Nutrition-related education intervention to improve cognitive development among impoverished small children in rural Uganda:
A cost-effectiveness analysis

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Abstract

Background

Inadequate nutrition intake in early childhood can lead to long-term deficits in cognitive development. The previous trial found that education intervention had improved cognitive development among small children in rural Uganda. However, cost and cost-effectiveness had not been performed. This add-on study, I aimed to see whether the education intervention is cost-effective compared with the control group considering both cost and effect. Thus, the intervention can be implemented on a large-scale in Uganda or similar countries.

Research objective

The objective of this thesis was to assess the cost-effectiveness of the education intervention compared with the control group to improve cognitive development among small children in rural Uganda.

Methods

Health effect data was regenerated from the previous RCT. Cost data was sought via interviews with researchers involved in processing the intervention. This study considers a healthcare provider perspective for a two-year time horizon. For the future implementation of this intervention, control group considered as a do-nothing strategy. A standard cost-effectiveness analysis was conducted to assess an incremental cost-effectiveness ratio. Uncertainty around the result was characterized using one-way, two-way and bootstrap analysis.

Results

The incremental cost-effectiveness ratio (ICER) for education intervention compared with do-nothing strategy was approximately $24.18 per cognitive composite score gained, with an incremental cost of almost $363.46 and an incremental cognitive composite score of 15.03. The education intervention compared with the control group, the ICER was almost $5.8. One-way, two-way sensitivity analyses, and a bootstrapping procedure indicated the robustness of these results. ICER is sensitivity to change in the cost of personnel and cognitive composite score.

Conclusion

The nutrition educational intervention can be considered cost-effective to improve cognitive development for small children in rural Uganda. The outcome of this study, including the cost, health outcome, cost-effectiveness, and sensitivity analyses, can be a useful tool to inform the policymaker in the resource's allocation process.

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List of abbreviations

AUC	Area under the curve
ASQ	Ages and Stages Questionnaire
BSID-III	Bayley Scales of Infant and Toddler Development-III
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CUA	Cost-utility analysis
CEAC	Cost-effectiveness acceptability curve
DALY	Disability-adjusted life year
ECD	Early Childhood Development
ICER	Incremental cost-effectiveness ratio
NGOs	Non-government organizations
QALY	Quality-adjusted life year
RCT	Randomized control trial
WHO	World Health Organization
WTP	Willingness to pay

1 Introduction

Undernutrition in early childhood is a critical factor in determining subsequent cognitive development (1). Globally 2 in 3 children aged 6-23 months are not eating the minimum recommended diverse diet for healthy growth and cognitive development (2). Specifically, in low- and middle-income countries more than 200 million children under the age of five are currently having lack of development potential due to poverty, malnutrition, poor health and unstimulating home environment (3-5). Uganda is a low-income country, where 29% of children aged 6-59 months are stunted, 4% are wasted (thin for their height), and 11% are underweight (6). Undernutrition is common in rural Uganda, especially among children below five years (7). Consequently, few interventions targeted on nutrition have been implemented in Uganda (8, 9).

Studies conducted in 40 developing countries show that early childhood interventions can have a reliable and positive effect on cognitive development (10). In low and middle-income countries, health promotion for parenting programs has consistently been linked to Early Childhood Development (ECD) and cognitive development (8, 11-13). However, studies consensus is varying in method, population and type of intervention. For instance, the most noticeable approach is an intervention of improving mother's knowledge which is related to improved child health and survival, nutrition and cognitive development (8, 14, 15). In particular, parenting intervention in rural Uganda (8) and Bangladesh (16) found significantly higher cognitive scores in the intervention group. Another approach is the community-based interventions which have been potential in improving children cognitive and psychosocial development (17, 18). Community health workers delivered a scalable integrated parenting program that has improved children cognitive development in rural China (19, 20). Concerning the education intervention, delivery through the health services resulted in improved nutrition in small children as well as decreased in the prevalence of stunted growth in childhood (21).

Although the evidence base for the importance of educational intervention for cognitive development has grown, there is less agreement about the most effective and efficient ways to enhance cognitive development. Cost-effectiveness analysis of early childhood development interventions is rarely conducted in resource-constrained countries (22). In addition, there are very few national statistics available on the development of young children in developing countries (23) and inadequate data on the effectiveness of the integrated intervention (5).

A project titled “Nutrition, hygiene, and stimulation education to improve growth, cognitive, language, and motor development among infants in Uganda: A cluster-randomized trial” conducted by Iversen et al., (2018) will serve as the data source for this thesis (24). Nutrition-related education intervention delivered to mothers has improved cognitive, language, and motor development for small children in rural Uganda (24, 25). However, cost and cost-effectiveness analysis had not been performed for their researches. Child cognitive development might be improved with a relatively low-cost for a nutrition-related education intervention. To the best of my knowledge, a cost-effectiveness analysis of nutrition-related education intervention compared with the control group to improve cognitive development among small children does not exist.

A significant policy challenge is how nutrition intervention programs can be delivered at large scale. In particular, policymakers often requires more precise information than is currently available to make early childhood development investment decisions (22). Apart from the clinical effectiveness of the nutrition educational intervention, the economic aspect of the intervention plays an important role in the decision-making process (26, 27). This study assumes that nutrition education intervention will be cost-effective in Uganda and also in similar countries. An economic evaluation of this education intervention will provide information on costs and health outcomes. The outcome of this study, including the cost, health outcome, cost-effectiveness, and uncertainty analysis, can be a useful tool to inform the policymaker in the resource’s allocation process. Another aspect is that this education intervention was largely managed and implemented by local personnel and using local village health teams (VHTs). Thus, the cost-effectiveness finding of the intervention has the potential to be replicated and scaled up in other low-resource, community-based settings. Furthermore, early childhood development programs come to be recognized as a critical period for cognitive development, and potential influences for human capital development in later life (16, 28, 29).

The objective of this thesis is to perform the cost-effectiveness of the education intervention compared with the control group to improve cognitive development among small children in rural Uganda. This thesis was performed a full economic evaluation of the education intervention to compare both costs and health effect for two alternatives. I have aimed at defining a control group that will be relevant if local decision-makers would consider a future scale-up of the educational intervention. For the future implementation of this intervention, there will be no control group. Thus, a cost-effectiveness analysis was performed considering comparator as a do-nothing strategy. In support of the main objective, the following sub-objective and outcomes will be addressed:

1. To assess cost-effectiveness analysis of education intervention compared with the do-nothing strategy considering both cost and health effect.
2. To assess the incremental cost-effectiveness ratio (ICER)
3. To observe the source of uncertainty by conducting a one-way and two-way sensitivity analysis, as well as a bootstrap analysis will be conducted.

This cost-effectiveness analysis was planned after the RCT. The health effects were obtained directly from the intervention group of the RCT, while the costs are estimated based on interviews with key project personnel. The control group is a “common practice” alternative. For the control group, the health effects were obtained directly from the control group of the RCT. The cost was estimated for a healthcare provider perspective for a two-year time horizon. A standard cost-effectiveness analysis was used to assess this analysis.

The rest of this study is laid out as follows. Section 2 presents the relationship between nutrition education and cognitive development, an overview of the health system in Uganda. Also, an overview of the earlier RCT in Uganda. Section 3 reviews the theory of economic evaluation and provides definitions of terminology used in this study. Section 4 provides an outline of the method, cost description and analysis. Section 5 presents the results of the incremental cost-effectiveness ratio, also sensitivity analysis, bootstrap result, scatterplot and cost-effectiveness acceptability curve. Section 6 is devoted to discussion, limitations and direction for further research, and section 7 is concluding with remarks on this analysis.

2 Background

This section presents the relationship of nutrition education with cognitive development. In addition, this section also describes an overview of the healthcare system in Uganda and a summary of the previous RCT that was implemented in rural Uganda.

2.1 Relationship between nutrition education and cognitive development

Cognitive development can be defined broadly as expected gain in language, thinking and understanding (10). Nutrition-related education can be defined as a set of learning experiences designed to facilitate eating and other nutrition-related behaviours conducive to health and well-being.

During early childhood, nutrition-related educational and health interventions have a significant effect on cognitive development. There are positive associations between effective educational interventions and cognitive development during the first 2 years of life (30). Review studies of different early childhood interventions have shown that children received substantial cognitive gains, behavioural change, health gains and schooling benefits (31). Nutrition educational intervention is crucial for child development. In developing countries, evidence shows that cognitive stimulation at early ages of life has increased cognitive development (32, 33). Across countries, nutrition education interventions have a direct and persistent effect on cognitive development. For instance, earlier interventions are associated with early cognitive development (34). In particular, the first few years of children's lives are particularly important because vital development occurs in all domains (35). Specifically, children younger than three years are especially vulnerable and dependent on their mothers for nutrition and stimulation (36). Thus, adequate nutrition is essential to lay the foundation for brain development (37, 38). Consequently, early childhood has come to be recognized as a critical period for brain development (39).

On the other hand, inadequate diets drive malnutrition up in early childhood and can adversely affect brain development. Child undernutrition is highly prevalent in low and middle-income countries, thus resulting in increasing child mortality rates (39). As a consequence, children living in poverty have poorer cognitive and languages development compared with more affluent peers (4).

2.2 An overview of the healthcare system in Uganda

In Uganda, the national health system is comprised of both private and public sectors. The health care system is managed by the Ministry of Health through a decentralized setting within national, districts and sub-districts. There are few primary sources of health financing such as the government, donors, employers, households/communities, and Non-government organizations (NGOs) (40). In the rural area most healthcare services are provided by the public and the private, not-for-profit sectors, also involving faith-based Catholic, Protestant and Muslim Medical Bureaus. Total expenditure on health per capita is $133 and the total expenditure on health as a percentage of GDP (2014) is 7.2 (41).

There was an overall decline of wasting and stunting from the period of 1995 to 2016 and the prevalence of stunting still remained alarming high at 29%, and the annual reduction rate of stunting and wasting was 0.45% and 0.01% respectively (42). The nutrition situation of the population is generally poor especially among children under the age of five; additionally, these conditions have not changed much over the past 15 years (43). In particular, the provision of psychosocial stimulation to children under 5 year age was low in Uganda, and the majority of the children were not engaged in learning activities (9). Thus, the Ministry of Health carries out a few health policies focused on health promotion and scale up nutrition (43).

2.3 Summary of the nutrition-related educational trial in Uganda

This thesis is incorporated with the previous RCT implemented in Uganda (24, 25). It was a community-based cluster-randomized trial in the Kabale and Kisore districts in South-Western Uganda. In detail, 511 mothers and children enrolled in an intervention group (41 villages, n=263) and control group (41 villages, n=248) at baseline (25). The target population was mothers with 6-8 months children. In the appendix, figure 11 illustrates the trial profile for the earlier RCT.

Child development was determined by the Bayley Scales of Infant and Toddler Development-III (BSID-III) on the subscales of cognitive, languages and motor development (44). Trained field-teams independently collected data. Both study groups were blinded to group allocation. They were fluent in English and local languages. The BSID-III scales were translated to the local language and translated back again to English. The raw cognitive scores were converted to composite scores according to BSID-III conversion tables (24). In addition, child development was assessed by the Ages and Stages Questionnaire (ASQ). ASQ was used to assess the social-emotional ability of the child such as communication, gross motors, fine motor, problem-solving and personal-social development scores (45).

Baseline characteristics and anthropometry assessment were done in October 2013 and lasted for six months. Education intervention including nutrition, stimulation, sanitation and hygiene were delivered to mothers in the intervention group. Child assessments were performed in a hired special room to avoid interruption and interference. Total duration per child was about 1.5 hours for the intervention group. On the other hand, the children in the control group were only assessed in relation to their health outcome, and mothers did not receive any educational information.

Children were evaluated for cognitive development at baseline and later in two-follow-up trials, at 12-16 months of age and 20-24 months of age, respectively. More description of the study area, participants, eligibility criteria, intervention and comparator, effect measurements have been described in section 4.1 and table 4.

3 Theoretical framework

Economic evaluation

In the healthcare industry, economic evaluation has played a vital role in the decision-making process. It can be used to inform wide-range of decision in a systematic approach; thus, the decision would be made based on scientific evidence and the likely effects with proper accountability (46). Economic evaluation is a tool linking costs and outcomes, aiming to provide evidence of the decision. Economic evaluation in healthcare can be defined as the comparison of alternative options in terms of their costs and health outcomes (47).

Depending on the nature of health outcome, there are three most common techniques can be used in economic evaluation: such as cost-benefit analysis (CBA), cost-utility analysis (CUA) and cost-effectiveness analysis (CEA) (47). The main difference between these techniques is an expression of health effects. For example, in CBA, both costs and health effects are expressed in monetary terms, whereas in CUA, the effects are quantified in quality-adjusted life years (QALYs). Cost-effectiveness analysis can be used to assess whether an intervention has more health effect relative to how much it costs in comparison to the comparator group. The effects are measured in a single unit of effect or natural units such as cognitive composite score, life-year gained, reduction in blood glucose level, etc. (46).

Approaches to economic evaluation

The most common form of economic evaluation is either a model-based economic evaluation or a randomized control trial based. In the trial-based studies, economics evaluation can be either alongside the trial or can be after the trial. Important of the randomized controlled trial in generating evidence for the evaluation of the health care programmes and intervention has seen it develop a role as a vehicle for economic evaluation (47).

Method for economic evaluation based on the RCT

Economic evaluation based on RCT involves the quantitative comparison of two or more intervention in terms of their cost and health benefits. Some key features should be clearly defined for this type of analysis, such as the target population, intervention, comparator, health outcome and study perspective etc. Economic evaluations are increasingly being conducted based on the clinical trials of health interventions. There are a growing number of economic evaluation studies, such as (48, 49) conducted based on the RCT.

The perspective of analysis is also crucial for cost estimation. In most cases, a societal perspective is taken, and it is the recommendation in cost-effectiveness analysis. Societal and healthcare perspectives are typical perspectives used on economic evaluation. Societal perspective provides an insight into the impact of the intervention to the society, including absence from work, transportation costs. One the other hand, the healthcare provider perspective only take into account costs incurred to the healthcare system (46).

Estimation of Incremental cost-effectiveness ratio (ICER)

The CEA will determine whether education intervention is cost-effective compared with the control group. The Incremental Cost-Effectiveness Ratio (ICER) will be determined using the following formula:

$$\text{ICER} = \frac{Cost^{Intervention} - Cost^{Control}}{CCS^{Intervention} - CCS^{Control}} = \frac{\Delta\text{Cost}}{\Delta\text{Cognitive composite scores}} --- (1)$$

Where $Cost^{Intervention}$ and $CCS^{Intervention}$ indicates to the cost in USD and effect in cognitive composite score of the intervention group children. While, $Cost^{Control}$ and $CCS^{Control}$ indicate the cost and cognitive composite score of the control group. The incremental cost is the difference in cost compared to the intervention and control group divided by the difference in cognitive composite score between intervention and control groups children (46).

Incremental cost-effectiveness plane

The incremental cost-effectiveness plane is a way of representing the likelihood of intervention being cost-effective compared to the comparator. This figure displays four different outcomes. It is separated into four quadrants: northwest, northeast, southeast, and southwest. Northeast quadrant indicates higher cognitive score also higher costs, southwest quadrant represents the cost-saving alternative, indicating a scenario that corresponds lower cost also lower health outcomes (47).

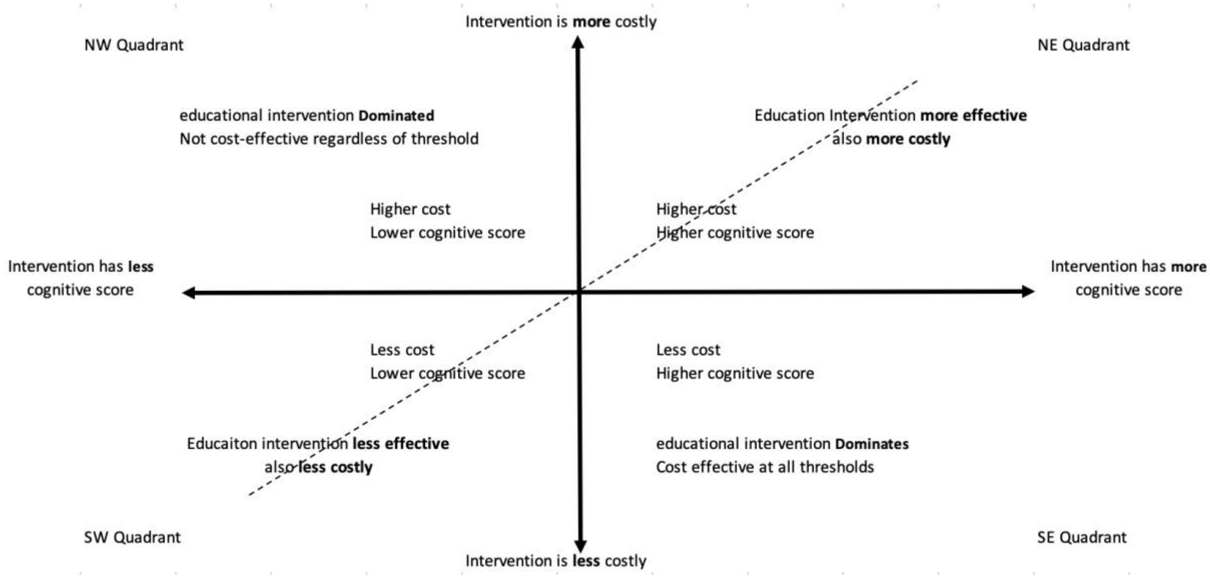

Figure 1. Cost-effectiveness plane for the nutrition-related education intervention

The ICER in the SE quadrant is the most preferred outcome because of less costly and higher health benefit. However, the opposite is true for the NW quadrant. Dominant intervention refers to the scenario that yields more health gain for a given cost, while dominated means that intervention with less health benefits but higher costs. NE quadrant show higher cognitive composite score also higher costs. The education intervention can be cost-effective depending on the willingness to pay threshold value. If the ICER is lower than the threshold value, then it will be considered as cost-effective. Whereas, if the ICER above the threshold value, then it will not be considered as cost-effective.

Sensitivity analysis

The uncertainty around the cost and health effect have variability within different populations. Thus, evaluated the sensitivity analysis will be a helpful tool for the generalisability of the study finding. Deterministic sensitivity analyses are the most common form of sensitivity analysis, where one or more input parameters is varied across a reasonable range. The bootstrapping procedure can perform sensitivity by all cost and effect measures with 1,000 repetitions to construct new ICERs.

One-way sensitivity analysis

Deterministic sensitivity analysis is called one-way sensitivity analysis when only one parameter is simulated at a time (50). A one-way sensitivity analysis is performed to deal with the issue of uncertainty around the decision. It provides a quick way to understand the quantitative relationship between changes in inputs and outputs. This sensitivity analyses represent uncertainty by varying parameter values by some specified amount, such as plus or minus a proportionate change in the mean value of each parameter and reporting the impact on cost-effectiveness (46). A tornado diagram can combine all result from one-way sensitivity analyses and illustrate their influence on the ICER. This analysis can be informative in describing which parameters have the least or lower effect on the ICER. However, one-way sensitivity analysis cannot combine uncertainty of all parameters within the analysis.

Two-way sensitivity analysis

Multiway sensitivity analysis can be conducted and represented was a two-way threshold analysis. It is assessing the robustness of the overall result when simultaneously varying the values of two key input parameters.

Bootstrap analysis

This process is a standard way of illustrating information and the surrounding uncertainty around the decision. The objective of this sensitivity analyses is to determine whether results are insensitive to substantial but plausible variation in a parameter. Bootstrapping is commonly used to estimate the empirical distribution of mean costs and health effects and from which confidence intervals can be estimated. It is a non-parametric technique which involves large numbers of repetitive computations to estimate the share of a statistics sampling distribution empirically (27, 51).

Cost-effectiveness acceptability curves (CEAC)

Cost-effectiveness acceptability curves are created by calculating the proportion of times education intervention has a higher probability compared to the comparator of being cost-effective at a number of different thresholds based on the result of the bootstrapped analyses. The acceptability curve presents much more information on uncertainly than do confidence intervals.

4 Method and data

4.1 Population, intervention, comparator and health outcome

The RCT was conducted in the Kabale and Kisoro districts in South-Western Uganda. Inhabitants were mostly small-scale farmers cultivating small plots of land. Both districts have similar socio-economic status, feeding practices, densely populated and a higher prevalence of stunting. A detailed description of participants, inclusion and exclusion criteria are outlined by Iversen et al, (24, 25).

Target population

The target population of this study consists of infants and small children aged between 6-24 months who have a higher prevalence of stunting, as complementary feeding is recommended to start at six months, and this age is most vulnerable to poor linear growth. A detailed description of the target population has described in table 4.

Intervention

The intervention consisted of educating mothers to increase dietary diversity to improve nutrition intake, also emphasizing stimulation, sanitation and hygiene demonstration (24, 25). Specifically, the intervention was to promote behavioural change by providing information and prompt practice through access to information and improved application. The main intervention strategies are as follows:

1) Nutrition education
2) Child stimulation
3) Cookery demonstrations
4) Hygiene and sanitation education

This intervention was based on the ten guideline principles of complementary feeding of breastfed children (52). The intervention was delivered to 26 groups of mothers at three main sessions with each group. In particular, mothers were also encouraged to practice responsive feeding and allow the children to feed themselves. The importance of hygiene and sanitation was given special emphasis. They focused on the washing of hand of mother and child and utensils used in cooking and feeding the child. In short, the intervention can be defined as "education intervention".

Comparator

The control group is an "old standard of care" group. Participants in the control group did not receive the nutrition-related educational intervention as part of the research protocol. The children of the control group were only assessed in their health outcome, and their mothers did not receive any information on nutrition education.

The previous RCT already found that education intervention had a significant effect compared with the control group to enhance cognitive development among small children in rural Uganda. Thus, for future implementation of this project, the control group will be considered as a do-nothing strategy. In simple, the control group will be similar to the general population. Therefore, health outcome for this group children will be the same as the control group in the RCT. However, there will be no health assessment for this group of children. Thus, there will be no cost associated with the control group.

Health outcome

The health outcome for this thesis is cognitive development, which measured by the cognitive composite score. Child cognitive composite score was determined by using BSID-III with subscales of the cognitive, language and motor development (44). BSID-III scales provide comprehensive development measures for children up to 42 months (53).

The previous RCT also generated a few more health outcomes, such as languages and motor development, communication, problem-solving, personal and social development, and mother knowledge in nutrition. Noted that cognitive development is interrelated with motor development (54, 55) and incorporated with languages development (56). Thus, cognitive development is connected with the rest of the health outcomes. Therefore, this thesis has considered the cognitive development as the only health outcome for the education intervention. The health effects for both groups were obtained directly from the previous RCT data. The health outcomes were summarised as the change from baseline to the last follow-up period.

In the previous RCT, concerning cognitive composite score, the number of participants was different from baseline to the last follow-up, such as participants ranged from 376 (first follow-up) and 390 (last-follow-up). However, for this economic evaluation, I have selected those children who continue throughout the trial period. Thus, I retained those children who were assessed at baseline and then continue throughout the last follow-up trial. Therefore, I kept 316 children participants for this analysis. Specifically, I obtained cognitive development composite scores for (n=166) children in the intervention group and (n=150) children for the control group.

4.2 Perspective, time horizon and discount

Study perspective

The healthcare provider perspective used in this economic evaluation of education intervention to improve cognitive development among small children in rural Uganda. With this perspective, only the cost related to intervention provided to the target population and health outcomes experienced by small children would be taken into consideration. Thus, other types of costs such as mother waiting time, productivity loss and future loss or gain for cognitive development are not included in this thesis. Considering the objective of this analysis and the data availability of this intervention, it is perhaps most appropriate to consider the healthcare provider perspective. One justification for this decision is the setting of Uganda. The lack of data availability and information for assessing the financial impact of having a consequence of cognitive development in small children in Uganda.

Time horizon

Economic evaluation requires a sufficiently long-time horizon to reflect on all the key differences between costs and effect. The ideal practice for most of the economic evaluation is the lifetime horizon. Longer time horizon represents a more accurate health outcome. However, economic evaluation based on randomized trials are usually follow-up for a shorter period and rarely follow-up a lifetime time horizon (47). The previous RCT had follow-up for two years' time horizon. Therefore, a two-year time horizon is considered to account for all related costs and health outcome of this economic evaluation.

Discount

A discount rate needs to be applied to future costs and health effects when used in a CEA (57). This thesis did not adhere to costs valuation for each follow-up or annual costs. The intervention under consideration lasts for two years, and the costs and effects have the same time profile. Given that the intervention period was relatively short, I think this study opted not to apply the discount. Because of the shorter period discount will not influence the results much. Therefore, this study did not apply a discount for costs and the health outcomes.

4.3 Costs description and analysis

This thesis considers cost for the healthcare provider perspective over the two-years. Costs were estimated through interviews with the researchers of the previous RCT. The cost calculations consist of three steps: identifying all relevant types of resources used; quantifying the resources used and assigning monetary unit values for each of the resources used. Once the cost has been identified, quantified and valued, then the difference between groups was summarized. Thus, estimates were made of total education intervention cost and the average cost per mother/children for the trial period.

4.3.1 Cost Identification, quantification and valuation

Cost Identification

I have followed the pathway on how nutrition education intervention is delivered to assess health outcome. This pathway indicates the cost associate with each activity (Figure 11). The structure of the education intervention pathway provides the basis for identifying relevant resources and costs. Costs were classified according to major expenditure lines to understand the depth of the RCT implementation and the associated costs. To identify detail costs item, I have also followed by Gowani et al. (2014) because of a similar cost-effectiveness study conducted in Pakistan (28). In addition, to define precise costs specification, this study also followed a few similar other studies (58-61). ISPOR guidelines recommend using planned costs and outcomes over the expected duration of intervention and its effect (57).

Table 1. Identification, quantification and valuation of the intervention costs (US$)

Cost categories	Sources of costs data: Published Literatures	Sources of costs data: Study Interviews	Valuation	Unit	No. of Unit	Unit price
Capacity building						
Baseline data collectors training		✚	Wages	5 Days	12	1.5
Data collector trainer's		✚	Wages	5 Days	1	15
Follow-up data collectors training		✚	Wages	6 Days	4	14
Follow-up trainer		✚	Wages	6 Days	1	15
Follow-up trainer		✚	Wages	6 Days	3	14
Child development tools -Training		✚	Wages	6 Days	4	75
Child development tools -trainer		✚	Wages	6 Days	1	1000
Personnel						
Leader - Clinic psychologist	✚		Wages	(3.5;4; 6 month)	1	1607
Leader - Nutritionist	✚		Wages	(3.5;4; 6 month)	1	1607
Baseline & Anthropometry	✚		Wages	60 Days	12	9.5
Baseline Psychological tests		✚	Wages	60 Days	6	14
Intervention (Nutrition Education)		✚	Wages	150 sessions	4	14
Adherence to intervention		✚	Wages	Days	3	736.1
Facilitation of intervention (VHTs)		✚	Wages	18months/VHT	32	5.5
Data collection - (12-16m)	✚		Wages	60 Days	6	14
Data collection - (20-24m)	✚		Wages	60 Days	6	14
Materials and other costs						
Bayley scales kit (base case)	✚		Real costs	n=166; n=150	316	5
Bayley scales kit (12-16m)	✚		Real costs	n=166; n=150	316	5
Bayley scales kit (20-24m)	✚		Real costs	n=166; n=150	316	5
Food demonstration (Purchases)		✚	Real costs	150 sessions	150	145
Toys (pencils, paper)	✚		Real costs	n=166; n=150	316	0.6
Data collection (scales, tapes)	✚		Real costs	9	3.03	27.7
Transportation cost of Team		✚	Rides			
Baseline				Personnel	10	96.1
12-16 months				Personnel	10	96.1
20-24 months				Personnel	10	96.1
Car rent for Intervention		✚	Rides	150 sessions	150	17.5
Incentives - (T-Shirt)		✚	Operation	n=166; n=150	316	7.7
Refreshments		✚	Operation	Operation		
12 - 16months				Mother & Child	1022	0.6
20 - 24 months				Mother & Child	1022	0.6
Incentives to mothers		✚	Operation			
12 -16 months				Mother	316	1.1
20 - 24 months				Mother	316	1.1
Transportation cost of mothers	✚		Operation			
12 -16 months				Mother	316	0.7
20 - 24 months				Mother	316	0.7
Capital costs						
Hired special rooms	✚		Operation	Operation		
12 -16 months		✚		Testing centers	50	1.3
20 - 24 months		✚		Testing centers	15	1.3
Mobile Tent		✚	Operation	Testing Centers	1	850
Telephone		✚	Operation	Operation	3	41.6

Table 1 shows the cost identification, quantification and valuation by different cost categories. All costs were standardised and reported in 2014 US$. Costs are usually measured by accounting for all the resources used, in what quantities and their input price. Costing was done across four key categories which were identified as the main activities of the education intervention. Those were personnel, materials and other costs, capacity building and capital costs. It is also essential to identify which cost items need to be included or exclude for this study. Based on trial researcher's opinion, few costs items were excluded for this study because those costs were not relevant for the health outcome of cognitive development.

Quantification

Unit cost is daily participation for training, data collection, and health assessment costs and those were multiple by the number of days of the involvement and training; while, some personnel cost was on a daily basis (data collectors), and few were on a monthly basis (trial leaders and VHTs). A detailed quantification description of Bayley scales kit, transportation, nutrition education, food demonstration and follow-up session to adherence to intervention presents in table 1.

Sources of cost information

This thesis collected cost data by conducted meeting with the previous trial researchers and project leader. At first, few costs were identified from the review of the previous RCT literature (24, 25, 62). Next, costs data was sought via a telephone interview with one clinical psychologist, one nutritionist and one professor of clinical nutrition at the University of Oslo. Those people were chosen for their expertise in knowing the planning and executing throughout the intervention trial. The purpose of doing so is to ascertain whether the prescribed costs specifications are actually being used. Researchers were examining the project record to understand actual resource use. Those documents include general descriptions of the project budget and expenditure statement. Informant interviews validated the quantitative findings of the cost incurred during the education intervention

Valuing costs elements

Resources used in the intervention were valued according to the market price. A monetary value assessed for each resource used for the intervention. Personnel time used, such as psychologist, nutritionists, data collector, and mothers, are an estimate by combining salaries and benefits.

Currency

The intervention was implemented in Uganda. Therefore, all costs incurred in local currency (Uganda Shillings). The previous RCT budget and expenditure statement also updated from local currency (Uganda Shillings, UGX) to United State Dollar (USD) currency. This study has confirmed that all prices were converted from the local currency (Uganda Shillings, UGX) and converted to United States Dollars (US$). All costs were standardised and reported in 2014 US $, by use of the exchange rate of $1=UGX 2,523.

4.3.2 Specification of units and unit costs

The cost items that are included also have a clearly specified statement of purpose in the intervention. The degree of specificity and accuracy in cost listing depend upon their overall contribution to the total cost of the intervention. Costing was specified across four major categories which were identified as the four activity of the nutrition education intervention.

Capacity building

The capacity building has consisted of training and follow-up study. The intervention was mainly delivering education and information related to nutrition. Thus, the essential task was to recruit and a train of health workers to implement the intervention. Capacity building was providing information and promoting practices such as demonstrations of preparing food and stimulation of the children (24). At baseline, 12 data collection personnel participated in a 5 days training session to ensure uniform and standardized procedures and each individual was compensated with $1.5; while, the data collector trainer was compensated with $15 for daily participation.

A six-day intensive training (follow-up training) session on the use of the BSID-III was conducted by a clinical phycologist to assess child growth and cognitive development. There are four health workers that received six days of intensive training for follow-up data collection process. Trainers were compensated $15 for her time spent on each day.

They are four personnel received six days of training for child development tools (BSID-III, ASQ). Only one personnel trainer spends her time training those data collectors. They all received a daily wage rate, and those details are described in Table 1. All capacity building costs were shared equally between the groups because the health personnel divided their time equally between intervention the groups. Table 1 show the full detail of all unit costs.

Personnel

Health workers are the most significant element to implement this education intervention. Full-time personnel, part-time employees and local health worker were engaged for the implementation of this intervention. The management team supporting the intervention was led by a clinical psychologist and supportive supervision composed of nutritionists who were trained in administering the child development tools and scoring the performance of the children.

Table 2. Nutrition education intervention staff

Personnel categories	Description	Number	Salary
Leader - clinic psychologist and nutritionist	Management team supporting intervention lead by the clinic psychologist	2	Monthly
Data collection - Baseline	Advance level of education and bachelor's degree gradates	12	Part-time
Data collection - follow up	Two nutrition graduates and two child development graduates collected child development data at baseline (6-8 months) and follow-up at 12-16m and 20-24m	4	Part-time
Village health team (VHTs)	leader or a mother was selected by consensus in the group to facilitation the intervention for 18 months	32	Monthly

Table 2 indicates the number of staffs, categories, description and salary arguments. The clinic psychologist and nutritionist played the most significant role in the implementation of the intervention. Both were offered competitive monthly salary packages. The leaders spent around three and a half months at baseline, and for the two-follow-up period, they spent four months and six months, respectively. The data collection team comprised of part-time health workers, and they were offered a unit price for their daily participation. All personnel were listed according to their qualifications and time commitments. Qualifications refer to the nature of training, experience and specialised skills required for this intervention. Start-up costs included recruiting and training the health workers and group leaders.

A total of 60 days of anthropometry and data collection was conducted and facilitated by six people. They were equally compensated with $9.5 for each day. At baseline, for the psychological test, a trained field-team independently collected data for 60 days. The health workers were compensated $14 for their time spent on each day. There are 4 health workers who demonstrated nutrition education to the mothers, a total of 150 sessions, and they were equally compensated with $14 for each session. A village health team (VHTs) leader or a mother leader was selected by consensus in the group to facilitate the intervention. Facilitators conducted village visit efficiently to help with the intervention process. A total number of 32 mothers/leaders have received a $5.5 monthly salary for 18 months. The health workers also facilitated the follow-up data collection at the age of 12-16 months and 20-24 months and each follow-up last lasted for 60 days. The health workers were compensated $14 for their time spent on each day.

Materials and other costs

The majority of the materials and other costs are equally shared between groups. For instance, transportation costs of team, data collection materials, the incentive (t-shirt) and refreshment costs were shared equally between the intervention and control group of mother and children. Scales, tapes, length boards and picture booklets were only used during consultancy sessions.

Few specific materials were solely allocated only for the intervention group. Such as, nutrition intervention demonstration, adherence to intervention and facilitation of intervention. The food demonstration has a purchased unit cost of $14.5 and demonstrated a total of 150 sessions to enhance nutrition education for mothers (Table 9).

Other costs refer to cost that do not fit readily into the categories set out above. For instance, transportation, refreshment and incentive costs. All the participant's mothers have received a t-shirt as an incentive.

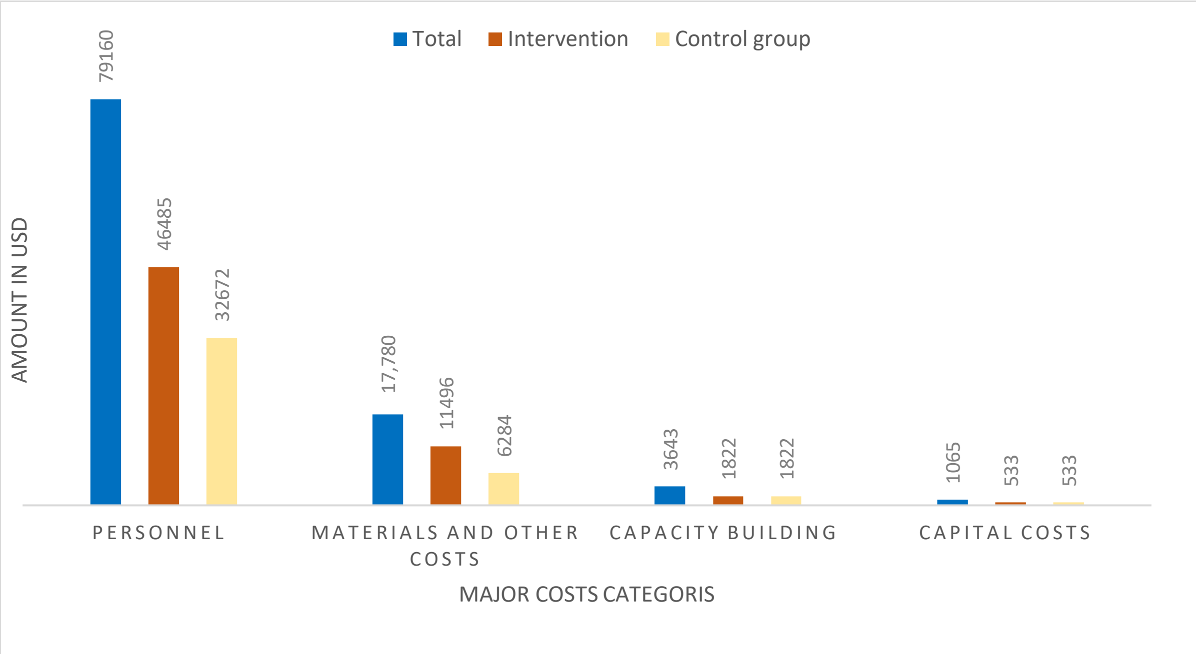

Figure 2. Cost comparison by cost categories

Figure 2 indicates total, intervention and control group cost by cost categories. The majority of resources used are associated with personnel, followed by materials then capacity building costs. The cost of personnel has been estimated to a total of $79,160 for the intervention group $46,485 and $32,675 for the control group.

Capital costs

The proportion of capital costs spent on this intervention were low, accounting for around 1% of the total cost (Table 9). The total capital cost amounted to only $1,065. Child assessments were performed in hired special rooms in the villages. In addition, they also used one mobile tent in cases where rooms were not available. A mobile tent had a fixed cost, and the rented room had a monthly expenditure, and both places accommodated baseline and follow-up assessments for the respective mothers and children. The trial team members used three mobile phones throughout the period.

4.3.3 Total costs and average costs

Total Costs

Table 3. Cost of intervention group and percentage within intervention input (US$)

Cost categories	Intervention group	% of Intervention costs	% within Intervention inputs
Capacity building	**1 822**	3%	100 %
Baseline data collectors training	45		2%
Data collector trainer's	38		2%
Follow-up data collectors training	168		9%
Follow-up trainer	45		2%
Follow-up trainer	126		7%
Child development tools -Training	900		49%
Child development tools -trainer	500		27%
Personnel	**46 485**	77%	100 %
Leader - Clinic psychologist	10 847		23%
Leader - Nutritionist	10 847		23%
Baseline & Anthropometry	3 420		7%
Baseline Psychological tests	2 520		5%
Intervention (Nutrition Education)	8400		18%
Adherence to intervention	2208		5%
Facilitation of intervention (VHTs)	3 203		7%
Data collection - (12-16m)	2 520		5%
Data collection - (20-24m)	2 520		5%
Materials and other costs	**11 496**	19%	100 %
Bayley scales kit (base case)	830		7%
Bayley scales kit (12-16m)	830		7%
Bayley scales kit (20-24m)	830		7%
Food demonstration (Purchases)	2 175		19%
Toys (pencils, paper)	115		1%
Data collection (scales, tapes)	42		
Transportation costs of Team			
Baseline	481		4%
12-16 months	481		4%
20-24 months	481		4%
Car rent for Intervention	2625		23%
Incentives - (T-Shirt)	1 291		11%
Refreshments			
12 - 16months	353		3%
20 - 24 months	353		3%
Incentives to mothers			
12 -16 months	194.2		2%
20 - 24 months	194.2		2%
Transportation costs of mother			
12 -16 months	111		1%
20 - 24 months	111		1%
Capital costs	**533**	1%	100 %
Hired special rooms			
12 -16 months	35		7%
20 - 24 months	11		2%
Mobile Tent	425		80%
Telephone	63		12%
Total Cost	**60 335**	**100**	
Cost per mother/child	**363.46**		

Total costs were defined as the sum of the costs incurred by the trial. Table 9 indicated that total project costs were estimated to be $101,648, and the intervention group cost accounting $ 60,335 and control group cost $ 41,313.

Table 3 indicates the total cost for the intervention group by intervention input categories. Total intervention costs amounted to $60,335 with personnel accounting for the largest proportion (77%). This was followed by the materials with 19%, capacity building with 3% and capital costs with 1%. In the largest cost contributor, personnel, the major cost driver was leaders' costs, which accounted for (23+23) =46%. The car rental cost and food demonstration cost accounted for 23% and 19%, respectively of the materials and other costs.

Average costs

Overall, most costs were shared across the intervention and control group. The only difference is the control group did not receive nutrition-related educational information. All of the capacity building costs were shared equally between the trial groups. Costs varied based on the implementation and monitoring of the education intervention and extra materials used by the intervention group. The cost per mother/child was expressed as the total costs divided by the total number of children for each group. There are 166 mothers/children in the intervention group and 150 mothers/children in the control group. Thus, the average cost per mother/child for the intervention and control group was $363.46 and $275.42, respectively (Table 9). Keep in mind that the total cost was divided by the number of participants to define cost per children. This process gave the same amount of cost for each child.

4.4 Cost-effectiveness analysis

Following ISPOR guidelines (57) and considering health outcome, this study used a standard cost-effectiveness analysis in assessing the economic evaluation of the education intervention compared with the control group. This thesis also following a few similar studies, where a parenting intervention conducted by the RCT, and the health outcome assessed by the BSID-III. For instance, a cost-effectiveness analysis of early childhood intervention that includes responsive stimulation is more cost-effective than a nutrition intervention in promoting children's early development (28). In addition, I have also followed the procedure of economic evaluation for the other type of interventions. For instance, a cost-effectiveness of group support psychotherapy delivered by trained health worker for depression treatment among people with HIV in Uganda (60), a pharmacist-led information technology intervention for medication errors (63).

In accordance with ISPOR guidelines, this study used trial endpoints as the outcome of this analysis (57). Therefore, this analysis illustrates the cost and effect of the endpoint (last follow-up) for this nutrition education intervention.

There are three-phases followed to assess cost-effectiveness analysis: At first, identifying cost item based on published literature and then by interviewing with researchers of the previous RCT. Secondly, regenerated cognitive composite scores from the previous RCT record. The third phase, defining the cost-effectiveness ratio with discussion and recommendation. In addition, a one-way, two-way sensitivity, and bootstrap analysis was also performed.

Incremental cost-effectiveness ratio (ICER)

In the deterministic analysis, the mean value of cost and cognitive composite score will be used for calculating the incremental cost-effectiveness ratio (ICER). At the last follow-up, when children were 20-24 months, the difference between the intervention group with control group costs and cognitive score were estimated. This gave incremental costs and health outcome; the differences in the study groups costs divided by the difference in the group's cognitive composite score. Calculations were based on equation 1. When Both cost and effect was positive, it means that intervention is costly and also more effective (46). The incremental cost-effectiveness ratio (ICER) will provide the cost per unit of cognitive composite score gained.

4.5 Sensitivity analyses

To decide on the implementation of the education intervention, the uncertainty of the input parameters is of important besides the base-case result. The results of the RCT or other clinical studies provide estimates that are imprecise because they usually come from sampled data (47). Thus, in principle, with the collection of more information, such as a larger sample size can be reduced uncertainty. The incremental cost-effectiveness ratio is reported as a point estimate. Therefore, some uncertainty is expected from the inputs of the intervention. The sensitivity analyses show that the decision is less threatened by uncertainty in costs and cognitive development of nutrition education intervention. This study estimated one-way, two-way sensitivity analyses and non-parametric bootstrap analysis.

One-way sensitivity analyses

To investigate the robustness of the costs and cognitive composite score, one-way sensitivity analyses were performed. The key cost components of this intervention were personnel, capacity building and materials costs. Those costs can be varied for future implementation of the educational intervention. Therefore, one-way sensitivity analyses will calculate the ICER for different values of the unit costs, showing whether the cost makes a lot of or a little difference in the economic evaluation results.

At first look at health outcome, the cognitive composite score has a significant impact on the ICER. Thus, 95% confidence intervals were obtained from the last follow-up health outcome for this sensitivity analyses. Lower boundary and the upper boundary of 95% confidence intervals were used to test for this sensitivity analyses.

Concerning cost, for large-scale implementation of this intervention, the cost of personnel will be gradually decreasing with the increasing number of participants. However, the cost of personnel can also be increased for adjusting inflation of the price. To make this in balance, I have tested the cost of personnel from 50% reduced to increased up to 20% for one-way sensitivity analyses.

Similar to personnel, I have tested the capacity building cost from 50% reduction to an increase of up to 20%, noted that capacity building cost is gradually decreasing with the increasing number of study participants.

However, in regard to materials and other costs, I applied a range of ±20% from the baseline price. This can be explained by the fact that if the number of participants increased, the materials and other costs also increase. For instance, each child requires a BSID-III test kit for each assessment of the health outcome. This type of cost will depend on the number of participants. Specifically, increasing participants will lead to an increase in the cost, while reducing the number of participants will lead to a lower cost.

Noted that capital costs were around 1% of total costs (Table 9). Thus, the same range of ±20% was applied to test sensitivity analysis for the capital cost.

I varied the key cost items by plus or minus 20% in the one-way sensitivity analyses and analysed the effect on the ICER and the consequential decision into a tornado diagram. This can be explained that it is very difficult to set a different range for each cost items. Thus, a range of ±20% was applied to test sensitivity analysis for major cost items.

On the contrary, education intervention compared with the control group, all costs categories were verified by plus or minus 20% in a one-way and two-way sensitivity analyses and analysed the effect on the ICER and the consequence decision. Concerning health outcome, lower boundary and the upper boundary of 95% confidence intervals were used to test for this sensitivity analyses.

Two-way sensitivity analyses

Table 3 indicates that more than 96% of intervention group costs were associated with the cost of personnel in combination with materials and other costs (77% +19%). Thus, two-way sensitivity analyses were performed to check the impact on the ICER. This two-way sensitivity analyses followed the same range as used in the one-way sensitivity analysis.

Two-way sensitivity analyses were also performed for education intervention compared with the control group. Similar to one-way sensitivity analyses, all costs were verified by plus or minus 20% to check the impact on the ICER.

Bootstrapping

Bootstrapping is a potential method for calculating confidence intervals for cost-effectiveness ratios (51). The bootstrap method is quite similar to the probabilistic sensitivity analyses (PSA), and this estimates a new mean, standard error and variation by drawing a random sample with replacement and constructing a number of equally sized resamples of the existing dataset. Bootstrapping assess all cost and health effect measures with 1,000 repetitions to construct new ICER (51). The presentation of bootstrapping results on the cost-effectiveness plane and the use of CEAC gives a useful impression of the overall uncertainty in this nutrition educational intervention.

Cost-effectiveness threshold

This study also reported the cost-effectiveness plane and cost-effectiveness acceptability curves. The cost-effectiveness acceptability curve indicates the likelihood of this intervention to be cost-effective according to different levels of willingness to pay (WTP). A willingness to pay (WTP) threshold can be set by evaluation of the importance of health outcome. However, there are no authorized willingness to pay (WTP) threshold ranges in Uganda for the children cognitive development. When the official recognized WTP threshold is not available, the World Health Organization (WHO) recommends the most commonly cited cost-effectiveness thresholds to be a country's per-capita gross domestic product (GDP) (64). However, this WTP approach is only applicable when comparing health outcome as a Quality-adjusted life year (QALY) or disability-adjusted life year (DALY) averted. It was out of the scope of this study to convert the cognitive development composite score to QALY, or DALY averted approach.

There are few studies assuming a threshold value when there is no explicit threshold exact for that intervention. For instance, Saing et al., (65) assumed a threshold value for community-delivered consultation to improve infant sleep problem and maternal well-being. Considering the efficacy of cognitive development and setting of Uganda, this study will assume a threshold of $100/per cognitive composite score gained in Uganda. In addition, instead of an explicit WTP threshold value, a decision-maker can consider the nutrition-related education intervention will likely to be a cost-effective strategy for the above ICER value of per child cognitive scores.

4.6 Key Assumptions and ethical procedures

This thesis can be considered as a pilot cost-effectiveness analysis. Thus, this economic evaluation of nutrition education intervention made a few reasonable assumptions concerning the objective of this study. Thus, this analysis considered the following assumptions:

1) The previous RCT found that education intervention had significantly improved cognitive development for small children. Thus, for future implementation of this

intervention, the comparator will be a general population or do-nothing strategy considering both cost and health outcome.

2) The current study considered the cognitive composite score as the only health outcome. However, the previous RCT had a few more health outcomes, such as languages and motor development, communication, problem-solving, personal and social development and mother's knowledge in nutrition. Cognitive development is correlated with the rest of the health outcomes and very crucial for childhood and later life. Thus, this thesis considered cognitive development as the only health outcome.
3) It has been assumed that nutrition status and cognitive development have quite a similar impact in the other parts of Uganda and also for countries with similar attributes.
4) Given there is no explicit threshold in Uganda for children's cognitive score, this study assumed a threshold of $100/per cognitive composite score gained

Ethical procedures

The previous RCT was approved by the Norwegian Regional Committee for Medical and Health Research Ethics. In December 2019, this add-on study was reviewed and approved by the previous randomized control trial committee. Thus, this add-on study is approved by ethical procedures.

4.7 Statistical analyses

The assumption underpinning each statistical method needs to check. To define which test to be used, we can do this by a taking look at the histogram for the dependent variable. This study has two groups to compare. Therefore, to compare baseline characteristics of the study participants for both groups, the chi-square test is used for categorical variables and two-sample t-test is used for continuous normally distributed variable. P-value of <0.05 was considered significant.

Chi-square test measure how well the observed distribution of data fits with the distribution that is expected if the variables are independent. This test gives a number and percentages. Baseline and demographic characteristics of mother/children such as children gender, breastfeeding frequency, started complementary feeding, dietary diversity scores category were categorical data. Thus, chi-square was used for analysing those categorical data. One the contrary, child age at inclusion month, growth indicators (cognitive, languages, motor development), maternal and household characteristics were continuous and normally distributed data. Therefore, a two-sample t-test was applied to define mean, standard deviation (SD) and p-value.

Health effect of the intervention was measured by two-sample t-test. I have changed unbalanced randomisation to ensure a flow of participants sufficient to fill the group from baseline to last follow-up period. This process helps to handle the missing data. All participants had rich baseline data; then some children were missing for the later follow-up trials. Thus, I have adjusted the data which ensures the same children were tested throughout the trial. I retained 316 children participants for this economics evaluation from a range of 376-390 participants in the previous RCT. This process confirms (166 versus 150) mother's/children for the intervention and control group throughout the trial. This helped to investigated differences in group cognitive score for baseline and later two follow-up study. Therefore, I assessed the area under the curve and used it to calculate the cognitive composite score by using two-sample t-test (Figure 3).

Section 4.5 has already discussed detail statistical analyses of one-way, two-way and non-parametric bootstrap analysis.

Health and cost data were prepared using Stata/SE 15.1 to estimate the required statistical analyses and bootstrap analysis. Bootstrapping procedure was generated using Stata/SE 15.1 and also by Microsoft Excel 2019. I used Microsoft Excel 2019 to summarise the cost data. Table and graphs were generated using the same software.

5 Result

5.1 Background information on the participants

Table 4. Demographic and dietary characteristics of mothers and children at baseline

Characteristics	Intervention (n=263)	Control (n=248)	P-value [c]
Child age at inclusion (months) [b]	7.38(0.8)	7.25(0.9)	0.09
Children Gender [a]			0.46
Male	139(52.8)	123(49.6)	
Females	124(47.1)	125(50.4)	
Breastfeeding frequency [a]			0.23
Breastfeeding on demand	170(64.6)	172(73.8)	
Breastfeeding <= 8 time a day	92(35.1)	61(26.8)	
Started complementary feeding [a]			0.42
Yes	254(96.5)	236(95.1)	
No	9(3.4)	12(4.8)	
Dietary diversity score category [a]			0.15
Low dietary diversity	149(56.6)	168 (67.7)	
Medium dietary diversity	83(31.5)	65(26.2)	
High dietary diversity	31(11.7	15(6.0)	
Growth indicators [b]			
Weight-for-age z-score	-.62(1.1)	-.72(1.1)	0.34
Weight-for-length z-score	0.12(1.2)	0.14(1.1)	0.81
Length-for-age z-score	-1.07(1.1)	-1.20(1.2)	0.21
Head circumference z-score	.68(1.0)	.56(1.1)	0.25
Cognitive development (BSID-III) [b]			
Cognitive	101.99(12.8)	103.52(13.8)	0.22
Languages	103.56(14.3)	100.13(14.0)	0.01
Motor	104.81(13.7)	104.40(14.6)	0.75
Maternal [b]			
Maternal education (years)	4.84(2.8)	4.91(2.7)	0.78
Maternal age (years)	26.17(5.9)	26.97(6.6)	0.15
Number of children per mother	3.42(2.2)	3.34(2.2)	0.67
Mother age during first child	19.57(2.6)	19.60(3.01)	0.89
Household (HH) [b]			
HH head age (years)	31.36(7.8)	33.05(10.7)	0.04
HH head education (years)	6.38 (3.0)	5.90(3.0)	0.09
household size	5.46(2.0)	5.47(2.0)	0.96
Household poverty score	47.84(11.6)	47.61(11.3)	0.82
Likelihood to be below poverty line	14.57(15.9)	15.04(15.7)	0.73

[a] Values are number (percentages)
[b] Values are mean (standard deviation)
[c] P-value is for the difference between the two groups at each study time point

Table 4 shows the baseline and dietary characteristics of 511 households with children between 6 and 8 months. For the continuous and normally distributed variable used two-sample t-test and for the category's variables used chi-square test. A details procedure of statistical analyses has described in section 4.7. The baseline difference between the two randomized groups was tested to confirm the success of the RCT. At baseline, child age at inclusion month, children gender, breastfeeding frequency, complementary feeding, dietary diversity score, growth indicators, cognitive composite score, maternal and household characteristics were similar between groups (p-value>0.05). The most important variable was child age at inclusion month, and (p-value>0.05) indicates that both groups were of similar age. The mean age of index children in the intervention and control group was 7.38 and 7.25 months, respectively. In addition, there was a similar number of male and female participants. Apart from languages, all the variables have (p-value>0.05). Therefore, it is fair to say that both groups were similar for their baseline and demographic characteristics.

5.2 The cognitive composite score gained during follow-up (area-under-the- curve)

At the baseline, the mean cognitive composite score was similar for the intervention and the control groups. Between group there was a small difference of 0.92(102.66<103.58) cognitive composite score, also not significant (p-value>0.05).

Table 5. The trend of the cognitive composite score over the trial period

	Intervention group (n=166)		**Control group (n=150)**		Between group difference		
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean difference	95% CI	P value
Baseline 6-8m	102.66 (12.41)	100.76-104.56	103.58 (14.05)	101.31-105.84	0.92	-2.00-3.85	0.53
Follow-up 12-16m	110.90 (12.13)	109.04 -112.76	104.06 (12.28)	102.08-106.04	6.83	4.13-9.54	0.00
At last follow-up cognitive composite score							
Follow-up 20-24m	114.88 (22.13)	111.48-118.27	99.85 (17.78)	96.98 -102.72	15.03	10.55-19.50	0.00
Health care provider perspective cost							
Cost	363.46 (0)	363.46- 363.46	275.42 (0)	275.42-275.4	88.04	88.04-88.04	0.00

Numbers are given in mean (standard deviation) and 95% confidence interval
P-value is for the difference between the two groups at each study time point

Table 5 indicates cognitive composite scores from baseline to the last follow-up for the sub-sample of participants who continue throughout the trial period. For the cognitive development, a transient effect occurred at 12-16 months, with a significant interaction of intervention with time (p-value=0.00). Finally, at the last follow-up phase, children in the intervention group had, on average, 15.03 higher cognitive composite score than those assigned to the control group. The education intervention effect was significant (p-value=0.00) for both follow-up phases.

Table 10 indicates cognitive composite scores from baseline to the last follow-up for the previous RCT. In the RCT, concerning cognitive composite score, the number of participants was different from baseline to the last follow-up. For instance, at first follow-up, the number of children for the intervention and control was 198 and 178, respectively. In contrast, at the last follow-up, this number of children became 204 and 186, respectively. At baseline, the mean cognitive development composite score for both intervention and control groups had a difference of 1.53(101.99<103.52). However, at the last follow-up trial, children in the intervention group had significantly higher cognitive scores than children in the control group.

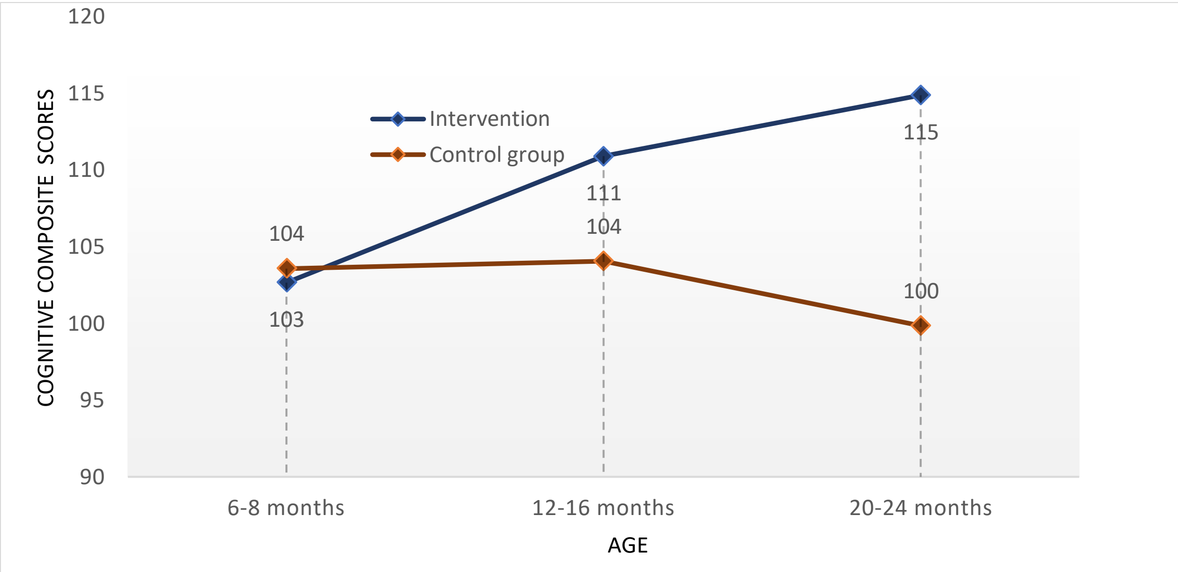

Figure 3. The cognitive composite score gained during follow-up (area-under-the- curve)

Figure 3 illustration the cognitive composite scores from table 5. This figure shows the cognitive composite score of the intervention using the area under the curve (AUC). In terms of incremental effectiveness, intervention group children experienced an increase of 15.03 cognitive composite scores over their control group counterparts for the 24 months trial period. This AUC drawing is comparing intervention and comparator group by observing cognitive composite scores from baseline to last follow-up period. Specifically, the AUC figure shows the incremental improvement between the intervention and control groups by comparing the mean cognitive composite scores.

A detailed cost description and analyses presented in section 4.3

Concerning cost-effectiveness analysis of education intervention compared with do-nothing strategy has presented on the rest of the result section. Graph and table for the cost-effectiveness of the education intervention compared with the control groups has presented in the Appendix.

5.3 Cost effectiveness analyses

Incremental cost-effectiveness ratio

Mothers and children were not receiving any education intervention for the do-nothing strategy. Thus, the incremental cost of the intervention was the same as the implementing cost of the intervention. The health-care cost per children for the educational intervention was $363.46, and the do-nothing strategy had zero costs, resulting in an incremental cost for the education intervention of $363.46 per child. The previous RCT found that without receiving education intervention, the control group had a cognitive composite score of 99.85. The health outcome for the do-nothing strategy was the same as the control group.

Table 6. Cost-effectiveness result for the intervention versus do nothing strategy

Deterministic result					
Program	Costs	Cognitive score	Incremental cost	Incremental cognitive score	ICER
Do Nothing strategy	N/A	99.85	N/A	N/A	N/A
Intervention	363.46	114.88	363.46	15.03	24.18

Table 6 indicates the deterministic result of the education intervention compared with the do-nothing strategy. At the last follow-up, the cognitive composite score of the intervention group was 114.88, while for the do-nothing strategy, the score was 99.85. Incremental cognitive composite scores gained 15.03. Both the cost increment and cognitive scores increment was positive, leading to a positive value of ICER. It means adopting the educational intervention resulted in additional expenses of approximately $24.18 per cognitive composite score gained. There is no explicit official threshold value for cognitive development in Uganda. Thus, this study finding shows that education intervention is likely to be a cost-effective strategy for the WTP threshold above $24.18 per cognitive composite score gained.

Table 11 indicates a deterministic result of the education intervention compared with the control group. The cost per children with the education intervention was $363.46 and for the control was $275.42 per child. The incremental cost of the educational intervention was approximately $88.04, and the incremental cognitive development was $15.03. Therefore, the educational intervention ICER was $5.86 per cognitive composite score gained. That means implementing educational intervention resulted in additional expenses of approximately $5.86 per cognitive composite score. The education intervention is likely to be cost-effective compared with control for the willingness-to-pay threshold of above $5.86 per cognitive composite score.

5.4 Sensitivity analyses

5.4.1 Deterministic sensitivity analyses

Key paraments such as cost of personnel, materials and other costs, capacity building, and cognitive composite score were found to have a significant impact on ICER. Section 4.5 presents a detailed description of the range chosen for the sensitivity analysis of one-way and two-were explained.

One-way sensitivity analyses

Personnel was the most crucial part for the implementation of educational intervention. Cost of personnel was found to have a significant impact on ICER values.

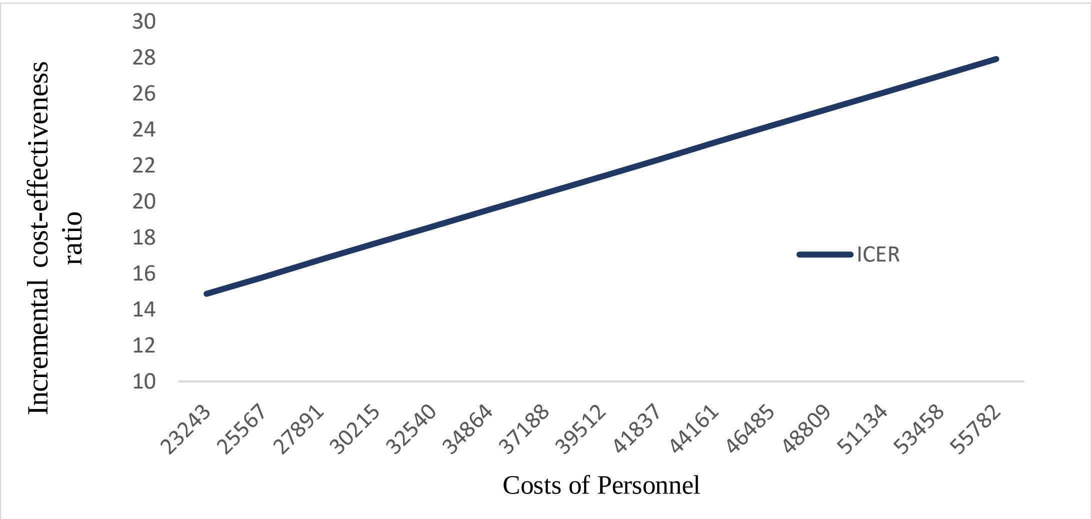

Figure 4. Effect of personnel cost on ICER

As illustrated in figure 4, the one-way sensitivity analyses showed that when personnel cost is reduced by 50%, which is $23,243 instead of the original cost $46,485 the ICER would be around $15. While, if personnel costs increased by 20%, then ICER would be increased to $28. Thus, the cost of personnel has a significant effect on the ICER. Noted that all costs were incurred only in the intervention group, as we are comparing with a do-nothing strategy.

Figure 12 shows the one-way sensitivity analyses of education intervention compared with the control group. The cost of personnel had a significant effect on the ICER. When the cost of personnel increased by 20%, then ICER became $9.6; when the cost of personnel decreased by 20%, then ICER became $2.

Sensitivity analyses of cognitive score

Table 5 shows the 95% confidence interval of the cognitive composite scores ranging from the lower bound of almost 111 to the upper bound of nearly 118 and the one-way sensitivity analyses checks the cognitive composite scores effect on ICER, between the mentioned bounds.

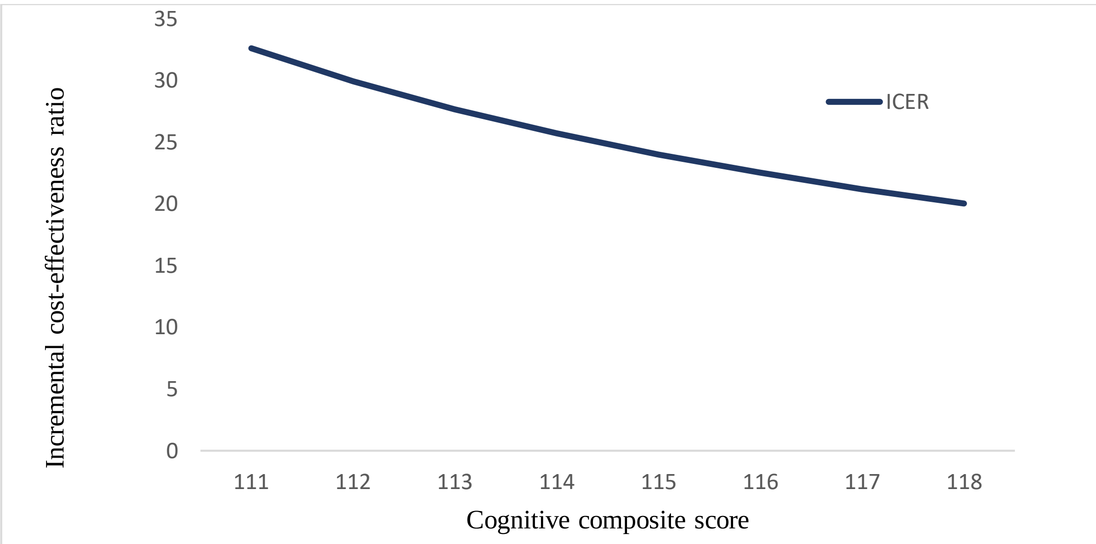

Figure 5. Effect of cognitive composite score on ICER

Figure 5 indicates that cognitive composite scores had a significant effect on ICER. Lowering the cognitive composite score from 118 to 111 resulted in the ICER increasing from $20 to $32. The resultant ICERs show that cost-effectiveness of education intervention is very sensitive to its cognitive composite scores.

Figure 13 tested the impact of the cognitive composite score on the ICER for the education intervention compared with the control group. A 95% confidence intervals of the cognitive composite score for last follow-up and sensitivity analyses have been performed with lower and upper values (Table 10). Lowering the cognitive score from 119 to 112 resulted in the ICER increasing from $4.5 to $7.2.

Tornado plot of cost categories and cognitive score

The results of the cost categories and cognitive composite score are combined into a tornado diagram and are presented in figure 6. In this case, cognitive score ranges from 111 to 118 to show the combined effect for costs and health outcome on ICER. Cost of personnel and capacity building ranged from 50% lower to 20% higher cost. Materials and capital costs used 20% lower and upper costs.

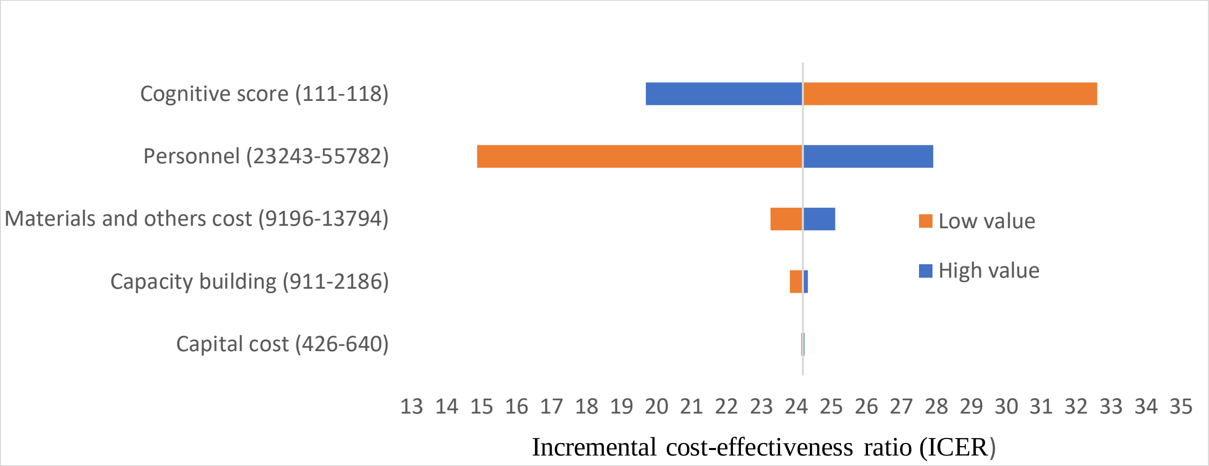

Figure 6. Effect of cost categories and cognitive composite score on ICER – tornado diagram

Figure 6 combined a one-way sensitivity analyses of cost categories and cognitive composite score into a tornado diagram. The ICER value ranges from almost $15 to $33. The cognitive scores impact on the ICER was not linear. Specifically, the lower bound of the cognitive composite score cause a comparatively higher impact on the ICER than the upper bound of the cognitive composite score. One-way sensitivity analyses showed that capacity building and capital cost categories have a small impact on the ICER. Cognitive composite score and cost of personnel had a significant effect on the ICER.

Figure 14 indicates a tornado diagram of cost categories and health outcome for the educational intervention compared with the control group. Overall, the ICER was most sensitive to changes in the personnel cost. If the cost of personnel were $55782 instead of $46,485 used in the base case, the ICER would be approximately $9.6

Summary of one-way sensitivity analyses for key cost items

One-way sensitivity analyses were also performed on the most important cost items considered to have uncertainty. Specifically, leaders, nutrition education, baseline data collection and anthropometry were considered to have an impact in the ICER.

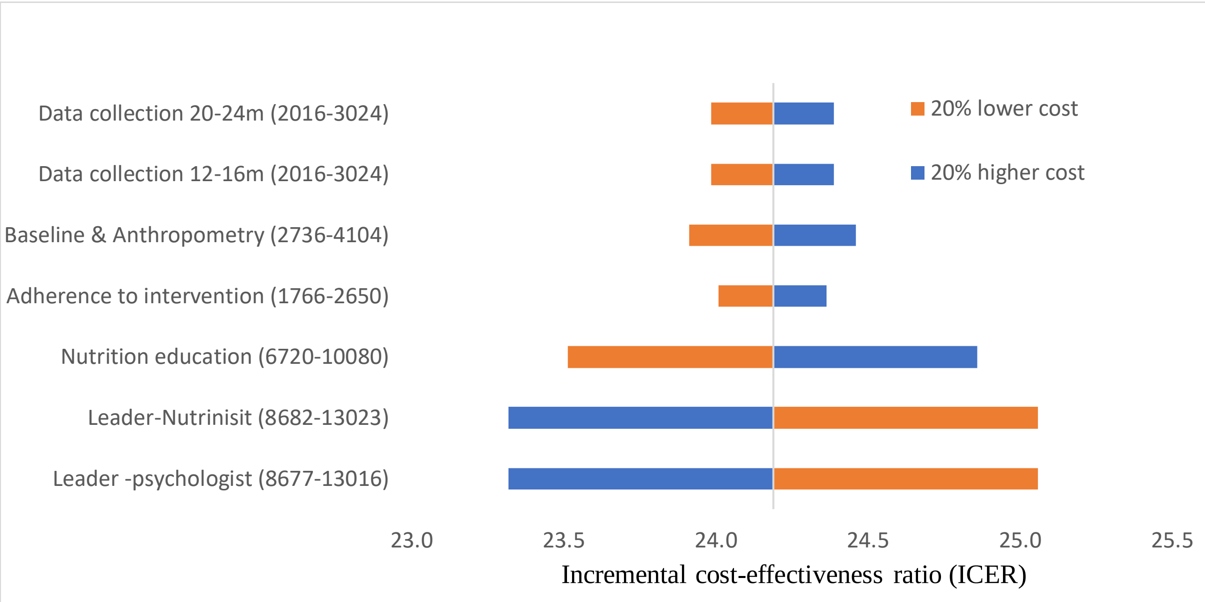

Figure 7. Effect of major cost items on ICER – tornado diagram

Figure 7 presents the summary of one-way sensitivity analyses for the main cost items in the intervention group are combined into a tornado diagram. For every cost item an upper and lower bound of ±20% from baseline level was introduced. The figure shows that, apart from leaders' cost and nutrition education cost, the remaining cost items have a small effect on ICER. The ICER value ranges from $23.3 to $25.6. All key cost items have the same effect on ICERs. Specifically, it is indicated that a percentage change in the cost items will also be associated with a similar percentage change in the ICER.

Two-way sensitivity analyses

Cost of personnel and materials and other costs were the most expensive items for this intervention. Two-way sensitivity analyses were used to examine the effect of simultaneous changes in these two cost items.

Table 7. Effect of personnel and materials costs on ICER

		Cost of materials and other costs							
		9196	9771	10346	10921	**11495**	12070	12645	13220
Costs of personnel	23243	13.9	14.2	14.4	14.6	14.9	15.1	15.3	15.6
	27891	15.8	16.0	16.3	16.5	16.7	17.0	17.2	17.4
	32540	17.7	17.9	18.1	18.4	18.6	18.8	19.1	19.3
	37188	19.5	19.8	20.0	20.2	20.5	20.7	20.9	21.2
	41837	21.4	21.6	21.9	22.1	22.3	22.6	22.8	23.0
	46485	23.3	23.5	23.7	24.0	24.2	24.4	24.6	24.9
	51134	25.1	25.4	25.6	25.8	26.1	26.3	26.5	26.7
	55782	27.0	27.2	27.5	27.7	27.9	28.1	28.4	28.6

Table 7 shows the two-way sensitivity analyses for the costs of personnel and materials and other costs effect on the ICER. Two key parameters (personnel and materials) showing the impact on the ICER for each combination of values within a given range. Light orange color indicates a value above deterministic ICER ($24.18). When both the costs of personnel and materials are increased by 20%, then the ICER will reach to $28.6. However, when the cost of personnel decreased to 50% and materials decreased by 20%, this resulted in an ICER of $13.9. The above two-way sensitivity analyses reveal that the ICERs is very sensitive to the cost of personnel compared to the cost of materials. The cost of personnel was found to have a significant impact on ICER values, ranging from $13.9 to $27.

Table 12 indicates a two-way sensitivity analyses for the cost of personnel and materials impact on the ICER for the education intervention compared with the control group. Both costs increased by 20%, resulting in an ICER of $10.5. When both costs reduced by 20%, resulting in an ICER of $1.2. Overall, cost of personnel had a significant effect on ICER values, ranging from $1.2 to $8.7.

5.4.2 Bootstrapping

As described in section 4, method and data, the difference in cognitive composite scores and costs between intervention and the do-nothing strategy is estimated in 1,000 ICERs.

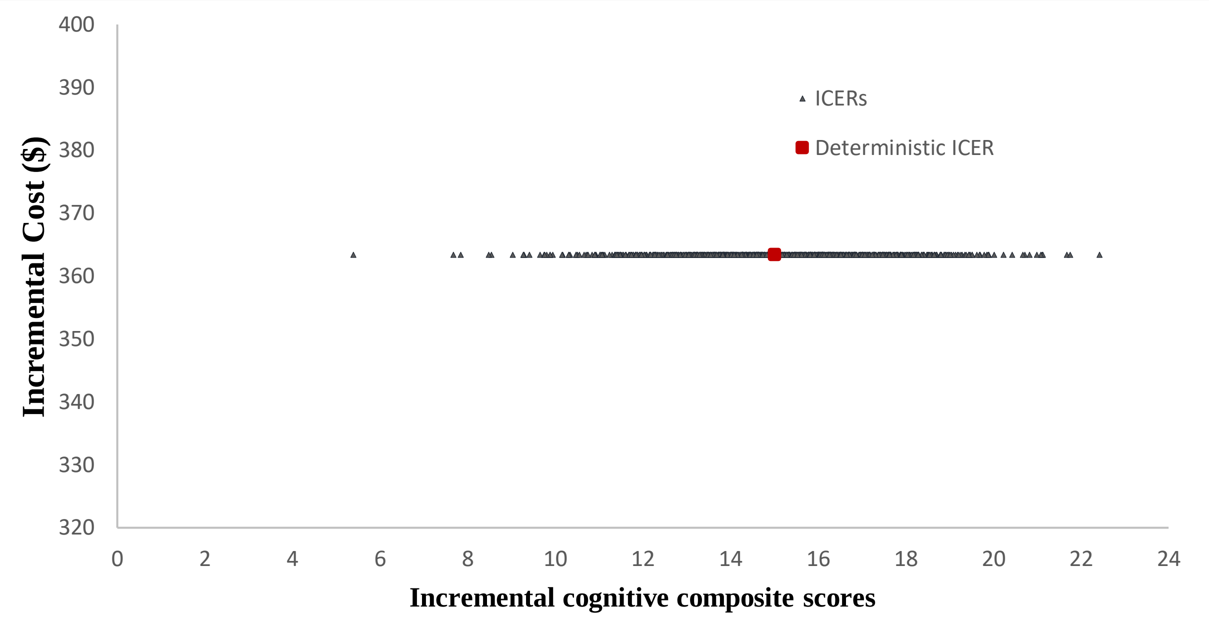

Figure 8. Scatterplot displaying uncertainty on costs and cognitive composite scores

Figure 8 indicates the scatterplot of the bootstrapped ICERs for the education intervention compared with the do-nothing strategy. This figure also presents a graphical method of a cost-effectiveness plane. The vertical axis shows the incremental cost and the horizontal axis indicates incremental cognitive composite scores. This education intervention has the same amount of cost per child, but each child had a different health outcome (cognitive development score). For this reason, bootstrapped ICERs were not scattered all over the cost-effectiveness plane; rather, all ICERs were laid on the straight line. All the ICERs scatter are lying in the north-east quadrant. It indicates that the incremental cost among 1000 iteration was the same with a mean of $363.46, while the mean incremental cognitive composite score during the 2-year period after bootstrapping was 15.2. That may suggest the relative health outcome of the education intervention over do nothing strategy; each child has the cost of $363.46.

Figure 15 indicates the cost-effectiveness plane of the bootstrapped ICERs for the education intervention compared with the control group. All of 1,000 ICERs are within the NE-quadrant. Thus, indicating that educational intervention has more costly while also providing better cognitive development. The mean increment effect after bootstrapping was $15.2 while the mean incremental costs after bootstrapping was $88.

Table 8. Incremental cost and cognitive score for the intervention

	Cognitive composite scores		Costs		Incremental outcome	
	Do-nothing	Intervention	Do-nothing	Intervention	Cognitive scores	Costs
Mean	99.7	114.9	-	$363.4	15.2	$363.4
Minimum	94.4	108.3	-	$363.4	5.4	$363.4
Maximum	104.7	120.1	-	$363.4	22.4	$363.4
Standard deviation	1.5	1.7	-	-	2.3	-
2.5th percentile	96.8	111.5	-	$363.4	10.5	$363.4
97.5th percentile	102.4	118.0	-	$363.4	19.4	$363.4

Table 8 shows the bootstrap result of incremental costs and cognitive development scores for education intervention compared with the do-nothing strategy. The incremental cognitive score among 1000 iterations has a wide variation with a mean of 15.2, ranging from 5.4 to 22.4. The costs had no variation because of the same amount of cost per child.

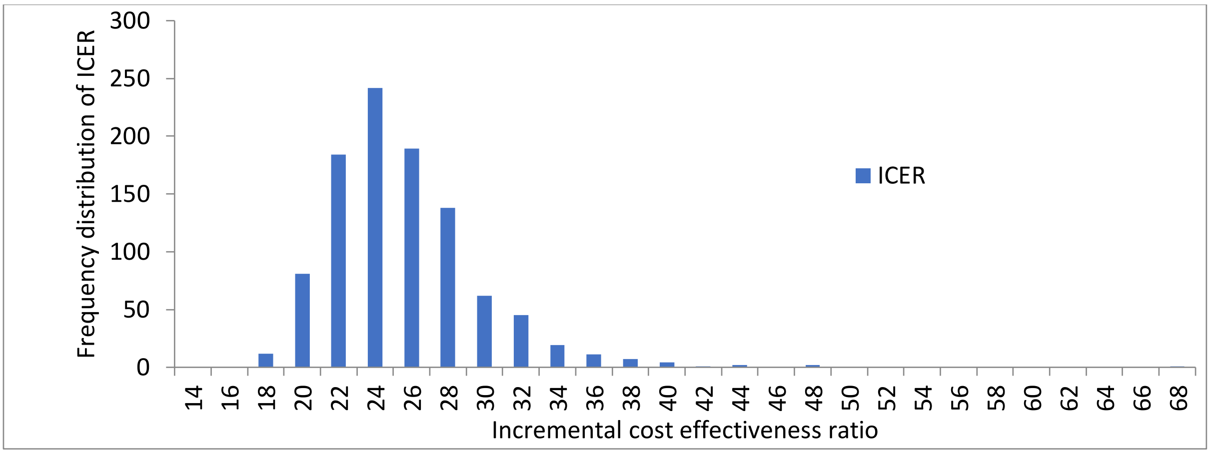

Figure 9. Frequency distribution of incremental cost-effectiveness ratio

From figure 8 the scatterplot of the bootstrapped ICERs, it is not easy to see the cost-effect pairs. Therefore figure 9 generated a histogram based on the ICER distribution from the bootstrap analyses. The majority of the ICERs range from $22 to $26, while the ICERs value of $24 contains a total of 242 cost-effect pairs of ICERs.

Figure 16 indicates the frequency distribution of the ICER for the education intervention compared with control. The majority of the ICERs range from $5 to $8. While the ICER value of $6 contains a total of 448 cost-effect pairs of ICERs

Cost-effectiveness acceptability curves (CEAC)

The uncertainty surrounding a decision is usually presented with the cost-effectiveness acceptability curve (CEAC).

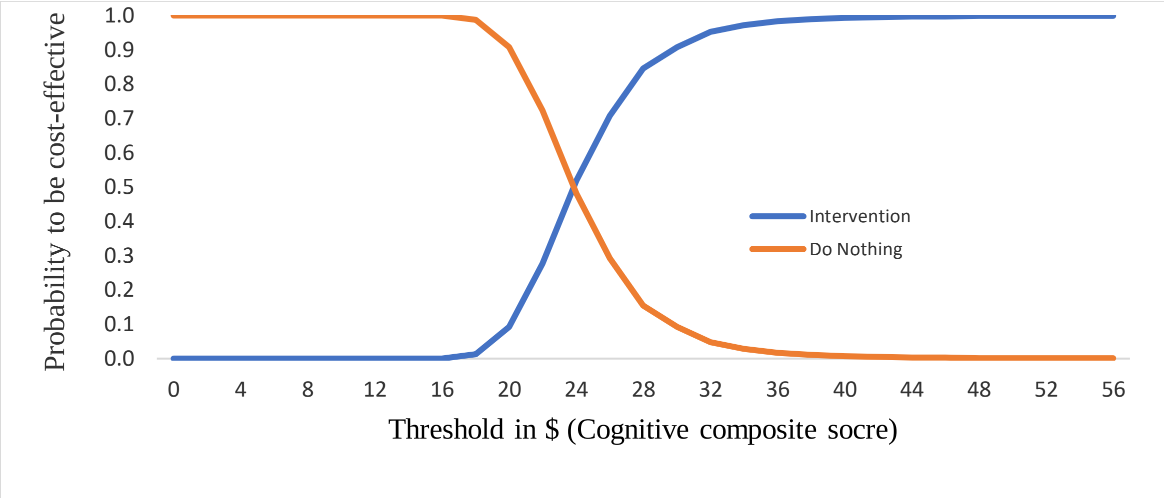

Figure 10. CEAC of educational intervention compared with the do-nothing strategy

Figure 10 gives the cost-effectiveness acceptability curve for a range of cost ceilings. A net monetary benefit analysis was performed with the results from the bootstrap analyses. This study assumed $100 as a WTP threshold value. This curve indicates the probability that the educational intervention is cost-effective compared with the do-nothing strategy, given the observed data for a range of threshold ICERs. At a threshold of $24, the education intervention has a likelihood of around 50% of being cost-effective. At a threshold of around $34, the nutrition education intervention has a 100% probability of being cost-effective. The probability of the education intervention being to be cost-effective increased from 0-100% from WTP ranging from $0 to $34 and reached a plateau afterwards.

Figure 17 indicates CEAC for the education intervention compared with the control group. At a threshold of around $9 the education intervention has a 100% probability of being cost-effective compared with the control group and reached a plateau afterwards.

6 Discussion

The previous RCT found that nutrition education intervention had improved cognitive development of small children in rural Uganda (24). However, cost and cost-effectiveness analyses had not been performed for that intervention. This thesis assessed the cost-effectiveness on education intervention compared with the control group, considering health care provider perspective over the two-year time horizon. For the future endeavours of this intervention, there will be no comparator group. This study also assessed the cost-effectiveness of educational intervention compared with the do-nothing strategy for costs and cognitive development. The objective of this CEA was to aid the decision-makers by proving an economic evaluation of health outcomes and costs.

I considered two important concerns in this economic evaluation. That is within a future large-scale implementation of the education intervention; the personnel and capacity building cost will gradually decrease because of the cost per child is correlated with the number of participants. Another aspect that needs to be considered for future implementation of this intervention is comprised of time horizon, target population, and assumptions that need to coincide with the setting of Uganda.

To my best knowledge, this study is the first cost-effectiveness analyses of an education intervention to improve cognitive development among small children in Uganda. I also did not find any other existing cost-effectiveness analysis of cognitive development from a global perspective.

6.1 Main finding

The main results indicate that educational intervention can be considered cost-effective compared with control from the health care provider perspective in Uganda. The cognitive composite score for the intervention group was 144.88 in contrast to 99.85 for the control group. The nutrition education was more costly compared to the control group by $88.04 over two years and yielded an additional cognitive composite score gain of 15.03. Therefore, the intervention had an ICER of $5.86 per cognitive composite gained. Thus, the educational intervention can be considered cost-effective compared to the control group for a WTP threshold of above $5.86 per cognitive composite score in the context of Uganda.

Concerning future implementation, the cost of nutrition education intervention is $363.46 and brings 114.88 cognitive composite scores, while a do-nothing strategy costs $0 and provides 99.85 cognitive composite scores. Therefore, the incremental cost-effectiveness ratio is $24.18. Thus, the education intervention is likely to be considered cost-effective compared with the do-nothing strategy if the willingness to pay exceeds $24.18 per cognitive composite score gained.

For a future large-scale implementation, higher participants will lead to lower average costs. Specifically, capacity building cost is a one-time cost, and this cost will be equally distributed among the participants. High personnel costs are common in educational intervention programmes and tend to decrease marginally over time with the increasing number of participants (59). However, few expenses can differ, such as money spent on t-shirts (incentive cost) for all participating mothers. This incentive cost can vary because it depends on how the response of people to a specific type of stimulus and the amount of the intervention budget.

Uncertainty surrounding the decision from this CEA has been addressed by performing one-way, two-way sensitivity, and non-parametric bootstrap analysis. Based on the one-way and two-way sensitivity analyses results personnel and materials costs have a significant influence on the ICER. In particular, the result of the one-way deterministic sensitivity analyses indicates that cost of personnel had significant effect on ICER. This gives a clear message that if the cost of personnel could be reduced, education intervention will be an attractive policy choice for the decision-makers.

Concerning health outcome, the cognitive composite score also affects in the ICER. Figure 5 and 6 revealed that the ICER is very sensitive to the cognitive composite score. The impact of the cognitive composite score is even greater than the cost of personnel. The deterministic sensitivity test shows that the ICER reached $33 when the cognitive composite score reduced towards the lower boundary. Thus, the lower value of the cognitive composite score will lead to higher ICERs. It also highlights an important message for future implementations of this intervention; similar training and supervision should be highly prioritized to maintain the quality of the education intervention. Greater focus on capacity building and personnel proficiency should be considered. If the nutrition education intervention is not maintained to the same standard, it can lead to the lowered of the cognitive composite score, consequently a higher ICER.

Figure 6 combined a one-way sensitivity analyses of main cost categories and cognitive composite scores into a tornado diagram which shows ICERs ranged between $15 and $33. The implication from the tornado diagram indicates that the ICER is very sensitive to the cost of personnel and cognitive composite score. Remaining cost categories had a minimal impact on ICER. Findings from one-way sensitivity analyses confirmed that the ICER and consequence decision would vary with the changing of the cost of personnel and cognitive composite score.

Personnel and materials costs are main contributing to the total cost of this intervention. Health workers providing the nutrition education intervention was seen as the main driving force behind the differences incurred in both groups' costs. Two-way sensitivity analyses for the costs of personnel and materials costs impact on the ICER shows that the ICER is very sensitive to the cost of personnel compared to the cost of materials.

The cost-effectiveness plane showed the result of the uncertainty in costs and cognitive composite score. All bootstrap ICERs are laid out at the north-east quadrant; hence the intervention had a higher cost and higher composite scores. Thus, bootstrap results indicated that the intervention has a higher probability to be cost-effective as compared with the do-nothing strategy. This intervention has a likelihood of 100% to be cost-effective with a WTP threshold above $34. The decision depends on the threshold value and the likelihood of the education intervention to be cost-effective. Therefore, considering a small cost of ICER, this intervention can be considered cost-effective compared with the do-nothing strategy.

6.2 Comparison to previous research

Several studies focused on the efficacy of nutrition education that has been conducted using the Bayley Scales of Infant Development (10, 16). Studies are discussing different types of nutrition education delivered to mothers and children. Regardless of the type of education intervention, the intervention group always had higher health outcomes compared with the comparator group of children (16, 21, 48). For instance, In Uganda, the efficacy of a parenting intervention to address maternal psychological wellbeing, child development and growth has been assessed (8). Integrated parenting intervention results indicated improvement in child development and maternal well-being in rural Uganda. At the last follow-up, children in the intervention group had significantly higher cognitive and language scores than children in the control group.

Cost-effectiveness analysis of nutrition education intervention delivered to mothers to enhance children cognitive development has been rarely conducted. Due to the lack of cost-effectiveness studies with the same intervention and health outcome, merely an indirect comparison of studies might be appropriate. I have found only one CEA study for education intervention to improve cognitive development.

In Pakistan, a similar cost-effectiveness study was performed on early child development (28). Authors have experimented on randomized trial on children from birth to 24 months in rural Pakistan. The study looks at the cost-effectiveness of a randomized cluster trial for the groups of enhanced nutrition, responsive stimulation, integrated and control group. Their analysis proved that early childhood intervention that includes responsive stimulation is more cost-effective than nutrition intervention alone in promoting children early development. At the trial cognitive composite score difference between with response stimulation compared without responsive stimulation were 81.7 and 74.1, respectively.

6.3 Strengths and Limitations

Strengths

This study aims to contribute to the intervention literature of cost-effectiveness on the impact of parenting educational training, analysing the potential impact on the cognitive development of children in resource-constrained countries.

One of the main strengths of this analyses is based on a previous randomized trial, which minimizes selection bias. In particular, a rigorous randomization procedure reduces selection bias. Table 4 also indicates that at baseline and dietary diversity, both groups were similar. In particular the mean age of index children were similar between groups.

Missing data can potentially violate the results. I have adjusted these missing data. This study retained only those children who were assessed at baseline and then continue throughout the last follow-up trial. Therefore, missing data were omitted for this analysis. However, reducing the number of participants also correlated with increasing per child cost. Thus, one-way and two-way sensitivity analyses revelated lower and higher costs impact on the ICER.

This study performed a standard cost-effectiveness analysis. This procedure did not use various sources for costs and health effect data. Both the health outcome and costs data were carried over from the previous RCT. The trial provides the sole source of evidence on resources use and health effect that, together with external valuation data (47). Therefore, this analysis indicates the possibility of full-scale implementation in order to examine the CEA of nutrition education intervention.

This study also incorporated a different amount of uncertainty through wide-ranging sensitivity analyses, such as the bootstrap analyses resulting in CEAC. In addition, I also performed one-way and two-way sensitivity analyses. Specifically, in the sensitivity analyses, I tested a range of values that were most likely to capture the extreme changes in costs and effects.

Limitations

This study has a few potential limitations. I have searched the literature for evidence to support this cost-effectiveness analyses. My literature search showed no other similar cost-effectiveness studies of nutrition education intervention which was based in Uganda or with a global perspective. However, there are several studies revealing the efficacy of nutrition education for children's cognitive development. However, economic evaluation has rarely been conducted on this topic. Thus, it was challenging to assess this cost-effectiveness analysis. Therefore, I was cautious about making reasonable assumptions regarding the aim of future endeavours of this educational intervention.

Data was collected via meetings with the previous RCT researchers. They do not have cost data from explicitly on each period basis; rather, they have costs record based on some activities incurred during the intervention. Therefore, differentiating between the cost item from baseline to the last follow-up was beyond the scope of this study. Thus, this analysis illustrates the costs and effect at the endpoint of the intervention. Implying that both cost and effect can be separated then it will be easier to see how the ICER is changing throughout the trial period.

One of the main limitations can be the accuracy of cost data. Cost data was sought via an interview with the researchers, rather than observing project budget and expenditure record. Thus, the cost can be varying for actual implementation. In addition, an ideal practice for a cost-effectiveness analysis should be conducted along-side the RCT (57). Noted that this cost-effectiveness analysis was planned after conducting the RCT. Therefore, it became challenging to identify all relevant costs item for this cost-effectiveness analysis. The RCTs cannot always inform resource allocation decisions unless the costs of interventions are considered alongside their effects (59). I have received full access for health outcome data, but it was beyond this study scope to observed project budget and expenditure record.

The previous RCT might be more expensive to compare with the future implementation of the education intervention since the previous trial had assessed more health outcomes. Specifically, personnel spent 1.5 hours on average to assess individual child health outcomes. While using BSID-III scale, it requires, on average 40-60 minutes to assess health outcomes (44). It is beyond the scope of this thesis to separate personnel explicit working hours spent only for the using of BSID-III scale. It might reflect on the education intervention costs when distributing costs down to per child. One-way and two-way sensitivity analyses showed that increasing personnel costs had a significant impact on the ICER.

A quality-adjusted life-year (QALY) is the preferred measured of health outcome when conducting economic evaluations (46). However, there are some efficacy studies (8, 16, 28) where education intervention delivered to mothers and health outcome represent by cognitive composite score instead of converting quality-adjusted life-year (QALY) or Disability-adjusted life year (DALY) averted. To my best knowledge, there is no standard conversion procedure available to convert the cognitive composite score to QALY or DALY averted. Thus, it was beyond this study scope to convert the cognitive composite score to QALY or DALY averted.

CEA results can differ based on the perspective chosen in the analysis. This study assessed the healthcare provider’s perspective and possible arguments for taking into consideration the societal perspective. Social planners are driven by the given budget to maximize the return of the investment. The optimal goal for this study will be a large-scale implication of the nutrition education intervention for enhancing small children’s cognitive development. A broad view would be appropriate for this study. In particular, including indirect costs from mothers and future loss or gain of cognitive development for the children. Cognitive development impacts are not only childhood life but also has a vital effect on the rest of life, human capital development and spills over effects to health. However, it is quite challenging to assess societal costs and health benefits for the Ugandan setting because of the lack of data availability and research. Thus, to assess the financial impact of having a consequence of cognitive development in small children becomes challenging.

6.4 Recommendation for further research

There is still a knowledge gap to be filled in the area of nutrition education intervention. The current study only considers the health outcome of a nutrition education intervention for up to two years. Further research can be taken into consideration for a long time. A CEA of a long time can be taken into consideration to provide more reliable empirical evidence of the education intervention.

7 Conclusion

This thesis, I verify whether nutrition-related education intervention is cost-effective compared control group to improve cognitive development among small children in rural Uganda. For the potential implementation of this intervention, control group considered as a do-nothing strategy. A standard cost-effectiveness analysis was used to assess this analysis.

The main result is that nutrition duction is likely to be considered cost-effective compared with the control group if the willingness to pay exceeds $5.86 per cognitive composite score. For the future implementation of this intervention, there will be no comparator group. Therefore, this study also performed a cost-effectiveness analysis considering comparator as a do-nothing strategy. This study finding shows that educational intervention can be considered cost-effective compared with the do-nothing strategy for the willingness-to-pay threshold above $24.18 per cognitive composite score gained. In addition, uncertainty around the cost-effectiveness ratio is explored with the support of one-way, two-way sensitivity and bootstrap sensitivity analysis. Summary of one-way and two-way sensitivity analyses revealed that the cost of personnel and cognitive composite scores have a large impact on ICER. Rest of cost items had a minimal impact on ICER.

Based on this thesis result, it is valuable to explain why a pilot study is required for this intervention before kick-off a large-scale implementation. In implementing this intervention through nutrition education, an initial trial could be instrumental in setting up future cost-efficiency analysis. Cost-effectiveness analysis should be continuing alongside the trial. This process will provide more reliable evidence for the future a large-scale implementation of this intervention. Thus, the outcome of a pilot trial, including cost, health outcome, cost-effectiveness analyses and sensitivity analysis, can be a helping tool to inform decision-makers in the resource allocation process in Uganda or similar countries.

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Appendix

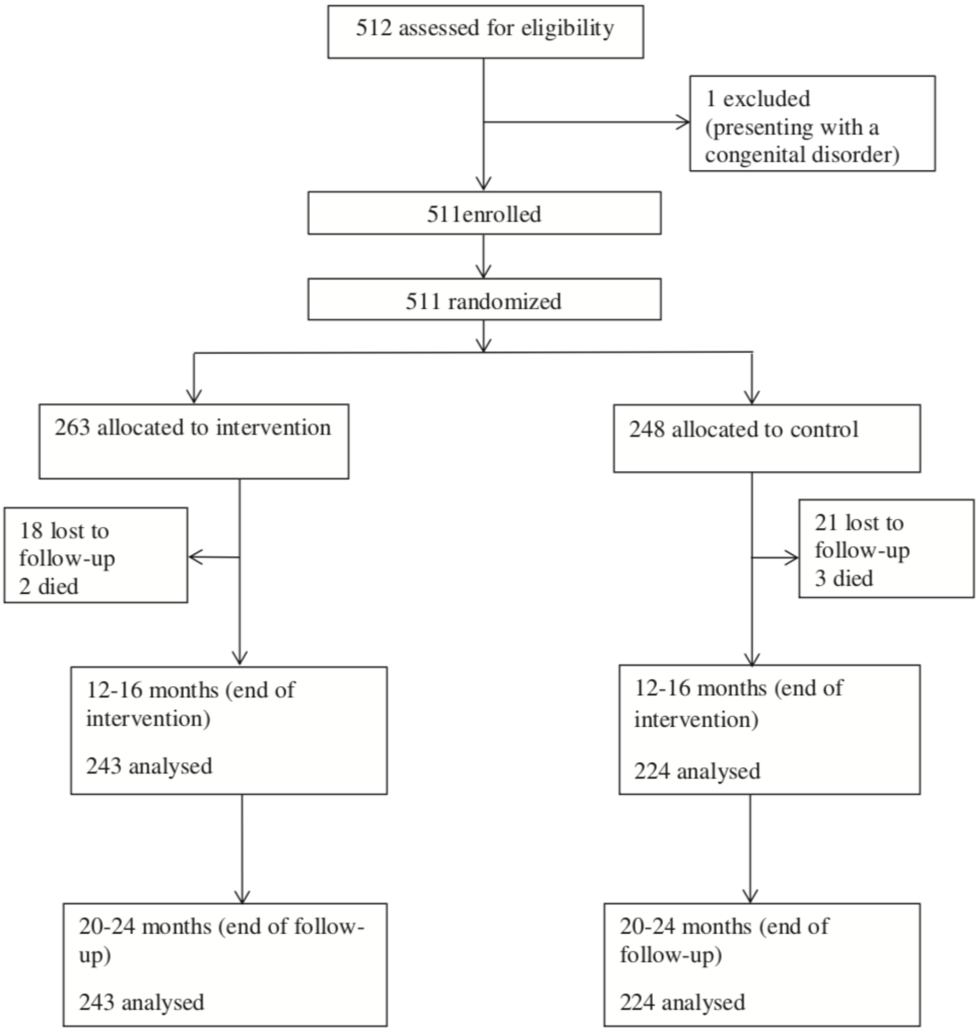

Figure 11. Trial Profile for nutrition-related education intervention

Source: Iversen et al, (24)

Table 9. Total, average and percentage of cost for the intervention and control group (US$)

Cost categories	Total costs	Intervention group	Control group	% of total costs	% of Intervention costs	% of Contorl costs
Capacity building	**3 643**	**1 822**	**1 822**	4 %	3 %	4 %
Baseline data collectors training	90	45	45			
Data collector trainer's	75	38	38			
Follow-up data collectors training	336	168	168			
Follow-up trainer	90	45	45			
Follow-up trainer	252	126	126			
Child development tools -Training	1 800	900	900			
Child development tools -trainer	1 000	500	500			
Personnel	**79 160**	**46 485**	**32 675**	78 %	77 %	79 %
Leader - Clinic psychologist	21 695	10 847	10 847			
Leader - Nutritionist	21 695	10 847	10 847			
Baseline & Anthropometry	6 840	3 420	3 420			
Baseline Psychological tests	5 040	2 520	2 520			
Intervention (Nutrition Education)	8 400	8400				
Adherence to intervention	2 208	2208				
Facilitation of intervenion (VHTs)	3 203	3 203				
Data collection - (12-16m)	5 040	2 520	2 520			
Data collection - (20-24m)	5 040	2 520	2 520			
Materials and other costs	**17 780**	**11 496**	**6 284**	17 %	19 %	15 %
Bayley scales kit (basecase)	1 580	830	750			
Bayley scales kit (12-16m)	1 580	830	750			
Bayley scales kit (20-24m)	1 580	830	750			
Food demonstration (Purchases)	2 175	2 175				
Toys (pencils, paper)	218	115	104			
Data collection (scales, tapes)	86	42	42			
Transportation costs of Team						
Baseline	961	481	481			
12-16 months	961	481	481			
20-24 months	961	481	481			
Car rent for Intervention	2 625	2625				
Incentives - (T-Shirt)	2 458	1 291	1 167			
Refreshments						
12 - 16months	705	353	353			
20 - 24 months	705	353	354			
Incentives to mothers						
12 -16 months	370	194,22	175,5			
20 - 24 months	370	194,22	175,5			
Transportation costs of mother						
12 -16 months	223	111	111			
20 - 24 months	223	111	111			
Capital costs	**1 065**	**533**	**533**	1 %	1 %	1 %
Hired special rooms						
12 -16 months	70	35	35			
20 - 24 months	21	11	11			
Mobile Tent	850	425	425			
Telephone	125	63	63			
Total Cost	**101 648**	**60 335**	**41 313**	**100 %**	**100 %**	**100 %**
Cost per monther/child		**363.46**	**275.42**			

Table 10. Child cognitive development status based on the previous RCT

	Intervention group		Control group		Between group difference		P-value
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean difference	95% CI	
Baseline 6-8 months (intervention = 239 and control=216)	101.99 (12.84)	100.35-103.62	103.52 (13.8)	101.66-105.38	1.53	-.928 - 3.99	0.22
Follow-up 12-16 months (Intervention =198 and Control=178)	110.60 (12.30)	108.81 -112.33	103.84 (12.27)	102.03-105.66	6.75	4.26-9.25	0.00
Follow-up 20-24 months (Intervention = 204 and Control =186)	115.53 (22.53)	112.42-118.65	99.34 (17.53)	96.80 -101.88	16.19	12.14-20.24	0.00

Numbers are given in mean (Standard deviation) and 95% confidence interval
P-value is for the difference between the two groups at each study time point

Table 11. Cost-effectiveness result for the intervention compared with the control group

Deterministic result					
Program	Costs	Cognitive score	Incremental cost	Incremental cognitive score	ICER
Control	275.42	99.85	N/A	N/A	N/A
Intervention	363.46	114.88	88.04	15.03	5.86

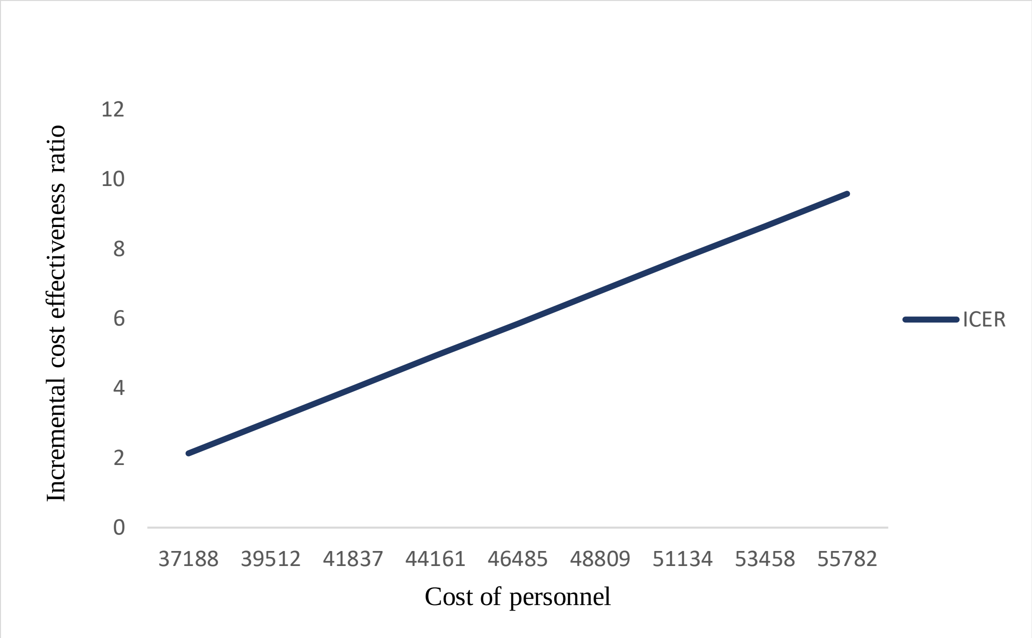

Figure 12. Effect of personnel cost on ICER – intervention versus control group

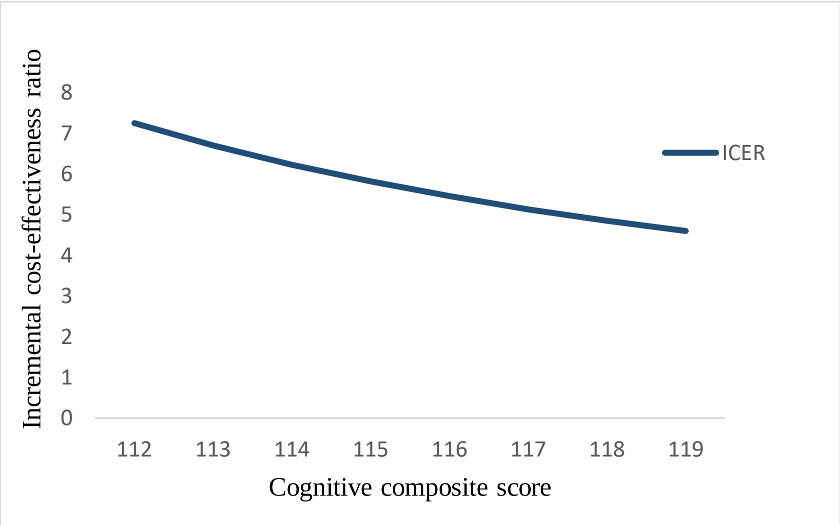

Figure 13. Effect of cognitive composite scores on ICER – intervention versus control group

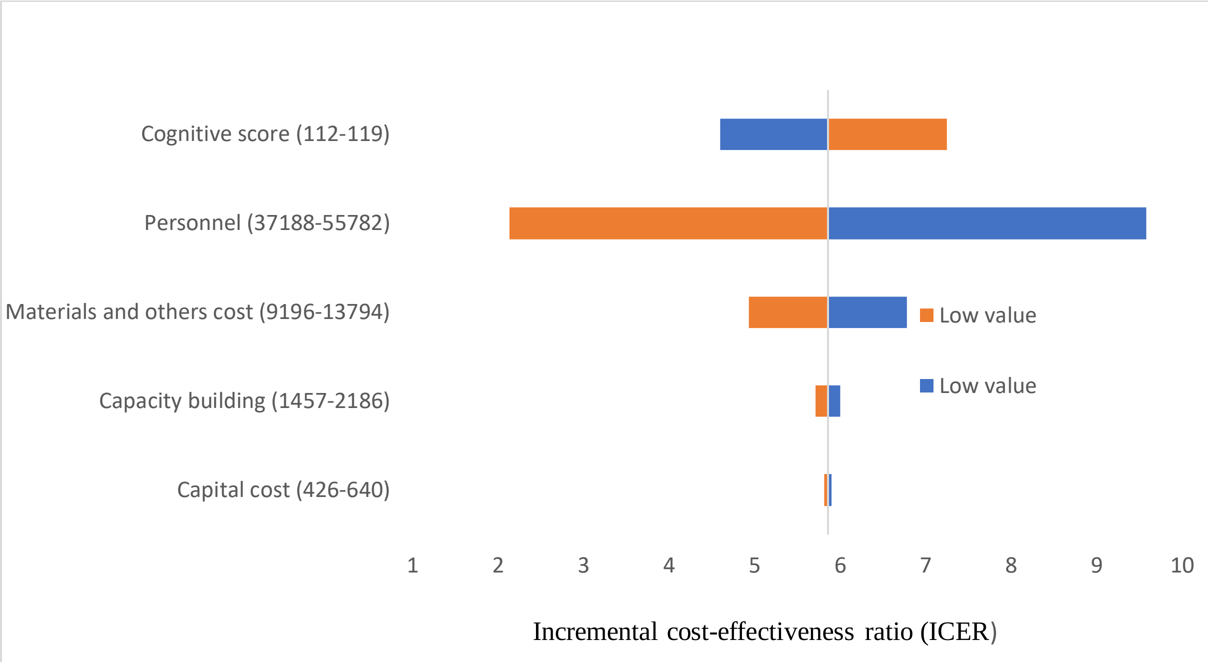

Figure 14. Effect of cost categories and cognitive composite score on ICER – tornado plot for intervention versus control

Table 12. Effect of personnel and materials costs on ICER – intervention versus control

Cost of personnel	Materials and other costs								
	9196	9771	10346	10921	**11495**	12070	12645	13220	13794
37188	1.2	1.4	1.7	1.9	2.1	2.4	2.6	2.8	3.1
39512	2.1	2.4	2.6	2.8	3.1	3.3	3.5	3.8	4.0
41837	3.1	3.3	3.5	3.8	4.0	4.2	4.5	4.7	4.9
44161	4.0	4.2	4.5	4.7	4.9	5.2	5.4	5.6	5.8
46485	4.9	5.2	5.4	5.6	5.9	6.1	6.3	6.6	6.8
48809	5.9	6.1	6.3	6.6	6.8	7.0	7.3	7.5	7.7
51134	6.8	7.0	7.3	7.5	7.7	8.0	8.2	8.4	8.6
53458	7.7	8.0	8.2	8.4	8.7	8.9	9.1	9.3	9.6
55782	8.7	8.9	9.1	9.4	9.6	9.8	10.0	10.3	10.5

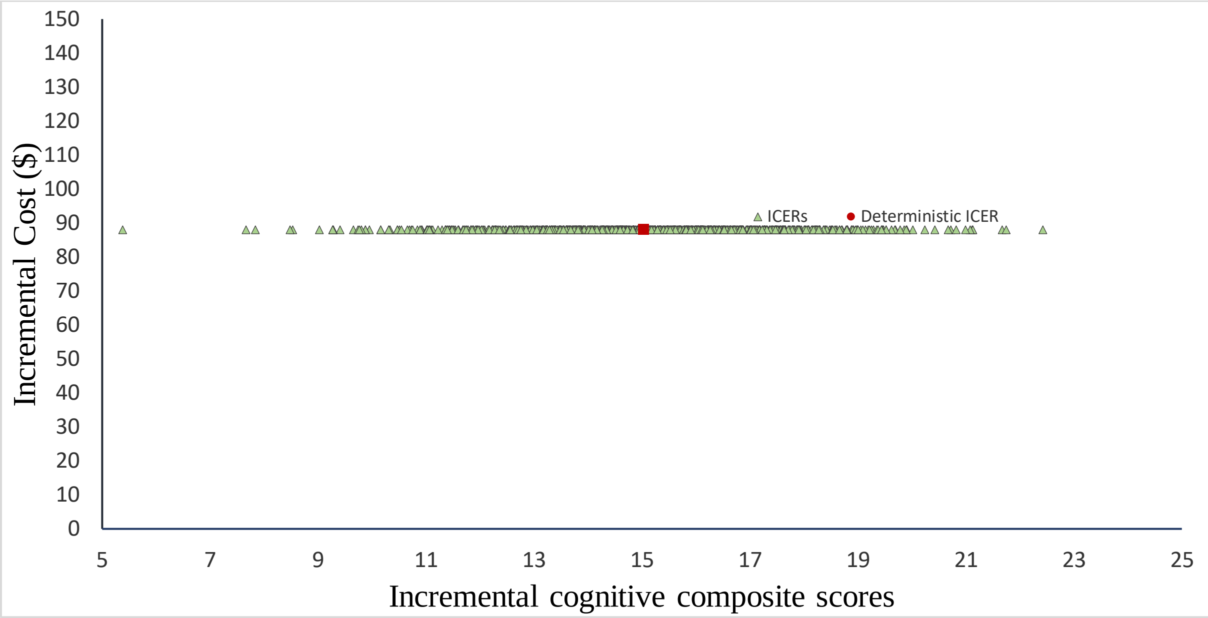

Figure 15. Cost-effectiveness scatter plane - intervention versus control group

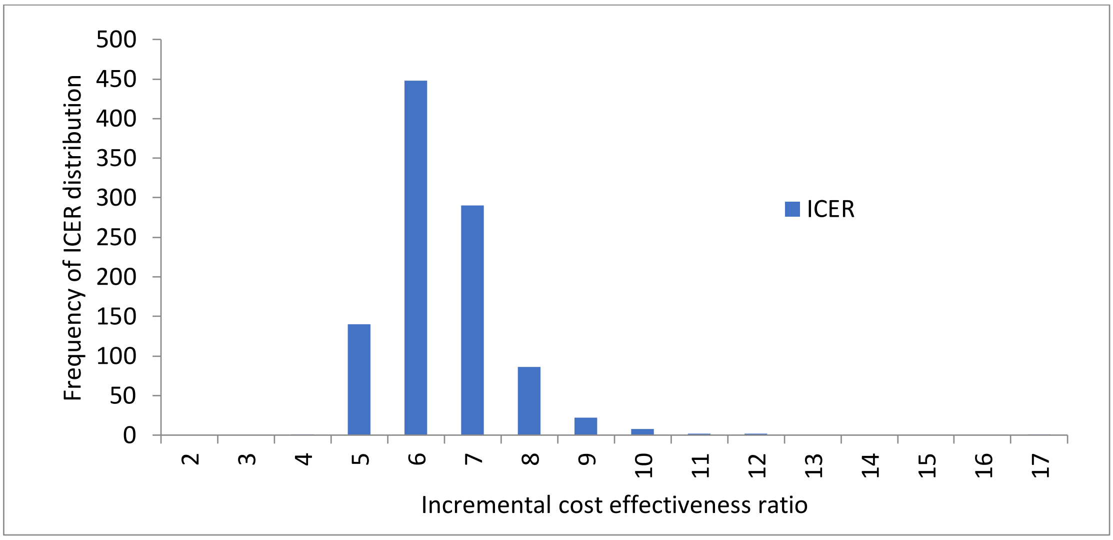

Figure 16. Frequency distribution of ICERs for intervention versus control group

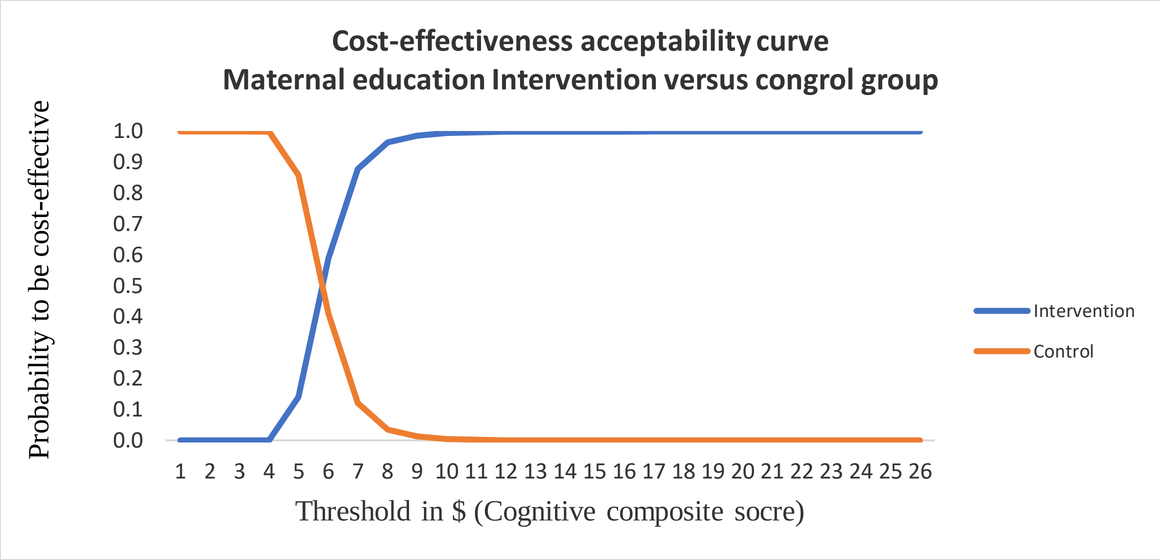

Figure 17. CEAC of the educational intervention versus control group