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# Early palliative care in newly diagnosed cancer in Ethiopia: feasibility randomised controlled trial and cost analysis

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/spcare-2022-003996).

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Received 18 October 2022
Accepted 2 November 2022



**To cite:** Reid EA, Abathun E, Diribi J, *et al*. *BMJ Supportive & Palliative Care* Epub ahead of print: [please include Day Month Year]. doi:10.1136/spcare-2022-003996

## ABSTRACT

**Objectives** Globally, cancer deaths are rising. In low-and-middle-income countries, there is a gap in access to palliative care (PC). We designed a feasibility trial to study the initiation of early PC in patients with cancer in Addis Ababa, Ethiopia.

**Methods** A randomised controlled trial (RCT) of standard cancer care versus standard cancer care plus in-home PC was conducted. Follow-up was at 8 and 12 weeks. Primary outcomes were: (1) feasibility, (2) patient-reported PC outcomes (African Palliative Care Association Palliative Outcome Scale (APCA POS)), and (3) costs.

**Results** Of 95 adults randomised (mean age 49.5 years; 66% female), 27 completed 3 study visits. Of these, 89% had stage III or IV disease. Recruitment was feasible, but attrition was high. APCA POS use was feasible, with significant within-arm improvements: 24% versus 18% reduction (p<0.0002, p<0.0025) in PC versus standard care, respectively. Standard care subjects reported higher out-of-pocket payments (5810 Ethiopian birr) (ETB) and lost wages of informal caregivers (74 900 ETB), multiple times an average Ethiopian salary (3696 ETB).

**Conclusion** It is feasible to conduct an RCT of early PC for patients with cancer in Ethiopia. Retention was the biggest challenge. This study revealed opportunities to improve care, and important feasibility results to inform future, larger scale PC research in Ethiopia and beyond.

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

⇒ PC adds value to medical care in developed countries.
⇒ Similar health economic data are missing from low-and-middle-income countries.

**WHAT THIS STUDY ADDS**

⇒ It is feasible to conduct a pilot randomised controlled trial of early palliative care (PC) in this fragile setting.

**HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY**

⇒ Future, similarly designed but larger research is needed to define the value of PC in fragile settings.

## INTRODUCTION

Globally, non-communicable disease continue to rise, constituting more than 70% of deaths worldwide.[1] As a result, people are living longer while accruing tremendous costs for seeking medical care.[2] Palliative care (PC) aims to reduce pain and suffering for those with incurable disease.[3] The benefits of early PC are numerous and well studied in high-income settings, including improved quality of life and increased value in healthcare spending.[4–6] However, these outcomes are missing from low-and-middle-income countries (LMIC) and with it, the momentum to increase publicly available PC.[7–9] We therefore designed a pilot, feasibility randomised controlled trial (RCT) of early PC in newly diagnosed cancer patients in Addis Ababa, Ethiopia.

## METHODOLOGY

### Study design

Our rationale and study design were previously published.[10] Briefly, a feasibility, single-blinded RCT of early, in-home PC plus standard cancer care versus standard cancer care alone was conducted. All cancer care took place at Tikur Anbessa Hospital Oncology Clinic. Critically important is that treatments in both arms represent the standard of medical care in this resource-constrained

location, including medication stock-outs, delays in diagnosis, and preferential oncological treatment given to 'high priority' patients, defined by a high likelihood of treatment response for example, oncologic emergency (spinal cord compression, space-occupying intracranial lesion, airway compromise) and certain cancers (germ-cell, testicular, lymphoma).

### Participants

Ninety-five adults with newly diagnosed, high-priority cancers were recruited and randomised in a 1:1 ratio to standard cancer care or standard cancer care plus PC. The web-based tool used to generate the randomisation scheme is open access and available at: www.randomization.com. Those randomised to early PC met with a PC provider at time of enrolment and at follow-up visits in their homes. All participants were assessed via questionnaire at enrolment and follow-up visits at 8±4 and 12±4 weeks, scheduled at the treating, blinded Oncologist's discretion.

### Outcomes

#### Feasibility

Outcomes include (1) recruitment, retention, the intervention implementation and (2) the practicality of the study, including positive/negative effects on the target population.

#### Patient-reported outcomes

A composite survey contained demographic information, the APCA POS, and five questions assessing out-of-pocket payments for medical care and lost wages.

#### Costs

Of those participants who completed all three study visits (N=27), 20 hospital charts were available for adjudication of hospital-generated costs. An expert local panel assigned costs to units of healthcare and estimated the cost of delivering home-based PC at 265 Ethiopian birr (US$9.25) per home hospice visit.

### Statistical analysis

The sample size was calculated based on the results of our previous research, which demonstrated that patients in a standard oncological care group had a mean APCA POS of 37.1±4.5. A sample size of 47 per group (N=94) is needed to provide 80% power to detect of difference of 3 at week 12 on the APCA POS score at a 2-sided significance level of 0.05 and attrition rate of 25%, assuming SD of 4.5 for both groups. For the APCA score, a two-sample t-test was used to determine whether the mean scores differed. The study is registered at clinicaltrials.gov: NCT03712436.

### Adaptations in response to the COVID-19 pandemic

In March 2020, the first COVID-19 cases were reported in Ethiopia. At a virtual meeting of stakeholders, initial modifications identified those PC patients suitable for phone follow-up. In August 2020, case numbers continued to rise, and the study transitioned to a safety plan: phone interviews were used to complete PC follow-up visits for all outstanding patients.

## RESULTS

### Feasibility

We reached our target recruitment and recruited according to the planned timeline. We faced a delay in study start due to a nationwide morphine stock-out; however, once we had begun enrolment, there were no further stockouts or delays. For those subjects randomised to receive in-home PC, all subjects received the intervention.

Our Oncology clinic-based research team cohesively worked with oncology staff to find the best window of time to complete case report forms while not delaying care or prolonging visits. The team successfully completed case report forms for each study subject at each follow-up visit. At study end, charts were retrieved from medical records, unfortunately seven charts could not be located.

While our target recruitment was reached (N=95), by the third visit, our population had decreased to 27. This attrition was multifactorial but advanced stage of illness and death was a driving factor, further complicated by limited death documentation (less than 5% of deaths in Ethiopia are recorded), and difficulties reaching patients by phone. The attrition did impair the degree to which we were able to execute the research, nevertheless, by study end, 27 subjects remained and we were able to study the feasibility of the intervention, its effects on quality of life as well

**Table 1** Demographic information

| | Standard cancer care | Standard cancer care plus palliative care |
|---|---|---|
| RCT | | |
| N | 53 | 42 |
| Mean age | 47.5 | 50.9 |
| Female% | 62.3 | 65.7 |
| Cost consequence analysis | | |
| N | 11 | 9 |
| Mean age | 47 | 48 |
| Female % | 70 | 78 |
| Type of cancer, n (%) | | |
| Breast | 4 | 0 |
| Lung | 3 | 0 |
| Cervical | 1 | 1 |
| Ovarian | 1 | 0 |
| Head and neck | 1 | 4 |
| Gastrointestinal | 1 | 2 |
| Prostate | 0 | 2 |
| Stage III or IV disease, n (%) | 11 (100%) | 7 (77.8%) |

RCT, randomised controlled trial.

as costs of care. This represents a success in the study execution despite the main difficulty of attrition.

### Practicality

Despite the aforementioned attrition, we saw positive effects of the intervention in our population with improved patient-reported outcomes and improved cost burden. Both are further presented below.

### Demographics

Ninety-five participants were randomised between February 2019 and March 2020. The mean age was 49.5 years and 66% were female. Over 89% of the population at follow-up visit 3 was diagnosed with stage III or IV disease (table 1). See online supplemental figure 1 for a Consolidated Standards of Reporting Trials diagram.

### Patient-reported outcomes

At baseline, our participants reported moderate pain. The pain score improved over the course of the study in both arms: the average APCA score for the study population was 0.49 points lower at visit 2 (p=0.0002) and 0.51 points lower at visit 3 (p=0.0025) compared with the baseline visit. This represents significant within group differences (24% vs 18% reduction in score in PC vs standard care; p<0.0002, p<0.0025). However, the average APCA score was not significantly different between the two arms.

### Cost analysis

Of those participants who completed all three visits (n=27), 20 hospital charts were available for adjudication of hospital-generated costs. Mean total costs were 40 430 Ethiopian birr (US$979) with mean PC costs of 765 Ethiopian birr (US$19) per subject. See online supplemental table 1.

Our population reported substantial out-of-pocket payments for medical care and lost wages, multiple times an average salary in Ethiopia (US$70) at 5810 Ethiopian birr (US$140.8) and 74 900 Ethiopian birr (US$1814.9).[11] Those receiving standard cancer care reported higher out-of-pocket payments for medical care and increased lost wages of an informal caregiver. An important trend of decreased healthcare utilisation and increased mortality was seen in those receiving PC.

## DISCUSSION

It is feasible in this fragile setting to conduct a pragmatic RCT, to recruit and randomise patients into a study examining outcomes of an integrated PC intervention. It was feasible to incorporate early, in-home PC at the time of a new cancer diagnosis. Patients were retained in the study, although attrition due to death and further complicated by limited death documentation in Ethiopia, made it difficult to obtain mortality data. Otherwise, the outcome measures chosen were acceptable and informative.

A caveat to the following discussion is that this was a feasibility study; however, the results are important in developing initial impressions and informing a larger, definitive study. Our results indicate that PC improves patient-reported outcomes in patients with late-stage cancers in this low-resource setting. We expected a greater improvement in APCA score in those receiving PC. There are potential explanations for why this was not observed: “high-priority” patients are preferentially given chemotherapy; thus, it is possible they responded to their treatment with improved symptoms. Second, analgesia is now regularly prescribed in this clinic, a hopeful and positive change from the time of our needs assessment (2017).[9] Finally, the impact of COVID-19 adaptations to phone follow-up for our PC arm may have minimised differences between groups: PC is a holistic approach to physical and non-physical care which is likely less effective when reduced to a phone call.

The second important finding is that home delivery of PC is not only effective but also achievable in this resource-limited setting, at low cost. Due to small numbers in the cost analysis, our analysis was exploratory and between-group differences are interpreted with great caution. Despite randomisation and blinding, we report higher mortality in those receiving PC. This may be because those receiving PC decided to forgo aggressive, expensive treatments, resulting in lower costs and increased mortality. This finding in particular will be important to explore in a larger study, with longer follow-up.

## CONCLUSION

Despite the limitations and challenges of conducting an RCT in what became a particularly challenging environment and time, our results suggest that it is feasible to conduct an RCT of early PC with oncology care in Ethiopia. The study revealed opportunities to improve care for those with advanced cancers while informing future, larger research on the health economics of PC in Ethiopia and other similar settings.

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**Acknowledgements** We wish to thank our study participants, who despite their cancer diagnoses, showed profound humanity in their willingness to share their thoughts, fears and experience living with cancer within a fragile health system, in order to improve the care of future patients in Ethiopia.

The study would not have been possible without the support of Addis-based research staff and nurses in the Department of Oncology at Tikur Anbessa Hospital. Finally, we wish to acknowledge the Yale Department of Emergency Medicine for funding the study and particularly Dr. Steve Bernstein, who believed enough in this project to continue funding despite significant budget cuts due to COVID-19.

**Contributors** EAR conceptualised the research, was awarded funding for the project, designed the methodology, supervised, conducted formal analysis and validation, wrote the original draft and edited subsequent drafts. EA was responsible for data curation, project administration, investigation, methodology and writing-review and editing. JD was responsible for data curation and writing-review and editing. YM and TW was responsible for conceptualisation, supervision and writing-review and editing. PH was responsible for methodology, formal analysis, writing-original draft and writing-review and editing. MF was responsible for conceptualisation, methodology, writing-original draft and writing-review and editing. LG was responsible for conceptualisation, writing-original draft and writing-review and editing.

**Funding** This study was funded by Yale University School of Medicine, Department of Emergency Medicine, through a New Investigator mechanism awarded to Dr. EAR.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** Ethical approval was obtained from Addis Ababa University College of Health Sciences School of Medicine and Yale University School of Medicine. All subjects signed/thumb-printed informed consent. The study conformed to the principles embodied in the Declaration of Helsinki.

**Provenance and peer review** Not commissioned; internally peer reviewed.



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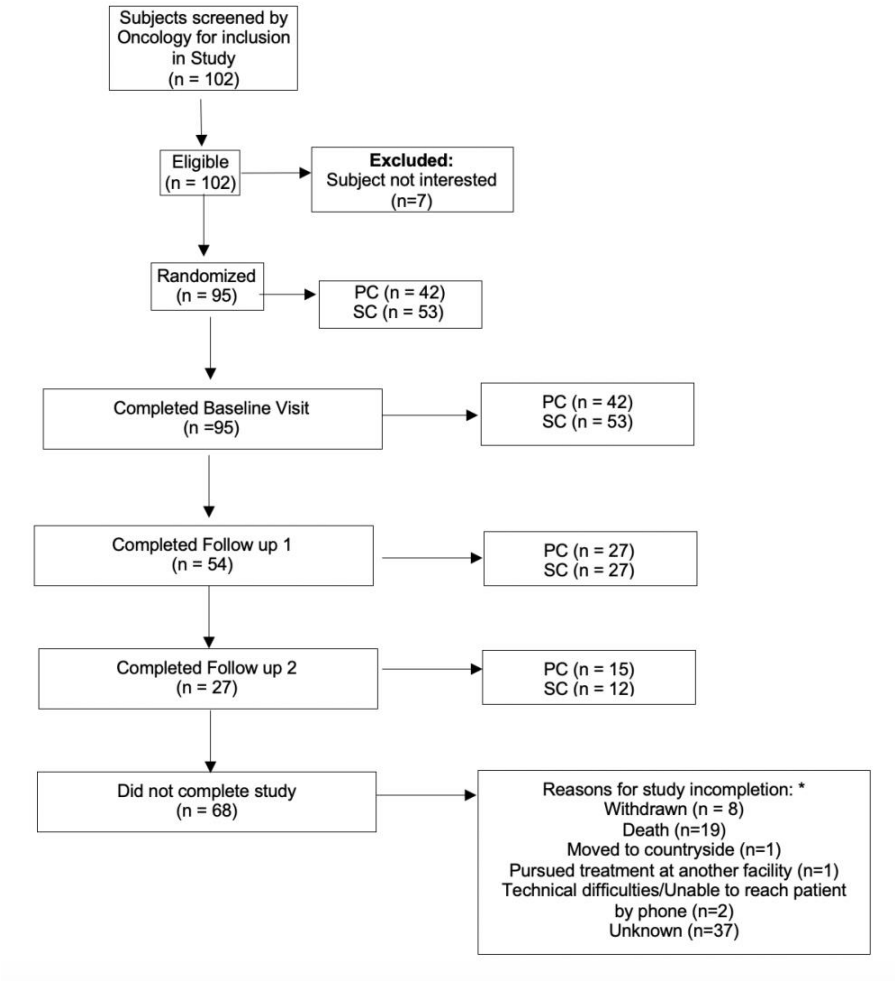
Subjects screened by Oncology for inclusion in Study (n = 102)
Eligible (n = 102)
Excluded: Subject not interested (n=7)
Randomized (n = 95)
PC (n = 42) SC (n = 53)
Completed Baseline Visit (n =95)
PC (n = 42) SC (n = 53)
Completed Follow up 1 (n = 54)
PC (n = 27) SC (n = 27)
Completed Follow up 2 (n = 27)
PC (n = 15) SC (n = 12)
Did not complete study (n = 68)
Reasons for study incompletion: *
Withdrawn (n = 8)
Death (n=19)
Moved to countryside (n=1)
Pursued treatment at another facility (n=1)
Technical difficulties/Unable to reach patient by phone (n=2)
Unknown (n=37)

| | Total population (N=20) | Standard Cancer Care (n=11) | Standard Cancer Care Plus Palliative Care (n=9) |
|---|---|---|---|
| **Days Hospitalized** | 18.8 | 22.2 | 14.7 |
| **Cycles Chemo** | 4.2 | 6.4 | 3 |
| **Fractions Radiotherapy** | 7.5 | 8.6 | 6.2 |
| **Surgery** | 0.9 | 0.9 | 0.85 |
| **MRI** | 0.7 | 0.6 | 0.75 |
| **CT** | 2.2 | 2.2 | 2.1 |
| **OPD visits** | 18.3 | 19.4 | 17.1 |
| **Total Hospital Costs*** | 40,430/979.70 | 53,588/1330.5 | 24,349/604.6 |
| **Out of pocket payments*** | 5810/140.8 | 7,768/192.8 | 4,271/106.1 |
| **Lost wages*** | 74,900/1814.9 | 120,591/2994.2 | 36,238/899.7 |
| **Palliative Care Costs*** | 765.5/19.1 | N/A | 765.5/19.1 |
| **Waiver holder** | 9(45%) | 5(50%) | 4(44%) |

| | | | |
|---|---|---|---|
| **Stage III or IV disease (Number, %)** | 18 (90%) | 11 (100%) | 7(77.8%) |
| **Alive at study end** | 10 (50%) | 7 (64%) | 3 (33%) |