

# Home-based Palliative Intervention to Improve Quality of Life in Children with Cancer: A Randomized Controlled Trial

Murti Andriastuti<sup>1\*</sup>, Pricilia Gunawan Halim<sup>1</sup>, Elnino Tunjungsari<sup>2</sup>, Dwi Putro Widodo<sup>1</sup>

## Abstract

**Objective:** Over the past few years, an integrated approach of palliative care (PC) to chronic and/or life-threatening conditions care has been widely used. Home-based PC (HBPC) service is developed to meet the needs of patients at home; however, it has not been used widely. This study is aimed at determining the benefits of integrated HBPC for the quality of life (QoL) and symptoms intensity in Indonesian children with malignancies. **Method:** A randomized controlled trial was carried out to compare the quality of life between patients who were given PC (a three-month home visit) and those who did not receive PC (control group). Each group was constituted of thirty children with cancer and aged 2-18 years old and were consulted by a palliative team. The participants were randomly allocated to two groups. In the first and twelfth weeks of the intervention, all patients were assessed using the Pediatric Quality of Life Inventory (PedsQLTM) questionnaire cancer module 3.0 (report by proxy or self-report). Symptoms intensity (pain, anorexia, sleep disturbance) were scored by using Edmonton Symptoms Assessment Scale (ESAS). The mean score and each dimension score of both groups were compared and analyzed using bivariate analysis. **Results:** In total, fifty participants were included in the study. A significant difference was found between the two groups in terms of the mean total score in control group 62.39 and intervention group 81.63 ( $p < 0.001$ ). The QoL was improved in the intervention group, while it was declined in the control group as the disease progressed. The main improvements were in the pain and nausea aspects ( $p < 0.001$ ), followed by procedural anxiety ( $p = 0.002$ ), treatment anxiety ( $p = 0.002$ ), and worry ( $p = 0.014$ ). Palliative intervention significantly reduced sleep disturbances ( $p = 0.003$ ) and anorexia ( $p < 0.001$ ). **Conclusion:** Home-based PC improved several aspects of QoL and caused better symptom management in children with malignancies. An early intervention concurrent with the underlying treatment can improve QoL in these children.

**Keywords:** Home visits- palliative- pediatric- cancer- quality of life

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## Introduction

There have been significant developments in treating chronic and life-threatening conditions. However, the morbidity level is high, if not the highest (Ramchandran et al., 2015). This decrease in mortality is linked with the increase in patients' morbidity because of the improved life expectancy and the longer treatment periods. During the treatment, patients and their families encounter various physical, psychological, and spiritual disturbances and a lower quality of life (Greer et al., 2013). Palliative care (PC) is an essential component in the treatment of chronic and life-threatening illness. Its purpose is to prevent and decrease patients' burden through early identification, assessment, and treatment of symptoms as well as other problems such as physical, psychosocial, and spiritual symptoms (Zhi and Smith, 2015; WHO, 2013; Bakitas et al., 2009).

At first, PC was only aimed at children in end-stage

diseases; however, now it is used widely from the initiation of the disease (Bakitas et al., 2009). Several studies have proven that PC could improve physical and psychosocial quality of life (QoL), quality of end-of-life care, treatment cost, and even life expectancy (Bakitas et al., 2009; Hui et al., 2014; Temel et al., 2010; Yennurajalingam, 2011). Palliative care could be given either in hospitals, communities, or in long-term care facilities such as home, homestay, and clinic (Kelley and Morrison, 2011). In the developed countries, a major part of PC is given at home and long-term care facilities where patients stay (Zhi and Smith, 2015). Home visits are believed to have important roles in PC to provide a continuity of care and psychosocial support to both patients and their parents or guardians (Shoemaker et al., 2012; Chong and Khalid, 2016). Several healthcare facilities in the developed countries have established home visit programs based on PC, called home-based palliative care (HBPC) (Shoemaker et al., 2012; Chong et al., 2018).

<sup>1</sup>Department of Child Health, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

<sup>2</sup>Pediatric Nursing, Cipto Mangunkusumo Hospital, Jakarta, Indonesia. \*For Correspondence: murtiandri@yahoo.com

Until recently, there has been no standard procedure regarding the application of early PC in children with malignancy, especially involving home-based palliative interventions in Indonesia. Many healthcare providers provide palliative intervention only at the end of life and when patients are hospitalized. This has no significant impact on critically ill children's quality of life. The knowledge about early palliative interventions and HBPC needs to be improved to provide the best standard of care for children with malignancy. There has been no study on the advantages of giving PC and home visit programs to children with malignancies in Indonesia. This research is the first randomized trial in Indonesia to prove the advantages of palliative care integration with home visit models for children with malignancies.

## Material and Methods

### *Research Design and Sampling*

This study is a randomized controlled trial to compare the QoL and symptoms intensity between children with malignancies who were given palliative intervention and those who were not. The study was conducted in the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, from January to June 2019. To examine the differences between two independent populations with 95% confidence interval and 80% power, the minimum number of participants was obtained 30 for each group (1:1 ratio). Estimated sample size was calculated using the mean difference formula of two independent groups. Mean difference of 20 was considered significant for QoL (Varni et al., 2002). The number of subjects who left the study was less than 20%; therefore, the study remained valid for further analyzes. The inclusion criteria consisted of pediatric patients with malignancies who were referred to the palliative team in the Department of Child Health, Cipto Mangunkusumo Hospital, during the research period, all patients with malignancies aged 2-18 years old fulfilling the criteria for PC (score of  $\geq 4$  in Cipto Mangunkusumo Hospital's palliative screening form), and patients and/or parents accepting palliative intervention. Patients living outside Jakarta were considered unreachable and excluded from this research. Sampling method was done by consecutive sampling and the patients were divided into two groups randomly (intervention group (A) and control group (B)) using a blocked randomization (AABB) method. The patients and families were not aware of the randomization.

### *Intervention*

The patients were given home visits as the intervention. It was done by trained and certified medical professionals who oversaw Cipto Mangunkusumo Hospital's Pediatric Palliative Care (PPC) team. The interventions were given for three months, by providing two-way communications between trained medical professionals, patients, and parents. The intervention was divided into six visits (once every two weeks), focusing on educating parents on problem solving and symptom management including the medications, self-care, communication, decision making, and continued care plan using standard procedures. Each

session lasted about sixty minutes and could be done either at home or at homestay. Hospitalization history of more than seven days was not accounted for in the follow-up period. The patients were examined in terms of QoL on the first and twelfth week of intervention. Symptom intensity (pain, anorexia, and sleep quality) was evaluated at first and then at every visit. During their participation in this study, the patients were treated according to Cipto Mangunkusumo Hospital's Pediatric Hematology-Oncology Division's treatment protocol. The participants in both groups were not aware about the type of intervention during study.

### *Assessment of QoL and Symptoms Intensity*

The patients' quality of life was evaluated using PedsQLTM cancer module 3.0 which consisted of eight dimensions (pain, nausea, procedural anxiety, treatment anxiety, worry, cognitive, physique, and communication). Pediatric HRQOL measurement instruments must be sensitive to cognitive development and include both child self-report and parent proxy-report. The PedsQL Measurement Model consists of appropriate forms for children ages 2-4, 5-7, 8-12, and 13-18 years. Pediatric self-report is measured in children and adolescents in the 5-18 age range, and parent proxy-report of child HRQOL is measured for children and adolescents in 2-18 age range. The Children aged 2-7 years old were evaluated based on the questionnaires filled by their parents, while children above seven years old either had their questionnaires filled by parents or had help from their parents to fill the questionnaires themselves. The questionnaire consisted of close-ended questions and the subjects needed to choose one alternative between 0 and 4. Each question presented a problem, while the alternatives showed how often the said problem was experienced by the respondent in everyday life (0 = "never", 1 = "almost never", 2 = "sometimes", 3 = "often", and 4 = "almost always"). Each answer is scored as 0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0. The score of each dimension is equal to the sum of scores of all relevant questions divided by the number of answered questions. If the case that more than 50% of the questions of one dimension are not answered, that dimension would be excluded from the analysis. The total quality of life score was the sum of the scores of answered questions divided by the number of answered questions of each dimension. The higher the scores, the better the QoL.

Symptom intensity was evaluated using Edmonton Symptom Assessment Scale (ESAS). In this study only the three most common symptoms; pain, anorexia, and sleep disturbances were measured. The intensity was scored from 0 to 10; 0 being the lowest and 10 the highest intensity. The questionnaires could be filled either by the patients (assisted by their parents), the parents themselves, or by the palliative team. The respondent needed to be the same person throughout the study as well.

### *Statistical Analysis*

The results from this study were statistically analyzed using SPSS version 20.0. Bivariate analysis using Mann-Whitney formula was used to determine the mean difference of QoL and symptoms intensity from the

two groups in this study. The test was done with 95% confidence interval.

## Results

Sixty participants were enrolled in the study and four and six participants were lost in the control and intervention groups respectively during the study. By the end of this study, fifty participants were included in the study (Figure 1).

No significant difference was found between the two groups in terms of their sociodemographic and clinical characteristics; except for the anorexia score (Table 1). As for the patients' quality of life, 41 subjects (68,3%) answered the questionnaires by proxy and only 19 subjects

(31,6%) directly answered the questionnaire.

### Quality of Life

In total, 26 subjects from the control group and 24 subjects from the intervention group completed the study. The intervention group's QoL was significantly higher than that of the control group (81.63 vs 62.39,  $p < 0.001$ ). There was a significant improvement in the functional areas of pain, nausea, procedure anxiety, treatment anxiety, and worry. However, other functional areas such as physique, cognitive, and communication did not meet the required cut-off to make a significant difference between the two groups. The results from the QoL assessment of the two groups are listed in Table 2.

### Symptoms Intensity

The symptoms with significant improvement of intensity following the palliative intervention were sleep disturbances and anorexia. The mean score for sleep disturbances in the intervention group was  $1.73 \pm 1.57$ , while it was  $2.87 \pm 2.21$  in the control group ( $p = 0.003$ ).

Table 1. Participant's Characteristics.

Demographic Characteristics	Control n (%)	Intervention n (%)
Sex		
Male	14 (46.7)	21 (70)
Female	16 (53.3)	9 (30)
Age (years old)		
2-4	10 (33.3)	9 (30)
5-7	4 (13.3)	5 (16.7)
8-12	10 (33.3)	8 (26.7)
13-18	6 (20)	8 (26.7)
Diagnosis		
Lymphoma	1 (3.5)	1 (3.5)
Solid tumor	17 (58.6)	12 (37.9)
Leukemia	12 (37.9)	17 (58.6)
Disease duration		
< 1 year	21 (70)	19 (63.3)
≥ 1 year	9 (30)	11 (36.7)
End-of-life		
Yes	5 (16.7)	5 (16.7)
No	25 (83.3)	25 (83.3)
Ongoing chemotherapy		
Yes	28 (93.3)	25 (83.3)
No	2 (6.7)	5 (16.7)
Initial ESAS	Mean (SD)	Mean (SD)
Pain	2.43 (1.92)	3.2 (2.62)
Sleep disturbances	2.07 (1.84)	2.03 (2.22)
Anorexia	4.70 (1.86)	3.63 (2.22)
Karnofsky score	75 (14.80)	75.17 (19.2)
Quality of life score		
Pain	63.70 (32.14)	65.83 (24.7)
Nausea	61.33 (24.39)	62.07 (23.2)
Procedure anxiety	40.03 (31.81)	46.55 (34.5)
Treatment anxiety	66.70 (30.06)	73.28 (24.8)
Worry	74.70 (21.82)	71.28 (27.1)
Physique	79.47 (33.92)	83.97 (22.2)
Cognitive	75.17 (22.41)	66.10 (19.5)
Total	65.64 (16.47)	65.45 (14.6)

Table 2. Patient's Quality of Life Score by the End of the Study

Domain	Mean (SD)		P
	Control (n=26)	Intervention (n=24)	
Pain	56.23 (26.75)	86.04 (25.37)	<0.001
Nausea	51.92 (21.17)	82.83 (21.15)	<0.001
Procedure anxiety	41.04 (31.83)	68.48 (27.22)	0.002
Treatment anxiety	67.69 (30.09)	93.13 (11.14)	0.002
Worry	68.88 (22.97)	83.57 (26.07)	0.014
Physique	82.54 (29.07)	92.43 (15.26)	0.357
Cognitive	71.15 (21.61)	80.30 (18.42)	0.119
Communication	61.00 (27.99)	67.69 (29.55)	0.315
Total	62.39 (15.75)	81.63 (14.61)	<0.001

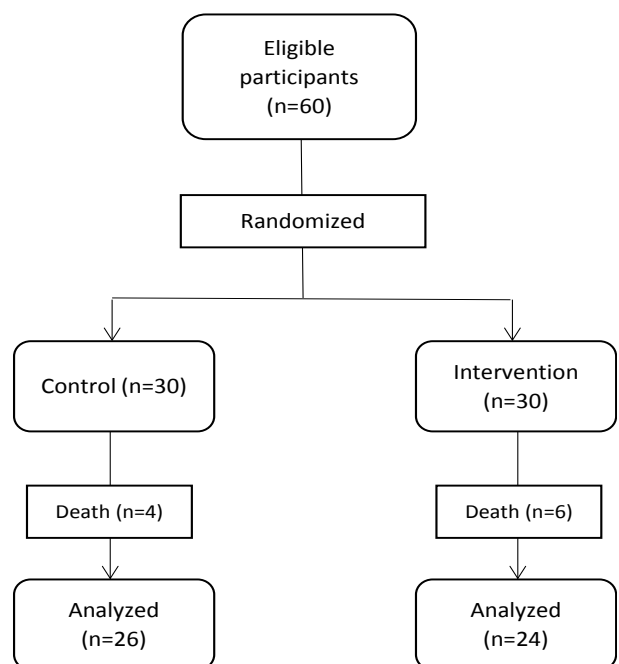


Figure 1. Participant's Enrollment.

Table 3. Mean Score for Each Symptom Intensity in the Final Phase of the Study

Symptoms Intensity	Mean (SD)		P
	Control	Intervention	
Pain	3.47 (2.56)	2.48 (1.86)	0.123
Sleep disturbance	2.87 (2.21)	1.73 (1.57)	0.003
Anorexia	5.07 (5.07)	3.27 (1.86)	<0.001

The mean score for anorexia in the intervention group was  $3.27 \pm 1.86$  while this figure in the control group was  $5.07 \pm 1.82$  ( $p < 0.001$ ) (Table 3). The final score for pain in the intervention group was  $3.47 \pm 2.56$  while this score in the control group was  $2.48 \pm 1.86$  ( $p = 0.123$ ). However, compared to the early phases of this study, the mean score in the intervention group decreased (from 3.20 in the early phase to 2.48). On the contrary, there was an increase in the intensity of pain in the control group (2.43 in the early phase to 3.47).

## Discussion

Sixty pediatric patients with malignancy were studied in the span of twelve weeks; so that this study was the first randomized controlled trial on the role of home-based pediatric palliative intervention in Indonesia. There was no significant difference between the two groups in terms of the sociodemographic data. The initial assessment of the quality of life in the intervention group showed no significant difference in terms of total mean score and the dimensions (Table 1).

In the final assessment, the intervention group obtained a significantly higher score compared to the control group. This shows that palliative intervention, concurrently done with treating the underlying disease could improve pediatric cancer patients' quality of life. This finding is consistent with another study by Bakitas et al. (2009), which stated that early palliative intervention in adult patients could improve quality of life. Several other studies have also reported similar results so that palliative intervention can provide a better QoL and also improve the end-of-life stage (Davis et al., 2015; Brumley et al., 2007; Gade et al., 2008; Pantilat et al., 2010). Another study by van der Geest et al. (2016) reviewed the HBPC service in children with incurable cancer and the healthcare provider and showed that they were satisfied with the quality of HBPC that they provide (van der Geest et al., 2016). Palliative intervention is preventive rather than curative and its objective is to improve the quality of life through early identification, accurate assessment, and treatment of pain and other symptoms, such as physical, psychosocial, and spiritual symptoms. Health providers, together with patients and their families could decide about the goal of care (curative or palliative). Palliative intervention could improve patients' outcome, including, but not limited to, physical, psychosocial, patients' satisfaction, and even the quality of life (Hui et al., 2014; Temel et al., 2010; Yennurajalingam et al., 2011; Zimmermann et al., 2014).

The QoL of the intervention group increased by the end of this study, while the QoL in the control group

decreased. This shows that pediatric cancer patients have declining quality of life as the disease progresses, and it reaches its lowest during the end-of-life stage (Vlachioti et al., 2016). Decreasing quality of life in children can be due to a wide range of factors, such as the shock of being diagnosed, as well as the inexplicable duration of the treatment. This process will continue to progress if not intervened immediately and QoL will continue to decline during the first 3-5 months after diagnosis. Psychological problems, low self-worth, even depression issues often arise (Vlachioti et al., 2016). It is extremely important for health providers to be able to comprehend the ideal QoL patients should have (Evan et al., 2012). The results of this study supported the idea of the necessity of palliative intervention on pediatric cancer patients from the early stages of the disease progression and throughout the disease trajectory.

There was a significant improvement in pain and nausea. The most common side effects in the treatment of pediatric cancer are pain and nausea (Kelley and Morrison, 2015). This study showed that palliative intervention can help improve the QoL of these children by decreasing pain and nausea symptoms. Mahmood et al. (2014), also stated that early palliative consultation was feasible in pediatric cancer patients, especially the high-risk ones. Palliative care could provide assistance on symptoms control and communication between parents, patients, and health providers. The physical, cognitive, and communication aspects did not improve significantly in the intervention group. Therefore, the results of this study are not consistent with the theory that states palliative consultation could assist the communication between parents, patients, and health providers (Mahmood et al., 2014). Since this study did not involve child psychiatrists, such discrepancy is expectable, because disruption in communication cannot be treated optimally by a palliative team. Disruption in communication can be due to the child's psychological disturbances caused by lack of activities, frequent hospitalization, and fear of the future (Vlachioti et al., 2016). This asserts the need for a child psychiatrist's role in the integrated palliative program. In a limited resources setting, family meeting and consultation with the support group and religious support group can be an option.

Most of the assessment for QoL in this study was done by proxy. Not all the questionnaires were self-report, because most of the subjects (76,7%) were children under twelve years old. Various cognitive and verbal intelligence between each child made self-report a more challenging task. Based on the recommendation made by Varni et al. (2007), a questionnaire designed to be filled by parents/guardians should be used for small children, cognitive-impaired children, gravely ill children, or those who are too exhausted to fill a questionnaire. Parents/guardians' questionnaires should be replaced by self-report questionnaires, when the child is able to fill a questionnaire (Varni et al., 2007). A meta-analysis stated that in general, there is a good level of synergy between the parents and the children's reports, with correlation score of  $r > 50$  in physical, functional, and symptoms aspects (Eiser

and Morse, 2001). In this study, PedsQLTM cancer module 3.0 was used in the domains of functional and symptoms, making the synergy between parents and children's reports considerably good. From a QoL assessment viewpoint, self and parent-proxy reports are distinguishable because each of them consisted of different questions.

Sleep disturbances and anorexia were significantly alleviated in this research. One of the major roles of PC was symptoms treatment or management while patients were being cared for. In cancer patients, the five most common symptoms are pain, anorexia, sleep disturbances, difficulty breathing, and exhaustion (Kelley and Morrison, 2015). Palliative approach can help solve non-medical problems that arise while patients undergo treatment, especially in the cases of lack of a cure or non-optimal medical treatment (WHO, 2013). The use of antiemetic agents was limited in this study due to the restrictions on using them in the country (only given for three days after chemotherapy). The use of sedatives or tranquilizers in children are only recommended in certain cases, under the supervision of child psychiatrists. This study proved that HBPC could be one of the modalities to be used in managing such symptoms in pediatric cancer patients.

The final pain score at the end of the intervention was lower in the intervention group compared to the control group, even though statistically insignificant. There was also a form of symptomatic treatment given to all subjects of our study (including the control group) by giving analgesics, as per the standard of pain treatment, since pain is one of the obligatory symptoms to be treated with medicines. However, the decreasing pain score in the intervention group was lower than that in the control group, showing that palliative intervention can help reduce pain in synergy with medical intervention. The combination of pharmacologic therapy and palliative approach would elucidate better pain management for pediatric cancer patients.

Integrated PC gives health providers chances to deliver comprehensive treatment to patients, consisting of aspects such as psychological, developmental, spiritual, and better symptoms management. Ideally, all pediatric cancer patients should automatically meet the criteria for PC, even if they are in the early stages of the disease. In fact, however, many clinicians do not have enough understanding about the importance and the roles of early PC initiations in children with chronic or life-threatening illnesses (Basol, 2015; Cheng et al., 2019). Palliative approach is offered during the time of diagnosis up until the end of the disease's progress—either in health or death (Friedrichsdorf et al., 2015). As a developing country, Indonesia is still being faced with challenges in providing the ideal PC for children with malignancy. Although we have proved that HBPC can be conducted and is feasible to be the standard of care for children with malignancy, there remain barriers, such as lack of medical insurance coverage and human resources. This can be dealt with through cooperation among non-governmental organizations working in the palliative field in Indonesia. With this study, we tried to encourage healthcare providers to provide HBPC for these children. As the results showed, HBPC was a better option to provide

early palliative intervention in children with malignancy. Hospitals are not equipped with the facilities to manage patients' and their families' psychosocial problems and there is a very limited place to provide a palliative intervention during the disease course except for patients in death bed (Allo et al., 2016). Hospital-based oncologic treatment is limited to the hospital and does not include providing continuous care for physical, psychosocial, emotional, and spiritual symptoms in patients and their families (Chong et al., 2018).

These barriers make optimal PPC services difficult to achieve. Home-based PC is way to overcome them and through it we can help patients and their families manage the symptoms, anxieties, and psychological distress (Basol, 2015). Palliative intervention in the form of home visits is beneficial for improving QoL as well as better symptom management in pediatric cancer patients.

This intervention is recommended for all pediatric cancer patients. By this study, the authors hope to raise awareness about the importance of PC for children with malignancy and support the promotion of HBPC service in Indonesia and other countries.

#### *List of abbreviations*

AAP : American Association of Pediatric  
ESAS: Edmonton Symptom Assessment Scale  
PedsQLTM: Pediatric Quality of Life Inventory  
PC: Palliative Care  
PPC: Pediatric Palliative Care  
QoL: Quality of Life

#### **Author Contribution Statement**

MA : Planning the research project, analysis, writing, edited the manuscript with significant intellectual contribution and approved the final script, PGH: Planning the research project, data collection, analysis, and writing the manuscript, DPW : Edited the manuscript with significant intellectual contribution and approved the final script, ET : Data collection.

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#### *Declarations*

All the authors have read and approved the manuscript.

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#### *Ethics approval and consent to participate*

This study was approved by Fakultas Kedokteran Universitas Indonesia's Ethics Committee with the number of 1368/UN2F1/ETIK/XI/2018. This study was also enlisted in ClinicalTrials.gov with the ID of NCT04067687. Written and signed informed consent

were obtained from parents and assent were obtained from children before the commencement of study.

*Consent to publish*  
Not applicable

*Data availability*

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

*Study registration*

This study has been retrospectively registered in ClinicalTrials.gov ID: NCT04067687 (August, 22nd 2019).

*Conflict of interests*

The authors declare that they have no competing interests.

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