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# Red blood cell transfusions in advanced cancer near the end-of-life: narrative review

Daniele Marelli <sup>1</sup>, Michela Romelli,<sup>1,2</sup> Cristina Cornali,<sup>2</sup> Daniela Martinelli,<sup>2</sup> Andrea Sbrana,<sup>3</sup> Cosimo Chelazzi <sup>1,2</sup>

<sup>1</sup>Dipartimento di Specialità Medico-Chirurgiche, Scienze Radiologiche e Sanità Pubblica, Università degli Studi di Brescia, Brescia, Italy

<sup>2</sup>ASST Spedali Civili di Brescia, Brescia, Lombardy, Italy

<sup>3</sup>Azienda Ospedaliero Universitaria Pisana, Pisa, Italy

## Correspondence to

Professor Cosimo Chelazzi;  
cosimo.chelazzi@unibs.it

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## ABSTRACT

**Background** Red blood cell (RBC) transfusions are commonly used to manage anemia-related symptoms, such as fatigue and dyspnea in patients with advanced cancer. Their use in palliative care (PC) remains controversial due to the lack of clear guidelines, potential risks, and ethical considerations.

**Objective** This narrative review aims to evaluate the role of RBC transfusions in patients with advanced cancer and those at the end of life.

**Methods and data sources** A comprehensive review of relevant existing literature was performed in various databases, using combinations of relevant keywords. Only studies published in English were considered.

**Findings** Anemia affects up to 77% of men and 68% of women with advanced cancer in palliative care. RBC transfusions may offer temporary symptomatic relief, but evidence supporting their routine use in palliative cancer patients is inconclusive. Studies report subjective response rates ranging from 31% to 70%. Benefits on fatigue and dyspnea often last <2 weeks and 23–35% of patients die within two weeks after the transfusion, raising concerns about futility. Variability in transfusion practices across different palliative care settings highlights the influence of clinician attitudes, resource availability, and institutional policies.

**Conclusion** RBC transfusions in advanced cancer and end-of-life care should be considered on a case-by-case basis, prioritizing patient-centered decision-making and ethical considerations. Though the benefit is often short, they may improve the quality of life for highly selected patients. Risks such as adverse reactions and resource allocation concerns must be considered. Further research is needed to establish evidence-based guidelines and standardized assessment tools to evaluate transfusion efficacy in this population.

## WHAT WAS ALREADY KNOWN?

- ⇒ Anaemia-related fatigue and dyspnoea are frequent in advanced cancer.
- ⇒ Red blood cell transfusions may relieve symptoms and support autonomy.

## WHAT ARE THE NEW FINDINGS?

- ⇒ Up to 70% of patients benefit, often temporarily.
- ⇒ Practices are widely variable.

## WHAT IS THEIR SIGNIFICANCE?

- a. Clinical: transfusions may improve quality of life; benefit to be balanced with prognosis and futility.
- b. Research: need for guidelines/tools to assess efficacy in palliative care.

## INTRODUCTION

### Clinical Vignette

A previously healthy, young adult woman presented with a left humeral sarcoma and received initial chemotherapy, which led to severe myelosuppression. This was managed with granulocyte colony-stimulating factor and blood transfusions, resulting in 1 year of clinical remission.

After 1 year, she developed shortness of breath and pain. Diagnostic work-up revealed disease progressed involving distant bone sites, the liver, lungs and pleura. Red blood cell (RBC) transfusions alleviated her anaemia-related fatigue, allowing for second-line chemotherapy and radiotherapy, which achieved another year of disease control.

Following an additional year of clinical and functional stability, she developed worsening fatigue, anorexia and cachexia. Imaging confirmed widespread skeletal metastases. With no remaining disease-modifying treatment options, she was referred to home-based palliative care (PC). At this point, with a haemoglobin level of 7.8 g/dL and experiencing



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severe fatigue, she requested another RBC transfusion, recalling previous symptomatic relief.

The interdisciplinary team considered a palliative transfusion, but ultimately decided to forgo it due to her advanced disease stage, limited life expectancy and the potential for discomfort from the procedure.

After multiple discussions about her goals of care, she understood and accepted the plan for end-of-life care and passed away peacefully at home 3 weeks later.

## Background

This fictional yet realistic clinical vignette illustrates a common scenario in the context of supportive and PC for adults with advanced or metastatic solid cancer nearing the end of life.

In this population, anaemia is both multifactorial and prevalent, affecting up to 68% of women and 77% of men receiving hospice care.<sup>1–3</sup> Symptoms such as fatigue and dyspnoea are frequently associated with anaemia, occurring in approximately 80% and 70%, respectively.<sup>4,5</sup>

These symptoms contribute substantially to patient discomfort and significantly impair quality of life (QoL) across both physical and non-physical domains. RBC transfusions can rapidly increase haemoglobin levels, thereby improving oxygen delivery and tissue oxygenation. This may alleviate symptoms like fatigue and dyspnoea, enhance functional capacity and potentially improve QoL, even in patients approaching the end of life.<sup>5</sup>

Although several guidelines address the diagnosis, evaluation and management of anaemia, fatigue and dyspnoea in cancer patients,<sup>5–12</sup> there is no clear evidence supporting the routine use of RBC transfusions in the PC setting or near end of life.

On the contrary, concerns exist regarding potential adverse reactions and ethical tensions, particularly between the principles of beneficence and justice.<sup>13</sup>

In the absence of definitive evidence, PC teams must make individualised, case-by-case decisions, often guided by differing attitudes and sensitivities.

In this narrative review, we aim to explore these challenges by providing a problem-oriented synthesis of the current literature.

## METHODOLOGY

Relevant papers relevant for this narrative review were identified through a comprehensive search conducted across PubMed, EMBASE, The Cochrane Library (Cochrane Database of Systematic Reviews) and CINAHL, using various combinations of the following keywords: “palliative care”, “supportive care”, “oncology”, “end-of-life”, “hospice care”, “transfusion”, “red blood cells”, “anemia”, “fatigue”, “dyspnea”. To supplement these database searches, the reference lists of included studies and pertinent review articles were manually screened to identify additional relevant papers that may not have been captured in

the initial search. Only peer-reviewed papers and documents published in English were considered, with no restrictions on publication date, allowing for the inclusion of historically relevant literature where appropriate. Studies were selected based on predefined inclusion and exclusion criteria to ensure both relevance and methodological quality. Inclusion criteria included: (1) studies focusing on adult populations ( $\geq 18$  years) in palliative or supportive care settings, particularly in oncology; (2) studies examining transfusion practices, anaemia management, fatigue or dyspnoea in end-of-life or hospice care settings; and (3) studies providing original empirical data (eg, randomised controlled trials, cohort studies, case-control studies or qualitative research). Exclusion criteria included: (1) studies involving paediatric populations and (2) non-English language publications. Final paper selection was conducted through panel discussions among the authors, based on the quality of evidence and its relevance to the topic.

## DISCUSSION

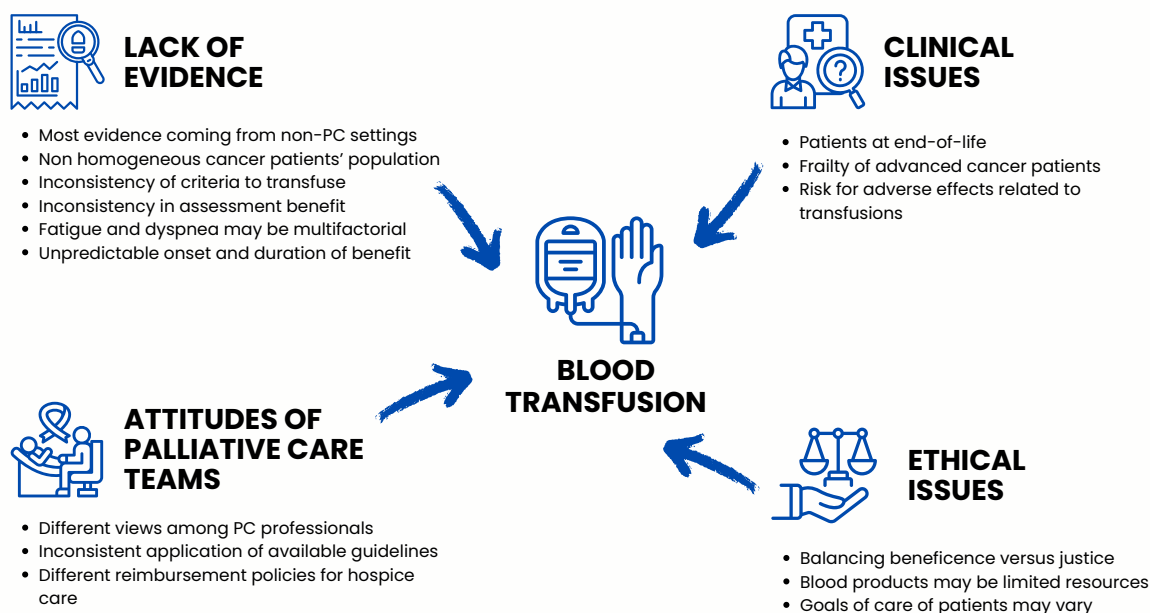
### Overview of the evidence

A 2012 Cochrane review on blood transfusion for anaemia in advanced cancer patients found no randomised clinical trials.<sup>5</sup> The authors identified 12 before-and-after studies involving 653 participants, reporting a subjective response rate to transfusions ranging from 31% to 70%. Five studies that used validated fatigue scales demonstrated early improvements in fatigue following transfusion, which declined by day 14. Similar trends were observed for breathlessness. Overall survival ranged from 2 to 293 days; however, a significant proportion of participants (23% to 35%) died within 2 weeks post-transfusion.<sup>5</sup> Since then, a number of papers have been published addressing some of the issues raised by the review. The clinical heterogeneity of the palliative population limits the generalisation of the findings and prevents the implementation of a systematic approach. These challenges and findings, including those building on the 2012 Cochrane review, are summarised in [figure 1](#).

The American National Comprehensive Cancer Network recommends treating anaemia as part of various strategies for optimal fatigue management at the end of life.<sup>11</sup> In contrast, UK guidance is more tentative, with National Health Service Scotland’s PC guidelines suggesting that blood transfusions may benefit some patients.<sup>12</sup>

Despite these general indications, only a minority of patients receive RBC transfusion for anaemia-related fatigue and dyspnoea in the late stages of solid cancer, particularly at the end of life.

Differences are evident across various PC settings, with transfusion rates ranging from 3.3% of hospice patients to 13% of in-patients admitted to PC units and 16% of patients cared for at home. These differences may reflect the diverse attitudes of PC teams working



**Figure 1** Summary of Key Challenges and Considerations in RBC Transfusions for Palliative Care. PC, palliative care.

in different settings, as well as varying clinical features of patients, such as symptom burden and short-term prognosis.<sup>9 13 14</sup> Such factors may influence a more conservative approach. Economic and reimbursement considerations may also play a role in countries where PC hospice care is not universal.<sup>13</sup>

While some studies suggest that transfusions may help improve symptoms like fatigue and shortness of breath in PC patients,<sup>15–18</sup> others report less promising results.<sup>3 13 19</sup> This conflicting evidence makes it difficult to definitively determine how effective transfusions are at reducing symptom burden in this patient cohort,<sup>20 21</sup> and the topic remains a subject of ongoing debate.

One possible explanation for the lack of consensus is that the population of oncologic patients enrolled in PC is not homogeneous, particularly in terms of disease history. Some included patients both in an earlier stage and more advanced stage. Some patients are in a simultaneous or early PC phase, where RBC transfusions are appropriate as part of a supportive care strategy to treat chemotherapy side effects or alleviate symptoms in otherwise functional patients. For these patients, appropriate treatment and resolution of anaemia can allow the continuation of active treatment with the right dose intensity, positively impacting both QoL and overall survival.

On the other hand, some patients with advanced-stage disease may still be undergoing active cancer treatment and may benefit from transfusions to support daily activities, reduce anaemia-related symptoms burden and improve QoL.

Finally, some patients at the end of life or those who are moribund may experience only temporary relief from RBC transfusions, which do not influence disease trajectory or fatigue.<sup>13</sup> For these patients, transfusions may be considered ethically disproportionate, with the risks outweighing the potential benefits. These differences make it challenging to find a ‘one size fits all’ approach for RBC transfusions in this population.

Another possible reason for lacking evidence is that the symptoms commonly associated with anaemia such as fatigue, dyspnoea and tachycardia- are non-specific. In advanced-stage patients, these symptoms may result from other common issues (eg, respiratory failure due to lung involvement or lung toxicities, heart failure, sarcopenia with muscular distress) and may not always be thoroughly assessed in oncologic PC patients.<sup>22</sup>

As mentioned, the causes of dyspnoea and fatigue in PC cancer patients are often multifactorial, and the relationship between anaemia and these symptoms is not always straightforward. Determining the contribution of anaemia to the onset of these symptoms is also complex.

These factors can influence the approach of PC teams towards investigating and treating the underlying causes of fatigue and dyspnoea, sometimes leading them to attribute these symptoms primarily, or exclusively, to anaemia, and thus recommend transfusions.<sup>23 24</sup> In some cases, even in advanced patients still on some active treatment, alternative approaches to managing anaemia, such as erythropoiesis-stimulating agents (ESAs) or iron supplementation, may be considered.<sup>7</sup> The availability of multiple biosimilar ESAs has

significantly reduced their cost, making them likely less expensive than RBC transfusions.<sup>25</sup> When indirect costs, such as logistics, monitoring and resource utilisation are considered, the cost-effectiveness of ESAs compared with transfusions becomes even more pronounced.<sup>26</sup>

Another barrier to detecting clear evidence of benefit from RBC transfusions is the unpredictable onset and duration of symptom control in this patient population. Different studies define ‘short-term’ or ‘long-term’ post-transfusion effects in arbitrary ways. A critical point in deciding whether to transfuse is that the expected benefit typically lasts no longer than 2 weeks.<sup>27</sup> This short duration underscores the importance of considering the patient’s life expectancy and care goals, as transfusions may be less appropriate for those with a very limited prognosis where symptom relief may not justify the intervention.

Monti *et al* reported that only 51% of 246 terminally ill cancer patients admitted to a PC unit reported a subjective benefit the day after a blood transfusion, regardless of their pre-transfusion haemoglobin level.<sup>28</sup> In an earlier paper by Gleeson and Spencer, 97 PC patients with malignancy completed visual analogue scales to assess the impact of blood transfusions on dyspnoea, weakness and overall well-being. The median pretransfusion haemoglobin value was 7.9 g/dL. Of those patients, 76% and 72% reported feeling better at 2 and 14 days after transfusion, respectively.<sup>29</sup> The difference in results between the studies may be due to the timing of the assessment. Additionally, the subjective improvements observed in both studies raise the possibility that psychological factors, such as the placebo effect, may partly influence these outcomes, especially given the variability in reported benefits despite similar interventions. While neither study directly investigates this, existing research suggests that patient expectations and contextual factors can enhance perceived symptom relief in advanced cancer settings, though further evidence is needed to clarify the extent of this effect in the context of blood transfusions.<sup>30</sup>

This time-related effect may also depend on the changing levels of 2,3-diphosphoglycerate (2,3-DPG).<sup>31</sup> It is important to note that positive effects from transfusions generally cannot be expected before 24–48 hours, as oxygen release from haemoglobin depends on the 2,3-DPG level in RBCs. It may take up to 72 hours for the levels of 2,3-DPG in erythrocytes to return to normal, which affects haemoglobin’s oxygen affinity.<sup>31</sup> An evaluation of transfusion benefits should be made at least 2–3 days post-transfusion, not within 24 hours. This may explain why some studies did not observe a post-transfusion benefit, highlighting the variability in patient responses. The delayed physiological impact of 2,3-DPG further suggests that immediate subjective benefits may be influenced more

by psychological factors, like the placebo effect, than by rapid improvements in oxygen delivery.

The impact of transfusions can also vary depending on objective factors such as the patient’s pretransfusion haemoglobin level and the number of transfused units. The National Institute of Health and Care Excellence (NICE) recommends a restrictive approach, considering RBC transfusions only when haemoglobin levels fall below 7 g/dL (8 g/dL in acute coronary syndrome).<sup>32</sup> However, PC teams often do not strictly follow these guidelines.<sup>23</sup> Studies show a wide range of pretransfusion haemoglobin thresholds in PC patients with cancer, from 4.9 g/dL to 10.7 g/dL.<sup>15 29</sup>

The lack of homogeneity in how studies evaluate the effects of RBC transfusions further complicates the interpretation of their benefits. Different studies use various assessment tools across different patient groups, making comparison difficult. Moreover, subjective measures of symptoms, such as self-reported tools on fatigue and shortness of breath, do not always align with objective measures like post-transfusion haemoglobin levels,<sup>17 33</sup> adding complexity to understanding the true impact of transfusions. In the PC setting, the absence of a precise haemoglobin cut-off reflects the fact that decisions are primarily driven by care goals—whether active treatment or exclusive palliation—and symptom management rather than absolute Hb values alone. For instance, a patient with an Hb of 8.5 g/dL in early PC, undergoing active treatment and possibly with cardiac comorbidities, may benefit from transfusion, while a patient with a similar Hb level but a life expectancy of 48 hours might not, as the intervention could be futile in such cases. This illustrates the tailored nature of these decisions.

This inconsistency in assessment methods highlights the need for standardised tools to evaluate transfusion efficacy. For instance, Brown *et al* used the Functional Assessment of Cancer Therapy–Fatigue (FACT-F) Fatigue Subscale and the Brief Fatigue Inventory (BFI) to assess the impact of RBC transfusions on fatigue in patients admitted to specialist PC units.<sup>15</sup> The FACT-F, a well-validated and widely accepted tool, measures fatigue on a 0–52 scale, with higher scores indicating less fatigue. A change of 3 points on this scale is considered clinically significant. Similarly, the BFI is a reliable tool that rates fatigue severity and impact.<sup>33</sup> In contrast, To *et al* linked post-transfusion improvement in the Australian-modified Karnofsky Performance Status, which is less validated in advanced cancer patients, to symptomatic benefits like fatigue relief, breathlessness and reduced weakness.<sup>34</sup> There is also the possibility to use another validated questionnaire, the FACT-An, which includes an anaemia-specific subscale.<sup>35</sup> This highlights the variability in assessment approaches.

Standardising the evaluation process, potentially favouring established tools like the FACT-F, would allow for more consistent and comparable results across studies.

The issue is complex since, in palliative cancer care, RBC transfusions primarily aim to alleviate symptoms, enhance autonomy and improve QoL, differing from standard clinical approaches. Decisions should consider clinical thresholds and the individual context, focusing on anaemia-related symptoms like fatigue and dyspnoea. Though not life-saving, the potential benefits are quality-preserving and should be evaluated based on symptomatic improvements rather than numerical data. This complexity makes room for other considerations.

#### End-of-life

Transfusions can still be administered at the end of life despite the mentioned challenges in predicting benefits and outcomes.

In a recent paper by Ostan *et al*, 179/1108 (16.2%) patients with solid or haematological cancers enrolled in home PC were given at least one RBC transfusion. Interestingly, half of the patients underwent the transfusions less than a month before death, and the duration of the assistance was positively correlated with the period from the last transfusion to death ( $p < 0.001$ ).<sup>14</sup> However, mixing the solid and haematologic cancer population may introduce biases, since the pathogenesis and effects of RBC transfusions are different in the two populations.

Indeed, Preston *et al* reported that between 23% and 35% of patients comprised by the studies included in their Cochrane died within 2 weeks after the transfusion.<sup>5</sup>

In the study on hospice patients by Woodward, only 3% of patients were transfused, and of these, 50% died within 4 weeks of transfusion, with 11% occurring in the first week.<sup>13</sup>

This may suggest not only that this population is particularly frail but also that the short-term prognosis may be crucial in the decision of transfusing.

RBC transfusions may also cause discomfort to patients (eg, venous access, monitoring) and may pose the risks of adverse effects, which may be particularly unfavourable in a PC population at the end of life.<sup>36</sup>

#### Attitudes of the PC teams

The lack of consistent evidence regarding RBS transfusions for advanced cancer patients in PC has led to varying professional attitudes. A survey by Leibovitz *et al*, which included 500 specialists (100 medical oncologists, 100 general internists, 100 geriatricians, 100 family doctors and 100 nurses) revealed that most, particularly nurses, support transfusions as standard care for patients at the end of life. The criteria for transfusion included haemoglobin levels of 7 g/dL, dyspnoea, weakness, active bleeding and functional decline.<sup>24</sup>

More recently, a UK-based survey of Neoh *et al* found that more than half of palliative medicine physicians responded in a way that was not in accordance

with NICE guidelines on red cell transfusion, generally adopting a more liberal transfusion approach.<sup>23</sup> Seniority played a role in the decision to transfuse, with certified specialists being the most liberal and training doctors adhering more closely to the guidelines. Due to their limited experience, training doctors are likely to follow the guidelines more strictly, influenced by recent exposure to evidence-based practices and restrictive transfusion policies in acute care settings.

Other, less clinical considerations may also influence the decision of PC teams to transfuse. A US-based cross-sectional survey conducted in hospices revealed limited access to palliative transfusions. Only 2.7% of health agencies always offered transfusions, 40.7% offered them sometimes, and 54.9% never provided them.<sup>37</sup> However, the American Society of Hematology issued a statement in 2019 supporting palliative blood transfusions in hospice settings, advocating for improved access to this intervention for symptom relief.<sup>38</sup> Additionally, in July 2021, the US Senate introduced Bill S. 2566, the Improving Access to Transfusion Care for Hospice Patients Act, to test separate payments for transfusions outside the Medicare hospice per diem payment. This legislation, however, was not enacted.<sup>39</sup> For-profit hospices were found to have the most restrictive policies.

In the PC setting, home transfusions may be beneficial; however, their use is limited by significant logistical and safety challenges. These include the need for reliable venous access, continuous monitoring for transfusion-related adverse events and strict protocols for the transport and storage of blood products. As highlighted by Shaw *et al*, while home transfusion services are technically feasible, their implementation requires extensive coordination and resources, thereby limiting their scalability and routine application in home-based PC.<sup>40</sup>

This lack of access to RBC transfusions was identified as a significant barrier to hospice care, particularly for blood cancer patients. Respondents suggested that increasing reimbursement for transfusions could be a key intervention to improve access.<sup>37</sup>

Patients with leukaemia who are transfusion dependent may be referred late to hospital care, despite having a high level of needs.<sup>41</sup>

In a survey on haematologic oncologists, most of the respondents found that inpatient hospice care would be appropriate for patients with blood cancer, considering their round-the-clock need of care, and that they would be more likely to refer their patients if transfusions were made available.<sup>42</sup>

Additionally, in cases where PC patients experience acute, treatable bleeding events, such as gastrointestinal haemorrhages that can be managed with endoscopy, transfusions may stabilise the patient and facilitate treatment.<sup>19</sup> In these situations, RBC transfusions can

impact short-term prognosis even in patients with advanced stages of disease.

Thus, while there has been a general shift towards more restrictive blood transfusion practices, attitudes towards transfusions for cancer patients in PC have remained relatively consistent.

In this context, with unclear evidence coming from non-homogeneous factors and a focus on quality-preserving rather than life-saving care, a solid ethical approach could aid in decision-making.

### Ethical considerations

In general, both delivering and withholding transfusion in advanced oncologic patients enrolled in PC are complex decisions.<sup>43</sup>

Offering a therapy that relies on the use of a limited resource to a patient with no probability of survival is ethically problematic, particularly from the standpoint of resource allocation.<sup>44</sup> However, the practical impact of blood scarcity varies across settings and over time, and may, in some contexts, remain more of a theoretical concern. Alignment with patients' decisions is paramount, and patients must consent to RBC transfusions, fully understanding the associated risks and discomfort. This alignment presupposes that patients are adequately informed about their prognosis and the realism of their care goals, as unrealistic expectations may complicate ethical decision-making about scarce resources, such as blood products.<sup>45</sup> In their ethical analysis of four paradigmatic cases, Smith *et al* argue that because blood products are scarce resources, the allocation requires a prudent and reasoned approach.<sup>46</sup> PC teams should act in the patient's best interest and align with their goals of care. Advance care planning is crucial for this population. However, the use of limited blood resources may also conflict with the principle of social justice, which advocates for the fair distribution of resources to those with the highest chance of benefit and survival. Transfusing patients nearing end-of-life becomes even more ethically challenging.<sup>46</sup>

The authors suggest that transfusions should not be discouraged if an occasional transfusion is likely to alleviate primary symptoms, such as severe fatigue. However, transfusions in openly medically futile situations should be avoided. If the frequency of transfusions exceeds two times a week and begins to strain resources for other patients, the authors propose that the request should be reviewed by the transfusion medicine service.<sup>46</sup>

Indeed, our healthcare system uses many resources to treat patients at the end of life. Since the ethical principles of beneficence and social justice need not conflict, it would be critical to have consistent guidelines that limit product use but can be adjusted for unusual individual circumstances.<sup>47</sup> To address these ethical dilemmas, establishing interdisciplinary ethics committees could provide case-specific guidance, integrating clinical data, patient values, perspectives from

diverse healthcare professionals and resource considerations, thus creating a standardised yet adaptable decision-making framework.

However, given the many factors mentioned above that can impede robust evidence on RBC transfusions in cancer patients in PC, the decision-making process in challenging cases should be understanding of ethical principles as well as the possibility of clinical ethics consults.<sup>46</sup>

### CONCLUSIONS

The decision to transfuse RBC in patients with advanced cancer or at the end of life involves a complex interplay of clinical evidence, timing, ethical considerations and resource allocation. While RBC transfusions can improve QoL by alleviating anaemia-related symptoms, such as fatigue and dyspnoea, these benefits are often short-lived. The absence of clear guidelines and the subjective nature of symptom relief make these decisions challenging. Ethically, the principle of beneficence—aiming to improve patient well-being—must be balanced with the principle of justice, which calls for the equitable distribution of finite health resources, particularly in settings where transfusions may offer limited long-term value. Ultimately, a patient-centred approach is essential. This approach carefully weighs the potential benefits against ethical and practical concerns, ensuring that transfusion decisions align with health care goals and prioritise comfort and dignity at the end of life. Even if their conduction is not easy, prospective studies or RCTs should be encouraged and are needed to establish evidence-based thresholds for transfusion in these populations.

These studies could clarify the balance between symptom relief and resource use, helping to inform standardised guidelines.

### LIMITATIONS

This review has some limitations. The available evidence is heterogeneous, and few recent studies specifically address RBC transfusions in PC. Existing guidelines on blood transfusions focus on non-PC patients. A narrative, problem-oriented, non-systematic approach was intentionally chosen to account for this variability, with study selection based on the authors' expertise and consensus. Only English-language publications were included, which may have excluded relevant studies in other languages. Additionally, this review deliberately excluded papers exploring ESAs, as the scope was intentionally limited to transfusion practices in palliative and end-of-life care settings. While this focus aligns with the review's objectives, it may overlook alternative strategies for managing anaemia and related symptoms, potentially limiting the comprehensiveness of the discussion.

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and analysed the data. CCor did the search and analysed the data. DMart did the search and analysed the data. AS revised the data and drafted the manuscript. CC do-designed the work, analysed the data, reviewed the manuscript and supervised the implementation of the work. All Authors contributed to drafting the manuscript and approved it. CC is the guarantor.

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#### ORCID iDs

Daniele Marelli <http://orcid.org/0009-0005-1527-2118>

Cosimo Chelazzi <http://orcid.org/0000-0002-5156-8638>

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