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REVIEW ARTICLE

Supportive and palliative care in hemato-oncology: how best to achieve seamless integration and subspecialty development?

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Abstract

While recent medical advances have led to cure, remission, or long-term disease control for patients with hematologic malignancy, many still portend poor prognoses, and frequently are associated with significant symptom and quality of life burden for patients and families. Patients with hematological cancer are referred to palliative care (PC) services less often than those with solid tumors, despite higher inpatient mortality and shorter interval between first consultation and death. The complexity of individual prognostication, ongoing therapeutic goals of cure, the technical nature and complications of treatment, the intensity of medical care even when approaching end of life, and the speed of change to a terminal event all pose difficulties and hinder referral. A modified palliative care model is an unmet need in hemato-oncology, where PC is introduced early from the diagnosis of hematological malignancy, provided alongside care of curative or life-prolonging intent, and subsequently leads to death and bereavement care or cure and survivorship care depending on disease course. From current evidence, the historical prioritization of cancer care at the center of palliative medicine did not guarantee that those diagnosed with a hematological malignancy were assured of referral, timely or otherwise. Hopefully, this article can be a catalyst for debate that will foster a new direction in integration of clinical service and research, and subspecialty development at the interface of hemato-oncology and palliative care.

Keywords Hematology · Oncology · Cancer · Supportive care · Palliative

Introduction

Palliative care (PC) is a multidisciplinary approach to symptom management, psychosocial and spiritual support, assistance in treatment decision-making for patients and their families, and medical home care for patients facing life-limiting illnesses. PC is established as an essential and integral part of cancer care [1]. Prior studies suggest that benefits of PC include significantly reducing physical symptoms, as well as alleviation of psychosocial distress, improving quality of life, end-of-life quality-care outcomes, cost of care, and improved survival in certain disease entity [2–5].

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PC was originally intended for patients with non-hematological neoplasms, and relatively few studies have assessed palliative care in patients with hematological malignancies. While recent medical advances have led to cure, remission, or long-term disease control for patients with hematologic malignancy, many still portend poor prognoses, and frequently are associated with significant symptom and quality of life burden for patients and families. Patients with hematological cancer are referred to palliative care (PC) services less often than those with solid tumors, [6] despite higher inpatient mortality and shorter interval between first consultation and death [7].

Palliative care needs and challenges in hematological malignancies

One of the major challenges in caring for patients with hematological cancer is deciding when referral to a PC unit should take place. The complexity of individual prognostication, ongoing therapeutic goals of cure, the technical nature and complications of treatment, the intensity of medical care even when approaching end of

life, and the speed of change to a terminal event all pose difficulties and hinder referral [8, 9].

To optimize end-of-life care, it is important for clinicians to rethink the PC needs of hematological malignancy patients and to call for development of collaboration between PC and hematology. Hematological cancer patients in the advanced disease phase may have a significant symptom burden resulting from cytopenia and clinical complications of bone marrow failure (e.g., fatigue, dyspnea, bleeding, and infections). In addition, psychological burden is often intense for this group of patients. As demonstrated in a previous study, a high frequency of anxiety and depression was detected by the Hospital Anxiety and Depression Scale in about one-third of acute myeloid leukemia patients at diagnosis [10]. The rapid onset and fluctuating course of hematological malignancies, with frequent life-threatening complications, suggest that anxiety symptoms including post-traumatic stress disorder may be a common accompaniment [11]. Furthermore, terminal hematological cancer patients may suffer from other problems identical to those of the general cancer population, including loss of autonomy and disability [12]. In the final phase of disease, bleeding complications and intensive level of blood products and antimicrobials requirement often prevent the use of palliative home care [13, 14].

The increase in global life expectancy could impose additional challenge in the care of older adults suffering from hematological malignancies. Hematological malignancies are typically a disease of the elderly. This point is illustrated by the median age at diagnosis in many of the most frequent types of blood cancer like myelodysplastic syndromes (MDS) and multiple myeloma (75 years) as well as in acute myeloid leukemia (AML), diffuse large-B cell lymphoma (DLBCL), and chronic lymphocytic leukemia (CLL) (70 years) [15]. Elderly patients generally have multiple medical issues and are treated with multiple pharmaceutical agents. These circumstances contribute to an increased risk of drug interactions and the consequent management of toxicities. Manifestations of common toxicities or severe side-effects may increase both morbidity and mortality in the elderly due to age-associated functional deficits in multiple organ systems. One important factor in the elderly patient is the age-related decline in immunity, including the diminished capacity of response to stimulus such as infection or myelo-suppressive treatments [15]. For instance, acute myeloid leukemia (AML) is mostly a disease of the elderly with a median age at diagnosis of 65–70 years [16]. More than 70% of all AML patients are over the age of 60, and in spite of new treatment strategies being present, the mortality is higher and survival is shorter than in the younger groups. PC collaboration could assist in discussing goals of care, advance care planning, enhance psychosocial support, and facilitate community care of elderly cancer patients [17].

Collaboration between hemato-oncology and palliative care

From current evidence, the historical prioritization of cancer care at the center of palliative medicine did not guarantee that those diagnosed with a hematological malignancy were assured of referral, timely or otherwise. A key concern has been that patients with a hematological malignancy were most likely to end life, amid escalating technology in search of a cure, without access to PC. There are special considerations for hematology patients with regard to PC such as the rapid change to a terminal trajectory, whether to include the administration of blood products during end-of-life care, and management of various infectious complications [14, 18]. However, these challenges can be addressed by a proactive hematology practice with a positive attitude toward the integration of PC. The special care need of hemato-oncology patients compared with solid tumor is summarized in Table 1.

Primary PC in the form of excellent communication about treatment options, prognosis, and attention to symptom management can be provided by the primary hematological oncology team when staff members all have appropriate training and skills. Specialty-level PC consultation teams should be available to patients with complex and challenging symptom distress and to patients and families requiring additional psychosocial support. Communication is also challenging for hemato-oncology patients who developed life-threatening complications associated with anticancer treatment (e.g., neutropenic fever, torrential bleeding, and septic shock). Balancing hopes and fears require both honesty and compassion. Hope-worry statements, for instance, “We are hoping for the best, but it would be wise to start planning for the worst. Knowing the full picture now, what is important to you and your loved ones at this time?”, might be helpful at prognosis disclosure in the face of uncertainty. When faced with limitations in therapy and guarded prognosis, open and honest discussions are needed between the hematological oncologist and the patient about the reality of the disease and limitations of treatment. Palliative care team is well placed to support this process, which is often challenging. Goals of care might then be switched from life-prolonging to one focused mostly on comfort, patient centered, and quality of life.

Collaboration between hematology and a PC team has had demonstrated success in symptom management, alleviation of psychosocial burden imposed by hematological cancer and its treatment, discussion of advance care planning, home care provision, enhancement of hospice transfer during end of life, and bereavement support for family members [17, 18]. Even at an advanced stage of disease, patients may still benefit from anticancer treatment (including chemotherapy and adjuvants such as high-dose steroids). As well, patients may have high dependency on blood products and be predisposed to different infectious complications. Therefore, we must ensure good

Table 1 Supportive and palliative care (PC) needs of hematological malignancy compared with solid tumor

	Solid tumor	Hematological malignancy
Disease trajectory	-Physical decline is stable and predictable until a steep and short period of decline before death	-Disease trajectory remains unpredictable and life-threatening; patient could experience episodes of sudden and acute detrioration related to treatment (e.g., neutropenic sepsis, torrential bleeding) -Diverse disease spectrum from those with an acute manifestation and poor survival (e.g., elderly AML) to those with a chronic nature (e.g., multiple myeloma)
PC model of collaboration	-Concurrent mode: early PC integration and care of palliative intent gradually increases over time	-Integration model: PC is introduced from the diagnosis of a hematological malignancy and provided alongside with curative or life-prolonging treatment -Can subsequently lead to death and bereavement care or cure and survivorship care depending on natural disease course
Place of death	-Identify preferred place of death of patients and provide support from PC home care -More often die at home, nursing home and hospice	-The intensive level of medical care even when approaching end of life, and the speed of change to a terminal event may limit the utilization of palliative home care -More often hospitalized and die in hospital
Subspecialty development	-Better recognition of "palliative oncologists" -"Palliative oncologists" could provide dual role in anticancer treatment and holistic palliative care -Clear training pathway as dual board-certified medical oncologist and PC physician	-Huge variability in practice around the world -PC member often embedded as part of the care team at joint rounds and patient care conferences -In countries where PC is not an accredited discipline and less developed, the process of obtaining formalized training is particularly challenging

communication among various clinical teams, namely, hematology, PC, microbiology, and infectious diseases, as well as blood bank services. Integration of hemato-oncology and palliative care requires an in-depth understanding of each discipline as well as how providers can work together most effectively. The historical stereotypes of hematologists who press on till late in disease course and palliative care physicians who give up too early are no longer helpful in the era of personalized cancer treatments and comprehensive supportive care. It is important to end the false dichotomy to choose between hemato-oncology and palliative care.

More recognition and research is needed

In a consensus among international experts on the integration of oncology and PC, it was recommended that a 1-month rotation by oncologists in PC is ideal. They believe that a clinical rotation helped oncologists gain knowledge of basic symptom assessment and management, communication and understanding of an appropriate PC referral, and establishment of a cohesive working relationship with the PC team [19]. It was shown in recent publication that a 4-week mandatory PC rotation could benefit hemato-oncology fellows' ability in symptom assessment, opioid prescription and opioid rotation, communication skills regarding advance care planning and do-not-resuscitate discussion, and coping with stress in facing terminal illness [20].

The lack of evidence-based knowledge and exploration could be another factor restricting palliative care involvement in hematological malignancies on how this should be achieved. When palliative care was first introduced, interventions were largely focused on patients with advanced cancers, particularly those with non-hematological neoplasms [21]. To a lesser extent, palliative care was also aimed at patients with other illnesses such as motor neuron disease [22] and acquired immune deficiency syndrome [23]. As a consequence of the initial target populations for palliative care, most published articles on palliative care report outcomes in patients with non-hematological neoplasms [24]. By contrast, relatively few studies have investigated palliative care in patients with hematological malignancies.

Several studies have found that patients with hematological malignancies tend to receive palliative care late and, therefore, sub-optimally [25, 26]. This situation is unwarranted given that the symptom burden in patients with non-hematological neoplasms and hematological malignancies is essentially equivalent [27]. Moreover, considering the growing evidence supporting the efficacy and cost-effectiveness of palliative care in cancer patients [28, 29] and other non-cancerous conditions [30–32], there is no reason to not consider palliative care interventions in this population. However, clear models and templates of integration of hematology and palliative care or services have been few and limited. Furthermore, there are only few research studies focusing on PC in onco-hematology especially randomized clinical trial [33] in comparison to cancer palliative care and other end-stage nonmalignant diseases. In the coming future, oncology and hematology journals should consider special issue or journal section focusing on end-of-life and symptom-directed clinical care [1, 34]. This might strengthen a sense of belonging to a community of

hematologists and healthcare professionals with common challenges and dilemmas in managing refractory hematological malignancies [35].

Palliative care model in hemato-oncology

Patient with a hematological malignancy could experience episodes of sudden deterioration related to the treatment or the underlying disease. However, it is not uncommon for patients to recover from episodes of "near-death" deterioration. Therefore, people suffering from hematological malignancy often experience a swift change in their goals of care, leaving little time for planning and preparation for death. A modified palliative care model might be needed in hemato-oncology, where PC is introduced early from the diagnosis of hematological malignancy, provided alongside care of curative or life-prolonging intent, and subsequently lead to death and bereavement care or cure and survivorship care depending on natural disease course [36]. This risk management approach may be the future of palliative care integration in the hematology setting and beyond as advances in medicine lead to more prognostic uncertainty [37]. Integrated care model of PC starting from diagnosis of high-risk hematological malignancy is depicted in Fig. 1.

In developed countries where palliative care is well-recognized, a palliative care member could be embedded as part of the care team. Joint rounds and patient care conferences could be held together. In countries in which PC is not an accredited discipline, the process of obtaining formalized training in palliative hemato-oncology is particularly challenging. Nevertheless, many hemato-oncologists are able to acquire the core skills through workshops, rotations and training programs, and focus their research in this area. Furthermore, it is important for PC units and hospice agencies to reconsider their transfusion support guidelines so that patients with hematologic malignancies can readily benefit from hospice enrollment and facilitate dying in place earlier in the course of their EOL care [38].

Conclusion

Establishment of collaboration would be a mutual learning experience for all involved parties. Tumor biology and anticancer treatment can be learned from hematologists, and knowledge about difficult symptom management and psycho-spiritual care could be gained from the interdisciplinary PC team. The diagnosis and treatment of blood cancers are changing rapidly and unpredictably. The role of physician is changing as well, in response to patient expectations, shifting regulations, and ongoing evolution in the structure of healthcare teams. However, the human experience of serious illness, as well as the importance of the physician's presence at the bedside, remains unaltered at core. Expertise of PC and hematology meet at their best in taking care of terminally ill hematology cancer patients.

While similar success in collaboration has been demonstrated in both cancer and other non-cancer life-limiting

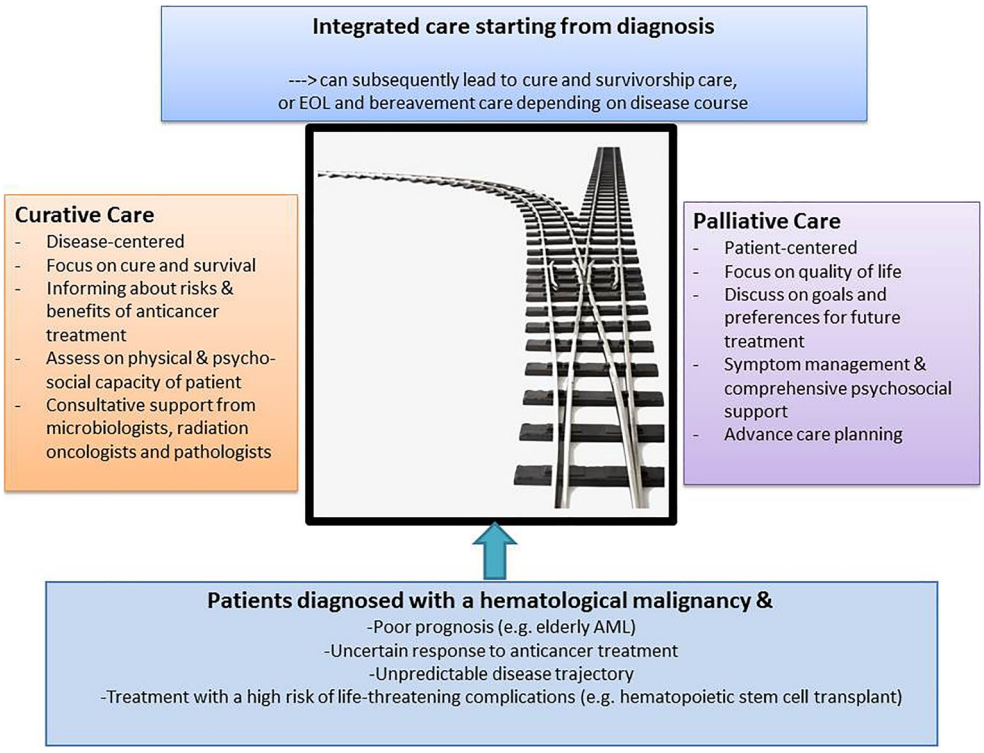

Fig. 1 Integrated supportive and palliative care (PC) model starting from diagnosis of high-risk hematological malignancy

diseases, there is scant work in the area of hematological oncology. As a result, there is an obvious need to call for development, research, and recognition of collaborative care models linking PC and hematology. Hopefully, this article can be a catalyst for debate that will foster a new direction in integration, research, and subspecialty development at the interface of hemato-oncology and palliative care.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

References

1. Kaasa S, Loge JH, Aapro M, Albreht T, Anderson R, Bruera E, Brunelli C, Caraceni A, Cervantes A, Currow DC, Deliens L, Fallon M, Gómez-Batiste X, Grotmol KS, Hannon B, Haugen DF, Higginson IJ, Hjermstad MJ, Hui D, Jordan K, Kurita GP, Larkin PJ, Miccinesi G, Nauck F, Pribakovic R, Rodin G, Sjøgren P, Stone P, Zimmermann C, Lundeby T (2018) Integration of oncology and palliative care: a lancet oncology commission. Lancet Oncol 19(11):e588–e653. https://doi.org/10.1016/S1470-2045(18)30415-7
2. Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leighl N, Oza A, Moore M, Rydall A, Rodin G, Tannock I, Donner A, Lo C (2014) Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet 383:1721–1730
3. Zimmermann C, Riechelmann R, Krzyzanowska M, Rodin G, Tannock I (2008) Effectiveness of specialized palliative care: a systematic review. JAMA 299:1698–1709
4. Morrison RS, Dietrich J, Ladwig S, Quill T, Sacco J, Tangeman J, Meier DE (2011) Palliative care consultation teams cut hospital costs for Medicaid beneficiaries. Health Aff (Millwood) 30:454–463
5. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, Dahlin CM, Blinderman CD, Jacobsen J, Pirl WF, Billings JA, Lynch TJ (2010) Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 363:733–742
6. McGrath P (2002) Qualitative findings on the experience of end-of-life care for hematological malignancies. Am J Hosp Palliat Med 19(2):103–111. https://doi.org/10.1177/104990910201900208
7. Bruera E, Russell N, Sweeney C, Fisch M, Palmer JL (2002) Place of death and its predictors for local patients registered at a comprehensive cancer center. J Clin Oncol 20(8):2127–2133. https://doi.org/10.1200/JCO.2002.08.138
8. Cheng HW (2015) Optimizing end-of-life care for patients with hematological malignancy: rethinking the role of palliative care collaboration. J Pain Symptom Manag 49(5):e5–e6
9. Cheng BH, Sham MM, Chan KY, Li CW, Au HY (2015) Intensive palliative care for patients with hematological cancer dying in hospice: analysis of the level of medical care in the final week of life. Am J Hosp Palliat Care 32(2):221–225
10. Zimmermann C, Yuen D, Mischitelle A, Minden MD, Brandwein JM, Schimmer A, Gagliese L, Lo C, Rydall A, Rodin G (2013) Symptom burden and supportive care in patients with acute leukemia. Leuk Res 37(7):731–736. https://doi.org/10.1016/j.leukres.2013.02.009
11. Rodin G, Yuen D, Mischitelle A, Minden MD, Brandwein J, Schimmer A, Marmar C, Gagliese L, Lo C, Rydall A, Zimmermann C (2013) Traumatic stress in acute leukemia. Psychooncology. 22(2):299–307. https://doi.org/10.1002/pon.2092
12. Tendas A, Niscola P, Ales M, Baraldi L, Boschetto C, Caiazza E, Cupelli L, Giovannini M, Scaramucci L, Brunetti G, Cartoni C, Mandelli F, de Fabritiis P (2009) Disability and physical rehabilitation in patients with advanced hematological malignancies followed in a home care program. Support Care Cancer 17(12):1559–1560. https://doi.org/10.1007/s00520-009-0732-1
13. McGrath P, Leahy M (2009) Catastrophic bleeds during end-of-life care in haematology: controversies from Australian research. Support Care Cancer 17:527–537
14. Odejide OO, Steensma DP (2020) Patients with haematological malignancies should not have to choose between transfusions and hospice care. Lancet Haematol 7(5):e418–e424. https://doi.org/10.1016/S2352-3026(20)30042-9
15. Hassan M, Abedi-Valugerdi M (2014) Hematologic malignancies in elderly patients. Haematologica. 99(7):1124–1127. https://doi.org/10.3324/haematol.2014.107557
16. Klepin HD, Balducci L (2009) Acute myelogenous leukemia in older adults. Oncologist. 14(3):222–232. https://doi.org/10.1634/theoncologist.2008-0224
17. Cheng HW, Li CW, Chan KY et al (2015) End-of-life characteristics and palliative care provision for elderly patients suffering from acute myeloid leukemia. Support Care Cancer 23(1):111–116. https://doi.org/10.1007/s00520-014-2333-x
18. Epstein AS, Goldberg GR, Meier DE (2012) Palliative care and hematologic oncology: the promise of collaboration. Blood Rev 26(6):233–239. https://doi.org/10.1016/j.blre.2012.07.001
19. Hui D, Bansal S, Strasser F, Morita T, Caraceni A, Davis M, Cherny N, Kaasa S, Currow D, Abernethy A, Nekolaichuk C, Bruera E (2015) Indicators of integration of oncology and palliative care programs: an international consensus. Ann Oncol 26:1953–1959
20. Reddy SK, Tanco K, Yennu S, Liu DD, Williams JL, Wolff R, Bruera E (2019) Integration of a mandatory palliative care education into hematology-oncology fellowship training in a comprehensive cancer center: a survey of hematology oncology fellows. J Oncol Pract 15(11):e934–e941. https://doi.org/10.1200/JOP.19.00056
21. Saunders B (1980) The terminal care support team. Nursing 15:657–659
22. Borasio GD, Voltz R (1997) Palliative care in amyotrophic lateral sclerosis. J Neurol 244:S11–S17
23. Fontaine A, Larue F, Lassaunière JM (1999) Physicians' recognition of the symptoms experienced by HIV patients: how reliable? J Pain Symptom Manag 18:263–270
24. Teunissen SC, Wesker W, Kruitwagen C (2007) Symptom prevalence in patients with incurable cancer: a systematic review. J Pain Symptom Manag 34:94–104
25. Hui D, Bansai S, Park M (2015) Differences in attitudes and beliefs toward end-of-life care between hematologic and solid tumor oncology specialists. Ann Oncol 26:1440–1446
26. Manitta VJ, Philip JA, Cole-Sinclair MF (2010) Palliative care and the hemato-oncological patient: can we live together? A review of the literature. J Palliat Med 13:1021–1025
27. LeBlanc TW, Smith JM, Currow DC (2015) Symptom burden of haematological malignancies as death approaches in a community palliative care service: a retrospective cohort study of a consecutive case series. Lancet Haematol 2:e334–e338
28. Gomes B, Calanzani N, Curiale V (2013) Effectiveness and cost-effectiveness of home palliative care services for adults with

advanced illness and their caregivers. Cochrane Database Syst Rev 6:CD007760
29. Higginson IJ, Evans CJ (2010) What is the evidence that palliative care teams improve outcomes for cancer patients and their families? Cancer J 16:423–435
30. Oishi A, Murtagh FE (2014) The challenges of uncertainty and interprofessional collaboration in palliative care for non-cancer patients in the community: a systematic review of views from patients, carers and health-care professionals. Palliat Med 28:1081–1098
31. Murray SA, Boyd K, Sheikh A (2005) Palliative care in chronic illness. BMJ 330:611–612
32. Chan KY, Yip T, Yap DY et al (2016) Enhanced psychosocial support for caregiver burden for patients with chronic kidney failure choosing not to be treated by dialysis or transplantation: a pilot randomized controlled trial. Am J Kidney Dis 67(4):585–592
33. El-Jawahri A, Traeger L, Greer JA et al (2017) Effect of inpatient palliative care during hematopoietic stem-cell transplant on psychological distress 6 months after transplant: results of a randomized clinical trial. J Clin Oncol 35(32):3714–3721. https://doi.org/10.1200/JCO.2017.73.2800
34. Loprinzi CL, Canellos GP (2000) A new addition to the Journal of Clinical Oncology: the art of oncology–when the tumor is not the target. J Clin Oncol 18(1):3. https://doi.org/10.1200/JCO.2000.18.1.3
35. Steensma DP (2011) Art of oncology: new voices wanted. J Clin Oncol 29(25):3343–3344. https://doi.org/10.1200/JCO.2011.37.7242
36. Button E, Bolton M, Chan RJ, Chambers S, Butler J, Yates P (2019) A palliative care model and conceptual approach suited to clinical malignant haematology. Palliat Med 33(5):483–485. https://doi.org/10.1177/0269216318824489
37. Cheng HWB (2020) Palliative care for cancer patients with severe COVID-19: the challenge of uncertainty [published online ahead of print, 2020 Oct 1]. Support Care Cancer:1–3. https://doi.org/10.1007/s00520-020-05809-y
38. Medeiros BC (2018) Non-zero-sum game of transfusions: EOL in leukemia. Blood. 132(7):676–678. https://doi.org/10.1182/blood-2018-06-856336