting nutrition screening was completed ( $n = 56$ ) the Malnutrition Universal Screening Tool (MUST) (66.7%,  $n = 36$ ) was the most widely used. If a patient were identified as at risk of malnutrition during screening, 79.4% ( $n = 54$ ) of respondents advised they had a dietetic service they could refer to.

**TABLE 3** Respondent perceptions on potential barriers to prehab in UK haematopoietic cell transplantation (HCT) centres.

Theme	Subtheme	Total number of respondents <sup>a</sup> (N = 36)	Selection of exemplar quotes <sup>b</sup>	Respondent (identifier)
Staffing	Provision	18	“Lack of staffing, provision, and resources within therapies to provide a prehabilitation service. My concerns would be time taken away from inpatient work unless it was properly funded”	Dietitian (2)
			“Availability of professionals to complete it”	Haematologist (27)
			“Resources. We try our best but as our dietetic resources are spread across haematology, oncology and HCT we find it very difficult to see patients and implement plans prior to HCTs”	Dietitian (23)
	Skill mix	3	“Hard for smaller centres to implement with limited staffing. Likely more relevant to allogeneic transplant”	Haematologist (21)
			“My concern prehabilitation will be delivered by specialist nurses rather than using clinical AHP specialists such as dietitians and physiotherapists”	Haematologist (8)
			“A dedicated AHP team is required in order to delivery this service effectively, to ensure pre and rehabilitation needs are met”	Occupational Therapist (13)
Training	3	“For optimum quality and pt benefit, I would prefer it to be provided by haematology dietitians for haematology patients rather than generic “cancer” pre-hab which is often based on solid tumours and often for surgical pathways – very different needs often”	Physiotherapist (35)	
		“Appropriately trained individuals to deliver the same”	Haematologist (16)	
		“The service should be delivered by competent staff could be an issue. The staff should be appropriately trained”	Dietitian (28)	
Funding	14	“My concern would be a lack of staff and therapy resources to be able to implement a prehabilitation clinic. (Unless the appropriate and additional funding is provided)”	Nurse (1)	
		“Funding to support a prehab programme would be the main concern & barrier”	Nurse (11)	
		“Current funding is not substantive for dietetics & physio, so could be lost in 2021. It is also in pilot phase, so not embedded into all management pathways. This would require more than current available capacity”	Dietitian (14)	
Delivery	4	“Dedicated funding pathways or appropriately trained individuals to deliver the same”	Haematologist (16)	
		“Timing of initiative, patients are referred from multiple centres so difficult to find a good time to offer them prehab as they are going through other aggressive treatments”	Physiotherapist (5)	
		“Information overload!”	Haematologist (17)	
			“Concerns as some patients travel a distance and would not be able to easily attend a local program”	Dietitian (18)

Abbreviations: AHP, allied health professional; MDT, multidisciplinary team.

<sup>a</sup>The total no. respondents relates to the number of contributing comments related to the theme;

<sup>b</sup>The exemplar statements provided are indicative of the comments provided by the participants relevant to the theme but do not include all responses.

## Nutrition assessment

If the screening tool assessed someone as at risk, 61% ( $n = 41$ ) of respondents reported that patients would have a nutritional assessment by a trained professional >70% of the time. Most nutritional assessments within centres were conducted using the dietetic care process<sup>29</sup> (34.1%,  $n = 14$ ). Less frequently reported processes were patient generated subjective global assessment (2.4%,  $n = 1$ ) and handgrip strength (4.8%,  $n = 2$ ), a measure of function. MUST (12.2%,  $n = 5$ ) was reported as an assessment technique in the “other” response options by some respondents. Dietitians most commonly (91.6%,  $n = 22$ ) conducted assessments within centres. Handgrip strength, a measure of physical function was reported to be used as part of nutritional assessments by 32.2% ( $n = 19$ ) of 59 respondents.

## Biochemical monitoring

Respondents (87.9%,  $n = 58$ ) reported liver (86.2%,  $n = 50$ ) and kidney function (86.2%,  $n = 50$ ) alongside blood pressure (79.3%,  $n = 46$ ) were routinely checked >70% of the time pre-HCT. Blood glucose (46.5%,  $n = 27$ ) and lipid (32.8%,  $n = 19$ ) levels were not routinely collected. Where samples were collected, only 12.1% ( $n = 8$ ) were reported to be fasted; however, 45.5% ( $n = 30$ ) felt that fasted samples could be facilitated. Details of HCP perceived frequency of biochemical and nutritional systemic measures taken pre-HCT are provided in the Supporting information (Figure S1).

## Body composition assessment

Body composition pre-HCT was reported to be measured >70% of the time by 45.8% ( $n = 27$ ) of respondents ( $n = 59$ ). Methods of body composition were reported by 43 (65.1%) respondents. Body mass index (BMI) (70.2%,  $n = 33$ ) was the most common. More comprehensive methods such as triceps skin fold (4.3%,  $n = 2$ ), mid upper arm circumference (6.4%,  $n = 3$ ), waist circumference (2.1%,  $n = 1$ ) and bioelectrical impedance analysis (2.1%,  $n = 1$ ) were rarely used and 12.8% ( $n = 6$ ) did not know. Haematology specialist dietitians were most likely to be reported to conduct body composition measurements (39.7%,  $n = 23$  of 58). Of 61 respondents, BMI was felt to be most feasible in practice (82%,  $n = 50$ ). However, 86.9% ( $n = 53$ ) of HCPs felt centres had the equipment to conduct an alternative body composition measure to BMI.

## Dietary advice provision

More non-dietitians (64.1%,  $n = 25$ ) reported that all patients would receive routine (>70% of time) dietary advice

pre-HCT than dietitians (40.7%,  $n = 11$ ). This differed, however, when those who had been identified as at nutritional risk (clinically or via a screening tool) were considered with both non-dietitians (69.2%,  $n = 27$ ) and dietitians (74.1%,  $n = 20$ ) reporting similar likelihood of routine (>70% of time) dietary advice pre-HCT.

Forty-five respondents (68.2%) reported they provided dietary advice pre-HCT, accounting for 70% ( $n = 28$ ) of non-dietitians and 65.3% ( $n = 17$ ) of dietitians. When asked how often they “individualised” this dietary advice based on clinical circumstances or preferences over delivery of generic advice, 44 HCPs responded. Of the 44 respondents, all dietitians (100%,  $n = 17$ ) reported the personalisation of dietary advice >70% of the time compared to non-dietitians (59.3%,  $n = 16$ ). Information used for personalisation of dietary advice is available in the Supporting information (Table S1).

Of the 45 HCPs who reported they provided dietary advice, 71.1% ( $n = 32$ ) reported giving dietary advice on total energy intake, 46.7% ( $n = 21$ ) on protein, 44.4% ( $n = 20$ ) on fat and 24.4% ( $n = 11$ ) on fibre. Where respondents provided advice, there were variations by profession (Figure 2) but the most common patterns of dietary advice pre-HCT were high-protein, high-energy, high-fat and moderate fibre. The type of advice given by dietitians and non-dietitians is provided in the Supporting information (Figure S2a–d).

Sixty-one HCPs reported types of specialist dietary advice they gave, with just over half providing neutropenic dietary advice pre-HCT (54.3%,  $n = 19$ , non-dietitians vs. 61.5%,  $n = 16$ , dietitians). Provision of probiotic (14.3%,  $n = 5$  non-dietitians vs. 34.6%,  $n = 9$  dietitians) and prebiotic advice (2.9%,  $n = 1$  non-dietitian; 15.4%,  $n = 4$  dietitians) was less frequent and varied between dietitians and non-dietitians (see Supporting information, Table S2). Half of the respondents did not discuss micronutrients pre-HCT; where they were discussed, vitamin D was the most frequently advised on (17.1%,  $n = 6$  non-dietitians vs. 38.5%,  $n = 10$  dietitians). However, advice on vitamin and mineral supplementation was given more frequently by dietitians than non-dietitians (see Supporting information, Table S3).

## Enteral feeding provision

Of sixty-one HCPs, just over one-third (35.9%,  $n = 14$ , non-dietitians vs. 44.4%,  $n = 12$ , dietitians) reported the prophylactic placement of enteral feeding tubes pre-HCT. Where used, nasogastric (39.3%,  $n = 24$ ) or nasojejunal (21.3%,  $n = 13$ ) feeding tubes were the most frequently reported (see Supporting information, Table S4). The most common reported indications for prophylactic tube placement were BMI  $\leq 17.5$  kg/m<sup>2</sup> (26.2%,  $n = 16$ ), 10% weight loss in 6 months (21.3%,



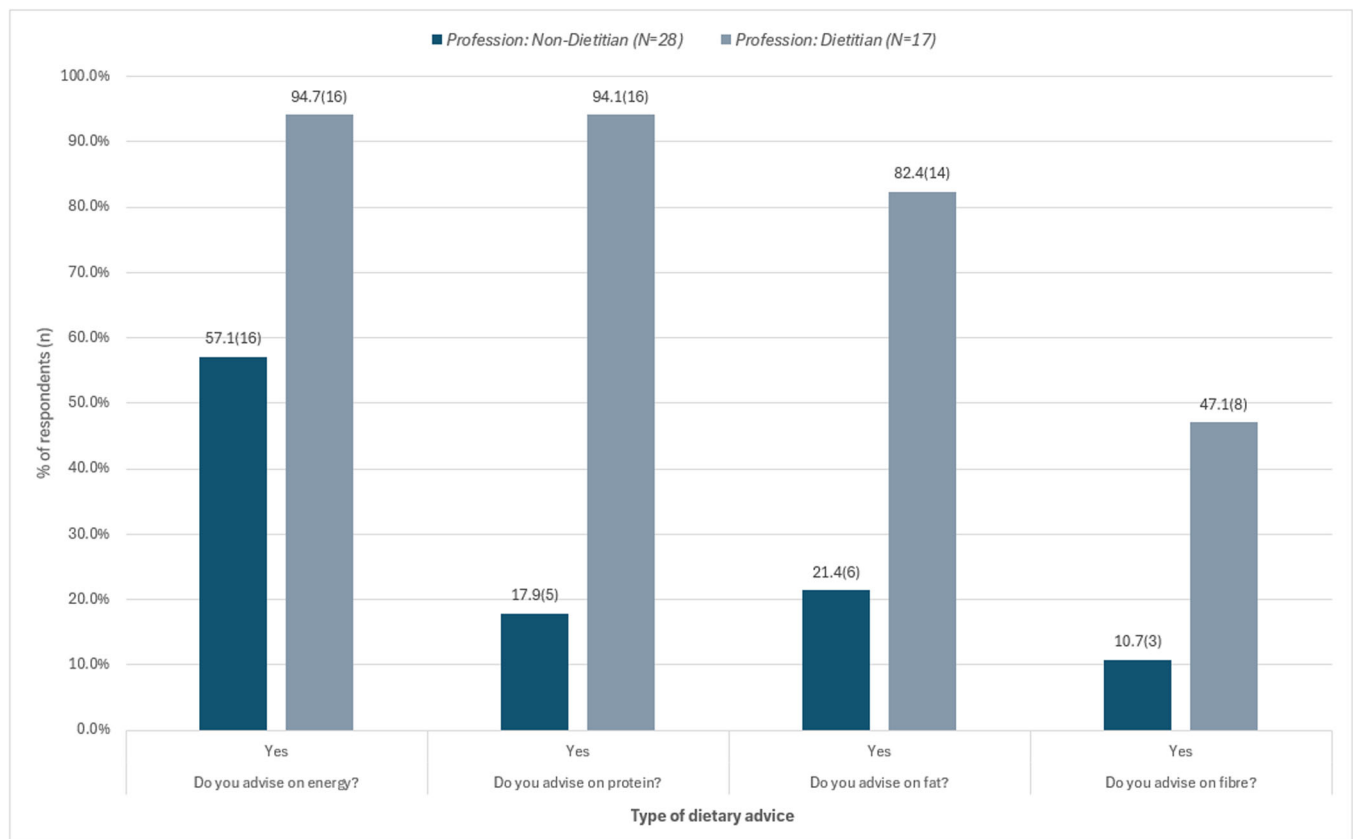


FIGURE 2 Types of dietary advice given by healthcare professionals (HCPs) pre-haematopoietic cell transplantation (HCT) ( $N = 45$ ).

$n = 13$ ) and BMI 17.5–19.5 kg/m<sup>2</sup> (19.7%,  $n = 12$ ) (see Supporting information, Table S5).

### Exercise advice provision

Of fifty-nine HCPs, less than half ( $n = 25$ , 42.4%) reported patients would receive physical activity advice as part of routine practice (>70% of time) pre-HCT. More specifically, 13.6% ( $n = 8$ ) reported exercise advice pre-HCT was given all the time, 28.8% ( $n = 17$ ) often, 25.4% ( $n = 15$ ) sometimes, 16.9% ( $n = 10$ ) rarely and 15.2% ( $n = 9$ ) never. Most HCPs (76.9%,  $n = 30$ ) reported that activity levels were rarely or never measured pre-HCT by questionnaire or physical assessment.

## DISCUSSION

This is the first UK survey to investigate HCP reported provision of prehabilitation and nutritional care pre-HCT. The findings highlight limited access to prehabilitation within centres, no standardisation of the constituents delivered and variable nutrition provision. Yet the value of both prehabilitation and nutrition was well recognised by HCPs.

### Defining prehabilitation in HCT

HCP perceptions on definitions for prehabilitation in the context of HCT have not previously been considered. Because 92.3%<sup>1</sup> of European HCT recipients will have a cancer diagnoses, the cancer prehabilitation definition by Silver and Baima<sup>22</sup> was reviewed by HCPs for relevance to HCT. Half the respondents reporting this definition could be directly translatable to HCT despite referring to cancer. A further one-third felt it needed refinement to reflect the multiphasic treatment cycles pre-HCT, potential acute presentation, non-malignant presentations, short lead in times and constituents considered important to future programmes.

In the proposed Miller et al., definition, physical wellbeing refers to nutritional adequacy, functional fitness, and appropriate management of side-effects to support activities of daily living. This may require a range of supportive interventions, for example nutritional care,<sup>17,30</sup> physical activity,<sup>31</sup> social support<sup>32</sup> (finance, carer support) and medical optimisation. In this definition, psychological wellbeing refers to a person's ability to be aware, manage and express their emotions in a way that improves life satisfaction, meaning and purpose and minimise the impact on their health outcomes. Strategies to support emotional

well-being may include self-help programmes, resources or talking therapies (cognitive behavioural therapy<sup>33</sup> or acceptance and commitment therapy<sup>34</sup>) facilitated by an appropriately qualified person.

Prehabilitation constituents, such as nutrition, emotional wellbeing, and physical activity were considered important by HCPs, as per other guidelines.<sup>17,26</sup> Additional, aspects such as multidisciplinary delivery, social and financial support, fatigue management and carer support were identified as important considerations for HCT. However, each prehabilitation programme will need to be personalised based on the person's diagnosis, circumstances, type of transplantation and any prior deconditioning leading up to HCT. Although the proposed definition by Miller et al. is informed by HCP perceptions of prehabilitation programme requirements, further refinement with those with lived experience is recommended.

### Delivering prehabilitation

Our capacity to understand optimal intervention, constituents, duration, intensity and timing of prehabilitation programmes is limited by low-quality heterogenous prehabilitation studies<sup>25,35</sup> and limited evidence in HCT. Elective surgical prehabilitation programmes are mainly delivered in the context of *de novo* treatment, which is not reflective of HCT pathways. More than 80% of HCT recipients receive up to three cycles of chemotherapy<sup>36</sup> with 2–4 weeks of cellular recovery pre-HCT. As such, HCT may have greater similarities to, and learning from,

prehabilitation in neo-adjuvant chemotherapy (three to six cycles) with its slightly longer 3–6 weeks of pre-operative cellular recovery<sup>37,38</sup> but evidence with respect to this is also lacking.<sup>26,39</sup>

More than 80% of respondents felt prehabilitation was deliverable between the end of consolidation treatment and admission for HCT (approximately 2–4 weeks), with 60.6% feeling earlier initiation at the end of first cycle of chemotherapy or at decision for HCT was possible. This reflects cyclical (multiphasic) provision through chemotherapy/treatment prior to HCT, comprised of both prehabilitation and rehabilitation<sup>40,41</sup> (Figure 3). Currently published protocols for prehabilitation trials in HCT report intervention windows as either pre-HCT only<sup>42–46</sup> or on a continuum (pre, peri and post),<sup>46</sup> with only one including personalised nutrition.<sup>43</sup>

### Nutritional care pre-HCT

The impact of obesity, malnutrition, and secondary sarcopenia on HCT outcomes<sup>3,8,12,47</sup> is well recognised. However, the implementation of nutritional practices that support the identification and management of these risks was variable. Malnutrition screening is a systematic approach used to identify those at nutritional risk, quickly and cost efficiently at scale. Although consensus is lacking on the optimal approach,<sup>17</sup> early screening for malnutrition is recommended<sup>17,48,49</sup> preferentially with a validated measure<sup>50</sup>; however, only 50% of UK centres screened pre-HCT using a validated tool (e.g., MUST).

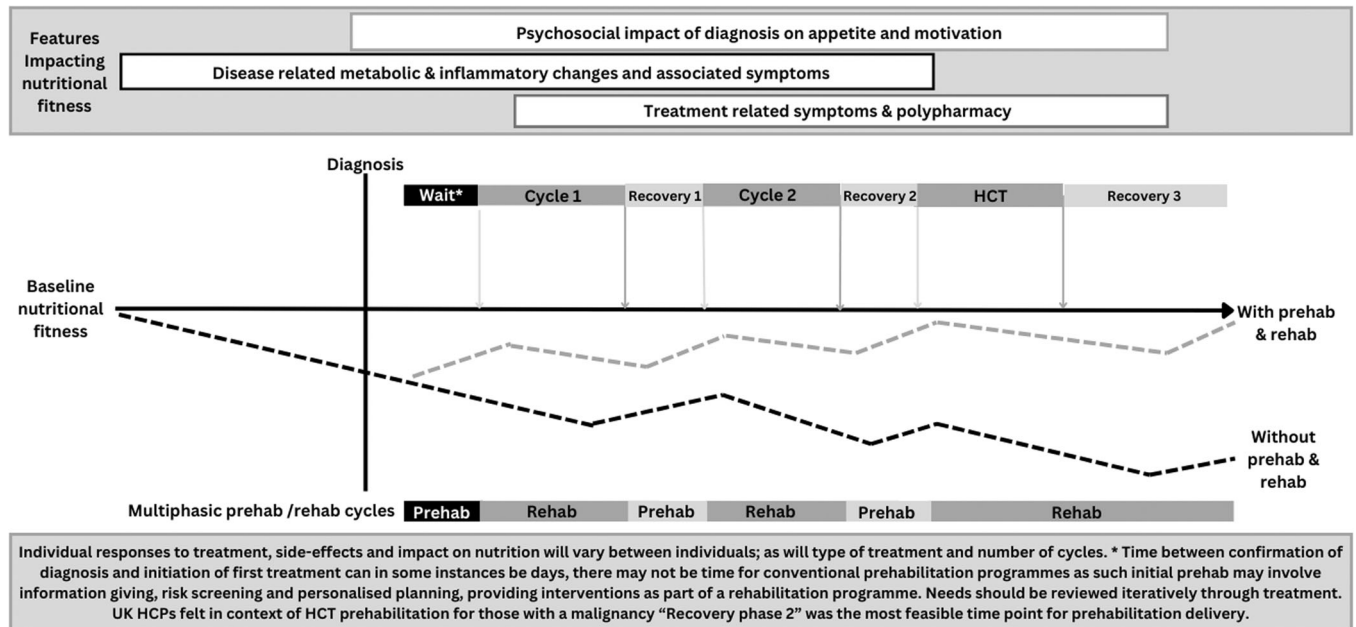


FIGURE 3 Example pathway for people with haematological cancer reflecting the potential impacts of multicycle chemotherapy prior to haematopoietic cell transplantation (HCT) and prehabilitation/rehabilitation considerations at each stage.

This compares to 57% of European Bone Marrow Transplant (EBMT) centres, with only 16% using a validated tool.<sup>16</sup>

For those identified as at risk of malnutrition during screening a more comprehensive assessment (e.g., Dietetic Care Process or Subjective Global Assessment) is then recommended.<sup>17</sup> The Global Leader's Initiative in Malnutrition (i.e., GLIM) published an evidence-based framework for the diagnosis and grading of malnutrition in adults<sup>50</sup> and this includes approaches for assessment. Five core diagnostic criteria were identified: three etiological (nonvolitional weight loss, low body mass index (BMI), reduced muscle mass) and two phenotypic (reduced food intake or assimilation and disease burden/inflammation).<sup>50</sup>

Weight and height were the most routinely reported measures to be collected prior to HCT. Non-volitional (unintentional) weight loss of more than 10% prior to HCT may be associated with poor treatment outcomes,<sup>51</sup> with impact varying dependant on diagnosis and type of transplantation.<sup>52</sup>

Body composition also impacts HCT outcomes<sup>53</sup> but there is a lack of standardised methodology between studies<sup>54</sup> on optimal approaches to measurements. Within this study, BMI was reported as the most feasible measure of body composition to be collected prior to HCT by HCPs. However, used alone, this significantly underestimates incidence of malnutrition compared to validated tools, particularly in people with obesity.<sup>55</sup> Alongside this, BMI does not differentiate between fat and fat free mass, where people of any weight and age can be sarcopenic (low muscle mass).<sup>30</sup> UK HCPs rarely used comprehensive measures (e.g., computed tomography, dual energy X-ray absorptiometry or bioelectrical impedance analysis) of body composition, limiting the potential to identify low muscle mass in practice. These approaches also allow monitoring of changes in fat mass, which have been shown to increase during HCT.<sup>56</sup> The clinical implications of these changes are less well described, but bone marrow adipocyte accumulation in both obesity and ageing has been linked to impaired haemopoiesis.<sup>57</sup>

Nutrition guidelines recommend the inclusion of strategies to diagnose and monitor for low muscle mass as part of nutritional/dietetic assessments.<sup>17,50</sup> The most appropriate method will depend on resources, staff and training available, alongside the target population.<sup>58</sup> As more research is published, there is also emerging data on population specific reference ranges and adjustment factors to ensure correct interpretation.<sup>58-60</sup>

Sarcopenic screening may help identify those at risk of low muscle mass, quickly at scale to support early intervention, in time and resource limited settings. Although there is a range of available screening approaches for sarcopenia,<sup>61</sup> most were

designed in the context of frailty and ageing<sup>62</sup> (primary sarcopenia) and not cancer (secondary sarcopenia<sup>11</sup>). These screening measures often incorporate measure(s) of function, rather than a discrete measure of low muscle mass. An example is the Strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) six-item questionnaire<sup>63</sup> or its derivatives (e.g., SARC-F-calf<sup>64</sup> [SARC-F plus calf circumference] and the paediatric SARC-F [PED-SARC-F]<sup>65</sup>). SARC-F-calf has shown good predictive potential<sup>64</sup> for low muscle mass in other cancer cohorts; however, further studies in HCT and within discrete populations (<60 years, ethnicity and BMI) are needed. Handgrip strength, can be used as a simple indirect or predictive measure of sarcopenia<sup>66</sup> and malnutrition risk,<sup>67</sup> but small samples and heterogeneity in procedural reporting limits comparisons between studies.<sup>68</sup> Calf circumference could also offer an alternative indicator of low muscle mass<sup>69,70</sup> and malnutrition.<sup>71</sup> Procedural recommendations include direct skin measures, and so there may be practical limitations as to where and how calf circumference may be collected in a clinic setting.

Less than half of the HCPs in centres reported routine provision of exercise advice and even less reported routine assessment of physical activity pre-HCT. However, the target audience for this survey were nurses, medics and dietitians because of its nutritional focus, and so this may reflect a lack of awareness or physiotherapist representation in the survey, such that further investigation is warranted.

Provision of dietary advice was interdisciplinary, and the level of personalisation delivered was determined by the profession delivering the advice. HCPs reported that dietary advice pre-HCT focused on total energy needs and high-fat dietary advice, with only one-third advising on protein and even less on fibre. This type of advice has potential limitations; for example, the optimisation of muscle mass and function requires protein, energy and nutrient advice.<sup>72</sup> The provision of specialist dietary advice such as pre- and probiotics, micronutrients and neutropenic diet was rare outside dietitians; this could be a result of recognised gaps in nutrition education and training of non-dietetic HCPs.<sup>73,74</sup> Vitamin D was the most frequently discussed vitamin pre-HCT, potentially reflecting its emergent role in anaemia,<sup>75</sup> infection and GvHD.<sup>75,76</sup> thus warranting further HCP training. Neutropenic dietary advice was routinely provided; however, the level of restriction advised was not evaluated in this study. While, neutropenic restriction is still practiced there is insufficient evidence to support very restrictive practices<sup>77</sup> the British Dietetic Association has recommended relaxation of restrictions as a result of gaps in the evidence base.<sup>78</sup> Prophylactic tube feeding was rare with unintentional weight loss and BMI as the primary indicators for feeding, which is in line with national and international recommendations.<sup>19,79</sup>

## Limitations

This survey was comprehensive and allowed greater understanding of interprofessional and between centre variation than similar studies. However, it was not possible to obtain representation from all centres or all target professionals within a site. There were notable discrepancies in reported provision of nutritional care between professionals within a site, raising important considerations for other surveys of multiprofessional intervention delivery. Increased knowledge of nutrition provision within centres and between HCPs could be improved via inclusion of allied services in multidisciplinary teams, documented processes and nutrition training. This study also focused on HCP perceptions of prehabilitation for HCT as a whole and did not explore HCP perceptions on differential service needs by type of transplant or diagnosis.

## CONCLUSIONS

Nutrition and prehabilitation in HCT are perceived as important and deliverable by HCPs, but current provision in UK centres is limited and inconsistent. Although limited, HCT prehabilitation research does exist, future studies should include detailed intervention descriptions in discrete haematological populations, including core outcome frameworks. Furthermore, although international HCT<sup>18</sup> standards recommend access to allied services, such as dietitians, they lack detail on minimum standards of pre, peri- and post-HCT nutrition, relative to the size, throughput and age range of the unit. Defining minimum nutrition standards in HCT via national organisations (e.g., BSBMTCT) or refined accreditation standards (Joint Accreditation Committee ISCT-Europe & EBMT)<sup>18</sup> may help address these unmet needs, reducing inequalities in access identified in this study, guiding centres and commissioners. Further research is warranted to quantify the impact of nutrition and prehabilitation interventions on survival outcomes, patient experience and health economics associated with HCT.

## TRIALS REGISTRATION

CTCS 19-01 (BSBMTCT CTSC). [Clinicaltrials.gov: NCT05352789](https://clinicaltrials.gov/ct2/show/study/NCT05352789).

## AUTHOR CONTRIBUTIONS

Laura J. Miller contributed to the concept, design, delivery, analysis and article drafting. Diana M. Greenfield contributed to design, qualitative analysis, critical review and revision of article. Vanessa Halliday contributed to design, critical review and revision of article. Guruprasad P. Aithal contributed to the design, critical review and revision of the article. John A.

Snowden contributed to the design, critical review and revision of the article. JL contributed to distribution of survey, coordination of some responses from centres and article review.

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## CONFLICTS OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICAL STATEMENT

The study was registered with the Health Research Authority who confirmed that ethics approval was not required. All local governance and GDPR processes were followed.

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## PEER REVIEW

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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