University of Modena and Reggio Emilia

PhD Program of Clinical and Experimental Medicine (CEM)

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EARLY PALLIATIVE CARE IN HEMATOLOGIC CANCER PATIENTS

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List of abbreviations

ECOG: Eastern Cooperative Oncology Group

EPC: Early Palliative Care

ESAS: Edmonton Symptom Assessment Scale

HADS: Hospital Anxiety and Depression Scale

PC: Palliative Care

PCI: Palliative Care Intervention

POS: Palliative Care Outcome Scale

SPCT: Specialist Palliative Care Team

RCT:Randomized control trial

PC: Palliative Care

MRC: Medical Research Council

SPCS: specialized palliative care service

CST: communication skill training

TtT: teach to talk

ASCO: American society of clinical oncology

BAS: breaking bad news assessment schedule

"YOU matter because you are, you matter to the last moment of your life and we will do all we can to help you not only die peacefully but also to live until you die"

Cecily Saunders

To all my patients

ABSTRACT (English version)

During my Phd, I've explored the integration between palliative care and hematologic cancer patient. Integration between early palliative care and standard haematologic care for advanced patients is worldwide suggested but little is known about its effect.
I first performed a systematic literature review to synthesize the evidence on the impact of early palliative care on haematologic cancer patients' quality of life and resource use.
The search terms were *early palliative care* or *simultaneous* or *integrated* or *concurrent care* and *haematologic* or *onco-haematologic* patients. The following databases were searched: *PubMed, Embase, Cochrane, CINHAL, and Scopus*. Additional studies were identified through cross-checking the reference articles. Studies were in English language, with no restriction for years. Two researchers independently reviewed the titles and abstracts, and one author assessed full articles for eligibility. A total of 296 studies titles were reviewed. Eight articles were included in the synthesis of the results, two controlled studies provided data on the comparative efficacy of PC interventions, and six one-arm studies were included. Since data pooling and meta-analysis were not possible, only a narrative synthesis of the study results was performed. The quality of the two included comparative studies was low overall. The quality of the 6 non-comparative studies was high overall, without the possibility of linking the observed results to the implemented interventions.
Studies on early palliative care and haematologic cancer patients are scarce and have not been prospectively designed. More research on the specific population target, type and timing of palliative care intervention and standardization of collected outcomes is required.
The systematic review was registered on PROSPERO and published in October 2020 in BMJ Support Palliative Care.

I consequently wrote a research protocol for a RCT on Early Palliative Care and Haematologic Cancer Patients: a palliative care intervention (PCI) integrated with standard haematological care. The aim of the protocol was focused on exploring the feasibility of the intervention by patients, professionals and caregivers and on assessing its preliminary efficacy.
It was a mixed-methods phase 2 trial.

The Specialist Palliative Care Team (SPCT) follow each patient on a monthly basis in the outpatient clinic or provide consultations during any hospital admission. SPCT and hematologists discuss active patient issues to assure a team approach to the patient's care.
This quantitative study is a monocentric parallel-group superiority trial with balanced randomization comparing the experimental PCI plus hematological standard care versus hematological standard care alone.
The primary endpoint will calculate on adherence to the planned PCI, measured as the percentage of patients randomized to the experimental arm who attend all the planned palliative care visits in the 24 weeks after randomization.
The qualitative study follows the methodological indications of concurrent nested design and was aimed at exploring the acceptability of the PCI from the point of view of patients, caregivers and physicians.
The trial was registered on ClinicalTrials.gov: NCT03743480 and Published in 2020 in BMC Palliative Care.

During my PhD I have concurrently explored and analyzed the dimension of breaking bad news from hematologists'point of view through a communication training program by my Palliative Care Unit and an ethnography study on the piloted training.
The development of the *Teach to Talk* training programme (TtT) identified the different components of the training course and a set of quality indicators together with its realization. The training was challenging for Haematology physicians, especially in the bed side component, suggesting it should be tailored on specific communication trainees' attitude and believes.

The RCT started in November 2018: in this trial, we will test the feasibility of an integrated palliative care approach starting when hematologists decide to propose the last active treatment to the patient, according to his/her clinical judgement. We decided to test this criterion because it is able to intercept a wide range of patients' needs. The feasibility of this approach requires that we enroll at least 60 patients and that more than 50% of them be followed by the palliative care team for at least 24 weeks. However, the enrollment for this protocol is difficult; only 15 patients and caregiver so far enrolled. We consequently decided to deep this difficulty togheter with other Specialists in this field realizing a realistic synthesis. The aims of the synthesis is

- to provide an overview of difficulties in patients enrollment in palliative care specifically address to hematologic malignancies, exploring the expert opinion point of view
- to elaborate a realist-inspired theory of enrollment, collecting data from interviews and the revised literature.

The results of this synthesis might be relevant for developing structured trial proposal regarding hematologic cancer patients.

Moreover, the final theory has the aim of providing a temporary, perfectible guide to answer the real-life problem that we, and others like us, have encountered.

ABSTRACT ITALIANO (Italian version)

Le cure palliative precoci insieme alle cure ematologiche standard per questo tipo di pazienti sono ritenute necessarie in tutto il mondo, ma poco si sa circa l'efficacia della loro integrazione.

È stata eseguita una **revisione sistematica della letteratura** per sintetizzare le prove di efficacia sull'impatto delle cure palliative precoci sulla qualità della vita e sull'uso delle risorse dei malati di cancro ematologico.

I termini di ricerca erano *cure palliative precoci* o *cure simultanee* o i*ntegrate* o *concomitanti* e *pazienti ematologici* o *oncoematologici*. Sono stati esaminati un totale di 296 studi. Otto articoli sono stati inclusi nella sintesi dei risultati, due studi controllati hanno fornito dati sull'efficacia degli interventi di cure palliative e 6 studi non comparativi sono stati inclusi. Poiché non è stato possibile realizzare una meta analisi, è stata eseguita una sintesi narrativa dei risultati dello studio.

Gli studi sulle cure palliative precoci e sui pazienti con cancro ematologico sono scarsi e non sono stati realizzati in modo prospettico.

La revisione sistematica è stata registrata su PROSPERO e pubblicata in Ottobre 2020

A seguire abbiamo scritto un protocollo di ricerca per uno studio randomizzato sulle cure palliative precoci e i malati di cancro ematologico: abbiamo sviluppato un intervento di cure palliative integrato con le cure ematologiche standard. L'obiettivo del protocollo è l'esplorazione della fattibilità dell'intervento integrato dal punto di vista dei pazienti, dei professionisti e dei caregiver e sulla valutazione preliminare della sua

efficacia.Lo studio prevede che un servizio specialistico di cure palliative segua mensilmente ogni paziente ambulatoriale o in regime consulenziale durante qualsiasi ricovero ospedaliero. I palliativisti e gli ematologi discutono dei problemi dei pazienti per assicurare un approccio integrato alla cura del paziente.
La parte quantitativa dello studio è monocentrico di superiorità a gruppi paralleli con randomizzazione bilanciata che confronta l'intervento di cure palliative sperimentale più la cura standard ematologica rispetto alla sola cura standard ematologica.
L'end-point primario verrà calcolato sull'aderenza all'intervento di cure palliative cosí come pianificato, misurato come la percentuale di pazienti randomizzati al braccio sperimentale che partecipano a tutte le visite di cure palliative pianificate nelle 24 settimane successive alla randomizzazione.
Il protocollo del trial è stato registrato su ClinicalTrials.gov: NCT03743480 e pubblicato nel 2020.

Durante il mio dottorato di ricerca ho contemporaneamente esplorato e analizzato la dimensione delle cattive notizie dal punto di vista degli ematologi attraverso un programma di formazione sulla comunicazione realizzato dalla mia Unità di cure palliative e uno studio etnografico sulla formazione eseguita.
Lo sviluppo del programma di formazione *Teach to Talk* (TtT) ha identificato, contestualmente alla sua realizzazione, le diverse componenti del percorso formativo e una serie di indicatori di qualità. La formazione è stata impegnativa per i medici ematologi, in particolare nella componente al "letto del paziente", suggerendo come il corso dovrebbe essere adattato alle abitudini e alle convinzioni rispetto al fare comunicazioni difficili dei partecipanti stessi.

Il trial è iniziato nel novembre 2018, tuttavia l'arruolamento a questo protocollo si è dimostrato lento e difficile; da quando è iniziato sono stati arruolati 13 pazienti coi loro caregiver.
Abbiamo quindi deciso di approfondire questa difficoltà insieme ad altri Specialisti internazionali del settore realizzando una intervista/survey. Lo scopo dell'indagine sarà quello di fornire una panoramica delle difficoltà nell'arruolamento dei pazienti in cure palliative specificamente indirizzate alle neoplasie ematologiche esplorando l'opinione degli esperti ed elaborare così una teoria dell'arruolamento di ispirazione realista, raccogliendo dati dalla nostra indagine e dalla letteratura rivista.

I risultati di questo studio verranno mostrati durante la discussione della tesi.

INTRODUCTION

A mutual understanding between Palliative care and Haematology has been starting during these last 10 years. Manitta et al.,[1] 9 years ago, described different barriers of collaboration between haematology and palliative care and proposed potential solutions to improve this collaboration. One advice to follow is 'Referral (to palliative care) should be based on needs rather than life expectancy'. Others have reemphasized this advice more recently.[2] Recent literature has underlined the message that focusing palliative care on poor prognostic and expected short-survival patients with haematological malignancies is not so simple for haematologists, and it has been recognized as one of the greatest barriers for palliative care in haematology.[3],[4] New strategies based on patients' needs are advocated.[5],[6]This needs-based idea raises many issues which need to be discussed when attempting to implement referrals to palliative care. These issues include who, how and when the patients' and their relatives' needs should be identified.

In some way, responding to these questions is linked to the model of integration with Haematology proposed. LeBlanc et al.,[7] discussing potential models for early palliative care in haematology, commented on the positive experiences of a 'trigger-based' model for patients admitted to undergo stem cell transplantation[8],[9] and the potential benefit of a 'co-rounding model' in inpatients, based on the experience published in non-haematological patients.[10] Another model postulated is the 'incorporation' into the haematology department of a specific haematology palliative care team,[11] based on the need of a better understanding and approach of the distinctive aspects of haematological malignancies. Other models that we can designate as 'cooperative' are based on early patients' and relatives' needs assessment and close cooperation with the haematology team, allowing mutual understanding and learning.[12]

Considering the different approaches and models suggested to overcome the barriers between palliative care and haematology, this probably means that a single palliative care model does not exist, and palliative care teams should be very adaptive to gain access to patients. Some authors also suggest to use of the denomination of the consult team as supportive care instead of palliative care as it was for some oncology reality.[6]

In my thesis, firstly I examined the relationship between early integration of Hematology and Palliative care as described in the literature; although palliative care is recommended to be integrated (and known to lead to benefits) early in the illness trajectory for people with a life-threatening illness, many hematologists still perceive palliative care as end-of-life care. Palliative care is integrated later and less consistently for people with a hematological malignancy compared to those with other types of cancer.

I consequently propose an ongoing model of integration in the Randomized Control Trial (RCT). Palliative care models have evolved and advanced over time. The original hospice model (the sequential model) transitioned to the concurrent model, allowing for earlier integration of palliative care alongside care of life-pro- longing intent.[13] In this model, care of palliative intent gradually increases over time. This may be more suited to people dying of many of the non-hematological malignancies where deterioration is often slow and predictable.[14]

In our RCT we propose a trigger criterion on hematologist clinical opinion about the last active treatment; I deeply explain this criterion in the research protocol we published. This model demonstrates the evolution of the palliative care model from terminal care to individualized care that is responsive to patients' needs and unpredictable illness trajectories. The model is appropriate for those who have slow, progressive incurable disease and those with acute aggressive disease who will undergo curative treatment with a significant chance of treatment-related mortality.

The successful application of the model requires patients and their families to be fully informed and play an active role in decision making. This requires skilled and sensitive communication from health care professionals that is tailored to the individual patients and their families and takes into account the vastly different illness trajectories experienced by people with a haematological malignancy. I personally believe to insist on mutual educative programs and contamination as I have showed with our experience on communication training programs for haematologists at the end of this thesis; I and my team first developed and piloted the *Teach to Talk* training program [15] and-recognizing the difficulty of completing it by hematologists-analyzed with a Focus Ethnography the heamatoligist' communication patterns during the course.

References

1. Manitta, VJ, Philip, JA, Cole-Sinclair, MF. Palliative care and the hemato-oncological patient: can we live together? A review of the literature. J Palliat Med 2010; 13(8): 1021–1025.
2. Moreno-Alonso, D, Porta-Sales, J, Monforte-Royo, C. Palliative care in patients with haematological neoplasms: an integrative systematic review. Palliat Med 2018; 32(1): 79–105.
3. Prod'homme, C, Jacquemin, D, Touzet, L. Barriers to end-of-life discussions among hematologists: a qualitative study. Palliat Med 2018; 32(5): 1021–1029
4. McCaughan, D, Roman, E, Smith, AG. Palliative care specialists' perceptions concerning referral of haematology patients to their services: findings from a qualitative study. BMC Palliat Care 2018; 17(1): 33.
5. Niscola, P, Tendas, A, Efficace, F. Early palliative care in patients with hematological malignancies: where do we go from here. J Pain Symptom Manage 2018; 55(4): e1–e2.
6. Vidal, M, Hui, D, Bruera, E. Palliative care in patients with leukemia: when and how? Curr Oncol Rep 2018; 20: 95.
7. LeBlanc, TW, Roeland, EJ, El-Jawahri, A. Early palliative care for patients with hematologic malignancies: is it really so difficult to achieve. Curr Hematol Malig Rep 2017; 12(4): 300–308.
8. El-Jawahri, A, LeBlanc, T, VanDusen, H. Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: a randomized clinical trial. JAMA 2016; 316(20): 2094–2103.
9. Loggers, ET, LeBlanc, TW, El-Jawahri, A. Pretransplantation supportive and palliative care consultation for high-risk hematopoietic cell transplantation patients. Biol Blood Marrow Transplant 2016; 22(7): 1299–1305
10. Riedel, RF, Slusser, K, Power, S. Early palliative care on an inpatient oncology unit: impact of a novel co-rounding partnership on patient and health system outcomes. J Clin Oncol 2014; 32(31 Suppl.): 3.
11. Ofran, Y, Bar-Sela, G, Toledano, M. Palliative care service incorporated in a hematology department: a working model fostering changes in clinical practice. Leuk Lymphoma. Epub ahead of print 25 January 2019.
12. Porta-Sales, J, Guerrero-Torrelles, M, Moreno-Alonso, D. Is early palliative care feasible in patients with multiple myeloma. J Pain Symptom Manage 2017; 54(5): 692–700.
13. Glare P and Clarke S. The interface of oncology and palliative care in tertiary hospitals: a concept in evolution. Cancer Forum 2002; 26(1): 6–8.
14. Porta Sales J. Hematology and Palliative Care: the needs are out there. Pal Med 2019. 33 (5) 481-82
15. S. Tanzi, L. De Panfilis, M. Costantini, G. Artioli, S. Alquati, S. Di Leo, Development and preliminary evaluation of a communication skills training programme for

hospital physicians by a specialized palliative care service: the 'Teach to Talk' programme, BMC Med. Educ. 20 (2020) 363. https://doi.org/10.1186/s12909-020-02275-2.

Early palliative care in haematological patients: a systematic literature review[1]

ABSTRACT

Background: Early palliative care together with standard haematologic care for advanced patients is needed worldwide. Little is known about its effect.

The aim of the review is to synthesize the evidence on the impact of early palliative care on haematologic cancer patients' quality of life and resource use.

Patients and Methods: A systematic review was conducted. The search terms were early palliative care or simultaneous or integrated or concurrent care and haematologic or onco-haematologic patients. The following databases were searched: PubMed, Embase, Cochrane, CINHAL, and Scopus. Additional studies were identified through cross-checking the reference articles. Studies were in the English language, with no restriction for years. Two researchers independently reviewed the titles and abstracts, and one author assessed full articles for eligibility.

Results: A total of 296 studies titles were reviewed. Eight articles were included in the synthesis of the results, two controlled studies provided data on the comparative efficacy of PC interventions, and six one-arm studies were included. Since data pooling and meta-

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analysis were not possible, only a narrative synthesis of the study results was performed. The quality of the two included comparative studies was low overall. The quality of the 6 non-comparative studies was high overall, without the possibility of linking the observed results to the implemented interventions.
Conclusions: Studies on early palliative care and haematologic cancer patients are scarce and have not been prospectively designed. More research on the specific population target, type and timing of palliative care intervention and standardization of collected outcomes is required.

INTRODUCTION

Palliative care (PC) is a holistic approach that aims to improve the quality of life of people with a life-threatening illness and of their families. PC should be integrated with curative treatment at every disease stage, from diagnosis to the end of life.[1] A growing body of literature has identified significant challenges in the provision of palliative care in the haematologic setting[2,3]; several barriers to integration are present, including haematologists' difficulty in prognostication, no research on haematology-specific patient needs, and misperceptions about palliative care and end-of-life care.[4-6] The haematologic population consumes a large amount of resources, has a low quality of life, exhibits high aggressiveness at the end of life, and has late access to palliative care services.[25-29]
It is difficult to adopt the classic criteria used in the oncologic population to refer to PC,[7,33,42,43] namely, stage IV metastatic disease, with no curative treatment options or limited estimated prognosis. Moreover, the term "early" is not used in a standardised, unequivocal way in oncologic settings; some authors define it as "just after the diagnosis of metastatic disease",[7] while others call for "early" integration based on the complexity of patients' needs (a more complex situation early on should have access to PC).[8]
In the field of haematology, little is known about the target population of a palliative care approach, the right time for an "early" referral to a palliative care service, the most appropriate palliative care interventions, or, the effect of integrating palliative care with standard care. A call for a new model of integration between palliative care and

haematologic services is strong[9,10]: from the beginning of advanced disease for some authors,[11] or modelled on the different patient needs for other authors.[2,8]
In this context, this systematic review aims to compare the effects of early palliative care interventions versus usual care/standard care on health-related quality of life, depression, symptom intensity, and resource spending among adults with a diagnosis of haematologic cancer.
This review is the first step of the Medical Research Council framework (MRC framework) for complex intervention,[12,13] the so-called phase 0, preliminary to the piloting of a new integrative model of palliative care and haematology required to synthesize evidence on the intervention.

METHODS

The research protocol was registered on PROSPERO, ID number CRD42020141322.

Eligibility criteria

Eligible studies included adult patients with a diagnosis of haematologic cancer. Studies on paediatric patients only were excluded; similarly, studies including a mixed population of haematologic and solid cancers were excluded if the proportion of the former group was lower than 75% and no subgroup analysis was reported.
For the purpose of this review, the term palliative care refers to every type of palliative care intervention, from consultations in the hospital setting to palliative care visits in the ambulatory settings, home care programmes, access to hospice care or any other palliative care service. Studies in which palliative care services were evaluated only as referral services were not considered to be interventions and were thus not included in the review.
For the purpose of this review, early palliative care means a palliative care intervention in haematologic patients undergoing transplant or undergoing ongoing active treatment. In this review simultaneous care is a synonym for early palliative care.
Both studies comparing early palliative care interventions with usual care and studies without a comparator were considered eligible.

Moreover, to be included, studies needed to report outcomes related to health-related quality of life and resource use.
Only quantitative research studies were included; we excluded reviews, qualitative studies, mixed methods studies, editorials, letters, discussions/experts' opinion papers and research protocols.

Information sources

The search was carried out using PubMed, Embase, Cochrane, CINHAL and Scopus. Reference lists of reviews or primary studies identified as relevant were cross-checked to identify further eligible studies. One author (C.B.) is an information specialist who guided the search criteria and the search itself.

Search

Medical subject headings (MeSH) terms were (early OR integrated OR simultaneous care OR concurrent) AND palliative care OR early palliative care OR simultaneous care AND (haematologic* OR haematologic* OR onco-haematologic*). Studies were in English, and there was no restriction for years (until February 7, 2020).

Study selection

Two researchers (S.T., S.L.) independently reviewed the studies' titles and agreed on the studies to include. Screening for full texts was undertaken by two authors (S.T., F.V.). Any discrepancy was discussed between the two authors, and when consensus was not reached, a 3rd author was also involved in the discussion (F.D.M).

Data collection process

To extract data from each study, we set up a data collection form. Two authors independently (FDM and LB) extracted data from each published study. Extracted data were discussed by the entire research team, and any disagreement was discussed with FV to reach a final decision.
There was no need to contact study authors to retrieve additional information.

Data items

We collected information on the study design, setting, participants (including number of patients, disease, treatment stage), intervention details, outcomes, results, type of comparison and timing of palliative care intervention.

Risk of bias of included studies

The quality of the included studies was assessed ~~only~~ for comparative studies using the Cochrane Risk of Bias tool 2.0 for randomized trials[14] and the Newcastle Ottawa Scale for nonrandomized studies (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). CARE guidelines were used for non-comparative studies.[50] Since no meta-analysis was feasible, we reported the quality appraisal criteria of individual studies for descriptive purposes. FV and ST discussed the studies included and their risk of bias.

Summary measures and synthesis of results

Since data pooling and meta-analysis were not possible, only a narrative synthesis of the study results was performed. The characteristics of the included studies are reported based on classic PICO criteria (patients, intervention, comparison, outcomes) in Table 1. For descriptive and comparative purposes, details on patients' characteristics and type of palliative care intervention are also reported (Table 2).

The summary statistics used in the included studies were used to report the results of comparative studies (Table 3) and one-arm studies (Table 4). A qualitative analysis of non-comparative studies was performed (Table 5). No additional analyses were performed.

RESULTS

Study selection

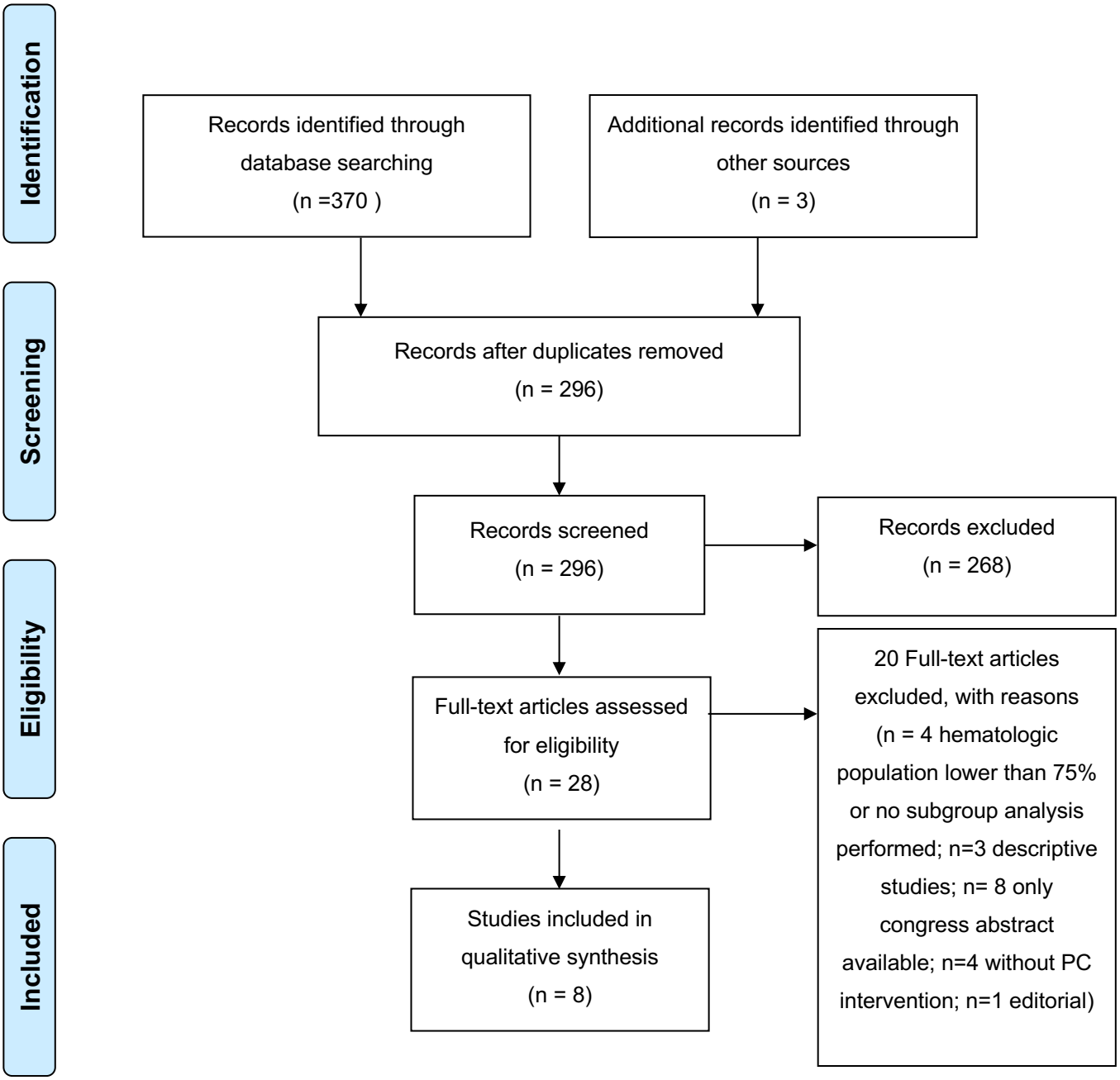
A total of 296 studies titles were reviewed.

Of the 28 full articles read, three were excluded because, being a description of experiences of haematologists and palliative care services, they lacked data.[25-28] Four

other studies were excluded because the haematologic population enrolled was under 75% of the total.[30-33] Another eight studies were excluded because only congress abstracts were available, [34-38,51-53] and one study [18] was excluded because it was an editorial.

Eight articles were included in the synthesis of the results (See PRISMA flow diagram).

PRISMA Flow Diagram of included studies



Characteristics of included studies

The study populations varied; they included haematologic patients with or without specified diseases, those in different treatment phases or those who were inpatients or outpatients. In most of the studies, patients were admitted patients. Palliative care service was an intervention arm/experimental arm in the two randomized controlled trials, set up as a classic PC unit with at least one specialized nurse and one physician. This basic team composition was present in all the studies analysed, but the type of services guaranteed differed between consultation services, home care programmes, hospice care, mobile teams and palliative care units. In most of the studies, PC services had no beds and functioned as consultation services. Haematologists sent patients to PC services at different time points to assess the suitability of PC services for patients candidate to transplantation very early in the disease stage,[15,16,19-21] but there were also a similar number of studies in which the patients were referred in the last stage of disease, near death.[17,18,22] Two controlled studies providing data on the comparative effectiveness of PC interventions and six one-arm studies were included. Different outcomes were measured: quality of life was collected in four studies,[15,16,19,20] while aggressiveness in end-of-life care and length of stay in hospice or palliative care services were collected in the others. See Table 1 for detailed characteristics.

Author and year	Design	Patients	Intervention	Type of comparison	Indicator/outcomes
El Jawahri 2016	Comparative Prospective RCT	160 haematologic pts	PC consultation	Standard care (transplant team)	QoL measures (FACT, BMT, HADS, ESAS, PTSD, PHQ-9)
Rodin 2020	Comparative Prospective RCT	42 haematologic patients	Tailored psychotherapy (EASE-Psy) Tailored physical screening (EASE-phys)	Usual Care	Traumatic stress (SASRQ), Physical symptoms (MSAS-phys), Pain (BPI), Depressive symptoms (BDI-II), Quality of Life (FACIT Sp), Satisfaction with care (FAMCARE)
Cartoni 2007	One-arm retrospective	144 haematologic patients	Home care programme	-	Use of resources (transfusions, CT scan, antibiotics, etc.)
Hung 2013	One-arm retrospective study	3156 solid cancer patients and haematologic patients	PC consultation	-	Transfer to hospice ward, time from hospital admission to PC referral, length of PC stay, time from PC referral to death
Loggers, 2016	One-arm prospective feasibility study	22 haematologic patients	PC consultation	-	Facit PAL, HADS, MDAS
Porta Sales 2017	One-arm retrospective study	67 haematologic patients	PC consultation	-	ESAS modified
Selvaggi 2014	One-arm retrospective study	256 cancer and haematologic patients	Palliative care implementation programme	-	Patients referred to hospice programme; physicians' satisfaction survey
Cheung 2020	One-arm retrospective study	11,127 haematologic patients	PC consultation, home care	-	Days spent at home before death

Table 1. Studies evaluating the efficacy of palliative care intervention and haematological patients.

Quality of included studies

The quality of the two included comparative studies was low overall. However, the quality of the RCTs was mainly affected by the intrinsic characteristics of experimental studies in this field, such as being almost necessarily open trials and assessing the impact on

patient-reported outcomes, potentially affected by the lack of blinding.[15] Details on the risk of bias assessment are reported in Table 5.

The quality of the non-comparative studies was high overall. Two of the eight items included in the guidelines we adopted[50] were not applicable to this kind of study (Table 6).

Study ID	Rating	Justification
Cartoni 2007		
Selection	yes	All patients
Ascertainment exposure	Yes	Hospital records
Outcome	Yes	Hospital records
Alternative causes	Unclear	Reduction in use of resources could be justified by a series of causes but is a typical impact outcome of palliative care
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	Costs and resources use during hospitalization were recorded within routine administrative data.
Reporting	Yes/no	Like all PC interventions, as the intervention is not a dose of drug administration, the reproducibility is not always so easy. PC intervention is not so well-described.
Hung 2013		
Selection	No	Not reported how patients were selected
Ascertainment exposure	Yes	Data on patients were recorded by a specialist nurse using a formulated symptoms record form during the first consultation. For outpatients, date of death was obtained from either the cancer registry center in our institute or the National Register of Death Database in Taiwan.
Outcome	Yes	
Alternative causes	Unclear	
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	Follow-up continued for all patients until death or the cutoff of this study on December 31, 2011.
Reporting	Yes	
Loggers 2016		
Selection	Yes	Potential study subjects were identified via screening of clinic schedules for eligible new patients arriving for transplantation. This review was performed by 1 author who is an experienced transplantation physician (S.J.L.). If a patient appeared to meet study criteria, the patient's attending physician was asked for permission to approach the patient for study consent.
Ascertainment exposure	Yes	High response rate to both baseline and post-intervention assessment
Outcome	Yes	
Alternative causes	Yes	
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	Day 90 surveys. Median follow-up of survivors is 14 months (range, 11 to 19 months
Reporting	Yes	

Porta Sales 2017		
Selection	Yes	We retrospectively reviewed the clinical charts of all patients who attended the MM-PAL from February to December 2013.
Ascertainment exposure	Yes	All patients underwent a comprehensive multidimensional assessment at the first visit conducted by a PC physician, including physical and emotional assessments, performance status, family structure, availability of emotional and practical support, and spiritual issues.
Outcome	Yes	After this first appointment, follow-up consultations were scheduled according to the patients' needs/wishes; when appropriate, phone follow-up by a nurse was scheduled to proactively assess the effect of any drug or dose modification and/or for emotional or practical support. We included in the final results only those patients who completed all three follow-up visits. Therefore, 58 patients (86.6%) were alive and attended the MM-PAL at the third follow-up visit.
Alternative causes	Yes	
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	The median time between the first visit at the MMPAL and the first, second and third follow-up visits was as follows: 14 days (IQR 7e14), 21 days (IQR 21e28) and 60 days (IQR 45e63), respectively.
Reporting	Yes	
Selvaggi 2014		
Selection	Yes	Between August 2006 and May 2010, 392 consults were performed on 256 individual patients with haematological malignancies. Of the 18 HM-BMT physicians who participated in the program, 78% (n = 14) completed satisfaction surveys.
Ascertainment exposure	Yes	As clinically indicated, daily assessments of pain characteristics were noted in the medical record. In addition, goals of care discussions, hospice enrolment, and confirmation of code status were documented
Outcome	Yes	Data regarding the acceptability, usefulness and effectiveness of the programme among clinicians were also collected through satisfaction surveys 18 months after programme initiation
Alternative causes	Yes	
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	Satisfaction surveys 18 months
Reporting	Yes	

Cheung 2020		
Selection	Yes	Residents of Ontario, Canada who died between 1 January 2005 and 31 December 2013, with cancer given as the cause of death in the death records of the Office of the Registrar General – Death (ORGD) were identified.
Ascertainment exposure	Yes	The Office of the Registrar General – Death (ORGD). The administration of palliative care services was defined by using the Health Quality Ontario definition based on physician billing codes specific for palliative consultation and receipt of palliative care documented in hospital or home care records
Outcome	Yes	We used public administrative databases to identify the total number of days spent away from home
Alternative causes	No	Since many variables can influence the care setting to exclude alternative causes is not feasible: "We cannot determine individual patient preferences or experiences, and appreciate that some patients may prefer not to die at home."
A challenge phenomenon	NA	
Dose-response effect	NA	
Follow-up long enough	Yes	180 days prior to date of death – days away from home
Reporting	Yes	The administration of palliative care services was defined using the Health Quality Ontario definition based on physician billing codes specific for palliative consultation and receipt of palliative care documented in hospital or home care records [5,17].

Table 5 risk of bias assessment

Study ID – Rodin 2020		
Risk of bias RCTs	**Authors' judgment**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The Princess Margaret Cancer Centre Department of Biostatistics, which is independent of the trial team, developed the randomization procedures, managed the logbook and provided the computer-generated randomization allocation to research staff after patients' completion of the baseline assessment.
Allocation concealment (selection bias)	Low risk	The Princess Margaret Cancer Centre Department of Biostatistics, which is independent of the trial team, developed the randomization procedures, managed the logbook and provided the computer-generated randomization allocation to research staff after patients' completion of the baseline assessment.
Blinding of participants and personnel (performance bias)	High risk	Unblinded participants and personnel.
Blinding of outcome assessment (detection bias)	High risk	Self-reported outcomes from unblinded patients.
Incomplete outcome data (attrition bias)	High risk	Starting from 124 eligible and contacted patients, only 42 accepted and were randomised. Of these, 32 completed the 12-week follow up.
Selective reporting (reporting bias)	Low risk	Main outcome and secondary outcomes consistent with the published trial protocol (Identifier: NCT023535599)

Table 6 risk of bias assessment comparative studies

Characteristics of haematologic patients and palliative care interventions in included studies

Patient characteristics and palliative care interventions differed among the included studies (see Table 2 for details).

Author	Disease	Number of patients, treatment phase, setting	Type of intervention and description of palliative care team and topic addressed (if specified)
El Jawahri 2016	No disease specified	160, transplant and active phase, hospital	Palliative care service. Team consists of an advanced nurse and a physician. They addressed symptom control and psychological needs.
Rodin 2019	AL	42, active phase, hospital	EASE Phys: multidisciplinary team plus consultation with palliative care nurse and physicians whenever physical symptoms were present. At least weekly for more than 4 symptoms during 8-week intervention
Cartoni 2007	No disease specified	144, active and terminal phase, home care	Home care programme Physicians, nurses, social workers and psychologists. General practitioner was involved and could request visits or consultations to the multiprofessional home care team.
Hung 2013	No disease specified	124, active and terminal, hospital setting	Palliative care consultation and weekly phone interviews. An interdisciplinary team (physicians, specialist nurses, social workers, Buddhists and volunteers). They provided holistic care for patients and family.
Loggers, 2016	AL, Hodgkin, chronic leukaemia	22, transplant and active phase, inpatients and outpatients	Palliative care consultation Expert physicians, nurses and social workers. It was a standard PC consultation addressing symptom control, spiritual and social needs assessments and goals of care.
Porta Sales 2017	MM	67, active phase, outpatients	Multiple myeloma palliative care clinic. The team conducted consultations and telephone assessment. The first visit was 1 hour, and follow-up appointments were 30 minutes. 1 PC physician and 1 nurse supported by the entire PC department, including the psycho-oncologist, social worker, physiotherapist and pain clinic. Multidimensional (physical, emotional and spiritual, social) assessment, treatment, support (family and patients) and follow-up.
Selvaggi 2014	Leukaemia, lymphoma, multiple myeloma, myelodysplastic syndrome	165, transplant and active phase, hospital setting	Palliative care consultation, PC team attended weekly interdisciplinary meetings, a PC member was present 2 hours a day in the ward after transplantation The intervention addressed symptom control and included discussions of the goals of care.
Cheung 2020	Acute leukaemias, aggressive histology lymphomas, indolent lymphomas, other	11,127, active and terminal phase, hospital setting, home care	

Table 2

Figure 1 illustrates how we grouped the studies based on outcome categories (patient-centred or care-centred) and treatment phase to present the overarching point of view of the topic of this article, namely, palliative care and haematologic cancer patients; most of the studies were care-centred and in the early treatment phase (transplant and active phase).

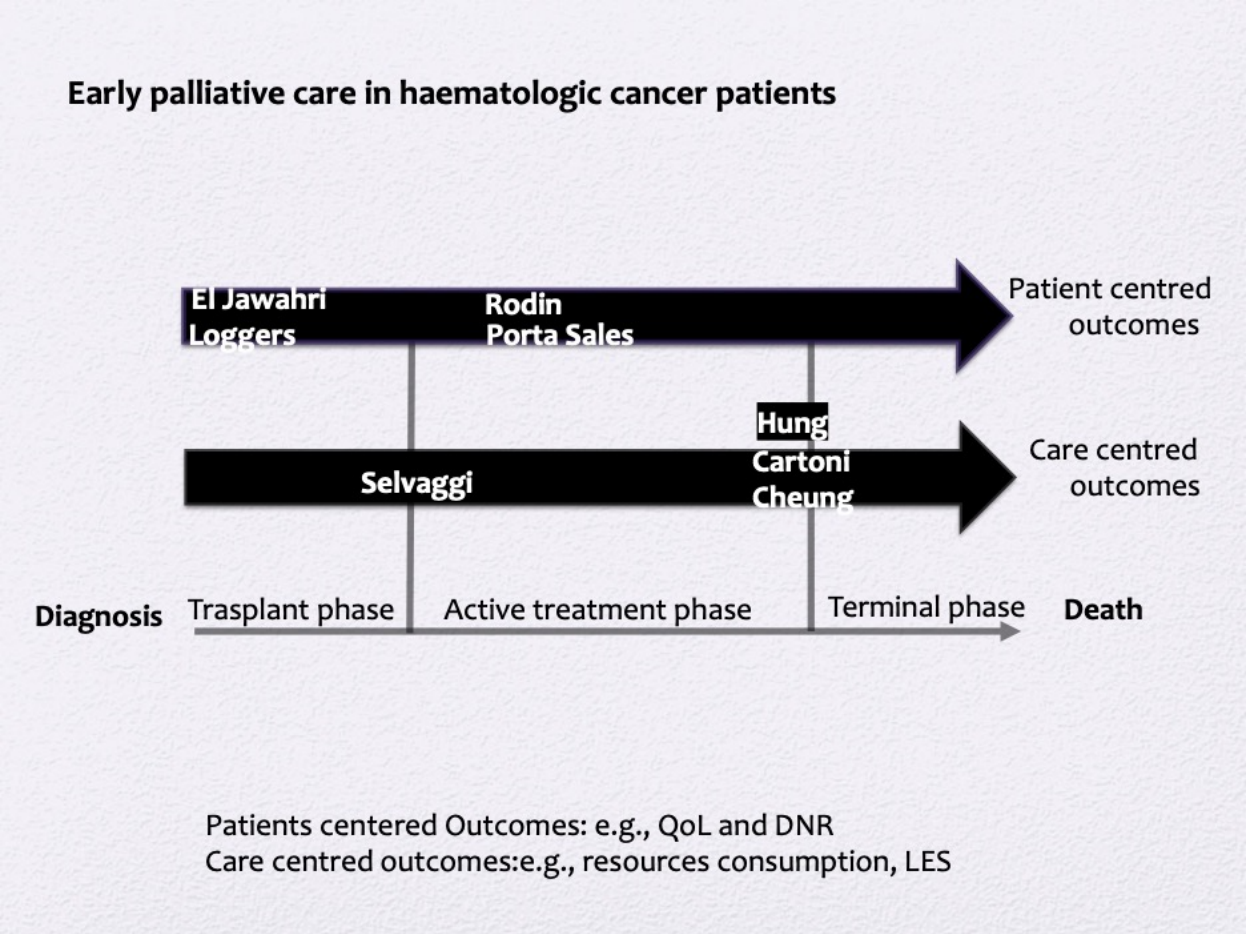


Fig 1. Results from included studies on health-related quality of life and resource use

Comparative studies

El-Jawahri et al.15 showed a significant improvement in the HADS-A hospital anxiety score ($p<0.001$) in the experimental arm. Intervention patients' had depression increased less, there was no difference in fatigue and symptom burden increased less.

In Rodin et al.,16 EASE was associated with significant reductions in traumatic stress symptoms and in clinically relevant symptoms of ASD or threshold ASD, pain intensity

and pain interference compared with UC. There were also promising non-significant trends favouring EASE over UC on most of the other secondary outcomes.
Data are reported in Table 3.

Table 3: Efficacy of palliative care in haematologically advanced cancer patients

Author and year	Type of comparison	Outcome	Results		
Rodin 2020 USA	EASE intervention (n=22) vs usual care (n=20)	Feasibility outcomes , traumatic stress, physical symptoms and quality of life, satisfaction with care	Significant traumatic stress differences at 4 and 12 weeks Difference in pain intensity and pain interference Individuals in EASE improvement in traumatic stress symptoms at 12 weeks, physical symptoms severity at 8 and 12 weeks, symptom-related distress at 8 weeks, number of physical symptoms at 4, 8 and 12 weeks, pain intensity at 4, 8 and 12 weeks and pain interference at 4 and 12 weeks compared with baseline		P= 0.048 e P=0.033 P=0.04 P=0.004 P<0.05 -
El Jawahri, 2016	PC (n = 80) vs standard arm (n = 77); week 2 change from baseline	Quality of life	-21.4 (standard)-14,72 (PC)	P = 0.02	-6.82, (95% CI: 0.16, 13.48)
		Depression	3,92 (standard) 2,43 (PC)	P < 0.001	-1.49, (95% CI: -2.78, 0.20)
		Anxiety	1,12 (standard) -0,80 (PC)	P = 0.09	- 1.92 (95% CI: -3.01, 0.83)
	PC (n = 79) vs standard (n = 77).	FACT fatigue subscale (higher = better)	-13,65 (standard) -10,30 (PC)	P = 0.03	- 3.34, (95% CI: -0.56, 7.25)
	PC (n = 75), standard (n = 77).	ESAS symptom assessment score (higher = worst)	23,14 (standard) 17,35 (Pc)	P = 0.03	

One-arm studies

Porta-Sales et al.[20] showed a significant improvement in pain and depressive mood ($p<0.0001$ and $p= 0.001$, respectively) between the 1st and 3rd palliative care

consultations (-68%, -92% and -62%, for the 1st, 2nd and 3rd consultations, respectively. The number of patients with no pain increased, and the interference of pain with insomnia and mood decreased.

In Logger et al.'s study[19], there were no statistically significant changes in scores over time in transplanted patients.

Selvaggi et al.'s study[21] showed an improvement from <5% to 41% in hospice referrals after programme implementation; the haematologists greatly appreciated the clinical recommendations of palliative care services on useful pain management.

In the Hung et al.[18] study, haematologic patients were significantly less frequently transferred to hospice than were solid cancer patients and were referred later to PCS after admission to the hospital ($p< 0.001$).

In the Cartoni et al.[17] study, patients discharged early and in the terminal phase required the highest mean monthly number of home visits (27.2 vs 24.1), transfusions (6.1 and 6.8) and days of care (22.8 and 19.7), respectively. Median monthly costs for terminal patients (€4300) and those discharged early (€3980) were higher than those for advanced (€2303) and chronic (€1488) patients.

In Cheung et al.,[22] 2932 (26.4%) haematologic cancer patients received palliative care and were able to spend more time at home than were patients who did not receive such services (median time at home increased by 3.2 days; $p<0.0001$).

The data are shown in Table 4.

DISCUSSION

Summary of evidence

Of the 296 titles screened, we included two studies providing evidence on the comparative effectiveness of early/simultaneous palliative care in haematologic cancer patients. The randomized control trial compared the palliative care intervention for 160 transplanted patients to standard care. The primary outcomes for this review (efficacy) were assessed, but the only difference favouring the experimental arm was a reduction in anxiety. The other comparative study, by Rodin et al.,[16] assessed the improvement of clinically relevant symptoms of ASD or threshold ASD, pain intensity, and pain interference compared with standard care in 22 AL patients.

The other six studies included were single-arm studies that provided only information on the population, setting and intervention characteristics, without the possibility of linking the observed results to the implemented interventions.

The interpretation of the available evidence should also carefully consider the overall low quality of the comparative studies included and the limitations of retrospective one-arm studies in providing strong evidence on the efficacy of interventions.

Moreover, the studies analysed showed heterogeneity in the population, palliative care intervention, disease trajectory and treatment phase.

A summary of the main characteristics of the studies included is shown in Table 2. The majority of patients were inpatients; hospitals or hospices seemed to be the appropriate setting for complex haematologic cancer patients.

Different care settings led to different palliative care interventions. Overall, palliative care services differed in composition (nurse and physicians, other specialists, composition not specified), issues addressed (symptoms, goals of care, spiritual needs, etc.), delivery modality (as consultation or phone calls) and frequency of consultations. Different models that integrate palliative care interventions with haematologic standard care are described; palliative care physicians could be consultants in the hematology department or in simultaneous care with ambulatory services or with dedicated beds of palliative care.

From this review we cannot identify the right time to refer to palliative care services hematologic cancer patients or the hematologic population that would most benefit from a palliative care intervention.

The timing of referral to any palliative care service depends on the individual patient, ranging from some days for those at the end of life to a referral from diagnosis for patients receiving a transplant; studies are divided between palliative care at the end of life[32,34,35] and a visionary concept of palliative care for non-advanced cancer patients.[15,16,18,20,21]

We identified two major criteria for identifying candidate patients for palliative care intervention: selection according to prognosis or high symptom burden (as in transplanted patients or in high-risk patients).

We identified an early approach in six studies.[15-17,19-21] For the purpose of this review an agreement was reached between the palliative care physician (ST) and haematologist (S.L.) who screened the title/abstract for the full text; patients receiving transplant and those with ongoing active treatment were included. In all the studies we identified as “early”, the basic components of a palliative care service of an expert palliative care physician and a specialized nurse were guaranteed.

During the screening phase of this review, while we did exclude some reviews, there was nevertheless general agreement on early integrated palliative care in haematology-malignancies assistance emerged.[44-47]

Moreno Alonso et al.[45] evidenced that haematology-oncology departments treating hematologic malignancies involve palliative care services only at the end of life. The authors suggested that specific clinical features of hematologic malignancies may impede timely referral to PC such as the hospice setting or home care. The authors of this review agree with Ruiz's paper on an early PC needs-centred model. Prognosis-linked referral is difficult due to the uncertainty of prognostication in many patients as shown by Oechsle [48] in his review; some specific symptomatic groups could benefit more from a PC assistance.

The model of integrating palliative care in haematology clinical practice is gaining much interest as a research question, and we also believe that hematologic patients should not be evaluated for CP based on their prognosis but rather based on their needs, including symptom control needs, social and spiritual needs and the need to discuss and plan therapies and life choices.

Patient pathways and illness trajectories for haematological malignancies differ considerably for chronic or acute patients[41]; as a result, the type of integration with palliative care should be flexible.

The recent review article by El Jawahri[49] hypothesized a potential approach for identifying the appropriate PC integration strategy in patients with low, moderate or high symptom burden and mortality; PC involvement as disease progresses, early intermittent PC or early longitudinal PC, respectively.

Limitations

The low quality and the heterogeneity of the studies included make the combination of study results not unfeasible, limiting the evidence synthesis on right time and haematologic patient's eligibility criteria for referral to palliative care interventions.

Moreover, the retrospective study design of most of the included studies is not appropriate for the collection of patient-reported outcome measures (PROMS) from the patients themselves after a palliative care intervention or of the usual outcomes evaluated in palliative care to measure quality of life.

Despite several limitations, our review provides a comprehensive overview of palliative care interventions in haematological patients, pointing out the gaps in knowledge in this field.

CONCLUSION

While there are no prospective studies on early palliative care and haematologic patients, some studies are ongoing; patients with acute leukaemia[39] and patients with high-risk acute myeloid leukaemia[40] experience relapse. Searching clinicaltrial.gov, three ongoing studies were found that integrate our eligibility criteria (NCT03743480, NCT04248244, NCT03800095): on multiple myeloma patients, on haematologic patients at their last active treatment[54] and on early palliative care in haematological malignancies. This indicates an increasing interest in the topic.

Most studies agree that referrals to PC occur too late for complex, multifactorial reasons. PC referrals should be guided by a needs-centred approach, overcoming the uncertainty of prognosis or the sudden deterioration in health of these patients.[36] PC specialists should be more confident in dealing with the specific clinical features of haematologic malignancies. PC specialists and haematologists should collaborate to assist dying inpatients.

Research is needed, with randomized control trials on homogeneous haematologic cancer patients using standardized palliative care interventions to evaluate their efficacy based on the patients' points of view.

References

1 Callaway MV, Connor SR, Foley KM. World Health Organization public health model: A roadmap for palliative care development. J Pain Symptom Manage 2018; 55: S6-S13.

2 Manitta VJ, Philip JA, Cole-Sinclair MF. Palliative care and the hemato-oncological patient: can we live together? A review of the literature. J Palliat Med 2010; 13: 1021-1025.

3 LeBlanc TW, Roeland EJ, El-Jawahri A. Early palliative care for patients with hematologic malignancies: is it really so difficult to achieve? Curr Hematol Malig Rep 2017; 12: 300-308.

4 Auret K, Bulsara C, Joske D. Australasian haematologist referral patterns to palliative care: lack of consensus on when and why. Intern Med J 2003; 33: 566-571.

5 Howell DA, Shellens R, Roman E et al. Haematological malignancy: are patients appropriately referred for specialist palliative and hospice care? A systematic review and meta-analysis of published data. Palliat Med 2011; 25: 630-641.

6 Corbett CL, Johnstone M, Trauer JM et al. Palliative care and hematological malignancies: increased referrals at a comprehensive cancer centre. J Palliat Med 2013; 16: 537-541.

7 Haun MW, Estel S, Rucker G et al. Early palliative care for adults with advanced cancer. Cochrane Database Syst Rev 2017; 6: CD011129.

8 Tuca A, Gomez-Martinez M, Prat A. Predictive model of complexity in early palliative care: a cohort of advanced cancer patients (PALCOM study). Support Care Cancer 2018; 26: 241-249.

9 Bandieri E, Apolone G, Luppi M. Early palliative and supportive care in hematology wards. Leuk Res 2013; 37: 725-726.

10 Roeland E, Ku G. Spanning the canyon between stem cell transplantation and palliative care. Hematology Am Soc Hematol Educ Program 2015; 2015: 484-489.

11 Odejide OO, Cronin AM, Condron NB et al. Barriers to quality end-of-life care for patients with blood cancers. J Clin Oncol 2016; 34: 3126-3132.

12 Campbell M, Fitzpatrick R, Haines A et al. Framework for design and evaluation of complex interventions to improve health. BMJ Support Palliat Care 2000; 321: 694-696.

13 Campbell NC, Murray E, Darbyshire J et al. Designing and evaluating complex interventions to improve health care. BMJ 2007; 334: 455-459.

14 Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928. doi:10.1136/bmj.d5928.

15 El-Jawahri A, LeBlanc T, VanDusen H et al. Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: a randomized clinical trial. JAMA 2016; 316: 2094-2103.
16 Rodin, G., et al. (2020). "Emotion And Symptom-focused Engagement (EASE): a randomized phase II trial of an integrated psychological and palliative care intervention for patients with acute leukemia." Supportive Care in Cancer 28(1): 163-176
17 Cartoni C, Brunetti GA, D'Elia GM et al. Cost analysis of a domiciliary program of supportive and palliative care for patients with hematologic malignancies. Haematologica 2007; 92: 666-673.
18 Eichenauer, D. A., et al. (2019). "Characteristics and course of patients with advanced hematologic malignancies receiving specialized inpatient palliative care at a German university hospital." Ann Hematol 98(11): 2605-2607.
19 Loggers ET, LeBlanc TW, El-Jawahri A et al. Pretransplantation supportive and palliative care consultation for high-risk hematopoietic cell transplantation patients. Biol Blood Marrow Transplant 2016; 22: 1299-1305.
20 Porta-Sales J, Guerrero-Torrelles M, Moreno-Alonso D et al. Is early palliative care feasible in patients with multiple Myeloma? J Pain Symptom Manage 2017; 54: 692-700.
21 Selvaggi KJ, Vick JB, Jessell SA et al. Bridging the gap: a palliative care consultation service in a hematological malignancy-bone marrow transplant unit. J Community Support Oncol 2014; 12: 50-55.
22 Cheung MC, Croxford R, Earle CC et al. Days spent at home in the last 6 months of life: a quality indicator of end of life care in patients with hematologic malignancies. Leuk Lymphoma 2020; 61: 146-155.
23 Tierney DK, Passaglia J, Jenkins P. Palliative care of hematopoietic cell transplant recipients and families. Semin Oncol Nurs 2014; 30: 253-261.
24 LeBlanc TW. Hope, phase I trials, and palliative care: so you're telling me there's a chance? J Oncol Pract 2017; 13: 675-677.
25 Hui D, Didwaniya N, Vidal M et al. Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study. Cancer 2014; 120: 1572-1578.
26 LeBlanc TW, El-Jawahri A. When and why should patients with hematologic malignancies see a palliative care specialist? Hematology Am Soc Hematol Educ Program 2015; 2015: 471-478.
27 Hui D, Kim SH, Roquemore J et al. Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. Cancer 2014; 120: 1743-1749.

28 Freeman AT, Wood WA, Fox A et al. Access to palliative care consultation and advance care planning for adults with high-risk leukemia. J Palliat Med 2018; 21: 225-228.

29 Hui D, Kim SH, Roquemore J et al. Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. Cancer 2014; 120: 1743-1749.

30 Bakitas MA, Tosteson TD, Li Z et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. J Clin Oncol 2015; 33: 1438-1445.

31 Amano K, Morita T, Tatara R et al. Association between early palliative care referrals, inpatient hospice utilization, and aggressiveness of care at the end of life. J Palliat Med 2015; 18: 270-273.
32 de Oliveira Valentino TC, Paiva BSR, de Oliveira MA et al. Factors associated with palliative care referral among patients with advanced cancers: a retrospective analysis of a large Brazilian cohort. Support Care Cancer 2018; 26: 1933-1941.
33 Prado BL, Haider A, Naqvi S et al. Changes in the care setting of first consults to palliative and supportive care over a seven-year period. J Pain Symptom Manage 2019; 57: 86-92.
34 Kedgley, E., et al. (2019). "Specialist palliative care (SPC) in haematological malignancy: Establishing practices in a UK tertiary cancer centre (TCC)." Annals of Oncology 30: v665.
35 VanDusen, H., et al. (2019). "Inpatient integrated palliative and transplant care to improve family caregiver (FC) outcomes of patients hospitalized for hematopoietic stem cell transplantation (HCT)." Journal of Clinical Oncology 34(26): 235-
36 Strand, J. J. and T. W. LeBlanc (2018). "Palliative care integration in haematological malignancies: towards a needs-based approach." BMJ Support Palliat Care 8(3): 289-291.
37 Alamgir, M. A., et al. (2017). "Early palliative care interventions in patients with hematologic malignancies prior to hematopoietic cell transplantation." Journal of Clinical Oncology 35(15).
38 Wood, C., et al. (2016). "The palliative care service and the stem cell transplant unit - A happy marriage." Biology of Blood and Marrow Transplantation 22(3): S363.
39 Barbaret C, Berthiller J, Schott Pethelaz AM et al. Research protocol on early palliative care in patients with acute leukaemia after one relapse. BMJ Support Palliat Care 2017; 7: 480-484.
40 Button E, Chan RJ, Chambers S et al. A systematic review of prognostic factors at the end of life for people with a hematological malignancy. BMC Cancer 2017; 17: 213.
41 Smith A, Roman E, Howell D et al. The haematological malignancy research network (HMRN): a new information strategy for population based epidemiology and health service research. Br J Haematol 2010; 148: 739-753.
42 Fulton JJ, Le Blanc TW, Cutson TM et al. Integrated outpatient palliative carefor patients with advanced cancer: a systematic review and metaanalysis. Palliat Med 2019;33:123-134
43 Ferrel B, Temmel JS,Temin S. et al. Integration of Palliative care into standard oncology care: American Society of Clinical oncology clinical practice guideline update. J Clin Oncol 2016;35:96-112
44 Webb JA, LeBlanc TW, El-Jawahri A. Integration of Palliative care into Acute myeloid Leukemia Care. Semin Oncol Nurs 2019; 35(6): 150959.

45 Moreno-Alonso D, Porta-Sales J, Monforte-Royo C et al. Palliative Care in patients with haematologic neoplasms;an integrative systematic review. Palliat Med 2017;32:79-105
46 Ruiz M, Reynolds P, Marranzini R. et al. Role of early palliative care intervention in hematological maiglnancies and bone marrow trasplant patients: barriers and potential solutions. American Journal of Hospice & Palliative Medicine 2018; 35(11): 1456-1460.
47 Ma JD, El-Jawahri AR, Le Blanc TW et al. Pain syndromes and management in adult hematopoietic stem cell transplantation. Hematol Oncol Clin North Am 2018; 32(3): 551-567.
48 Oechsle K. Palliative Care in patients with Hematological Malignancies Oncol Res Treat 2018; 42(1-2): 25-30.
49 El- Jawahri A, Nelson A.M., Gray TF et al Palliative and end of life care for patients with hematologic malignancies. JCO 2020
50 H.M. Murad, S.Sultan, S.Haffar et al Methodological quality and synthesis of case series and care reports. BMJ Evid Based Med.2018 Apr; 23(2):60-63
51 Cartoni, C., et al. (2015). "Hospital versus home care for patients with hematological malignancies in curative or terminal phase: Use of the resources analysis, symptom burden and cost-effectiveness study." Haematologica 100: 24
52 Federico, V., et al. (2013). "Early supportive/palliative care integrated with standard hematological care (simultaneous care) in multiple myeloma patients." Haematologica 98: 449.
53 Quirino, M., et al. (2012). "Supportive simultaneous care: A novel approach to frail cancer patients." Journal of Clinical Oncology 30(15).
54 Tanzi, S., et al. (2020). "Early palliative care versus standard care in haematologic cancer patients at their last active treatment: Study protocol of a feasibility trial." BMC Palliat Care 19(1).

Early Palliative Care versus standard care in haematologic cancer patients at their last active treatment: study protocol of a feasibility trial[2]

Abstract

Background

Patients with advanced haematological malignancies suffer from a very high symptom burden and psychological, spiritual, social and physical symptoms comparable with patients with metastatic non-haematological malignancy. Referral to palliative care services for these patients remains limited or often confined to the last days of life. We developed a palliative care intervention (PCI) integrated with standard haematological care. The aim of the study was focussed on exploring the feasibility of the intervention by patients, professionals and caregivers and on assessing its preliminary efficacy.

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Methods/design

This is a mixed-methods phase 2 trial.
The Specialist Palliative Care Team (SPCT) will follow each patient on a monthly basis in the outpatient clinic or will provide consultations during any hospital admission. SPCT and haematologists will discuss active patient issues to assure a team approach to the patient's care.
This quantitative study is a monocentric parallel-group superiority trial with balanced randomization comparing the experimental PCI plus haematological standard care versus haematological standard care alone.
The primary endpoint will calculate on adherence to the planned PCI, measured as the percentage of patients randomized to the experimental arm who attend all the planned palliative care visits in the 24 weeks after randomization.

The qualitative study follows the methodological indications of concurrent nested design and was aimed at exploring the acceptability of the PCI from the point of view of patients, caregivers and physicians.

Discussion

In this trial, we will test the feasibility of an integrated palliative care approach starting when the haematologist decides to propose the last active treatment to the patient, according to his/her clinical judgement. We decided to test this criterion because it is able to intercept a wide range of patients'needs. The feasibility of this approach requires that we enrol at least 60 patients and that more than 50% of them be followed by the palliative care team for at least 24 weeks.
The trial will include integrated qualitative data analysis; ~~this methodology can~~ to give essential information on feasibility and acceptability.
Trial registration: ClinicalTrials.gov: NCT03743480 (November 16, 2018)

Background

The most recent World Health Organization (WHO) definition of palliative care advocates that palliative care principles "…should be applied as early as possible in the course of any chronic, ultimately fatal illness" [1]. The difference to the previous WHO vision is substantial [2], as the earlier definition recommended palliative care to patients not responsive to curative therapy, limiting its role to the last period of life.

Evidence about the effectiveness of an early integration of palliative care has emerged in recent years for patients with solid tumours. A recent Cochrane systematic review identified seven eligible randomised clinical trials (RCTs) comparing the effects of early palliative care interventions versus standard cancer care on quality of life, depression, symptom intensity, and survival among advancer cancer patients [3]. The results of this review suggested that early palliative care had significantly beneficial effects on quality of life, with a standardised mean difference (SMD) of 0.27 (95% confidence interval (CI) 0.15 to 0.38), and on symptom intensity, with a SMD of -0.23 (95% CI -0.35 to -0.10), among patients with advanced cancer. Effects on mortality and depression remained uncertain [4]. The results of qualitative studies performed in different countries suggested that the early integration of specialised palliative care is well accepted by patients, relatives and, to a lesser extent, oncologists [5-8].

Patients with advanced haematological malignancies suffer from a very high symptom burden and psychological, spiritual, social and physical symptoms comparable with patients with metastatic non-haematological malignancy [9-11]. During the last 30 days of life, haematological patients are more frequently admitted to hospital settings, emergency departments and high-care wards and receive more aggressive treatments and more chemotherapy or biologically active treatments than patients with advanced solid tumours [12].

Conversely, referral to palliative care services for haematologic patients remains limited or often confined to the last days of life [13, 14]. Haematologic specialists show resistance to involving a palliative care service because of the perceived contrast between ongoing active treatments and palliative care, the latter being identified as terminal care [15].

In agreement with the new WHO vision [1], the evidence from studies performed in patients with solid tumours and haematologic patients' symptom burden suggests that an earlier and integrated provision of specialised palliative care has the potential to improve their quality of life and reduce resource consumption through effective management of

psychological and physical symptoms, appropriate relationships, effective communication and support in decision-making.

The call for an effective model of assistance integrating specialised palliative care and haematologic services is strong [16], although there is no agreement about what the best approach is. To some authors, palliative care should be integrated earlier in the trajectory of the advanced disease [17, 18], while others suggest an early integration according to patients' needs [19, 20] or when requested by the haematologist [21]. In some centres, integration of palliative care is assessed for patients undergoing stem cell transplantation [22].

A major challenge in designing a palliative care intervention that is early integrated with onco-haematological care is identifying the best timing for starting an integrated intervention.

The evidence of the effectiveness of an early integration of palliative care with onco-haematological care is poor and is based on few observational studies [10, 11, 23-26]. Only one randomised clinical trial assessed the effectiveness of a palliative care intervention (PCI) in patients hospitalised for haematopoietic stem cell transplantation [27]. The results showed a smaller decrease in quality of life for patients randomised to receive PCI 2 weeks after transplantation.

Following the WHO vision, we developed a PCI integrated with standard haematological care. This pilot study was primarily focused on assessing the feasibility of the PC intervention. Secondary aims include exploring its acceptability by patients, professionals and caregivers and collecting preliminary information on its effectiveness, which will be potentially useful for designing a randomised phase 3 trial. In this article, we describe the protocol of the study.

Methods

Trial design

According to the Medical Research Council framework for complex interventions [28, 29], this is a mixed-methods phase 2 trial on early integration of palliative care in patients with advanced haematological malignancies.

This quantitative study is a monocentric parallel-group superiority trial with balanced randomisation (1:1) comparing the experimental PCI plus haematological standard care versus haematological standard care alone (control arm).

The qualitative study follows the methodological indications of concurrent nested design [30], as both qualitative and quantitative data are collected during the same stage. The qualitative study will deepen the perceptions of patients, family members and physicians involved in the early integrated PCI (see table 1 for the interview topic guide)

Topic	Patients	Family members	Physicians
Early integration of PC	Could you please tell me what you thought when the haematologist proposed you this intervention? Did you talk with anyone about it? How did you experience it?	Could you please tell me what you thought when the haematologist proposed to your loved-one this intervention?	Could you please tell me what you thought about this intervention when you heard about it?
Relationship	Could you please tell me how is the relationship with the hematologist? And what about the palliativist?	Could you please tell me what is your relationship with the hematologist? And what about the palliativist?	How is your relationship as a physician with the patients in the study?
Perceived benefits/strengths	Regarding your participation in this study, could you please tell me what was good for you? What can be the positive aspects of this?	Regarding the participation in this study, could you please tell me what was good for you as caregiver? What can be the positive aspects of this?	Regarding this study, could you please tell me what the strengths of this intervention are, according to your opinion? If it impacted on your usual job, how did it do?
Concerns/weaknesses	Could you please tell me if you had concerns about the intervention? What can be the negative aspects of this?	Could you please tell me if you had concerns about the intervention? What can be the negative aspects of this?	Regarding this study, could you please tell me what the weaknesses of this intervention are?
Feelings	In general, could you please tell me how you felt during this study? Is there any example you would like to share? What about the support you received?	In general, could you please tell me how you felt during this study? Is there any example you would like to share? What about the support you received? And what about the support your loved-one received?	As professional caregiver, could you please tell me how you felt? How did you experience the relationship with the palliativist? And with the patients and their family members?
Decision-making and advance care planning	Could you please tell me how you made the decisions this intervention required? What did you think when you have been involved in the advance care planning?	Could you please tell me how the decision-making process went? What did you think when you have been involved in the advance care planning of your loved-one?	Could you please tell me your opinion about the decision-making process with patients and caregivers during the intervention? How did it go? What are you opinions/prerogatives about/in advance care planning?

Table 1 interview topic guide

Aims

Primary aim

The primary aim is to determine whether a specialised PCI integrated with standard haematological care is feasible in terms of adherence to the planned PCI.

Secondary aims

Quantitative secondary aims are to obtain Patient Reported Outcomes Measures (PROMS) estimates to assess the potential effectiveness of the intervention and to inform the sample size calculations for a future large-scale trial. More specifically, secondary aims include the following assessments in the 24 weeks after enrolment:

- compliance with the assessment of quality of life;
- the main dimensions of quality of life measured with the Palliative Care Outcome Scale questionnaire (POS);
- the severity of physical and psychological symptoms measured with the Edmonton Symptom Assessment Scale questionnaire (ESAS);
- The severity of symptoms of anxiety and depression measured with the Hospital Anxiety and Depression Scale questionnaire (HADS);
- the functional status of the patient measured with the Eastern Cooperative Oncology Group scale (ECOG Performance Status).

Qualitative secondary aims are to explore the acceptability, perceived benefits and concerns, and strengths and weaknesses of the PCI from the point of view of interviewed patients, caregivers and physicians.

Eligibility criteria

Inclusion criteria

- histologically or cytologically confirmed incurable haematological malignancy;
- age 18 years or more
- life expectancy more than 1 month, according the clinical judgement of both the haematologist and the palliative care physician;

- The patient will start the last potentially active treatment (chemotherapy or immunotherapy) as established by the haematological team. Another active treatment could follow this treatment according to evidenced best practice and/or the development of novel haematologic therapy. Agreement on the new treatment between referenced physicians is guaranteed.
- performance status of 0-3, according to the Eastern Cooperative Oncology Group (ECOG);
- ability to understand, read and fill in questionnaires in Italian;
- signed the written informed consent form.

Exclusion criteria

- patient without a caregiver;
- any physical, psychological or psychiatric condition that, in the opinion of the clinical team, makes participation to the study not appropriate.

Setting

Participants will be recruited from the Haematology Department of the Arcispedale Santa Maria Nuova of Reggio Emilia, Italy.

The Haematology division is located in the Santa Maria Nuova hospital, Centro Onco Ematologico of Reggio Emilia. It includes inpatient and outpatient services. The inpatient service consists of 16 beds, 6 of which are used for bone marrow transplantation (low microbial charge). The outpatient service consists of 4 rooms with a total of 6 beds and 3 armchairs and 10 rooms for medical examinations. Medical staff is made up of 14 haematologists organised by main area of haematology: inpatient and transplant, lymphomas, myeloproliferative disorders, and acute leukaemia. During 2018, there were 272 hospital admissions and 39479 ambulatory visits. The unit is certified by Jaice for bone marrow transplantation (autologous and allogenic) and is also certified for phase I trials.

The PCI is provided by the hospital Palliative Care Unit (PCU), integrated for the care of patients and relatives with severe psychological suffering with the hospital Psycho-Oncology Unit. The PCU can be classified as a specialised hospital-based unit with no

beds [31]. At present, it includes three senior physicians (one in advanced palliative care training) and two advance practice nurses, with a remit of specialist consultations in wards and in a clinic for advanced outpatients and their relatives.

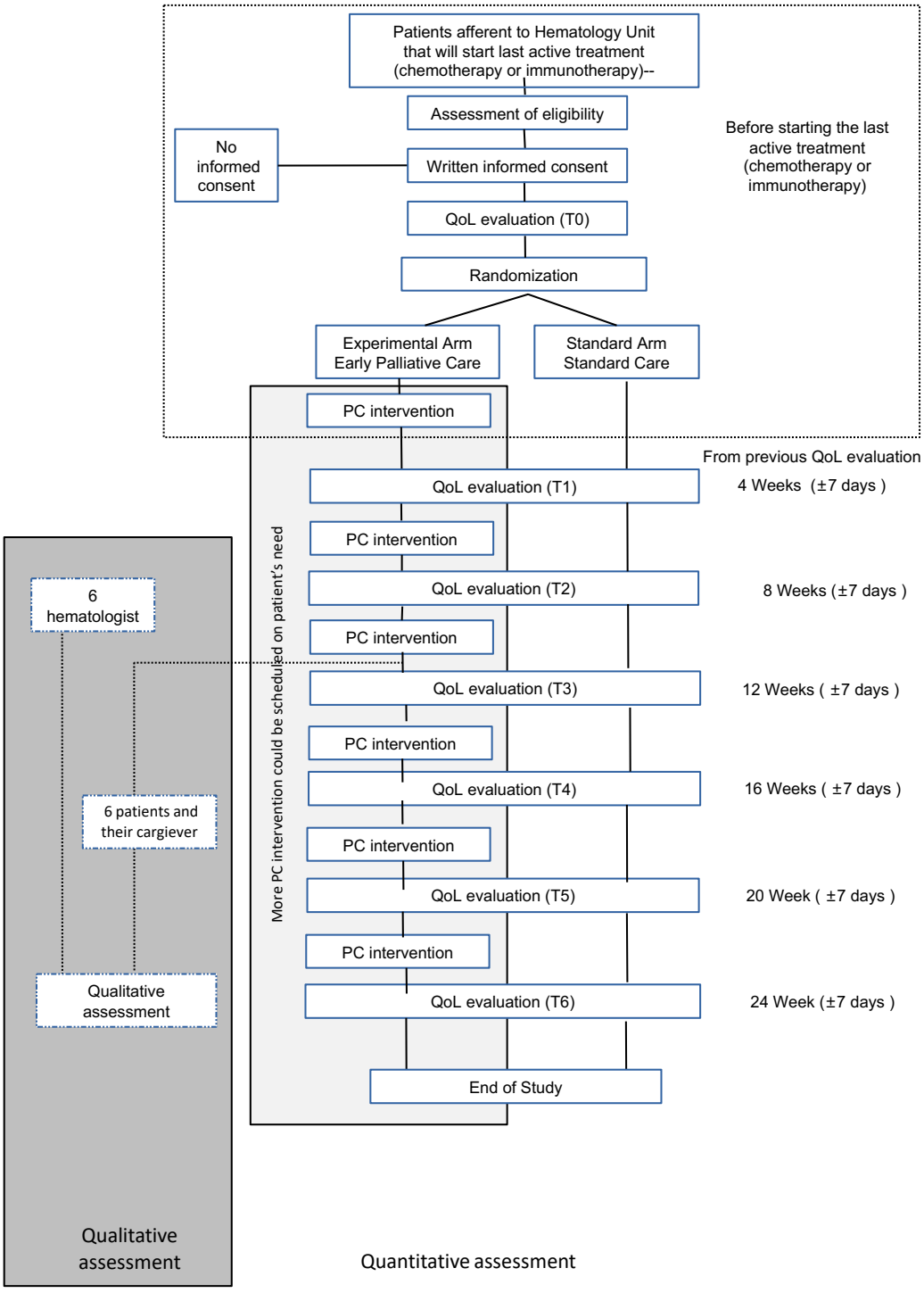
Screening and informed consent

All study procedures are described in Figure 1.
Haematologists and palliative care physicians identify potentially eligible patients during weekly case discussions in the Haematology Department.
We will register all potentially eligible patients and reasons for no accruement, patients who were asked to participate in the study, and patients who did not agree to participate.
A haematologist will give to each eligible patient a description of the study and will ask them to participate in the study.
Patients who agree to participate in the trial will be asked to sign the written informed consent.
To achieve adequate patient enrolment and reach the target sample size, the enrolment rate will be constantly monitored. To this aim, contacts with physicians will take place on a weekly basis.

Randomisation

All patients who agree to participate in the study will be randomly assigned to either the experimental or the control group (1:1 ratio) according to a computer-generated randomisation list created using permuted blocks of random (undisclosed) sizes and stratified by site (if other centres will join patient recruitment).
The allocation sequence will be generated by the Infrastruttura Ricerca e Statistica (I-RS) of the Azienda USL-IRCCS. Investigators involved in patient recruitment will call by telephone the central randomisation centre (I-RS), which will assign the patient a unique code and communicate the arm of allocation. The randomisation code will not be released before patient enrolment to ensure allocation concealment.

Figure 1: Flow chart EPC-EMA



Endpoints

Primary endpoint

- Adherence to the planned PCI, measured as the percentage of patients randomised to the experimental arm who attend all the planned palliative care visits in the 24 weeks after randomisation.

Secondary endpoints

- Compliance with the assessment of quality of life for each questionnaire (POS, ESAS and HADS) at the six planned times;
- Assessment of quality of life measured with the Palliative Care Outcome Scale questionnaire (POS);
- The severity of physical and psychological symptoms measured with the Edmonton Symptom Assessment Scale questionnaire (ESAS);
- The severity of symptoms of anxiety and depression measured with the Hospital Anxiety and Depression Scale questionnaire (HADS);
- The functional status of the patient measured with the Eastern Cooperative Oncology Group scale (ECOG Performance Status).

All questionnaires will be proposed to patients (control/experimental arm) for self-assessment by two trained researchers at the following time points: immediately after giving consent (t0), 4 weeks (± 7 days) after t0 (t1), 8 weeks (± 7 days) after t0 (t2), 12 weeks (± 7 days) after t0 (t3), 16 weeks (± 7 days) after t0 (t4), 20 weeks (± 7 days) after t0 (t5) and 24 weeks (± 7 days) after t0 (t6).

Self-assessment will be the standard procedure. If this is not possible, patients will be assisted by a research physician. Assessment by other professionals or caregivers is not allowed.

Baseline evaluation (t0) will be carried out in hospital. To reduce deviation from the protocol and the dropout rate, evaluations t1-t6 could be performed in hospital or at the patient's home, depending on the patient's preferences.

Four questionnaires will be used in this study:

- Palliative Care Outcome Scale (POS – version 2) in its Italian-validated version [32]. POS is a widely used questionnaire with a brief outcome measure. It is commonly used in patients with advanced illnesses in different settings: inpatient, outpatient, and

community. POS comprises 10 items, including physical and psychological symptoms, spiritual and emotional dimensions, communication with patients and families, and practical concerns related to disease stage. Each of the 10 items is scored with a Likert scale ranging from 0 to 4. POS also includes an open optional question to list the patient's main concerns.

- The Edmonton Symptom Assessment Scale (ESAS) in its Italian-validated version [33]. ESAS asks respondents to rate the severity of 10 common symptoms (pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, appetite, sleep, and feeling of well-being) during the previous 24 hours. It has been found to be valid and reliable in cancer populations.
- The Hospital Anxiety and Depression Scale (HADS) in its Italian-validated version [34]. HADS is a self-assessed 14-item questionnaire that has been tested in cancer patients. It has two 7-item subscales assessing depression and anxiety in the preceding week. The scale is considered appropriate for cancer patients because of the lack of items regarding somatic symptoms, which can confound the identification of psychiatric issues. The format consists of four responses (range 0 to 3) that quantify the degree to which an emotion is experienced by the patient. The score on each subscale ranges from 0 to 21, and a score greater than 11 is consistent with definitive depression or anxiety. A score of less than 7 is normal, and a score of 8–10 is considered borderline for depression and anxiety.
- The Eastern Cooperative Oncology Group (ECOG) Performance Status [35], a widely used scale to evaluate and measure the functional status of a patient.

Data Collection and Management

We will collect Information on the use of health care services including referral to hospice, hospital admissions,emergengy department visits and the date and place of death. In particular we will collect frequency and date of palliative care visits in each arm, type, setting and timing of all chemotherapy, number of hospitalizations, emergency visits and use of hospice services.

Data will be collected on an electronic Case Report File (eCRF) management system (Smarty Ver.3.85– Sinfo S.R.L), validated and handled in accordance to local and European regulatory requirements.

The qualitative assessment

A consecutive series of six patients enrolled in the experimental arm who attend at least three visits in the PC outpatient clinic and their family members will be asked to participate in the qualitative assessment. This assessment will also be proposed to a sample of six physicians involved in the care of recruited patients, selected among those who follow the highest numbers of patients. Patients, family members, and physicians who agree to participate in the qualitative study will be asked to sign the specific written informed consent for the interview and to give explicit permission to be audio-recorded.
Information will be gathered through individual semi-structured interviews [36]. The prompts are defined in advance and listed in three topic guides [37] whose responsibility is up to a team member, expert in qualitative evaluation in palliative care (Table 1). Researchers will explore the acceptability of the intervention giving the opportunity to the receivers (patients and family members) and the haematologists, involved in early integrated palliative care, to tell their experience. Given the intervention's characteristics discussed below, while the semi-structured interviews administered to patients and family members will focus on perceived benefits and concerns of the early PC intervention, the physicians' interviews will address the strengths and weaknesses of the intervention with reference to the respondents' views on patient and family caregiver experience.

Anonymity and non-traceability criteria will be duly presented to all interviewees. The interviewers will be two researchers with expertise in palliative care and basic knowledge of the intervention but who will not be involved in its implementation.
Training of all researchers involved in the study will be carried out before the enrolment of any patient to guarantee the study integrity.

The intervention offer

Haematologists will propose that a patient participate in a study that will include early PC intervention integrated with standard haematological care. To standardise the proposal,

a wording will be suggested to all the haematologists as requested in a previous focus group between haematologists and palliative care professionals in which haematologists addressed the difficulty of using words such as palliative care or palliative care intervention because perceived by patients as synonymous with terminal care. The standardised passage will be,

“I propose you participate in a study in which you will also be assisted by the staff of the palliative care unit. Palliative care addresses all quality-of-life domains, and we have been collaborating with this unit for several years. However, there are no studies anywhere in the world addressing the efficacy of this integrating model of assistance. We would highly appreciate your participation in this study. Even if you decide not to participate in the study, we will continue to assist you according to the best standard of care.”

The PCI in the experimental arm

The initial assessment of patients enrolled in the experimental arm will occur in the outpatient clinic or in the ward as a consultation before the beginning of the last active treatment. The Specialist Palliative Care Team (SPCT) will follow each patient on a monthly basis in the outpatient clinic or will provide consultations during any hospital admission. SPCT and haematologists will discuss active patient issues to assure a team approach to the patient’s care. We will also consider family meetings to improve communication among the patient, family members and health professionals in which we will share the patient’s status, goals of care and current plans. Patients will be followed until death, referral to PC community teams, refusal, or other reasons.

More specifically, the goals of integrating palliative care earlier during the disease include the following:

- Specific attention to individual preferences for information, including patient understanding/awareness of the prognosis;
- improved physical and psychological symptom detection and management;
- a continuous explanation of treatment goals and support for patient decision-making;
- elements of advance care planning, progressively introduced, according to the patients’ wishes;
- the possibility for relatives to meet the SPCT professionals.

Integration with the Haematology teams will be planned through the whole disease trajectory. Although we do not have a specific structure for liaising with haematologists, meetings and case conferences are performed periodically with specific attention to critical turning points such as periodical re-assessments, disease progression, and major modification of the therapeutic plan. Whenever possible, the two teams will have preliminary discussions to reach a shared clinical proposal for the patient to the maximum extent possible. All disagreements will be negotiated within the meetings.

The standard PCI in the control arm

Patients randomised to the standard care arm can be seen by the SPCT at the request of their haematologist at any time. The intervention will not be standardised but planned on the patients' needs.
The date of SPCT interventions will also be recorded for these patients.

Statistical methods

Statistical analysis
The feasibility of the early integrated PC intervention will be assessed by estimating the proportion of haematologic patients who agreed to participate in the intervention and attended the first PC visit. We plan to recruit 60 study participants. Feasibility will be achieved if >50% of patients remain in the programme 3 months after enrolment.
Secondary analyses include the quantitative evaluation of changes in the score of the four questionnaires (POS, ESAS, HADS and ECOG) within 6 months after enrolment.
Descriptive summaries of the scores will be presented by arm at each time point (baseline, 4, 8, 12, 16, 20 and 24 weeks from baseline). For each scale and for each time point, changes from baseline will also be presented with corresponding 95% confidence intervals. For each scale, differences between arms will be estimated using multi-level repeated-measures modelling adjusting for scores at baseline.
Statistical analyses will be performed by the staff of the Clinical Trials and Statistics Unit of the Azienda USL-IRCCS. To this end, the SAS System or R will be used according to availability and version in use.

Sample size estimation

The study was designed to randomise 60 patients. Feasibility will be achieved if >50% of patients remain in the programme 3 months after enrolment. It will be possible to assess the feasibility of the experimental intervention assuming a two-tailed type 1 error equal to 5% and a statistical power equal to 80% given the following assumptions:

1) planned statistical test: chi-squared test with 1 degree of freedom;
2) p-value calculation mode: exact (because of the small sample size);
3) alternative hypothesis: 75%;
4) allocation ratio: 1:1.

To reach the primary objective, the statistical test as cited in point 1 will be used according to specifications detailed in point 2; about the tested percentage, the exact two-sided 95% confidence interval will be calculated according to the Clopper-Pearson approach. Sample size was computed by using nQueryAdvisor, procedure POT0x, version 7.0.

The qualitative analysis

The qualitative analysis will be performed as described below. Recordings of the interviews will be transcribed verbatim and then analysed using thematic analysis to explore the content and context of responses [38, 39].

Each transcript will be independently labelled by two researchers, who will reconcile differences in labelling. Throughout an iterative process, they will inductively identify a few subthemes. Finally, a third researcher will revise both the transcripts and the preliminary thematic analysis and regroup and rename some themes and subthemes with the objective of describing them by highlighting commonalities and differences between the perspectives of the three ‘actors’ involved. This revision will be discussed and emended with the other researchers involved in the qualitative analysis.

Blinding

Allocation status cannot be blinded for the participants or trial personnel.

Ethics

Little evidence is available in the literature concerning the beneficial effect of early palliative care in advanced haematologic cancer patients. Furthermore, patients randomised to standard treatment receive the same treatment as they would have had if they had not entered this trial, including SPCT consultation at the request of their haematologist. These palliative interventions will be reported in a case report file.

The protocol has been approved by the local ethics committee (the Ethics Committee of the Area Vasta Emilia Nord, No. 2018/0056350 of 18 May 2018) as EPC-EMA1 and has been registered at www.clinicaltrials.gov (NCT03743480).

Any protocol amendment will be submitted in ethics committee and communicated to all the participants and to clinicaltrials.gov

Discussion

This is the first trial assessing the early integration of palliative care in patients with advanced haematological malignancies. Other prospective studies have included patients with acute leukaemia relapse [21] or patients with high-risk acute myeloid leukaemia [40].

Palliative care is a holistic approach that aims to improve quality of life in people with life-threatening illness and in their families [41]. A growing body of literature has identified significant challenges in providing palliative care in a haematological setting. [19, 42] Barriers for palliative care integration include difficulty in prognostication by haematologists, too little research specifically on haematological cancer patients' needs, and misperceptions about palliative care as end-of-life care [13-15].

Different haematologic diseases express different needs, but there are basic palliative care needs in all hematologic populations examined in many studies. The call for a new model of integration between palliative care and haematologic service is strong [16, 22]; some authors recommend such care just from the beginning of an advanced disease [17, 18], while other authors advocate its provision according to the patients' needs [19, 20].

Evidence supporting an effective model of integration is missing. In clinical settings, palliative care is usually offered by haematologists in the last days/weeks of life or according to symptom burden, for example, in leukaemia patients at high risk of relapse or who have undergone transplant [10, 11, 23-26]. In this trial, we will test the feasibility

of an integrated palliative care approach starting when the haematologist decides to propose the last active treatment to the patient, according to his/her clinical judgement. We decided to test this criterion because it is very simple to understand, not prognosis linked and, at the same time, able to intercept a wide range of patients and needs. Moreover, the inclusion criterion (judged by the hematologists) "the last active treatment" will include incurable patients.

The hematologist specialists underestimate PC needs and are reluctant to refer patients to a PC service. These problems, in our opinion make this population more homogenous than we could think according to the haematologic diagnosis.

We therefore decide to include different onco-hematologic diseases with different trajectories and characteristics but with the same palliative care unmet need.

The feasibility of this approach requires that we enroll at least 60 patients and that more than 50% of them be followed by the palliative care team for at least 24 weeks. Failure can derive from multiple reasons: a low rate of recruitment because either the haematologists or the patients do not believe in the effectiveness of the intervention; or a low proportion of patients followed for at least 24 weeks because the patients refuse to go on or because the intervention starts too late in the course of the disease.

Conversely, if the trial shows that this approach is feasible – more than 50% of patients are followed by the palliative care team for at least 24 weeks – the impact on quality of life can be potentially relevant, considering that the seminal Temel trial [43] was designed to assess the impact of an integrated PCI at 12 weeks after randomisation.We establish 24 weeks as integrated assistance length and, on the other hand, we include as inclusion criterion "life expectancy > one month"; is an attempt to avoid enrollment of end-of-life hematologic patients considering that literature showed an difficult in prognosis by hematologists.

The trial will include integrated qualitative data analysis to deeply explore the strengths and weaknesses of the proposed approach from patients' and professionals' point of view; this methodology can give essential information on feasibility and acceptability, especially for vulnerable people, such as those in palliative care, data that are difficult to obtain with questionnaires or quantitative data assessment. Moreover, the qualitative approach can provide useful information for identifying the "active ingredients" of the PCI. Regardless, this study, independently of the results, can provide useful information for modelling the most effective integrated PCI in advanced haematological cancer patients.

References

1. Sepulveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organization's global perspective. J Pain Symptom Manage. 2002;24:91-6.
2. World Health Organization. Cancer pain relief and palliative care. Technical Report Series 804. Geneva, Switzerland: WHO; 1990.
3. Haun MW, Estel S, Rucker G, Friederich HC, Villalobos M, Thomas M, et al. Early palliative care for adults with advanced cancer. Cochrane Database Syst Rev. 2017;6:CD011129.
4. Maltoni M, Scarpi E, Dall'Agata M, Schiavon S, Biasini C, Codeca C, et al. Systematic versus on-demand early palliative care: a randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. Eur J Cancer. 2016;69:110-8.
5. Back AL, Park ER, Greer JA, Jackson VA, Jacobsen JC, Gallagher ER, et al. Clinician roles in early integrated palliative care for patients with advanced cancer: a qualitative study. J Palliat Med. 2014;17:1244-8.
6. Zimmermann C, Swami N, Krzyzanowska M, Leighl N, Rydall A, Rodin G, et al. Perceptions of palliative care among patients with advanced cancer and their caregivers. CMAJ. 2016;188:E217-27.
7. Costantini M, Apolone G, Tanzi S, Falco F, Rondini E, Guberti M, et al. Is early integration of palliative care feasible and acceptable for advanced respiratory and gastrointestinal cancer patients? A phase 2 mixed-methods study. Palliat Med. 2018;32:46-58.
8. Sarradon-Eck A, Besle S, Troian J, Capodano G, Mancini J. Understanding the barriers to introducing early palliative care for patients with advanced cancer: a qualitative study. J Palliat Med. 2019;22:508-16.
9. Manitta V, Zordan R, Cole-Sinclair M, Nandurkar H, Philip J. The symptom burden of patients with hematological malignancy: a cross-sectional observational study. J Pain Symptom Manage. 2011;42:432-42.
10. LeBlanc TW, O'Donnell JD, Crowley-Matoka M, Rabow MW, Smith CB, White DB, et al. Perceptions of palliative care among hematologic malignancy specialists: a mixed-methods study. J Oncol Pract. 2015;11:e230-8.
11. LeBlanc TW, Smith JM, Currow DC. 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. 2015;2:e334-8.
12. Hui D, Didwaniya N, Vidal M, Shin SH, Chisholm G, Roquemore J, et al. Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study. Cancer. 2014;120:1572-8.
13. Howell DA, Shellens R, Roman E, Garry AC, Patmore R, Howard MR. Haematological malignancy: are patients appropriately referred for specialist palliative and hospice care? A systematic review and meta-analysis of published data. Palliat Med. 2011;25:630-41.

14. Corbett CL, Johnstone M, Trauer JM, Spruyt O. Palliative care and hematological malignancies: increased referrals at a comprehensive cancer centre. J Palliat Med. 2013;16:537-41.
15. Auret K, Bulsara C, Joske D. Australasian haematologist referral patterns to palliative care: lack of consensus on when and why. Intern Med J. 2003;33:566-71.
16. Bandieri E, Apolone G, Luppi M. Early palliative and supportive care in hematology wards. Leuk Res. 2013;37:725-6.
17. Odejide OO, Cronin AM, Condron NB, Fletcher SA, Earle CC, Tulsky JA, et al. Barriers to quality end-of-life care for patients with blood cancers. J Clin Oncol. 2016;34:3126-32.
18. Odejide OO, Cronin AM, Condron N, Earle CC, Wolfe J, Abel GA. Timeliness of end-of-life discussions for blood cancers: a national survey of hematologic oncologists. JAMA Intern Med. 2016;176:263-5.
19. Manitta VJ, Philip JA, Cole-Sinclair MF. Palliative care and the hemato-oncological patient: can we live together? A review of the literature. J Palliat Med. 2010;13:1021-5.
20. Tuca A, Gomez-Martinez M, Prat A. Predictive model of complexity in early palliative care: a cohort of advanced cancer patients (PALCOM study). Support Care Cancer. 2018;26:241-9.
21. Barbaret C, Berthiller J, Pethelaz AMS, Michallet M, Salles G, Sanchez S, et al. Research protocol on early palliative care in patients with acute leukaemia after one relapse. BMJ Support Palliat Care. 2017;7:480-4.
22. Roeland E, Ku G. Spanning the canyon between stem cell transplantation and palliative care. Hematology Am Soc Hematol Educ Program. 2015;2015:484-9.
23. Zimmermann C, Yuen D, Mischitelle A, Minden MD, Brandwein JM, Schimmer A, et al. Symptom burden and supportive care in patients with acute leukemia. Leuk Res. 2013;37:731-6.
24. Loggers ET, LeBlanc TW, El-Jawahri A, Fihn J, Bumpus M, David J, et al. Pretransplantation supportive and palliative care consultation for high-risk hematopoietic cell transplantation patients. Biol Blood Marrow Transplant. 2016;22:1299-305.
25. Bukki J, Scherbel J, Stiel S, Klein C, Meidenbauer N, Ostgathe C. Palliative care needs, symptoms, and treatment intensity along the disease trajectory in medical oncology outpatients: a retrospective chart review. Support Care Cancer. 2013;21:1743-50.
26. Porta-Sales J, Guerrero-Torrelles M, Moreno-Alonso D, Sarra-Escarre J, Clapes-Puig V, Trelis-Navarro J, et al. Is early palliative care feasible in patients with multiple myeloma? J Pain Symptom Manage. 2017;54:692-700.
27. El-Jawahri A, LeBlanc T, VanDusen H, Traeger L, Greer JA, Pirl WF, et al. Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: a randomized clinical trial. JAMA. 2016;316:2094-103.
28. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. BMJ. 2000;321:694-6.

29. Campbell NC, Murray E, Darbyshire J, Emery J, Farmer A, Griffiths F, et al. Designing and evaluating complex interventions to improve health care. BMJ. 2007;334:455-9.
30. Creswell JW, Clark VL, Gutmann ML, Hanson WE. Advances in mixed methods research designs. In: Tashakkori A, Teddlie C, editors. Handbook of mixed methods in social and behavioral research. Thousand Oaks, CA: Sage; 2003. p. 209-40.
31. Higginson IJ, Finlay IG, Goodwin DM, Hood K, Edwards AG, Cook A, et al. Is there evidence that palliative care teams alter end-of-life experiences of patients and their caregivers? J Pain Symptom Manage. 2003;25:150-68.
32. Costantini M, Rabitti E, Beccaro M, Fusco F, Peruselli C, La Ciura P, et al. Validity, reliability and responsiveness to change of the Italian palliative care outcome scale: a multicenter study of advanced cancer patients. BMC Palliat Care. 2016;15:23.
33. Moro C, Brunelli C, Miccinesi G, Fallai M, Morino P, Piazza M, et al. Edmonton symptom assessment scale: Italian validation in two palliative care settings. Support Care Cancer. 2006;14:30-7.
34. Costantini M, Musso M, Viterbori P, Bonci F, Del Mastro L, Garrone O, et al. Detecting psychological distress in cancer patients: validity of the Italian version of the hospital anxiety and depression scale. Support Care Cancer. 1999;7:121-7.
35. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the eastern cooperative oncology group. Am J Clin Oncol. 1982;5:649-55.
36. Rubin HJ, Rubin I. Qualitative interviewing: the art of hearing data. 2nd ed. Thousand Oaks, CA: Sage Publications; 2005.
37. Taylor MC. Interviewing. In: Holloway I, editors. Qualitative research in health care. Maidenhead, England: McGraw-Hill Education; 2005. p. 39-55.
38. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3:77-101.
39. Payne S. Qualitative methods of data collection and analysis. In: Haddington-Hall JM, Bruera E, Higginson IJ, Payne S, editors. Research methods in palliative care. New York, NY: Oxford University Press; 2007. p. 139-60.
40. Button E, Chan RJ, Chambers S, Butler J, Yates P. A systematic review of prognostic factors at the end of life for people with a hematological malignancy. BMC Cancer. 2017;17:213.
41. Callaway MV, Connor SR, Foley KM. World health organization public health model: a roadmap for palliative care development. J Pain Symptom Manage. 2018;55:S6-13.
42. LeBlanc TW, Roeland EJ, El-Jawahri A. Early palliative care for patients with hematologic malignancies: is it really so difficult to achieve? Curr Hematol Malig Rep. 2017;12:300-8.
43. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med. 2010;363:733-42.

Development and preliminary evaluation of a communication skills training programme for hospital physicians by a Specialized Palliative Care Service: The 'Teach to Talk' programme[3]

Abstract

Background

There is widespread agreement about the importance of communication skills training (CST) for healthcare professionals caring for cancer patients. Communication can be effectively learned and improved through specific CST. Existing CSTs have some limitations with regard to transferring the learning to the workplace. The aim of the study is developing, piloting, and preliminarily assessing a CST programme for hospital physicians caring for advanced cancer patients to improve communication competences.

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Methods

This is a Phase 0-I study that follows the Medical Research Council framework; this paper describes the following sections: a literature review on CST, the development of the Teach to Talk training programme (TtT), the development of a procedure for assessing the quality of the implementation process and assessing the feasibility of the implementation process, and the pilot programme. The study was performed at a 900-bed public hospital. The programme was implemented by the Specialized Palliative Care Service. The programme was proposed to 19 physicians from 2 departments.

Results

The different components of the training course were identified, and a set of quality indicators was developed. The TtT programme was implemented; all the physicians attended the lesson, videos, and role-playing sessions. Only 25% of the physicians participated in the bedside training. It was more challenging to involve Haematology physicians in the programme.

Conclusions

The programme was completed as established for one of the two departments in which it was piloted. Thus, in spite of the good feedback from the trainees, a re-piloting of a different training program will be developed, considering in particular the bed side component.

The program should be tailored on specific communication attitude and believes, probably different between different specialties.

Keywords

palliative care; communication training; oncology; complex intervention

Background

There is widespread agreement on the importance of communication skills training (CST) for healthcare professionals caring for cancer patients.[1,2] The literature indicates that

honest and open communication with cancer patients can improve adherence to treatment programmes[3,4] and lead to benefits for physicians.[4-6] Conversely, poor communication leaves patients alone with their worries and anxiety,[7] while professionals become more prone to dissatisfaction and burnout.[8]

As highlighted in a number of studies, physician-patient communication can be effectively learned and improved through specific training programmes [2,9-19]. Nevertheless, the transferability of trainees' acquired competences to the clinical setting is difficult for range of reasons:

- CST are usually intensive residential programmes held outside trainees' workplaces and attended by participants from different work environments and setting
- CST are usually implemented by psychologists or experts from psychiatry and behavioural sciences who, de facto, are not directly involved in physician-patient communications
- experiential learning techniques usually employed within these training, such as role playing with peers or trained actors, are not real encounters with real patients, which included in only a minority of programmes.

As many difficult conversations take place in hospitals, all health professionals should be trained to engage in them.

Any hospitals physician should be able to converse about a prognosis, the goals of treatment at the end of life and managing global suffering.[20] To achieve these objectives, a primary palliative care curriculum must be taught, and education about communication issues regarding advanced illness should be the starting point. It is widely documented that the development and implementation of a communication training course is necessary for generalist palliative care physicians to develop core competencies is this area.

Starting from limitations acknowledged by the literature about existing CST, we developed a novel communication training programme addressed to hospital physicians caring for oncologic patients with palliative care needs, conceived to be implemented inside participants' workplace (i.e. the hospital), held by specialized palliative care and including encounters with real patients among experiential learning techniques.

The SPIKES protocol, developed in USA with the aim of teaching communication skills at the end of life to medical oncology fellows, was the theoretical model that inspired the

programme [23] . It consists in a six steps protocol, each of which is associated with a specific skill (Setting up the interview, assessing the patients' Perception, obtaining the patients Invitation, giving Knowledge and information to the patients, addressing the patient Emotion, Strategy and Summary)

The training was developed, implemented, assessed and evaluated as a complex intervention[21,22] according to a phase 0-I of the Medical Research Council (MRC) framework[21,22].

Our paper describes the phases guiding this process:

- developing a communication training programme focused on hospital physicians caring for advanced cancer patients;
- developing an evaluation system to assess the quality of the implementation;
- launching and preliminarily assessing both the programme and the evaluation system

Methods

This is a mixed-method, Phase 0-I study that follows the MRC framework for the assessment of complex interventions.[21,22] According to this framework, it is useful to consider the process of development and evaluation of complex interventions as having several distinct phases. These can be compared with the sequential phases of drug development or may be seen as more iterative. Progression from one phase to another may not be linear. In many cases an iterative process occurs. Preliminary work is often essential to establish the probable active components of the intervention so that they can be delivered effectively during the trial. Identifying which stage of development has been reached in specifying the intervention and outcome measures will give researchers and funding bodies reasonable confidence that an appropriately designed and relevant study is being proposed.

The study was subdivided into three phases

Phase 1: developing the communication training programme

SPIKES protocol[23] was the theoretical model that inspired the programme. Besides, we performed a review of systematic reviews on existing communication training

programmes with a focus on oncology and palliative care. The PubMed, Embase, Cochrane Library CINHAL and Scopus databases were searched using the MeSH terms [cancer OR tumour OR neoplasm OR oncol*] AND [systematic] AND [communication skills OR communication strateg* OR communication training] for English language articles published until December 2015. An author (S.T.) reviewed the studies' titles and the abstracts. Screening for full texts was undertaken by two authors (S.D.L. and S.T.).
A sample of physicians who were potentially eligible for the training were preliminarily interviewed, with the aim of gathering information on their perceived training needs in this field and developing the programme accordingly. Interviewed physicians were 4 males and 2 females with a mean age of 52 years (range: 41-67) and an average professional experience of 25 years (range: 18-43). Interviews were analysed qualitatively through thematic analysis[66]. In table 1 interview's topic and questions are reported.

Phase 2: assessing the quality of the implementation

This phase was aimed at developing specific procedures to assess the consistency of the implementation process. A set of indicators was developed for a twofold purpose: the first was to assess whether the programme was delivered exactly as outlined and the second was to evaluate each component of the intervention. Thus, information on the objectives achieved or not achieved was collected for each component of the programme (table 2). The procedure included a semi-structured questionnaire on the perceived usefulness of the programme (table 3)

How helpful do you think the 4 components have been with regard to	Delivering bad news to patients and families, % quite/extremely	Exploring patient's concerns and wishes about illness, % quite/extremely	Building empathy, % quite/extremely
1) Lesson	100	86	86
2) Video screening	100	100	86
3) Role playing	86	100	100
4) Bed-side training	100	100	100

Table 3. Semi-structured questionnaire on the perceived usefulness of the TtT programme

Phase 3: assessing feasibility and implementation methods

This phase was aimed at assessing the feasibility of the implementation process within the hospital setting. Both the intervention and the procedure used to assess the quality of the implementation were implemented through a convenience sample of two hospital teams

We considered the programme feasible if:

a) the components of the training course were appropriately identified
b) the set of quality indicators was developed and implemented
c) the programme was completed as established for the two hospital departments.

Where feasibility was not achieved, the programme included interviews with trainees to detect difficulties and weaknesses of the programme itself. (table 4)

Topic	Physicians questions
Project involvement	Could you please tell me what you thought about this training program when you heard about it?
Expectations	What were your expectations in the project?
Perceived benefits/weakness	Regarding this project, could you please tell me what the strengths of this intervention were, according to your opinion? If it impacted on your usual job, how did it do? And what about its weakness?
Short report of the experience	Regarding this program, could you please tell me what do you remember about the lesson/the role play? Did you complete the training program in all its components?
Future suggestions	As health professional, could you please tell me any suggestions for future training program?

Table 4. Interview guide on physicians' difficulties in completing the programme

Population and context

The study was performed at the Arcispedale Santa Maria Nuova of Reggio Emilia. This is a 900-bed Italian research hospital, accredited as a Clinical Cancer Centre by the Organization of European Cancer Institutes (OECI). The Specialized Palliative Care Service (SPCS) is a specialized hospital-based unit with no beds whose mission is to perform clinical, training and research activities in palliative care. The unit was established in 2013, and at present, it includes two senior physicians and three advanced practice nurses, one of whom is devoted to training courses full-time. Psychologists from the hospital Psycho-Oncology Unit cooperate with the SPCS by holding clinical consultations and taking charge of SPCS staff training.

The training was overseen by the two palliative care physicians, the senior nurse specialized in training methodology from the SPCS, and three psychologists from the Psycho-oncology Unit. Based on prior experience in developing and leading communication courses in oncology and palliative care,[9,13,24,25] three of the training teachers (S.T., S.D. L and G. A) trained another palliative care physician (S. A.) before the beginning of the programme with the aim of providing her with the competencies needed to act as a teacher.

We proposed the programme to all physicians from the Medical Oncology and Haematology Departments. The Medical Oncology Department provides care for patients with advanced onco-haematological diseases. The department has 20 beds and four

physicians. The Haematology Department provides care to haematological patients at all disease stages. The department has 16 beds and 15 physicians. Trainees from both departments were senior physicians. Four were physicians from the Medical Oncology department, four from the Haematology ward, ten from the Haematology day care unit and one from the Haematology home care unit. Only one physician from the Medical Oncology Department had been previously involved in a training course in communication.

The study was approved by the Ethics Committee of Reggio Emilia on 12 June 2015 (n 861/12.6.2015) and was conducted in accordance with the Declaration of Helsinki.[65]

Data analysis

Phase 1

An author (S.T.) reviewed the studies' titles and the abstracts for the review of systematic review. Screening for full texts was undertaken by two authors (S.D.L. and S.T.).

The interviews with professionals before the implementation of the programme were recorded, transcribed, and analysed qualitatively with the objective of exploring in detail physicians' perceived training needs (table 5). Two researchers (ST and SDL) independently read the transcripts and categorized them into themes [66]. Any disagreement between the researchers was discussed, and a final categorization was determined.

Themes and subthemes	Representative quotations
Communication difficulties	
communicating the end of active therapy	"…Trying guide the patients through small steps toward their real situation [the end of curative treatments] is a sort of 'art of the relationship', to build through small steps" (Ph 2) "When you comes to this point [the end of curative treatments] there is a difficulty in transferring this information to the patient.. This conversation should be anticipated much earlier and not just when you stop the treatment" (ph 3)
Talking about prognosis	"Telling to a patient the prognosis ... There is always something to do but, from that precise moment, you start to lie ... Obviously, I can't say that there are four weeks of survival left! "(Ph 1) "Sometimes there is a sort of omission in communicating a poor prognosis to the hematological patient. This step can really missing… "(Ph 3) "Communicating the prognosis to a patient you have known for a long time. We always tend to show the glass half full… "(Ph 4)
Handling interference from relatives	"There are family members who 'overturn' the suffering of their loved one not to the disease but the work of health professionals" (ph 1) "Situations in which there is an oppositive behavior or even an aggression by family members, and these become the cases that are most difficult to manage" (Ph 2) "Families who do not give up, who cannot cut this sort of umbilical cord that unites them with their loved one…" (Ph 3) "The relative who continues to search and ask for treatments even when things are over" (Ph 5)
Source of communication competencies	
experience	I have to say that age and experience help me, so it is easy for me knowing both advanced cancer patient's previous history and how that history will continue in the future. Therefore, I can also 'touch' the sensitive points of what that patient would like to be told, to know… "(Ph 1) "It seems to me that I have absorbed some communication techniques ... I would not seem presumptuous" (Ph 2) "Our thirty years of experience, in my opinion, is enough! "" (Ph 6)
collaboration with colleagues	"In some situations, your resources are not enough. Then you ask for help to other specialists who will be the psychologist, or the palliative care physician, or your collaborators and colleagues" (Ph 1) "I learned communication from briefings, structured meetings, meetings with colleagues on more complex cases" (Ph 3) "The confrontation with our team ... with the psychologist" (Ph 4) "We improved in keeping a common line when we communicate with patients, and this helps " (Ph 5) "
personal attitude	"Patients and relatives confirm that I can establish a fairly empathic relationship with them. This probably derives from my previous training, from my personality, from my capacity of getting understandably and easily certain speeches" (Ph 2)" "Surely there is an attitude allowing me to easily establish relationship with patients ... an ability to listen to them ... an attitude in understanding them... adaptability ... sensitivity ... "(Ph 1)
Expectations toward the training	
becoming more empathetic	"Knowing how to leave a little hope even in the face of bad news" (Ph 6) "Knowing how to give more consolation when the epilogue cannot be favorable"(Ph 1)
improving communication with colleagues	"Knowing how to listen more my colleagues, other operators. The clinical eye of the nurse for example "(Ph 3) "Improving communication between operators" (Ph 5)
experiencing less stress	"Approaching myself in a less stressful way in the face of these bad communications that we have to deliver every day" (Ph 4)

Table 5. Themes, sub-themes and representative quotations from qualitative analysis of 6 physicians' interviews

Phase 2

An overview of the objectives achieved and not achieved for each component of the implementation of the programme was obtained through an analysis of the pilot implementation process (table 2). The answers to the semi-structured questionnaire about the perceived usefulness of each component of the programme (table 3) were analysed by means of descriptive statistics. The usefulness of each component (i.e. lesson, videoscreening, role playing, bed-side training) was assessed by considering the three main objectives of the training (i.e. delivering bad news, exploring patients' concerns and supporting them and building empathy).

Phase 3

The interviews with professionals concerning difficulties encountered by physicians in completing the implementation process (table 4) were recorded, transcribed, and analysed qualitatively with the objective of exploring in detail reasons related to problems with training completion (table 6). ST and SDL independently read the transcripts and categorized them into main themes according to the objective of the evaluation. Any disagreement between the researchers was discussed, and a final categorization was determined.

Results

Phase 1: developing the communication training programme

The literature review

The literature review selection process is summarized in the PRISMA diagram (Figure 1). The search identified 87 records. A total of 61 duplicates were removed, and 43 abstracts were excluded due to ineligibility. Fifteen systematic reviews of CST in oncology and palliative care were included in our review[14,26-39]

The following recommendations arose from the analysis of the retrieved papers:

- Communication training should be developed and delivered by professionals with both skills and expertise in the field. Facilitators should practice the skills they learn.[31,38,40]
- Courses should be addressed to small groups of professionals (4-6 persons).[40]
- Successful training courses should last at least one day, although there is evidence that the best results come from training courses conducted over a longer period.[27,30,32,36,37]
- Follow-up sessions are also indicated as a promising strategy aimed at reinforcing and maintaining acquired skills over time.[17,37,40]
- Courses should be learner-centred and practice-oriented and should use a combination of didactic and experiential methods,[27,30,32-34,40,41] such as role playing.[17,27,33-35,38,42]

The interviews with physicians

A convenient sample of 6 out of 19 physicians participating in the programme were interviewed one month before the implementation of the training course to collect their perceived training needs and consequently tailor the contents of the course to them. The major difficulties reported by the trainees concerned three topics: communicating the end of active therapy, talking about prognosis and handling interference from relatives with physicians' choices with regard to communication with patients about illness. The interviewees considered their communication competencies derived from either field experience, collaboration with colleagues, and nurturing personal attitudes such as sensitivity. Becoming more empathetic in communicating hope, improving communication with colleagues and experiencing less stress and emotional involvement during difficult conversations with patients and their relatives were the interviewees' expectations regarding the course (Table 1 and 5).

Topic	Question
Training needs	Could you please tell me which are your major difficulties in communicating bad news to advanced cancer patients and their relatives? Can you please give me any specific examples? According to your opinion which are the major difficulties of your colleagues?
Perceived self-strengths/resources	Regarding your difficulties in bad communication, could you please tell me what are the strengths of your communication, according to your opinion?
Expectations about the training program	Could you please tell me which are your expectations about the training program?

Table 1 : interview topic guide of training needs

The Teach to Talk programme

According to the literature, existing programmes suffer from a number of limitations: courses are usually residential and are implemented for trainees from different work environments, experiential learning techniques based on role playing with actors make use of simulated scenarios that are very different from real encounters with patients and relatives, facilitators are not directly involved in clinical practice, and training courses are not implemented within the real contexts in which physicians communicate with patients. Considering both the recommendations and criticisms raised from the literature review as well as the difficulties that emerged from the analysis of the interviews with physicians, we developed a novel intervention named“Teach to Talk” (TtT) training programme. The key features of the programme are the following:

1. the programme is implemented within the participants’ hospital ward, i.e., in the context in which participants are required to practice the communication skills they are learning;
2. the programme includes peer to peer role playing;
3. the programme includes bedside sessions with real patient encounters;
4. teachers are professionals from the hospital SPCS. They are supported by professionals with a psychosocial background, such as psychologists or counsellors.

Inspired by the contents of the SPIKES protocol, the “Teach to Talk” (TtT) programme is aimed at improving physicians’ competencies in the following three broad areas: 1) delivering bad news, 2) exploring patients’ concerns and supporting them, and 3) building empathy.

The SPCS delivers the intervention in five components: video screening, didactic lesson, role playing, bedside training and follow-up. The TtT components as well as the procedures concerning their implementation are described in detail in Box 1.

Phase 2: Quality assessment of the programme

The procedure to assess the quality of the programme included a list of indicators covering all of its components (see Table 2). With reference to the lesson, videos, role playing and bedside sessions, a 75% minimum attendance rate was estimated by researchers to be reasonable, which is consistent with the study aims. The time spent by the facilitators teaching the training course was also recorded

Dimension	Rationale	Indicators	Expected standard
General training in palliative care	A basic training on palliative care is necessary to educate the future trainees on palliative care topics (e.g., communication)	Proportion of ward physicians attending the 4-hour basic training	100%
Request to receive the communication training	A perceived need that training in communication is important for changing future behaviour	Call from the head of the department for communication training	Requested
Developing the documentation for the training	Specific documentation is mandatory	Received the documentation	Received
Didactic lesson	Little basic knowledge on delivering bad news is necessary	Proportion of ward physicians attending the didactic lesson	75% of the participants attend the didactic lesson
Videos	An overview of and a preliminary discussion on different teaching methods prepare students for the didactic lesson	Proportion of ward physicians participating in the video sessions	100%
Role playing	Experiential learning as role playing improve behavioural changes in trainees	Proportion of ward physicians attending at least 2 role playing sessions; proportion of ward physicians performing in at least 2 role playing sessions, at least one as a patient/relative and one as the physician	75%;75%
Bedside trainings	Real-life training improves participants' awareness of their communication style	Proportion of ward physicians attending at least 3 bed-side sessions	75% of the participants attend the bed-side training
Semi-structured questionnaire on the perceived usefulness of the programme	A self-evaluation of the usefulness of the training components can improve both the structure and contents of the programme	Proportion of physicians attending the whole programme and completing the questionnaires	100%
Bedside training follow up	Follow-up sessions control and re-enforce the maintenance over time of the training course	Proportion of ward physicians performing at least 2 bed-side session follow ups	75%

Table 2: quality indicators

Phase 3: Preliminary assessment of the programme: the evaluation system

The heads of the two departments and all 19 physicians from the two departments agreed to participate in the programme (table 7). The intervention was implemented between

December 2015 and June 2017.These stages are planned as shown in the Gantt Diagram (Table 8).

Department	Sex (male:female)	Age (years) Average	work experience (years) Average
Medical Oncology			
	2:2	56 (47-67)	27 (12-43)
Haematology			
	10:5	46 (36-60)	16 (4-32)

Table 7. Participants demographic characteristics

Tab 8. the Gantt diagram of the TtT training programme

Department	Theoretical lesson	Role Play	Bed Side	Follow up bed side
Medical oncology Department	November 2015	December 2015	December 2015	December 2015-January 2016
Hematology Department	January 2017	February 2017	February-June 2017	Not done

Table 9 summarizes the main findings of the pilot study. The staff from both wards had previously attended general palliative care training.

Dimensions	Medical Oncology Department	Haematology Department
General training in palliative care	100%	100%
Request to receive the communication training	Requested	Requested
Developing the documentation for the training	Received	Received
Didactic lesson	100%	100%
Videos	100%	100%
Role playing	100%	100%
Bedside trainings	100%	6% (1/15)
Semi-structured questionnaire on the perceived usefulness of the programme	100%	20% (3/15)
Bedside training follow up	75% (3/4)	0%

Table 9 The results of the TtT programme

After requesting communication training from the SPCS, these staff members were duly contacted to schedule the preliminary assessment of the participants' needs for communication training. The issues raised during the interviews were used as a framework to prepare both the lesson and the role-playing sessions. Other topics from the emotional domain were also considered.

The SPCS prepared the documentation for both the lesson and the role-playing session, as established at the outset. As was laid out in the programme, the training was conducted entirely in the participants' work environment in small groups. Both the lesson and the role-playing sessions were attended by all the participants. The goals to be achieved during the role playing were changed from those set out in the protocol because the researchers decided to use clinical examples proposed by the trainees. The staff from Medical Oncology completed the entire programme, while those from Haematology completed only part of the programme. Indeed, only one physician completed the entire programme in six months. Four did not perform any bedside training sessions. For two of staff members, the trainers did not deem it to be useful for them to complete three bedside training sessions, and the competences they had acquired were judged to be sufficient by the trainers. One physician completed the entire training. The remaining 8 physicians performed only one bed side session.

In addition to the training, follow-up was performed, as established by the programme, by only 3 physicians from the Medical Oncology Department.

The results from the semi-structured questionnaire administered to the physicians who completed the training showed that all the components, particularly the role playing and bedside training sessions, were evaluated as useful or very useful by participants.

Both the didactic lesson and the role-playing sessions were jointly conducted by a palliative care physician from the SPCS and a psychologist from the Psycho-oncology Unit. The synergic approach of the facilitators guaranteed a sort of double perspective in guiding the trainees, both in relation to learning and using appropriate communication skills and to recognizing and managing difficult emotions. Throughout the implementation of the programme, physicians facilitating the bedside training sessions were constantly supervised by the psychologists involved in the project and by a senior nurse training expert. A portfolio was used as a guide to the supervision process.

Findings from the interviews with the four physicians who did not request bedside sessions provide insights into criticisms concerning the implementation of this component, as well as on their comprehensive view on the training. Following, themes emerged from qualitative analysis are briefly described, representative quotations for each theme are reported in table 6.

Themes	Representative quotations
Global feedback on the training	"The only thing was my discomfort facing other people during role play I think that role play should be avoided in the presence of other colleagues. [...] Observer teachers are one thing, because they have to help you see some mistakes, your colleagues are another thing. "(Ph 1) "It was difficult ... Not so much when you play your part but when we analysed things ... Everyone has difficult cases outstanding ... It was difficult to cope with the return to the memory of cases that I had not yet worked out". (Ph 4) "I remember that during the theoretical lesson S.T. [the teacher] stated that we must be able to highlight with the patient the end of his/her life… and that we have to do this in a very clear way… which is something that I do not agree because… at the end you always have to give hope to the patient. Besides, our patients already know when their time has come, so there's no point in stressing it. Then if we want to underline it with family members, that's due! " (Ph 1) "I remember the role plays very well. […] Role plays have impressed me a lot. I don't remember anything in particular about the theoretical lesson ... "(Ph 3)
Organizational issues	"Also palliative care physicians have a number of things to do, and this could be a limitation…" (Ph 4) "With reference to the training, I think that It should be planned having in mind both the characteristics of haematological patients and our great workload" (Ph 2).
Misunderstandings about the structure of the programme	Interviewer "May I ask you if you have completed all the communication training? Did you carry it out in all its parts?" […] Ph 1: "Yes, I did. I had one problem only… My distress in front of other persons, during the role-playing sessions…" "It was a training including either a theoretical, a practical and a field component. I still have to achieve this part because when I needed to communicate some kind of diagnosis, I could not arrange for a meeting with S. [the trainee]. Thus, I still have to do it. I will call S.T. when I will have to communicate a 'bad' diagnosis". (Ph 3)
Problems in detecting the "right" situation	" I could not attend the bedside sessions because I needed to communicate an illness diagnosis, thus S.T. said that I should call her when I had to perform a truly difficult communication!" (Ph 4) ""Our patients can get worse from one moment to the next, so you make a good plan but ... it's hard to keep up with this!" (Ph 1)

Table 6 - Themes and representative quotations from qualitative analysis of interviews with physicians who did not complete the training

Global feedback on the training: Two physicians expressed some discomfort in participating to role plays, emphasizing in one case a feeling of embarrassment to be observed by colleagues and in the other an unpleasant sensation of arousal linked to the memory of some emotionally demanding relationships with patients. One physician reported on her disappointment toward a message acknowledged during the theoretical lesson, concerning the relevance of communicating to patients a poor prognosis. On the whole, interviewed physicians highlighted that the educational value of role plays and videos was greater than that of the theoretical lesson.

Organizational issues: Some participants referred to practical difficulties in predicting when they have the time to engage themselves in a critical communication with a patient concerning, for example, the end of the active provision of treatment. Problems also emerged because, according to interviewed physicians' opinion, the trainers themselves were very busy with their clinical activities.

Misunderstandings about the structure of the programme: One physician was convinced she had completed the entire training course, while another was still trying to arrange an encounter with the trainer.

Problems in detecting the "right" situation: A physician explained that, during the training, she had to communicate bad news concerning only illness diagnosis, a task perceived as less challenging and difficult than communicating a poor prognosis. Another physician highlighted her difficulty in knowing in advance whether she should have to cope with a difficult communication scenario due to rapid changes in patients' condition

Discussion

This study focused on the development of a communication training programme, indicators of the fidelity of the implementation, the different components of the intervention and its preliminary assessment. The programme was completed as established for one of the two departments in which it was piloted; for the Haematology department, bedside training and the consequent follow-up sessions were missing. Thus, in spite of the high perceived utility expressed from the trainees, major changes are needed to ensure the feasibility of this training program.

We developed our intervention and included all the components evaluated as essential in the last ASCO statements.[43] We chose to offer only one lesson, which was attended

by all the participants from both wards, and we used role-playing between peers to allow for safe interaction between colleagues within the small-group setting and peer-reviewed the feedback, which a number of studies stated were effective tools.[35,44-52] This approach was also highlighted in our pilot study, where participants evaluated the role playing sessions in which they took part as highly useful.

Regarding the bedside training, recent studies[53,54] have suggested and proved the importance of coaching after didactic modules because of its focus on individual learning goals and the possibility of tailoring training to personal weaknesses. One-to-one coaching by palliative care physicians was also the main tool used in the study by Clayton et al.[54] on a group of voluntary, junior doctors. Satisfaction with the course was expressed by the participants, but only one-third of the participants saw improvement in their communication skills.

In our pilot study, most physicians from the Haematology ward did not receive this coaching session (bedside training), even though there had been a formal request by the heads of the ward to participate in the training and the training met the specific needs expressed by physicians during the preliminary need assessment.

Two main reasons could explain the major limitation of our training programme: first, haematologists must address organizational issues, as declared in some interviews; second, theoretical and cultural issues underlying the haematologists' concept of palliative care and the palliative care approach should be taken into account as contributory factors.

The Teach to Talk programme has been implemented since 2015 by an SPCS inside the hospital. The interaction with the Haematology ward is well documented by the increasing number of year-to-year consultation requests. Interaction between palliative care and haematology has been explored by recent literature. Although the value of palliative care is recognized by haematologists, there still seems to be resistance to the reality and practicalities associated with the referral of haematologic patients to palliative care services.[55]

In literature a great amount of evidence underscores the difficult of hematologists to recognize patients' poor prognosis and talk with them about it:[67-69] in the study by Alexander, a lack of patients' involvement in decision about treatment, as well a tendency to avoid prognostic discussion emerge in the analysis of video recorded real encounters with patients. Hematologists participants in a qualitative research[55] acknowledge taking a paternalistic approach towards certain decisions and explained their therapeutic

optimism in order to bolster patients in toxic but curative treatments. The intention 'not to give up' was strengthened by the intense physician-patient relationship and by the unpredictable nature of the treatment itself.[55] The hematologic patient is described differently from the oncologic one for the no predictable disease's trajectory,[69,70] thus, the right moment to share a bad communication could be not so clear.

These difficulties were similar with problems raised by the haematologists in our study, for instance, with regard to the appropriate time to communicate with patients regarding the turning point of an illness (e.g., the end of active treatment or disease leading to poor prognosis). An international trial by Szekendi et al.[56] highlighted the impact of embedding a palliative care team with a selected non-palliative care service: non-palliative care physicians report an increase in comfort as well as in their skills in conducting care conversations.

As far as we know, few training courses in communication are addressed to haematologists and thus focus on their specific communication needs.[57] At the same time, communication remains a challenge for haematologists. Formal communication skills training and target interventions for patients with haematologic malignancies by palliative care staff have been called for by some authors.[58,59]

We developed a set of indicators to assess the quality of the implementation. We propose to take these indicators into account in every setting to expedite implementation. In particular, we believe the preliminary stages (general training in palliative care, requests to receive the communication training, communication need assessment) to be mandatory to improve core competencies in basic palliative care for other professionals.

Findings from this study need to be interpreted by acknowledging some limitations. We have initiated the programme at only one clinical cancer centre. Nevertheless, we launched our project within a coherent methodological framework. This approach involved the recommendation to assess the local feasibility of complex interventions so the project can be amended as necessary and evaluated on a larger scale.

The results of this study strongly suggest the need for developing a revised version of the TtT programme. In hospital settings, the duration of the intervention should be longer than eight weeks, depending on the specific characteristics of the ward in which it is implemented (e.g., number of physicians, professionals' training needs, frequency of bad news communication, organization of work). The number of bedside sessions per participant should be determined on the basis of the competencies acquired by single participants throughout the training in accordance with the facilitator's judgement.

Bedside sessions should be scheduled a priori with facilitators rather than self-managed by participants because self-management, an active and proactive behaviour, may facilitate concrete change in communication attitudes.

Conclusions

In the last ten years, research from the literature emphasized that training in communication skills is not enough to bring about real change in professional attitudes.[19,26,60,61] We implemented an educational intervention with a well-integrated palliative care team in order to overcome limitations of existing residential training programmes and to impact communicative behaviour in the contexts where professionals actually work. However, major changes are needed to ensure the feasibility of this training programme.

Turrillas et al.[62] argue that the most effective training method should be tailored to the environment and context. A re-piloting of a different training program will be developed, considering in particular the bed side component.

Moreover the program should be tailored on specific communication attitude and believes, probably different between different specialties as emerged in our interviews to haematologists. [4]

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[4] **Declarations**

Ethics approval and consent to participate

The study involves a specific information note and a consent form with the relevant resolution of the data. Informed written consent was obtained from all participants.

The approval of this study was subject to the opinion of the Provincial Ethics Committee of Reggio Emilia Comitato Etico di Area Vasta Emilia Romagna Nord (AVEN), in consideration of the Protocol, the privacy policy, the relative informed consent forms, the interview used in the and the questionnaire addressed to the professionals.

The study was approved by the Ethics Committee on 12 June 2015 (n 861/12.6.2015)

References

1. Block SD and Billings JA. A need for scalable outpatient palliative care interventions. Lancet 2014; 383: 1699–1700.
2. Stiefel F, Kiss A, Salmon P, et al. Training in communication of oncology clinicians: a position paper based on the third consensus meeting among European experts in 2018. Ann Oncol 2018; 29: 2033–2036.
3. Banerjee SC, Matasar MJ, Bylund CL, et al. Survivorship care planning after participation in communication skills training intervention for a consultation about lymphoma survivorship. Transl Behav Med 2015; 5: 393–400.
4. Bialer PA, Kissane D, Brown R, et al. Responding to patient anger: development and evaluation of an oncology communication skills training module. Palliat Support Care 2011; 9: 359–365.
5. Fujimori M, Shirai Y, Asai M, et al. Development and preliminary evaluation of communication skills training program for oncologists based on patient preferences for communicating bad news. Palliat Support Care 2014; 12: 379–386.
6. Gattellari M, Ward JE and Solomon MJ. Randomized, controlled trials in surgery: perceived barriers and attitudes of Australian colorectal surgeons. Dis Colon Rectum 2001; 44: 1413–1420.
7. Donovan-Kicken E and Caughlin JP. Breast cancer patients' topic avoidance and psychological distress: the mediating role of coping. J Health Psychol 2011; 16: 596–606.
8. Shanafelt T and Dyrbye L. Oncologist burnout: causes, consequences, and responses. J Clin Oncol 2012; 30: 1235–1241.
9. Baile WF, De Panfilis L, Tanzi S, et al. Using sociodrama and psychodrama to teach communication in end-of-life care. J Palliat Med 2012; 15: 1006–1010.
10. Costantini A, Baile WF, Lenzi R, et al. Overcoming cultural barriers to giving bad news: feasibility of training to promote truth-telling to cancer patients. J Cancer Educ 2009; 24: 180–185.
11. Lenzi R, Baile WF, Costantini A, et al. Communication training in oncology: results of intensive communication workshops for Italian oncologists. Eur J Cancer Care (Engl) 2011; 20: 196–203.
12. Lamiani G, Meyer EC, Leone D, et al. Cross-cultural adaptation of an innovative approach to learning about difficult conversations in healthcare. Med Teach 2011; 33: e57–64.
13. Morasso G, Caruso A, Belbusti V, et al. Improving physicians' communication skills and reducing cancer patients' anxiety: a quasi-experimental study. Tumori 2015; 101: 131–137.
14. Gysels M, Richardson A and Higginson IJ. Communication training for health professionals who care for patients with cancer: a systematic review of effectiveness. Support Care Cancer 2004; 12: 692–700.
15. Maguire P, Faulkner A, Booth K, et al. Helping cancer patients disclose their concerns. Eur J Cancer 1996; 32a: 78–81.

16. Kiss A. Communication skills training in oncology: a position paper. Ann Oncol 1999; 10: 899–901.
17. Fallowfield L, Jenkins V, Farewell V, et al. Enduring impact of communication skills training: results of a 12-month follow-up. Br J Cancer 2003; 89: 1445–1449.
18. Fallowfield L, Jenkins V, Farewell V, et al. Efficacy of a cancer research UK communication skills training model for oncologists: a randomised controlled trial. Lancet 2002; 359: 650–656.
19. Stiefel F, de Vries M and Bourquin C. Core components of communication skills training in oncology: a synthesis of the literature contrasted with consensual recommendations. Eur J Cancer Care (Engl) 2018; 27: e12859.
20. Quill TE and Abernethy AP. Generalist plus specialist palliative care--creating a more sustainable model. N Engl J Med 2013; 368: 1173–1175.
21. Campbell M, Fitzpatrick R, Haines A, et al. Framework for design and evaluation of complex interventions to improve health. BMJ 2000; 321: 694–696.
22. Campbell NC, Murray E, Darbyshire J, et al. Designing and evaluating complex interventions to improve health care. BMJ 2007; 334: 455.
23. Baile WF. Buckman R, Lenzi R et al SPIKES-A six step procol for delivering bad news:application to the patients with cancer. Oncologist 2000; 5:302–311.
24. Tanco K, Rhondali W, Perez-Cruz P, et al. Patient perception of physician compassion after a more optimistic vs a less optimistic message: a randomized clinical trial. JAMA Oncol 2015; 1: 176–183.
25. Priami D, Sollami A, Vivoli V, et al. Tutorship process in health care professions: a survey investigation in Emilia Romagna. Acta Biomed 2015; 86 Suppl 2: 97–103.
26. Barth J and Lannen P. Efficacy of communication skills training courses in oncology: a systematic review and meta-analysis. Ann Oncol 2011; 22: 1030–1040.
27. Gysels M, Richardson A and Higginson IJ. Communication training for health professionals who care for patients with cancer: a systematic review of training methods. Support Care Cancer 2005; 13: 356–366.
28. Gysels M and Higginson IJ. Interactive technologies and videotapes for patient education in cancer care: systematic review and meta-analysis of randomised trials. Support Care Cancer 2007; 15: 7–20.
29. Uitterhoeve RJ, Bensing JM, Grol RP, et al. The effect of communication skills training on patient outcomes in cancer care: a systematic review of the literature. Eur J Cancer Care (Engl) 2010; 19: 442–457.
30. Ong LM, de Haes JC, Hoos AM, et al. Doctor-patient communication: a review of the literature. Soc Sci Med 1995; 40: 903–918.
31. Moore PM, Rivera Mercado S, Grez Artigues M, et al. Communication skills training for healthcare professionals working with people who have cancer. Cochrane Database Syst Rev 2013; 7: CD003751.
32. Berkhof M, van Rijssen HJ, Schellart AJ, et al. Effective training strategies for teaching communication skills to physicians: an overview of systematic reviews. Patient Educ Couns 2011; 84: 152–162.
33. Libert Y, Conradt S, Reynaert C, et al. Improving doctor's communication skills in oncology: review and future perspectives. Bull Cancer 2001; 88: 1167–1176.

34. Rao JK, Anderson LA, Inui TS, et al. Communication interventions make a difference in conversations between physicians and patients: a systematic review of the evidence. Med Care 2007; 45: 340–349.
35. Lane C and Rollnick S. The use of simulated patients and role-play in communication skills training: a review of the literature to August 2005. Patient Educ Couns 2007; 67: 13–20.
36. Lannen P and Barth J. Do communication skills trainings improve behavior, attitude and patient outcomes equally? Evidence from a systematic review and metaanalysis. Psychooncology 2009; 18: S103.
37. Fellowes D, Wilkinson S and Moore P. Communication skills training for health care professionals working with cancer patients, their families and/or carers. Cochrane Database Syst Rev 2004: CD003751.
38. Bialer PA, Gilewski T, Kissane D, et al. The development and implementation of an institution-based communication skills training program for oncologists. J Clin Oncol 2010; 28: 9128.
39. Walsh RA, Girgis A and Sanson-Fisher RW. Breaking bad news. 2: what evidence is available to guide clinicians? Behav Med 1998; 24: 61–72.
40. Stiefel F, Barth J, Bensing J, et al. Communication skills training in oncology: a position paper based on a consensus meeting among European experts in 2009. Ann Oncol 2010; 21: 204–207.
41. Back AL, Arnold RM, Baile WF, et al. Faculty development to change the paradigm of communication skills teaching in oncology. J Clin Oncol 2009; 27: 1137–1141.
42. Aspegren K. BEME Guide No. 2: teaching and learning communication skills in medicine-a review with quality grading of articles. Med Teach 1999; 21: 563–570.
43. Gilligan T, Coyle N, Frankel RM, et al. Patient-clinician communication: American society of clinical oncology consensus guideline. J Clin Oncol 2017; 35: 3618–3632.
44. Nestel D and Tierney T. Role-play for medical students learning about communication: guidelines for maximising benefits. BMC Med Educ 2007; 7: 3. DOI: 10.1186/1472-6920-1187-1183.
45. Jackson VA and Back AL. Teaching communication skills using role-play: an experience-based guide for educators. J Palliat Med 2011; 14: 775–780.
46. Wearne S. Role play and medical education. Aust Fam Physician 2004; 33: 858.
47. Coyle N, Manna R, Shen M, et al. Discussing death, dying, and end-of-life goals of care: a communication skills training module for oncology nurses. Clin J Oncol Nurs 2015; 19: 697–702.
48. Epner DE and Baile WF. Difficult conversations: teaching medical oncology trainees communication skills one hour at a time. Acad Med 2014; 89: 578–584.
49. Brown B. AFC handbook: worth a look. Community Pract 2010; 83: 42–43.
50. Luttenberger K, Graessel E, Simon C, et al. From board to bedside - training the communication competences of medical students with role plays. BMC Med Educ 2014; 14: 135.
51. Tai J, Molloy E, Haines T, et al. Same-level peer-assisted learning in medical clinical placements: a narrative systematic review. Med Educ 2016; 50: 469–484.

52. Tai JH, Canny BJ, Haines TP, et al. Implementing peer learning in clinical education: a framework to address challenges in the "real world". Teach Learn Med 2017; 29: 162–172.
53. de Figueiredo MN, Rudolph B, Bylund CL, et al. Erratum to: ComOn coaching: study protocol of a randomized controlled trial to assess the effect of a varied number of coaching sessions on transfer into clinical practice following communication skills training. BMC Cancer 2015; 15: 596.
54. Clayton JM, Adler JL, O'Callaghan A, et al. Intensive communication skills teaching for specialist training in palliative medicine: development and evaluation of an experiential workshop. J Palliat Med 2012; 15: 585–591.
55. Wright B and Forbes K. Haematologists' perceptions of palliative care and specialist palliative care referral: a qualitative study. BMJ Support Palliat Care 2017; 7: 39–45.
56. Szekendi MK, Vaughn J, McLaughlin B, et al. Integrating palliative care to promote earlier conversations and to increase the skill and comfort of nonpalliative care clinicians: lessons learned from an interventional field trial. Am J Hosp Palliat Care 2018; 35: 132–137.
57. Christie D and Glew S. A clinical review of communication training for haematologists and haemato-oncologists: a case of art versus science. Br J Haematol 2017; 178: 11–19.
58. Odejide OO, Cronin AM, Condron NB, et al. Barriers to quality end-of-life care for patients with blood cancers. J Clin Oncol 2016; 34: 3126–3132.
59. Epstein AS, Goldberg GR and Meier DE. Palliative care and hematologic oncology: the promise of collaboration. Blood Rev 2012; 26: 233–239.
60. Bousquet G, Orri M, Winterman S, et al. Breaking bad news in oncology: a metasynthesis. J Clin Oncol 2015; 33: 2437–2443.
61. Verma A, Griffin A, Dacre J, et al. Exploring cultural and linguistic influences on clinical communication skills: a qualitative study of international medical graduates. BMC Medical Education 2016; 16: 162.
62. Turrillas P, Teixeira MJ and Maddocks M. A systematic review of training in symptom management in palliative care within postgraduate medical curriculums. J Pain Symptom Manage 2019; 57: 156–170.e4.
63. Artioli G, Bedini G, Bertocchi E et al Palliative care training addressed to hospital healthcare professionals by palliative care specialists: a mixed-method evaluation.BMC Palliat Care 2019;Oct 26;18 (1):88
64. Tanzi S, Di Leo S, Mazzini E, Castagnetti M. Turrà C, Peruselli C, Costantini M. Long-term sustainability of a quality improvement program on cancer pain management: a complex intervention in an inpatient setting. Tumori. 2019;Aug 28 [epub ahead of print]
65. http://www.wma.net/e/policy/b3.htm
66. Virginia Braun & Victoria Clarke (2006) Using thematic analysis in psychology, Qualitative. Research in Psychology, 3:2, 77-101
67. Alexander S, Sullivan M, Back A et al Information giving and receiving in hematological malignancy consultations. Psyco-oncology 2012;21: 297-306

68. Chhabra K, Pollak K., Lee S. Physician communication styles in initial consultation for hematological cancer. Patient education and counselling 2013;93; 573-578.
69. Manitta V, Philip J, Cole Sinclair M Palliative care and the hemato-oncological patient: can we live togheter? A review of the literature. J Pal Med 2010;13:1021-25
70. Roeland E, Ku Grace Spanning the canyon between stem cell transplantation and palliative care Palliative care in Haematological malignancies. Hematology 2015.484-489

Not just a matter of skills: an ethnographic study on breaking bad news in hematology[5]

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ABSTRACT

Objective: To explore the behavior of hematologists during difficult conversations and provide new insights regarding how to teachs kills to communicate bad news.

Methods:This study used focused visual ethnography (FE). The research question was, “what are hematologists’ behavioral patterns in communicating bad news to patients and families?” The FE was performed during training on communication using role playing and bedside sessions.

The collected data included 1) video recordings of role-playing sessions; 2) observational field notes (FNs) taken during bedside sessions; and 3) interviews with hematologists after the end of the training.

Results: The analysis highlighted 4 cross-cutting categories of behaviors: 1) a defensive technical pattern, 2) an authoritative pattern, 3) a relational-recursive pattern, and 4) a compassionate sharing pattern. Based on triangulation of the data, we concluded that the major difference between the simulated data and the real-life events during the bedside sessions involved the compassionate sharing pattern; the hematologists had difficulty expressing compassionate caring and empathetic comprehension.

Discussion: Communication skills remain a challenge for hematologists. Fostering personalized communication with patients could help them feel less uncertain about difficult issues.

Practical value: The study of behavioral patterns can lead to increasingly targeted training interventions for specific learner populations.

Introduction

Patients with hematological malignancies are unique in terms of the challenges they face during their illness until the end of their life, as the trajectory of the disease is irregular and unpredictable [1,2]. In addition, the severity of a hematological malignancy diagnosis also heavily depends on the medical team involved, who typically develop close and long-term relationships with their patients [3], which may affect their communication behavior. Therefore, the right conditions (related to timing and the doctor-patient relationship) in which to share bad news may not be so clear.

In the literature, many studies have shown the difficulties hematologists have with recognizing the poor prognosis of patients and disclosing that information to them [1,4,5]; discrepancies between the hematologists' communication of the prognosis and the patients' understanding have also been highlighted [6]. Several factors limiting patient-centered communication in the hematology-oncology context have been investigated: insufficient information exchange, the misalignment of treatment goals, and discordant role preferences in treatment decision making [7].

Hematologists working with hematological malignancies in particular need to practice good communication skills. These include sharing bad news and helping patients and families negotiate difficult decisions [8]. According to Wright [9], hematologists participating in past qualitative research have acknowledged that they take a paternalistic approach towards certain decisions and explain their therapeutic optimism in order to support patients during toxic but curative treatments. The intention to 'not give up' is reinforced by intense doctor-patient relationships and the unpredictable nature of the treatment itself. Furthermore, the therapeutic possibilities allow doctors to think, "Maybe we can pull another 'rabbit out of the hat'", given the possibilities offered by different therapeutic lines [10].

Strategies such as effective communication of patients' prognosis and the integration of palliative care (PC) for patients with hematological malignancies may improve their quality of life and care [11].

Training hematologists in communication skills is a way to help them meet their specific communication needs, but courses on the topic seem to be rare [8]. Some researchers have called for formal training in communication skills and targeted interventions for patients with hematologic malignancies from PC staff [3,12].

Since there is room for improvement in communication in hematology, in 2015, we implemented a training on communicating bad news [13]. This study aimed to explore the behavior of hematologists in difficult conversations during both this specific training and in real-life situations.

Methods

Methodological approach

We applied an ethnographic approach previously used by Ng et al. for studying health professionals' education and practice [14]. Using this approach, we employed a specific method called focused ethnography(FE) [15]; it entails entering the field with a defined research question [14], undertaking fieldwork in a short timeline [16], and restricting the field of enquiry to a specific phenomenon within a planned event with key informants [17]. As a consequence, its results do not entail lengthy records but instead produce rather direct and short reports, providing insights into the narrow research focus [16]. Visual data plays an important part in the present FE [18], connecting it with visual ethnographic traditions. For our study, we formulated the following research question: "What are the hematologists' behavioral patterns related to communicating bad news to patients and families?".
The study report follows the COREQ checklist [19]

The organizational setting

The present work was carried out at the Hematology Department of the Clinical Cancer Centre of Reggio Emilia (Azienda USL – IRCCS). In this Centre, operated the PC unit (PCU) whose goals are developing and implementing training programs aimed at improving HPs' PC competencies, especially those related to communication.
The Hematology Department provides inpatient and outpatient services. The medical staff includes up to 15 hematologists organized according to their different areas of expertise. The hospital's PCU is a specialized hospital-based unit with no beds. At present, it includes three senior physicians and two advance practice nurses, with a remit of specialist consultations in different wards and in a clinic for advanced outpatients and their relatives.

The training: the teach to talk program

A training program titled the “Teach to talk training program” was implemented within the participants’ hospital ward [13]. Different teaching methods were employed: lectures, peer-to-peer role playing, briefing sessions (with video recordings of the role playing), and bedside sessions during real patient encounters. The teachers were professionals from the hospital PCU, and all of the hospital’s hematologists participated after the head of the department called for a training.

Data collection

We collected several types of data, as shown in Table 1:

1. video recordings of role-playing sessions;
2. observational FNs taken during bedside sessions along with BAS checklists [20]; and
3. interviews with hematologists after the end of the training.

Roleplaying	**Average duration**	**Range**
Duration of each roleplaying session	35 minutes	5-40 minutes
Duration of video for each simulated session	12 minutes	8 - 16 minutes
Time of analysis for each video	2 hours	1.30 -2.30 hours
Bedside Sessions	**Average duration**	**Range**
Duration of each bedside session	28 minutes	10-60 minutes
Final debriefing with the BAS	15 minutes	12-17 minutes
Interviews	**Average duration**	**Range**
Interviews post training	18 minutes.	15-22 minutes

Table 1 Collected data characteristics: roleplaying video recordings, field notes from bedside sessions, interviews

An external researcher (GA) was involved as an observer in 14 role play sessions, which were video recorded. The recordings were then descriptively transcribed. GA and LG put the transcriptions into a table and annotated the patients' nonverbal behaviors during role-playing next to the participants' words, along with providing observational notes (ON).
The bedside training took place after performing the role play sessions. Immediately after the training, FNs obtained from bedside training were documented by ST and SA, who were the training facilitators.
Observations and visual data enriched the data set and allowed the researchers to understand the communicative behaviors both during training and in real-life situations.
One year after the end of the training, GA administered semistructured interviews with 9 hematologists to explore 3 main topics:

- Their experiences with difficult communication during their clinical activity;
- Their perceived emotions and feelings;
- The content of their difficult communication.

The interviews allowed the researchers to contextualize, in clinical practice, what has been identified in the observation of simulated situations. The interviews were audio-recorded and transcribed verbatim.
Taken together, the data collected by means of different collection strategies and within a variety of situations, allowed researchers to reach what practitioners had to say about why they behave as they did [29].

Data analysis

GA began the analysis while collecting data, as recommended by Roper and Shapira [21] and Hammersley and Atkinson [22], and the data was then triangulated [23].
The first analysis concerned the role-playing sessions. Participants' verbal and nonverbal communication behaviors along with the ONs were labeled and described in order to facilitate further analysis. An example of role play analysis was shown in table 2.

Table 2 Example of the analysis of a roleplaying interview with the doctor (D) and a caregiver (CG)

Minutes of video	Transcription of the minutes Deregistration: caregiver and doctor	Description of the nonverbal and paraverbal communication	General interpretation
22'40-22'45	D -Please, come in, come in.	Doctor goes to the desk with the two chairs and stands in front of the CG with his back to her. He does not look at her but looks at the ground until he turns towards the CG, pointing to the chair. He uses a firm tone.	The doctor looks cold and detached, the welcome in the moment is missing. There is no direct contact with the CG.
22'45-22'49	D- I looked for you because I wanted to…	Initially, there is no eye contact with the CG. They sit facing each other. While sitting down, D. rolls up his right sleeve, and once seated, he reaches out towards the CG, with his hands and forearms resting on the desk. The position adopted looks like a closing pose. He approaches the chair, keeping his legs apart. He looks up at the CG.	The doctor begins to set up a speech. He appears 'closed off', and the doctor's discomfort is evident.
22'49-23'00	D - I wanted to see you for a moment to take stock of the situation because things are hmm… They have evolved quite quickly (.....)	M begins to open up to his interlocutor, occupying more space and reaching out to the other person. M is seated on the tip of the chair, maintaining a position in which he leans towards the CG and has his forearms resting on the top of the desk. He gesticulates with his hands, always leaning on his arms. He looks down at his hands, and while explaining the situation, he rotates his wrist to emphasize the evolution of the situation. He looks for words to explain and pauses during the speech. The rhythm of speech slows down, and the tone becomes firmer at the word 'evolved'. (....)	He immediately gets to the point of communication, without exploring the experience of the CG. There is an initial sense of insecurity in introducing the discourse. The choice of the word 'evolved' is not very empathetic. There are no words or gestures that convey empathy. (....)

In addition, FNs and interview transcripts were subsequently added to the data set, which was analyzed using a five-step process [24]. The transcribed FNs, interviews and role-playing recordings were inductively analyzed using triangulation, with the intent of providing a more in-depth and holistic understanding of the phenomenon [15].

Rigor and Reflexivity

The data collection was carried our iteratively. Since this study was a focused ethnography and required descriptions of a particular event, saturation could not be applied [30].

As to reflexivity, the external researcher in this study GA has a master's degree in nursing and works as a research nurse in the PCU. She had previous experience conducting qualitative studies as a tutor for the Master's degree in PC. The training was supervised by two PC physicians. All had prior experience developing and leading communication courses in oncology and PC [13,25,26]. ST and SA had frequent contact with hematologists during their work as consultants in PC. LG, who has a background in education and social science research and is an expert in qualitative methodology, served as an external auditor during the whole research process.

Ethical consideration

The study was approved by the local ethics committee (in-house Prot. N. 2015/0014578, 24/06/2015).

Results

The hematologists were 10 males and 5 females. Their average age was 46 years old (range 36-60), and their average work experience was 16 years (range 4-32).

Fourteen role-playing scenarios with different themes were video recorded, as shown in Table 3.

N° RP	TYPE OF INTERVIEW	PURPOSE OF INTERVIEW	COMPLICATING FACTOR
	INTERVIEW WITH PATIENT	**PROGRESSION OF THE DISEASE**	
		Doctor suggestions	
RP 1	Communication with a woman with Hodgkin's recurrence	A compassionate drug is proposed	The woman does not seem to have understood her illness well; has severe anxiety
RP 5	Interview with a patient in an advanced stage of the disease	The patient is expected to change therapies	The doctor has a hard time creating an empathetic relationship with the patient and his wife.
RP 6	Interview with a patient who has already undergone a bone marrow transplant with no success	Palliative therapy is proposed after the other therapies stop being effective	The patient has already undergone several lines of therapy with no results
RP 8	Interview with a patient whose disease is progressing	It is proposed that chemotherapy be resumed	The patient had already stopped therapies in the past, only to then resume them and then have to stop again due to the disease's progression
RP 13	Interview with a patient with leukemia	The doctor seeks to understand how the patient will manage his life as the disease worsens	There is a handicapped daughter in the family
RP 14	Interview with a patient with hematological pathology	The patient is in disease progression and hospitalization is proposed	The patient is depressed and absolutely does not want to accept hospitalization, as treatment no longer makes sense to him
		Poor Prognosis	
RP 10 (RP 9 case is repeated)	Interview with a patient with hematological pathology	Communication of the poor prognosis directly to the patient	Complex interview in which the doctor must talk to the patient about his situation, explaining the terminal phase his pathology is entering
RP 11	Interview with a patient with a new oncological pathology	Communication of the prognosis of a new disease and its treatment	Doctor has to talk about diagnosis and a new therapy to a patient who has already been treated with chemotherapy for Hodgkin's lymphoma
		Proposal of new treatment	
RP 7	Interview with a patient with leukemia	Monoclonal therapy is proposed in anticipation of transplantation	The patient is very anxious
RP 12	Interview with a patient diagnosed with myeloma	The doctor proposes chemotherapy	The patient refuses any type of therapy for fear of side effects

	interview with CAREGIVER	PROGRESSION of the disease	
RP 2	Communication with the patient's caregiver (daughter)	It is proposed that the patient move from active care to palliative care due to the disease's progression and the refractory disease	The daughter does not want the communication to be shared with her mother and does not accept the proposal of hospice
RP 3	Communication with the patient's caregiver (wife)	The patient has experienced a sudden and severe deterioration and needs support	The caregiver is shocked by the sudden and worsening evolution of the patient's condition. In addition, the doctor and patient know each other
RP 4 (RP 3 case is repeated)	Communication with the patient's caregiver (wife)	The patient has experienced a sudden and severe deterioration and needs support	The caregiver pours all her anger onto the doctor and tries to attack him.
		POOR PROGNOSIS	
RP 9	Communication with the patient's wife	Communication of the poor prognosis	The patient is the father of 4 children, and his wife is in a precarious economic condition

Table 3: role plays' themes

Fourteen bedside sessions were performed, ultimately involving 11 out of the 15 hematologists.

A convenience sample size of 9 physicians was interviewed one year after the training ended.

An analysis of the data collected throughout the ethnography highlighted 4 cross-cutting categories: 1) a defensive technical pattern, 2) an authoritative pattern, 3) a relational-recursive pattern, 4) a compassionate sharing pattern.

Pattern details and verbatim quotes from the role plays are shown in Tables 4-7.

Bed-side session evaluations are shown in Table 8

Table 8 Bedside evaluation

Breaking bad news scale items	Trainees' evaluation (number of bedside sessions with the item achieved/bedside sessions in total)	Trainees' evaluation (number of bedside sessions with the item achieved/bedside sessions in total)	Trainees' evaluation (number of bedside sessions with the item achieved/bedside sessions in total)
In your opinion, how were the encounters conducted by the trainees? See each item below.	Very/extremely well (4-5)	Quite well (3)	Slightly well, not at all well (1-2)

1. Did the doctor carefully arrange the environment?	13/14	1/14	0
2. Did the doctor use an appropriate greeting and introduction?	14/14	0/14	0/14
3. Did the doctor show interest in the patient's current state of well-being and personal circumstances at the beginning of the interview?	9/14	1/14	4/14
4. Before breaking the news, did the doctor check what the patient knew already?	8/14	5/14	1/14
5. When breaking the news, did the doctor introduce it with sensitivity?	6/14	4/14	4/14
6. When delivering the news, did the doctor allow the patient to decide the level of detail and language used?	7/14	6/14	1/14
7. Did the doctor allow the patient to set the pace for the delivery of the news?	7/14	5/14	2/14
8. Did the doctor use an appropriate pause after giving the news?	6/14	5/14	3/14
9. Did the doctor specifically invite questions?	7/14	4/14	3/14
10. Did the doctor explicitly attempt to obtain a complete list of the patient's concerns?	5/14	4/14	5/14

11. Did the doctor explicitly check which areas were most important to the patient?	3/14	2/14	9/14
Information giving 12. Did the doctor give information tailored to the patient's expressed concerns?	7/14	5/14	2/14
13. Did the doctor clearly explain any information given so that the patient understood?	11/14	1/14	2/14
14. Did the doctor manage to focus on any positive aspects?	14/14		
15. Was the content of the interview factually accurate?	8/14	6/14	0/14
General considerations 16. How many concerns did the patient air?	5/14	6/14	3/14
17. How many of the key areas of the patient's concerns were touched upon?	4/14	5/14	5/14
18. Were the psychosocial issues that the patient noted during the interview explored?	7/14	3/14	4/14
19. Did the doctor manage to appear supportive during the interview?	12/14	2/14	0/14
20. Did the doctor use appropriate body language during the interview?	12/14	2/14	0/14
21. Did the doctor avoid appearing clumsy during the interview?	11/14	3/14	0/14
22. Did the doctor tailor the pace of the interview to suit the patient?	11/14	3/14	0/14

23. Didi the doctor manage the available time well?	9/14	4/14	1/14

- Defensive-technical pattern: This pattern is defined by the use of many technical and clinical terms, which were sometimes difficult for the patient and/or caregivers to understand. This occurred when the doctor kept speaking in the interview when faced with patient questions that were potentially embarrassing.
- Authoritative pattern: In this pattern, the doctor used authoritativeness and even courteousness to try to explain the situation to the patient and/or the caregiver.
- Relational-recursive pattern: In this pattern, the doctor-patient relationship was used by the doctor to convey the chances of recovery based on the patient's past history using a narrative marked by positivity or opportunities for recovery.
- Compassionate sharing pattern: In this pattern a compassionate relationship established between the doctor and patient activated reciprocity and sharing in the conversation, with particular attention paid to emotions.

Defensive-Technical Pattern

The RP analysis showed that this behavior consisted of the substantial use of medical terms, including technical information on the disease and on tests and treatments to be carried out. The doctor was the main one speaking, leaving little space for the person to confirm his or her understanding or to ask questions.

The interview analysis showed that doctors admitted the following:

"(...) When we are in trouble, we use medical and clinical explanations, a technical language". (Int. 5,7)

In addition, side observations also confirmed this pattern throughout all the encounters. The use of technical terms and a large amount of unrequested information concerning the disease were highlighted by the facilitators in both the BAS checklist and the FNs.

Table 4 shows this pattern, its subcategories and verbatim quotes.

The defensive-technical pattern consisted of three subcategories confirmed by RP and FN:

A) using clinical content; b) not mentioning the pathology; c) using a pressing tone.

Table 4 Defensive-technical pattern and specific behavioural characteristics

FOCUSED ON	SUBCATEGORIES	QUOTES	VERBAL LANGUAGE	PARAVERBAL LANGUAGE	NONVERBAL LANGUAGE
THE DOCTOR ALSO USED CLINICAL CONTENT AS A DEFENSE MECHANISM	A) USES CLINICAL CONTENT	The doctor seems to have had difficulty since the beginning of the interview and he/she shows it by not maintaining eye contact, and his/her movements highlight this. He/she looks nervous and uncomfortable with the questions. (ON - RP 9) The doctor appears closed off from the patient's problems and shows a lack of attention". (ON- RP 6) "[There was] too much information… she started all in one go but then she asked for confirmation and was unconfirmed… bad time management "(FN) Doctor: "Moreover, platelets were the first problem (…) then from the TC scan we see a fungal pneumonia, by aspergillus … and oxygen is no longer enough to secure respiratory exchanges". (RP3)	Widely used: prevalent use of clinical content	Tone of the voice always the same, flat, sometimes pressing	Static posture and facial expressions
	B) DOES NOT MENTION THE PATHOLOGY	Doctor: "We can't know for certain … but it can be something worse than what you had previously". (RP 2)			
	C) USES A PRESSING TONE	Doctor: [With a loud and determined voice]: "I have an offer for you, we will certainly not do the last type of treatment". (RP 6) 'Caregivers' questions gave the doctor trouble; these are not topics he deals with, and he admits embarrassment about speaking of this because he can't give a proper answer'. (ON - RP 9)			

RP: roleplay; ON: observational note; FN bed side field notes

A) Using clinical content

The physicians tended to focus on clinical content, thus extending the conversation, which was not very useful and was not understood by the other person (see the verbatim quotes in Table 4).

For item 6 in the BAS schedule, 5 out of 6 partecipants used technical terms during bedside sessions and did not adjust their language to the patients' level.

In the bedside sessions, the facilitator observed in the FNs that there was first some embarrassment, and then the physicians calmed down as the conversation progressed, eventually giving information that patient and caregiver had not requested.

B) Did not mention the pathology

The doctors tended to avoid directly naming the disease, replacing it with paraphrasing.

During one bedside consultation, the doctor tried to alleviate the bad information by using weaker words;

Doctor:

"A little bit… in some way… until a certain point… there are still some cells". (FN 4)

C) Use of pressing tone

In some cases, the doctor used certain expressions and high-pitched tone that overpowered the patient's or caregiver's voice, even when the doctor admitted his or her own difficulty in giving pertinent answers

Authoritative Pattern

In this pattern, the doctor relied on his or her expertise and authority to communicate with the patients and their families. Despite the bad news, the doctor pointed out that there were still several possibilities for a cure on a scientific basis. Clinical skills helped the doctor communicate. In the interview, the doctor gave bad news but introduced a possible cure:

"Oh, it depends… there are different types of bad news. (...) We can omit things but do so from a perspective of care, (…) I try to give the news in the moment that I process a solution or an offer… I mean… I avoid giving bad news if I'm not sure what to do". Int. 9

In addition, this pattern was confirmed in the bedside sessions in both the FNs and the BAS score for item 21.

Table 5 shows this pattern, its subcategories and verbatim quotes.

Table 5 Authoritative pattern and specific behavioural characteristics

FOCUSED ON	SUBCATEGORIES	QUOTES	VERBAL LANGUAGE	PARAVERBAL LANGUAGE	NONVERBAL LANGUAGE
THE DOCT TRIED CONVINCE PATIENT AND CAREGIVER	A) USING HIS OR HER OWN EXPERTISE	Doctor: "Ok! … But if we set up a therapy that serves to control certain symptoms and … certain pains, we must, however, follow this therapy. … We cannot not take it partway." (RP 2) Doctor: "Well, I say that this pain treatment, to me, is not good … The CT scan didn't give us good news, and the treatments didn't give us the expected results." (RP8) 'He tried to give an image of himself as having the situation under control' (FN 5)	Used; words still prevail over other forms of commu nication	Sometimes moderate, sometimes used a high-pitched tone of voice	Prevailingly static posture and facial expressions
	B) TRYING TO CONVINCE THE PATIENT OF A SPECIFIC TREATMENT OPTION	Patient: "And if 'the beast' should reappear"? Doctor: "We will find another treatment to use, but we have to pursue one goal per day; I understand that with this mindset, moving on is hard." Patient: "Yes, I go on… I always go on…" (RP7) Patient: "There's no point in continuing the treatment. " Doctor: "The disease is continuing. This treatment can hold the illness, and you can go on living for months with a good quality of life." (RP 6) Physicians tend to underscore positive outcomes to reduce patients' expression of bad emotion or try to sugar coat the pill. (FN 2-3)			

RP: roleplaying; ON: observational note; FN: bed side field noters

The authoritative pattern was based on two behaviors described below:
A) Doctors using their own expertise and B) trying to convince the patient and their family of the positive possibilities. For the relevant quotes, see Table 5.
A) Using their own expertise
The doctor used his expertise to provide authoritative opinions to patients and family members.
B) Trying to convince
The doctor tried to 'convince' the person about what were, in his or her opinion, the best choices for treatment and quality of life.
Additionally, this aspect emerged in the bedside observations: item 14 was focused on this behavior, and all physicians applied it.

Relational-Recursive Pattern

This behavioral style was characterized by the establishment of a doctor-patient or doctor-family relationship in which there was reciprocity. One of the main characteristics of this pattern was the use of a narrative of the person's illness as a tool to strengthen the patient's ability to accept another piece of information.
The interviews showed an appropriate alternation between information and silences
Thirteen out of 15 physicians used this pattern, as confirmed in items 7 and 11 in the BAS.
Table 6 shows this pattern, its subcategories and verbatim quotes.
In the RPs, the recursive relational pattern was characterized by three essential features: A) listening to the person; B) paying attention to the person's emotions; and C) using a narrative approach.
A) Listening to the person
The doctor listened to the person and entered into a relationship with the person.
B) Paying attention to the person's emotions
The doctor was also attentive to the person's 'doubts', welcoming and understanding them and trying to offer other opportunities to the person (see RP 7 in Table 6).
C) Using a narrative approach
The doctor retraced the person's history of the disease in order to form an attachment that would help him or her continue his or her communication effectively.

The narrative approach was a communication skill taught during the training program. This skill was seen in almost all of the real encounters with the patients.
Moreover, the relationship between the patients and physicians had a quite long history over the course of the disease.
Items 2 and 4 in the BAS score were quite high because the presentation was not useful and the history of the disease was well known by both the patient and the physicians.

Table 6 Relational-recursive pattern and specific behavioural characteristics

FOCUSED ON	SUBCATEGORIES	QUOTES	VERBAL LANGUAGE	PARAVERBAL LANGUAGE	NONVERBAL LANGUAGE
THE RELATIONSHIP WAS FOSTERED BY RECOUNTING THE NARRATIVE OF THE ILLNESS	A) LISTEN TO THE PERSON	Patient: “But … if I don't do anything? … What can happen to me?” Doctor: “The disease goes on … Listen … If you want, we can do something; we can also talk about it with your daughter” (RP. 9) Patient: “It’s been two years since we began the treatment; do I have to stop it?” Doctor: “Hmm … I understand perfectly; this treatment that I want to propose…” Patient: “Yes, I understand, you are offering me other treatments, but I’m tired." (RP5)	Use of words and silence (the doctor left room to listen to the person)	Tone of voice was modulated and adapted to what the doctor was communicating	Alternation of stillness and dynamic of postures, gestures, and facial expressions
	B) ATTENTION TO THE PERSON’S EMOTIONS	Patient: "Indeed, I am tired … very tired…" Doctor: "In fact, you are right! … We don't really do it (that therapy), but now what we can offer you, if you want, is a therapy that contains the disease." (RP 6) Patient: “And … if I don’t make it…?” Doctor: “Healing, you know, it’s not certain…. We speak of a cure, not healing, and you know it … we could search and have other opportunities for treatment.”(RP7)			

	c) Using a narrative approach to describe the history of the person's illness.	Doctor: "When you came for the blood test that we did, we found some cells that weren't right …. Do you remember? We did the medullary needle biopsy because we needed to properly understand the situation—the most important thing is understanding that. So, Angela, the disease is confirmed." (RP 6) Doctor: "When we saw each other, we made a plan…. It could be an important disease, but we said, because it happened before, that maybe we could keep the disease in check." (RP 5) She doesn't rush, uses a narrative approach, shows proper knowledge of the patient and the caregiver. (FN 10)			

Compassionate Sharing Pattern

The analysis of the role-playing scenarios revealed a self-awareness with a conscious use of silence; the doctors, in fact, had developed active listening and understanding skills.

The doctors' compassion also triggered a great deal of emotions between the doctor and the patient during their encounters.

The interviews highlighted this intertwining of emotions.

Table 7 shows this pattern, its subcategories and verbatim quotes.

Table 7 Compassionate sharing pattern and specific behavioural characteristics

FOCUSED ON	SUBCATEGORIES	QUOTES	VERBAL LANGUAGE	PARAVERBAL LANGUAGE	NONVERBAL LANGUAGE
		Doctor says:			

THE EMPATHETIC RELATIONSHIP ACTIVATES RECIPROCITY AND SHARING	A) ATTENTION TO THE SETTING AND THE CONTROL OF EMOTIONS	"Time can be dedicated … in addition to the standard time that we use for a standard visit. We usually request the presence of a caregiver. And … [reflective pause] then, it's expected that you know the person". (Int. 7,2). "It is useful to prepare myself well before communication, knowing the patient and caregivers in dept". (Int. 6,4) From nonverbal language, you can see that the doctor is listening to the patient; he/she keeps eye contact, he/she doesn't seem bothered when stopped, but he/she starts listening again to his/her interlocutor. (ON. - RP 5)	Conscious use of intermixed words and silence (the doctor develops active listening and understanding)	Modulated tone of voice that adapts to the needs of understanding the other	Prevalence of dynamism and activity; involves leaning towards the person, a type of body language
	B) USING COMPASSIONATE CARE	From the notes, it's clear that the doctor is interested in the patient's family situation and understanding the possible logistical problems that are involved in the treatment plan. (ON - RP 13)			
	C) EMPATHETIC COMPREHENSION	From the notes, it's clear that the doctor is leaving some pauses throughout the conversation; he/she is expanding the time to allow patient to absorb the news and give			

		him/her time to interrupt (ON - RP6) The doctors interviewed were very sensitive to these dimensions due to their deep understanding of what the patient was experiencing, including crying. (ON - Int 4) Doctor: "I try to give the patient enough time to express himself and to cry." (Int. 4,8) Patient: "I'm really confused…" Doctor: "I know …. do you want to think about it for a while? I know …" Patient: "I'm afraid I won't make it." (RP7)			
	D) SHARING THE CARE	Doctor and caregiver seem to come to an agreement on what to say to the patient. The interview ends with an agreement from both of them and a smile from the doctor. The closure seems to be relaxed. Both interlocutors managed to find a compromise. The doctor seems relieved at the result. (ON - RP 9)			

RP: roleplaying; ON: observational note; Int: interview; FN bed side field notes

In the RPs, the compassionate sharing pattern consisted of 4 subcategories of behavior: A) attention to the setting and the control of emotions; B) the use of compassionate care; C) empathetic comprehension; and D) the sharing of care.

(Below, all notes by the observer are reported; compassion often did not show in the words, but nonverbal behaviors, which were recognized from the outside, were observed).

A) Attention to the setting and the control of emotions

The doctor created a 'favorable' climate (RP5; 8) to establish an effective relationship.

The physicians recognized that attention to the setting is fundamentally important; in interviews, they said the following:

"It is important to choose the setting and an appropriate moment for interview". (Int. 1, 4).

This pattern was confirmed for all physicians in Item 1 in the BAS score.

Twelve physicians out of 14 appeared supportive during the real encounters (items 19 and 20 in the BAS score).

B) Using compassionate care

The doctor deepened his or her knowledge of the person's history (RP10; 13) and showed sensitivity.

The interviews also highlighted this aspect:

"I try to have sensitivity towards a patient, even if it's difficult to catch his history; that goes beyond the one illness". (Int 2.9)

The analysis of the bedside sessions contrasted with this result; 29% of physicians did not exhibit sensitivity when sharing bad news (item 5 in Bas), and 5 out of 14 physicians did not explore the patients' concerns (item 10 in BAS).

Moreover, 5 out of 14 physicians mentioned supposed patient concerns in item 17: "The learner 'sticks' his own worries on the patient."(FN)

C) Empathetic comprehension

The doctor took his or her time, especially when he or she realized that the person was unable to understand what was happening to him or her.

The bedside observations did not confirm the presence of a deep understanding of and attentiveness towards the patients; 9 out of 14 physicians did not explicitly explore which quality-of-life dimensions the patients found important (item 11).

D) Sharing the care

The doctor shared with his or her interlocutor conclusions about the simulated visit (RP9; 11):

"From the notes it's clear that the end of the interview is loose; it seems that both speakers reached a compromise. The doctor seems satisfied with the result." (O.N. RP11).

The bedside observations confirmed this capacity to end the encounter at the right moment. Only 1 physician did not correctly manage her time (item 23 in the BAS).

Discussion and Conclusion

Discussion

The aim of this study was to explore the hematologists' behavioral patterns in communicating bad news. Four behavioral patterns were identified: a defensive technical pattern, an authoritative pattern, a relational recursive pattern, and a compassionate sharing pattern. These patterns were widely observed among the group of hematologists derived from both the intrinsic characteristics of the group and the training they attended. The major difference between the simulation data (the interviews and the role-playing sessions) and the real-life context of the bedside sessions was related to the compassionate sharing pattern; the PC physicians observed that the hematologists had difficulty expressing compassionate caring and empathetic comprehension. These two very important communication skills were only utilized by some hematologists, even though they had been taught by the PC physicians and were recognized as essential in difficult conversations.

Some of the hematologists didn't explore the quality-of-life dimensions not strictly linked to the disease; the hematologists were excellent specialists in their discipline but were not as competent in the patient's life as a whole, which is an attribute more typically associated with PC physicians. These data were confirmed by the scarce literature on this topic [4,5,8].

Communication skills remain a challenge for hematologists [4,5]. Research has shown a tendency among hematologists to 'broadcast' using monologues, particularly while delivering bad news during hematological cancer consultations [5].

In the study by Alexander et al. [4], audio-recorded consultations between patients and hematologists were analyzed; they found 4 main conceptual areas (framing the

consultation, presenting the prognostic information, discussing treatment options, and other topics). We saw similar patterns in our study, as the hematologists commonly discussed the disease and treatment but less commonly discussed other, more patient-centered topics such as preferences in decision making and information preferences. As specialized professionals in PC and facilitators of communication training [13], we try to teach deep attention to the values, preferences, quality-of-life dimensions and concerns of our patients during difficult conversations; this type of active listening and attention is fundamental for being supportive and actually being useful to vulnerable patients in the advanced stages of a disease. Hematologists—as shown in the authoritative pattern—frequently provide recommendations during their discussions about treatment, but on the other hand, they only very briefly a no treatment option. Additionally, in the study by Alexander et al., quality of life and the impact of treatment was under-evaluated; we believe that the hematologists felt confident and competent with topics such as disease treatment and tried to avoid other difficult topics, regardless patients' wishes to discuss them. In our study, the hematologists frequently had a long-term therapeutic relationship with their patients through treatment, which differed from the study by Alexander et al.; however, these difficult topics were still avoided in such cases.

Unlike the study by Alexander et al., our ethnographic study was enriched by an analysis of nonverbal behaviors. Especially in the compassionate sharing pattern, the analysis allowed us to underline the importance of professional compassion, a communication behavior recommended in our training course that could be taught and practiced [25].

In the study by Chhabra [5]—which started with the same training as in the study by Alexander et al. [4], the HEMA-Comm—the authors analyzed 20 consultation visits to study the behavioral patterns that emerged among hematologists; the authors found 4 main patterns (broadcasting, deferential, directive and inviting). The most ubiquitous finding was a pattern of lengthy physician monologues on disease mechanisms and history, treatment options, or prognostic information; this pattern was termed "broadcasting." In Chhabra's study, the author noted that the patients had not all given their consent, but some had rather given their assent to participate; during the encounters, there was no room for exchange, and the doctors conveyed only information about what was good for the patients. In this approach, the patient's values are not explored, and therefore, choices are not made according to the patient's preferences; this is in agreement with our observation that the important dimensions of the patient and personal concerns were not investigated.

Authoritative and defensive technical patterns may help physicians establish credibility and provide a general overview of relevant information, both of which are important objectives of these visits, but the concerns and needs of patients could be different. In PC, treatments involving chemo- or immunotherapy are not the only answer; therefore, hearing the desires and preferences of the patients opens up new dialogues and possibilities. Relational recursive behaviors are ways to show active listening and knowledge of patient history as well as to explore patients' disease awareness. This pattern was a focus in the training course. In a clinical review of communication training for hematologists [8], 5 studies were considered eligible, and they included 3 interventions for hospital fellows whose participation was usually voluntary; one strength of our study was that we could analyze the hospital's hematologist population in its entirety and in real work scenarios, thus revealing the group's patterns as a population, which included senior physicians and others who had already graduated from medical school.

One limit of our FE could be the simulated scenario we analyzed (the training course); however, simulation facilitates the research of complex phenomena that occur infrequently and involve vulnerable patient populations. The greatest challenge in simulation-based qualitative research, as identified in a recent review [27], is related to uncertain generalizability of simulations to reality; however, the triangulation of data, as shown here, can improve the reliability of qualitative findings, and a research design is the most effective when it involves experience-based experts, that is, people with lived experiences of the phenomena being explored, as was the case for our population [28].

Conclusion

In the context of the broadening scientific basis of medicine over the last 100 years, observers have commented on the decline of the art of physician-patient communication [8].

The study of patterns can lead to increasingly targeted training interventions for specific learner populations, aimed at evaluating the patient's own values and preferences. In this way, communication training should teach advanced communication skills, which does not involve doctors just convincing patients of their own specialist point of view but truly shares with care choices with the patients. As for hematologists, avoiding standard behavior patterns would allow them to foster personalized communication with patients without feeling uncertain about difficult issues.

Practical Implications

Our study suggests a potential future training program on difficult communication should teach attention to all dimensions of patients' lives as a whole. Active listening to real patient concerns is a challenge for hematology specialists. It is possible that broader training including more PC competences should be implemented to promote this advanced communication skill.

References

[1] V.J. Manitta, J.A.M. Philip, M.F. Cole-Sinclair, Palliative care and the hemato-oncological patient: can we live together? A review of the literature, J. Palliat. Med. 13 (2010) 1021–1025. https://doi.org/10.1089/jpm.2009.0267.

[2] E. Roeland, G. Ku, Spanning the canyon between stem cell transplantation and palliative care, Hematology 2015 (2015) 484–489. https://doi.org/10.1182/asheducation-2015.1.484.

[3] A.S. Epstein, G.R. Goldberg, D.E. Meier, Palliative care and hematologic oncology: the promise of collaboration, Blood Rev. 26 (2012) 233–239. https://doi.org/10.1016/j.blre.2012.07.001.

[4] S.C. Alexander, A.M. Sullivan, A.L. Back, J.A. Tulsky, R.E. Goldman, S.D. Block, S.K. Stewart, M. Wilson-Genderson, S.J. Lee, Information giving and receiving in hematological malignancy consultations, Psycho-Oncology 21 (2012) 297–306. https://doi.org/10.1002/pon.1891.

[5] K.R. Chhabra, K.I. Pollak, S.J. Lee, A.L. Back, R.E. Goldman, J.A. Tulsky, Physician communication styles in initial consultations for hematological cancer, Patient Educ. Couns. 93 (2013) 573–578. https://doi.org/10.1016/j.pec.2013.08.023.
[6] K.P. Loh, H. Xu, A. Back, P.R. Duberstein, S. Gupta Mohile, R. Epstein, C. McHugh, H.D. Klepin, G. Abel, S.J. Lee, A. El-Jawahri, T.W. LeBlanc, Patient-hematologist discordance in perceived chance of cure in hematologic malignancies: a multicenter study, Cancer 126 (2020) 1306–1314. https://doi.org/10.1002/cncr.32656.
[7] T.W. LeBlanc, W.F. Baile, S. Eggly, C.L. Bylund, S. Kurtin, M. Khurana, R. Najdi, J. Blaedel, J.L. Wolf, R. Fonseca, Review of the patient-centered communication landscape in multiple myeloma and other hematologic malignancies, Patient Educ. Couns. 102 (2019) 1602–1612. https://doi.org/10.1016/j.pec.2019.04.028.
[8] D. Christie, S. Glew, A clinical review of communication training for haematologists and haemato-oncologists: a case of artversusscience, Br. J. Haematol. 178 (2017) 11–19. https://doi.org/10.1111/bjh.14606.
[9] B. Wright, K. Forbes, Haematologists' perceptions of palliative care and specialist palliative care referral: a qualitative study, BMJ Support. Palliat. Care 7 (2017) 39–45. https://doi.org/10.1136/bmjspcare-2014-000689.
[10] M. Dowling, P. Fahy, C. Houghton, M. Smalle, A qualitative evidence synthesis of healthcare professionals' experiences and views of palliative care for patients with a haematological malignancy, Eur. J. Cancer Care (2020). https://doi.org/10.1111/ecc.13316.
[11] T.F. Gray, J.S. Temel, A. El-Jawahri, Illness and prognostic understanding in patients with hematologic malignancies, Blood Rev. (2020) 100692. https://doi.org/10.1016/j.blre.2020.100692.
[12] O.O. Odejide, A.M. Cronin, N.B. Condron, S.A. Fletcher, C.C. Earle, J.A. Tulsky, G.A. Abel, Barriers to quality end-of-life care for patients with blood cancers, J. Clin. Oncol. 34 (2016) 3126–3132. https://doi.org/10.1200/jco.2016.67.8177.
[13] S. Tanzi, L. De Panfilis, M. Costantini, G. Artioli, S. Alquati, S. Di Leo, Development and preliminary evaluation of a communication skills training programme for hospital physicians by a specialized palliative care service: the 'Teach to Talk' programme, BMC Med. Educ. 20 (2020) 363. https://doi.org/10.1186/s12909-020-02275-2.
[14] S.L. Ng, L. Bisaillon, F. Webster, Blurring the boundaries: using institutional ethnography to inquire into health professions education and practice, Med. Educ. 51 (2017) 51–60. https://doi.org/10.1111/medu.13050.
[15] P. Andreassen, M.K. Christensen, J.E. Møller, Focused ethnography as an approach in medical education research, Med. Educ. 54 (2020) 296–302. https://doi.org/10.1111/medu.14045.
[16] K. Harris, N. Jerome, S. Fawcett, Rapid assessment procedures: a review and critique, Hum. Organ. 56 (1997) 375–378. https://doi.org/10.17730/humo.56.3.w525025611458003.

[17] G.M.A. Higginbottom, J.J. Pillay, N.Y. Boadu, Guidance on performing focused ethnographies with an emphasis on healthcare Research, TQR 18 (2013) 1–6.
[18] H. Knoblauch, B. Schnettler, Videography: analysing video data as a 'focused' ethnographic and hermeneutical exercise, Qual. Res. 12 (2012) 334–356. https://doi.org/10.1177/1468794111436147.
[19] A. Tong, P. Sainsbury, J. Craig, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups, Int. J. Qual. Health Care 19 (2007) 349–357. https://doi.org/10.1093/intqhc/mzm042.
[20] S.J. Miller, T. Hope, D.C. Talbot, The development of a structured rating schedule (the BAS) to assess skills in breaking bad news, Br. J. Cancer 80 (1999) 792–800. https://doi.org/10.1038/sj.bjc.6690423.
[21] J. Roper, J. Shapira, Ethnography in Nursing Research, Sage, Thousand Oaks, CA, 2000.
[22] M. Hammersley, P. Atkinson, Ethnography: Principles in Practice, Routledge, New York, NY, 2007.
[23] N. Carter, D. Bryant-Lukosius, A. DiCenso, J. Blythe, A.J. Neville, The use of triangulation in qualitative research, Oncol. Nurs. Forum 41 (2014) 545–547. https://doi.org/10.1188/14.onf.545-547.
[24] S.G. Robinson, The relevancy of ethnography to nursing research, Nurs. Sci. Q. 26 (2013) 14–19. https://doi.org/10.1177/0894318412466742.
[25] W.F. Baile, L. De Panfilis, S. Tanzi, M. Moroni, R. Walters, G. Biasco, Using sociodrama and psychodrama to teach communication in end-of-life care, J. Palliat. Med. 15 (2012) 1006–1010. https://doi.org/10.1089/jpm.2012.0030.
[26] K. Tanco, W. Rhondali, P. Perez-Cruz, S. Tanzi, G.B. Chisholm, W. Baile, S. Frisbee-Hume, J. Williams, C. Masino, H. Cantu, A. Sisson, J. Arthur, E. Bruera, Patient perception of physician compassion after a more optimistic vs a less optimistic message, JAMA Oncol. 1 (2015) 176. https://doi.org/10.1001/jamaoncol.2014.297.
[27] S. Vemuri, J. Hynson, L. Gillam, K. Williams, Simulation-based research: a scoping review, Qual. Health Res. (2020) 104973232094689. https://doi.org/10.1177/1049732320946893.
[28] A. Boivin, T. Richards, L. Forsythe, A. Grégoire, A. L'Espérance, J. Abelson, K.L. Carman, Evaluating patient and public involvement in research, BMJ (2018) k5147. https://doi.org/10.1136/bmj.k5147.
[29] P.Salomon, B. Young Qualitative methods can test and challenge what we think we know about clinical communication-if they are not too constrained by methodological 'brands', patient Educ Couns (2018) 30037663 https://doi.org/10.1016/j.pec.2018.07.005.
[30] A.Finset. Qualitative methods in communication and patient education research, Patient Educ Couns (2008) 18762131 DOI: 10.1016/j.pec.2008.08.004

GENERAL CONCLUSION

My thesis is the real evidence that also a negative study (as the communication training program *Teach to Talk*) or a slow enrolling trial (15 patients and their caregivers enrolled so far in 2 years) can be useful to understand a process ongoing, like the “friendship” between Hematology and Palliative Care is.

The *Teach to Talk* programme in the component *bedside training* failed for the Haematology department and one main reason could be the theoretical and cultural issues underlying the haematologists’ concept of palliative care, as I discussed in the article. The same reason suggested for inadequate PC referral, in general; theoretical and cultural issues underlying the haematologists’ concept of PC and the PC approach should be taken into account.
In the ethnography study, we observed as the hematologists commonly discussed the disease and treatment but less commonly discussed preferences in decision making and information preferences. Moreover, active listening to real patient needs, especially regarding not disease-specific dimensions remains a challenge for hematology specialists; they were more focused on physical symptoms, treatment toxicity and decision but they were less confident on discussing patients ‘emotions, social or psychological needs, even if patients ask for them.

I believe that all the observations raised from our experience with our colleagues-both in training occasions and in the reality offered by the trial - are concordant and congruent.

More time to mutual knowledge and appreciation about specific competences is needed.

During my Ph D program, I deeply reflect on the trial from the beginning of its realization: the study design was discussed in 2018 with our hematology colleagues to better understand how to propose it and to decide the inclusion criteria suitable for the feasibility

trial including patients at their last active treatment. A dedicated research physician has been participating to multidisciplinary discussion and patient encounters. We have been improving different techniques to facilitate the enrollment (see table 1 below)

Difficulties with the trial realization and initiatives taken in response
Before we started writing the protocol, we met with the 2 referring hematologists expert in myeloma multiple and chief department to discuss inclusion criteria of the trial. Moreover, a focus groups was done to underline difficulties in enrollment and from this discussion a common proposal for the trial arose
During weekly multidisciplinary meeting with hematology team and palliative care researcher, the hematologists listed some difficulties: – it's hard to keep in mind the possibility of enrollment in this kind of protocol through ordinary care the suggested timeline for the enrollment can be an obstacle, as: – some patients potentially eligible for the intervention needed urgent access to palliation, and so were excluded from the protocol (as they couldn't be randomized and enrolled in the study) – sometimes clinicians needed to start the allegedly last line of therapy in a really short time, and palliative care evaluation and randomization wasn't possible – trial's design was aimed to maximize safety and benefit for the patient; as a consequence, patients that were randomized to the control group sometimes asked to have access to palliative care services anyway, immediately after. This might have negative influenced the clinicians' perceptions of the relevance of the trial intervention.
some initiatives were already in place from the start, as: – hand-delivery of written reminders for the office desk of hematologists – weekly in-person reminder, at scheduled ward's meeting – periodical reminders to formal leaders of the ongoing trial
as possible improvement strategies we tried to: – engage "trial champions", meaning that we asked to hematologists that showed particular interest in the trial to advocate for and sponsor the trial enrollment, to create some sort of peer pressure; – involve the formal ward's leadership, to gather their perceptions and ideas on the patients' enrollment and its dynamics
and as a result of this consultation, we decided to: – participate to the more specific meetings divided for disease's type (and not to the general meeting about all the hematological patients); in the team's tradition, these meetings focused more on serious patients

Table 1: difficulties and developed strategies

Despite of these efforts, I think that the best defense of my still unfinished trial is showing that problem is worldwide and not local.

Little is known about specifically research in Pc regarding hematologic cancer patients: in a rapid review for this work in Pub med, no studies specifically address this topic.

So have we decided to conduct a realistic synthesis based on published difficulties in Palliative Care research in general, barriers of referral to PC by hematologists, expert palliative care opinion about interaction in trials with hematology cancer patients. We have integrated this information with our experience-still rare worldwide- and experts opinions interviews.

Starting from the conclusion of our review *Early Palliative Care in Hematologic Cancer Patients* we consequently contact 7 experts with studies ongoing registered in clinical trial.gov or published as protocols.

According to realist analysis methodology, our first literature consultation aimed at the development of a rough theory that further research and expert consultation, conducted with a specifically derived questionnaire, aimed to refine the IRT, focusing on what seems to work better, for whom, and how, describing it through Context-Mechanism-Outcome (CMO) configurations. Step by step our process was

STEP 1: we revised the available literature, exploring different fields that could contribute to answer our question: we selected a first list of CMOs configurations that seemed likely to be applicable to our research's question.

STEP 2: we developed a check list, starting from the list of the retrieved CMOs, to have an operative summary of the main mechanism that seemed likely to have an impact on hematologic studies' enrollments.

STEP 3: we searched for relevant palliative care studies conducted with hematologic patients and for ongoing trials; using our checklist, we analyzed the available materials (published papers, protocols and abstract) to see how the selected CMOs were addressed.

STEP 4: we developed an interview guide based on the CMOs' checklist and the suggested guidelines for authors' interviews in realist evaluations; we then contacted the authors of the researches that we analyzed to gather additional information on their studies and to compare our.

The table below summarized some of our results with the proposed mechanism favoring or reducing enrolment in Palliative Care with subsequent suggestions.

The highlighted mechanisms often are common between PC *referral* mechanism in general (in red in the table 2) and PC *research*; if hematologists usually don't refer to PC they don't enroll in a PC trial equally.

Relevant Mechanism	Possible suggestions
Integrated (both teams work simultaneously) vs linear model (PC works after usual care) exist; some hematologists seem to prefer integrated care, but others might fear an early interference of palliative care	discuss preferences between integrated and linear model of care with hematologist
Leadership might vary; usually referring team is preferred	explicitly acknowledge that referring team has leadership on patient
Support a lead clinician	
Where PC is perceived as a continuation of usual care, is generally more used.	Discuss what is perception of PC in referring team Participation to multidisciplinary discussions and in/outpatients visits Pc rotation for hematology staff
Poor communication between the 2 staffs influences PC referrals	
If referring team has the perception of "failing" the patient in referring to PC, it might negatively impact the enrollment	
Generalists' perception of PC's competence might influence the referral; PC is perceived as "competent" if it shows good knowledge of disease trajectories and treatment options.	Mutual training between Palliative care and Hematology staff
Professionals prevent the researchers from approaching eligible patients related to not over burdening patients, lack of belief in research, seeing patients too distress, lack of beliefs in the intervention, randomization, fear to speak about prognosis	Partner education, personal repeated contact with referral
Symptom's absence can reduce enrollment in PC	Explain other expertise of PC discipline
Skilling vs deskilling: other specialists believe to lose some competences if refer to palliative care	Educate colleagues to basic pc domains during consultations
Self efficacy perceived by colleagues reduce PC referrals	Educate about PC as not only symptoms control but also Advance care planning (ACP), managing difficult communication, conflicting families and so on. Create a Competencies-based trust
On the other hand, if referring team perceived itself as incompetent in some PC topics, refers to PC	Educate referring team on specific dominion in PC (eg ACP, difficult communication with families, palliative sedation, complex pain etc)
PC accessibility: 24/24 7/7 is requested by other specialists to improve referral to PC	Guaranteeing a constant access to PC service
Multiprofessional PC team was perceived as unique and useful by other specialists	Guaranteeing a multi-professional PC team

Rebranding of *Palliative Care* term in *supportive* could improve PC referrals	Changing the name
The potential personal gain perceived by patients could improve the access to PC	Underline this aspect during trial proposal, as better symptoms control, better teams' integration to take care of them and/or an additional specialist to take care of them
Evoke a sense of altruism in patients	To underline the benefit for future patients during trial proposal and thank patients for this
The words *Randomization* and *Placebo* could be detrimental for patient's acceptance	Explain these words in a simple manner
In American culture, "a name in a bucket" is a better perceived image that the "flipping coin" one	Use metaphors perceived as more acceptable in the receiving culture
The trial proposal should be explained by a known person for the patients, a member staff	A professional already known by the patient should propose the trial
Caregivers/proxies or the referring doctor could influence trial participation	Educate doctors and caregivers on trial aims and flow
Research perception by the staff could influence the patient's participation/approval	Empathize the research priority in the professional agenda
A higher age (over 75) could reduce trial participation	Design trial not too tough for older people
Caregiver's fear of impact of emotional distress or pain for the patient could influence trial participations	Inform care giver to the possibility of interrupting the enrollment if condition worst
Trial communication in non-technical language is better accepted. Not using end of life or hospice language and underline quality of life aspects could be essential	Training specialists on good doctor-patient communication
It's difficult to identify patients with a bad prognosis	Give prognostic tool/broad study eligibility criteria
Lack of clinical equipoise could reduce accrual, both for patients and professionals' concerns	Replicate clinical practice as much as possible
Offering a palliative care symptom control usually not offered (outside the trial)	Using different trial study design as eg. cluster trial
Access to similar support service could reduce the enrollment or competing trial	
Minimize the burden of the intervention, both for patients and clinical staff	Consent by phone, recruitment in routine access in hospital, screening strategies, research staff on site
Recruiting setting far from the therapeutic setting could impact on QoL of patients and reduce the enrollment	Increase the number of recruiting centers
Making a pc referral was perceived as loss of hope, abandonment and rupture of	Changing the name from PC to supportive (see also above) Mutual training

therapeutic alliance. Close emotional bond resulted from knowing their patients over time	
Unrealistic expectation of cure, unwillingness to discuss prognosis and non-curative approach are attitude that hindered PC referral	Sharing visit, education, communication between staffs
Lack of space and time to discuss PC	Dedicated staff
Hospital culture directed towards cure hindered referral	PCU established in hospital. A PC professional embedded in hematologic team
The large number of professionals involved in patients care in hospital setting lead a higher change of mistakes and misunderstanding	Frequent and coordinate communication is essential
On the other hand, hospital setting can facilitate formal and informal education, mutual development of knowledge, joint decision making	Take advantage of the proximities in hospital
PC providers have incorrect perception about course of illness and treatment outcomes leading to inconsistence communications	Sharing visit, education, communication between staffs
Pc referral could risk curtailment of care for their patients	Sharing visit, education, communication between staffs
The research staff identify potential participants by accessing patients' list.	Split the proposal from the clinicians, improve a standardized approach by a referring list. This help to not burden hematologist and-on the other hand- not to confuse patients with a confused pc proposal (because the hematologist his/herself does really don't know PC in deep)
Define a population not prognosis linked but risk linked	For hematologic cancer patients with uncertain disease trajectory is simpler to identify by disease characteristics
Train the research staff with experiential learning technique on the enrollment visit	It was simpler to propose the trial in real life if before the research staff has simulated it

Table 2: Suggested Mechanisms and some suggestions to overcome barriers

This synthesis from literature and experts 'opinion allow us to answer about some questions which our previous review didn't: which hematological population beneficial more of Palliative care intervention? When propose palliative care? How?

In particular from experts' interviews emerged that the initial identified population should be a rich in symptoms burden to start building a collaboration with hematologists. Consequently, in a second time, end-of-life patients could be co-managed between the two staff. Moreover, being part of the hematologic team or being perceived like an insider seem to be the winning element in the RCTs realized until now.

Finally, trials with inpatients -as transplanted patients for example - could be easier to conduct for the high symptoms burden and the access facility to the ward.
On the other hand, failure experience collected from the interviewed experts are described as linked to the population target definition as “incurable”, a criterion not recognized by hematologists, as being to another department and not perceived as a continuum of care by professionals. Moreover, the hematologist point of view on Palliative Care is essential for both refer to PC and propose a PC trial.

Looking to these results and in conclusion of this PhD program I believe that:

1) the referral to PC- as the enrollment in a PC trial - should be tailored on patients’ needs and recognizing these palliative care needs is not simple for Hematologists.
2) a mutual knowledge of specific competences is required to promote integration between PC and Hematology; Palliative care is not only end of life and symptoms control but Advanced care Planning, support for complex families etc. Hematology is not only overtreatment and disease-oriented therapy.
3) to foster interaction between Palliative Care and Haematology, PC service should be incorporated in Hematology Department. The presence of a dedicated Palliative care physician could improve the hematologist capacity to see patients palliative care needs, favoring the mutual knowledge on specific competences and reduce reciprocal misconceptions.

In conclusion, I believe we are at the beginning a great history that we are writing by falls and successes remembering that

“For every complex problem there is an answer that is clear, simple and wrong”

H.L. Mencken

References

1. Salins N, Ghoshal A., Hughes S et al How view of oncologist and hematologists impacts palliative care referrals:a systematic review. BMC Palliative Care 2020 19:175
2. Bloomer MJ, Hutchinson AM, Brooks L. et al Dying persons'perspectives on, or experience of, participating in research: an integrative review. Pal Med 2018. 32(4) 851-860
3. Firn J, Preston N, Walshe C. What are the views of hospital based generalist palliative care professionals on what facilitates or hinders collaboration with in patients specialist palliative care team? A systematically constructed narrative synthesis. Pal Med 2015, 1-17
4. Schenker Y., Bahary N, Claxton R. et al A Pilot trial of Early Specialty Palliative Care for Patients with Advanced Pancreatic Cancer: challenge encountered, and lesson learned. J Pal Med 2018, 21 (1) 28-36
5. Dunleavy L., Walshe C, Oriani A et al Using the Social Marketing Mix framework to explore recruitment barriers and facilitators in palliative care randomized controlled trials?A narrative synthesis overview. Pal Med 2020 in press
6. Walsh E, Sheridan A. Factors affecting patient's participation in clinical trials in Ireland: a narrative review. Contemporary clinical trial communication 3 (2016) 23-31
7. Horton R, Rocker G, Dale A et al Implementing a Palliative Care Trial in advanced COPD: a feasibility assessment (the COPD impact Study). Journal of Palliative Medicine 16(1) 2013. 67-73
8. White C., Hardy J What do Palliative Care patients and their relatives think about research in palliative care? A systematic review. Support Care Cancer 2010. 18:905-911
9. Dowling, M., et al. (2020). "A qualitative evidence synthesis of healthcare professionals' experiences and views of palliative care for patients with a haematological malignancy." European journal of cancer care **29**(6).
10. Morikawa, M., et al. (2016). "Barriers to the Collaboration Between Hematologists and Palliative Care Teams on Relapse or Refractory Leukemia and Malignant Lymphoma Patients' Care: A Qualitative Study." American Journal of Hospice and Palliative Medicine 33(10): 977-984.
11. Bakitas MA, Tosteson TD, Li Z et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. J Clin Oncol 2015; 33: 1438-1445.
12. El-Jawahri A, LeBlanc T, VanDusen H, Traeger L, Greer JA, Pirl WF, et al. Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: a randomized clinical trial. JAMA. 2016;316:2094-103.
13. Barbaret C, Berthiller J, Schott Pethelaz AM et al. Research protocol on early palliative care in patients with acute leukaemia after one relapse. BMJ Support Palliat Care 2017; 7: 480-484.

14. El-Jawahri, A., et al. (2020). "Palliative and end-of-life care for patients with hematologic malignancies." Journal of Clinical Oncology 38(9): 944-953.
15. Ofran, Y, Bar-Sela, G, Toledano, M. Palliative care service incorporated in a hematology department: a working model fostering changes in clinical practice. Leuk Lymphoma. Epub ahead of print 25 January 2019.
16. McCaughan, D, Roman, E, Smith, AG. Palliative care specialists' perceptions concerning referral of haematology patients to their services: findings from a qualitative study. BMC Palliat Care 2018; 17(1): 33.
17. Decastro, G. and B. Earle (2017). "Palliative care in hematologic oncology: A needs assessment." Journal of Clinical Oncology 35(31): 137.