Effect of a Center-Based Early Childhood Care and Education Program on Child Nutritional Status: A Secondary Analysis of a Stepped-Wedge Cluster Randomized Controlled Trial in Rural Sindh, Pakistan

Effect of a center-based early childhood care and education program on child nutritional status: A secondary analysis of a stepped wedge cluster randomized controlled trial in rural Sindh, Pakistan

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Abbreviations:

BMI: body-mass index

BMIZ: BMI-for-age z score

CYL: Community Youth Leaders

ECCE: early childhood care and education

GEE: Generalized Estimating Equation

HAZ: height-for-age z score

HCZ: head circumference z scores

HICs: high-income countries

ICC: intra-cluster correlation coefficient

ITT: intention-to-treat

LEAPS: Youth Leaders for Early Childhood Assuring Children are Prepared for School

LMICs: low- and middle-income countries

LMM: linear mixed effect model

MUAC: mid-upper arm circumference

MUACZ: MUAC-for age z score

NCHD: National Commission for Human Development

OR: odds ratio

SDGs: Sustainable Development Goals

ToT: training of the trainer

WAZ: weight-for-age z score

WHO: World Health Organization

WHZ: weight-for-height z score

95% CI: 95% confidence interval

Abstract

Background: High-quality early childhood care and education (ECCE) programs can positively impact children's development. However, as an unintended consequence, ECCE attendance may also affect children's nutritional status.

Objective: We evaluated the effect of a center-based ECCE intervention on child nutritional outcomes in rural Pakistan.

Methods: This study utilized data from a stepped-wedge cluster randomized controlled trial of a center-based ECCE program that trained female youth to run high-quality preschools for children aged 3.5-5.5 years (LEAPS program) in rural Sindh, Pakistan. The program did not include any school meals. A total of 99 village clusters were randomized to receive the LEAPS intervention in three steps, and repeated cross-sectional surveys were conducted to assess the impact on children (4.5-5.5 years old) at four time points. Intention-to-treat analyses with multi-level mixed-effect models were used to estimate the effect of the intervention on child anthropometric outcomes.

Results: The analysis included 3,858 children with anthropometric data from four cross-sectional survey rounds. The LEAPS intervention was found to have a positive effect on child HAZ (mean difference: 0.13 z-scores; 95% confidence interval (CI): 0.02, 0.24). However, there was a negative effect on weight-based anthropometric indicators, -0.29 WHZ (95% CI: -0.42, -0.15), -0.13 BMIZ (95% CI: -0.23, -0.03), and -0.16 MUACZ (95% CI: -0.25, -0.05). An exploratory analysis suggested that the magnitude of the negative effect of LEAPS on WHZ, BMIZ, and WAZ was greater in the survey round during the COVID-19 lockdown.

Discussion: The LEAPS intervention positively affected child linear growth but had negative effects on multiple weight-based anthropometric measures. ECCE programs in low- and middle-income country settings should evaluate the integration of nutrition-specific interventions (e.g., school lunch, counseling on healthy diets) and infection control strategies to promote children's healthy growth and development.

Clinical Trial Registry: ClinicalTrials.gov, NCT03764436, https://clinicaltrials.gov/ct2/show/NCT03764436

Keywords: Children, preschool, anthropometry, child development, Pakistan

Introduction

Decades of research have demonstrated the crucial role of the first five years of life in shaping children's growth and development (1). However, poor child growth and suboptimal developmental outcomes persist in low and middle-income countries (LMICs), with an estimated 149 million children under the age of 5 years being stunted, 45 million wasted, and 250 million failing to reach their full developmental potential (2, 3). Children in LMICs are vulnerable to multiple risk factors that can contribute to both poor growth and developmental outcomes, such as preterm birth, low birth weight, small-for-gestational age, food insecurity, infections, low maternal education, maternal depression, and other exposures within the broader socioeconomic and environmental context (2, 4). The Sustainable Development Goals (SDGs) include multiple targets to improve child undernutrition and development (5), which has led to increased investment in child nutrition and early childhood care and education (ECCE) programs.

ECCE encompasses learning opportunities for children outside their homes, such as daycare, preschool, and pre-primary school programs, from birth to eight years old. A large body of research on ECCE in high-income countries (HICs) and LMICs has generally shown positive cognitive and social-emotional developmental outcomes for children (6-9). However, few studies have evaluated the effect of ECCE interventions on child nutrition outcomes in LMICs using experimental and quasi-experimental designs, and the evidence is mostly from studies that included a nutrition intervention. Three studies of ECCE programs that included school meals that varied in terms of the quality and quantity of meals provided found mixed effects on the nutritional status of the children (10-12). For example, a subsidized community nursery program in Colombia was found to have a positive effect on the linear growth of children aged 3-6 years (10), whereas a preschool program in Bolivia had a negative impact on the weight of children under age five years despite the fact that both studies included school meal equivalent to 70% of daily calorie requirements (11). Given that ECCE programs bring children together in groups, it is hypothesized that an increased risk of infectious disease transmission may contribute to the negative effects on morbidity and child weight in some settings. Therefore, research is needed to better understand the impact of ECCE programs on the nutritional status of children in LMICs, particularly in contexts with high risk of infectious diseases and food insecurity where these effects may be most pronounced.

Child nutritional status is a complex interplay of diet and infectious disease morbidities within a broader social, political, and economic environment (13). Leroy and colleagues, in their systematic review of daycare/ ECCE programs, used a program theory framework to identify pathways by which ECCE programs can directly and indirectly affect child health, nutrition, and developmental outcomes (9, 14). Provision of meals in the ECCE program, nutrition education, parents' social network, and parents' income opportunities are factors that may positively impact child health and nutrition. On the other hand, they note that hygiene and sanitation and increased contact between children in a group setting may elevate the risk of infection transmission and thereby negatively affect their nutritional status. Thus, an ECCE program's overall effect on child nutritional status may be determined by the balance between these positive and negative factors within the school and home environments. Given the high susceptibility of under-five children to infection and subsequent undernutrition, it is important to understand the effect of the ECCE programs in LMICs, where the majority of these programs are run in informal centers that do not provide school meals and nutrition education (9, 15).

We evaluated the effect of a center-based ECCE intervention, called LEAPS (Youth Leaders for Early Childhood Assuring Children are Prepared for School), on the nutritional status of children aged 4.5 to 5.5 years in rural Sindh, Pakistan. Given the need for early childhood education opportunities and considering the limited resources in LMICs, LEAPS preschools were conceptualized as a low-cost, innovative solution that was strategically situated in rural areas, utilized community spaces, and were operated by trained youth leaders. The LEAPS program was evaluated using a stepped wedge randomized controlled trial design with a primary outcome of children's school readiness. Nevertheless, the trial also provides the opportunity to estimate the causal effect of the program on multiple secondary outcomes, including the nutritional status of children at the population level. Findings from this study will provide critical insights that can inform the need and design of effective ECCE nutrition policies and programs in LMICs.

Methods

Study setting

The LEAPS trial was conducted in four rural districts of Dadu, Khairpur, Naushahro Feroze, and Sukkur in Sindh, Pakistan, from December 2018 to June 2021. The region has a low enrollment rate in early childhood education among children aged 3 to 5 years at 39% and a high burden of childhood undernutrition including stunting (62%), wasting (13%), and underweight (51%) (16, 17). Studies in the setting have identified multiple risk factors of childhood undernutrition, including low levels of women's literacy, poverty, high levels of food insecurity, and events such as seasonal floods and droughts (17).

Study design

A stepped wedge cluster randomized control trial was conducted to evaluate the impact of the LEAPS intervention (**Figure 1**). The primary outcome of the trial was school readiness at the population level as measured by the International Development and Early Learning Assessment (IDELA) (ClinicalTrials.gov, NCT03764436). Full details of the study methodology can be found in the published protocol (18). Briefly, villages with a primary school run by the National Commission for Human Development (NCHD) were selected for inclusion. Clusters that participated in the prior LEAPS efficacy trial (19), lacked community space for the preschool setup, had a safety concern, or lacked a female youth leader with a minimum of 10 years of education to support the preschool program were excluded. One hundred and nineteen clusters were screened, and 99 village clusters were selected from the four rural districts based on the study inclusion criteria. Village clusters were then block-randomized with a 1:1:1 ratio, stratified by district, to roll out the LEAPS intervention in three steps. All clusters started in the control state (no LEAPS intervention), and in each step, 33 clusters transitioned to the LEAPS intervention. Randomization was done using a computer-generated sequence by a study statistician not directly involved with study implementation. Due to the nature of the intervention, blinding the study participants was not possible. Blinding of the outcome assessors was attempted but blinding was limited due to visible community intervention activities.

Intervention

LEAPS was implemented in collaboration with NCHD and provided educational services for children in areas where the Ministry of Education of Pakistan has limited services. Initially, the LEAPS intervention support team, which consisted of five female trainers with master's degrees, conducted a five-day training of the trainer (ToT) course for 50 NCHD officers. The trained NCHD officers then recruited female youth leaders aged 18-24 years with at least a 10th-grade education through community-based recruitment workshops. The NCHD officers trained these youth leaders on the preschool curriculum and provided them with a "starter kit" to set up a LEAPS preschool with community support. Space for the LEAPS preschool was provided by the local community.

The youth leaders then enrolled children aged 3.5-5 years who were registered within the NCHD working areas in LEAPS preschools. The program team tried to ensure equal enrolment for boys and girls to promote gender equality. The LEAPS preschool classroom maintained a teacher-to-student ratio of 1:20 and followed the NCHD feeder primary school calendar, with six school days per week and each session lasting three hours (8:00-8:30 am to 11:00 am). Each preschool session includes individual and small group activities, indoor/outdoor play, snack time, and free play. Children were advised to bring their own snacks or food from home during school days. In case, they did not bring anything, the school provided them small packets of biscuits during snack breaks. The LEAPS curriculum included 4-5 sessions per school year on healthy eating given to preschool children to promote physical development. Hand washing and hygiene practices were promoted in the LEAPS classrooms. There was no education session on child health, nutrition, and development given directly to the caregivers.

Implementation of the LEAPS intervention started in March 2019 (**Supplemental Figure 1**). Due to the COVID-19 pandemic, LEAPS preschools remained closed from March to September 2020 during the lockdown period. At that time, NCHD implemented the LEAPS emergency plan to promote remote learning activities for the youth leaders and provided LEAPS workbooks for children to continue their learning at home. The youth leaders also met children in informal community gatherings to support learning during lockdown.

Following the lockdown, LEAPS preschools resumed operations in October 2020 and continued till March 2021. During this time, youth leaders received training in COVID-19 safety protocols. The protocols promoted practices such as handwashing, wearing masks, maintaining social distancing, identifying COVID-19 symptoms, seeking appropriate care, and adhering to guidelines for returning to work after a COVID-19 infection. The study provided essential supplies like masks, sanitizers, and disinfectants to ensure the implementation of safety precautions within LEAPS classrooms.

Data Collection

We used repeated population-based cross-sectional surveys to evaluate the impact of the LEAPS preschool intervention. The surveys were conducted at four different time points, including baseline (January-April 2019), round two (August-November), round three (February-March 2020 and June-August 2020), and endline (December 2020-March 2021) (**Supplemental Figure 1**). Due to COVID-19, round three data collection was interrupted in March-June 2020. The survey included children aged 4.5-5.5 years and their caregivers residing in the study clusters, regardless of their participation status in the LEAPS intervention. Children with severe health conditions or disabilities were excluded. Written informed consent was obtained from the parents, and verbal assent was obtained from the children.

Local women who were fluent in Sindhi and had at least a bachelor-level education were trained for ten days as study outcome assessments before the baseline survey. They also received one day of refresher training before each subsequent data collection round. If a cluster had more than 11 children, assessors used a random number generator to select 11 children who met the study inclusion criteria.

The assessors collected data on child, parent, and caregiver characteristics, household socio-demographic status, household food security, preschool readiness, child executive function, and child anthropometry (including height, weight, head circumference, and mid-upper arm circumference (MUAC)) during household visits at all four-time points. To measure height and weight, the assessors used portable Shorr boards (Weigh and Measure LLC, USA) and Seca 877 Digital Flat Scales, respectively. Height, weight, head circumference, and MUAC were measured in duplicate. Out of 3858 children surveyed, we had height measurements for 3843 children and weight information for 3844 children; <1% anthropometry information was missing. Head-circumference and MUAC measurements were available for 2153 out of 2155 children aged 4.5- 5 years. No data was collected on morbidity or prevalence of infectious diseases in the survey.

Statistical Analysis

First, we evaluated the sociodemographic characteristics of the study participants in each randomization step to assess the balance between groups. To estimate the effect of the LEAPS intervention on child nutritional outcomes, we utilized the intention-to-treat (ITT) analysis approach and followed the Hussey and Hughes analytical framework for analysis of stepped wedge randomized controlled trials (RCTs) (20). The two measures of height, weight, and MUAC were averaged prior to the calculation of z-scores. For children ≤60 months old, we estimated child anthropometric z-scores (height-for-age (HAZ), weight-for-age (WAZ), weight-for-height (WHZ), head-circumference-for-age (HCZ), and MUAC-for-age (MUACZ)) using the World Health Organization (WHO) Child Growth Standards (21). We used the WHO Growth Reference for School-Aged Children and Adolescents (5-19 years) to estimate anthropometric z-scores for children >61 months (22). We also analyzed the binary indicators of stunting (HAZ < -2), wasting (WHZ < -2 for children ≤60 months and BMIZ <-2 for children >61 months), and underweight (WAZ < -2).

A linear mixed effect model (LMM) was used to estimate the effect of the LEAPS intervention on continuous anthropometric indices (HAZ, WAZ, WHZ, BMIZ, HCZ, and MUACZ). Multi-level mixed-effect logistic models were used to estimate odds ratios for the binomial stunting, wasting, and underweight outcomes. Our primary ITT models included a random effect for clusters and fixed effects for stratified randomization and survey rounds as recommended by Hussey and Hughes for basic analysis of stepped wedged RCT with repeated cross-sectional samples(20). The assumptions of the model include i) a fixed effect for time accounting for a common underlying secular trend across all clusters, ii) a single term for the treatment, allowing a constant shift in this trend under treatment, iii) a uniform correlation structure, where the correlation between any two observations in the same cluster remains the same regardless of administered treatments and the duration between the periods of the observations given the random sampling of children from clusters in each survey rounds and iv) the data, collected at multiple discrete time points, pertain to different individuals considering children surveyed in different survey rounds are different.

Aligned with the trial protocol, we also conducted a per-protocol analysis by excluding 8 clusters that were randomized but did not roll out a LEAPS intervention either due to a lack of eligible children or insufficient space to establish a preschool in the community. There was no difference in baseline characteristics for clusters that were excluded from the per-protocol analysis as compared to clusters that were included in the analysis (**Supplemental Table 1**). Additionally, we examined as-treated effect of the intervention among children who attended LEAPS preschools in the intervention clusters as compared to children in the control clusters adjusted for child age, sex, birth order, number of children in the household, mother's education levels, father's education levels, family structure (nuclear/extended), household food insecurity level and the household wealth index.

As outlined in the protocol, we conducted the following sensitivity analyses to examine modeling assumptions of the basic stepped wedged RCT model proposed by Hussey and Hughes (20) i) adding a fixed effect for clusters to model intra-cluster correlation ii) incorporated a random effect interaction between cluster and times to adjust for potential effect modification between clusters and time if any , iii) included a random effect interaction between treatment and cluster to adjust for potential effect modification between treatment and clusters if any, iv) utilized a generalized estimating equations (GEE) model to account for variable cluster sizes, and v) employed a multivariable model adjusted for child age, sex, and birth order, the number of children in the household, mother's education levels, father's education levels, family structure (nuclear/extended), household food insecurity index, and the household wealth index to account for potential imbalances in baseline characteristics.

Additionally, we conducted an exploratory analysis to examine potential effect modification by COVID-19, by modeling interaction between the treatment and survey rounds, where round two represents the pre-COVID period and round three represents the COVID lockdown period. We also conducted exploratory subgroup analyses to examine potential modification ofthe treatment effect by child age (<5 years and ≥ 5 years), sex (male and female), household wealth (< median and ≥ median), and household food security(food secure, mild to moderate food insecure and severe food insecure). The likelihood ratio test was used to assess the statistical significance for models that explored effect modification.. All analyses were conducted using Stata 15.0 Special Edition statistical software.

Ethics

The study obtained ethical approval from the Aga Khan University Ethics Review Committee, the Pakistan National Bioethics Committee, and the Harvard T.H. Chan School of Public Health Institutional Review Board. Our study adhered to ethical principles governing human research. Written informed consent was obtained from parents, while children were asked to assent verbally in the local language, Sindh.

Funding

Dubai Cares and Saving Brains, Grand Challenges Canada funded the study. The funders had no role in the study design, implementation, data collection, or interpretation of study findings.

Results

The flow of the randomized LEAPS intervention roll-out and population-based surveys is presented in **Figure 1**. The population-based surveys included a total sample of 3,858 children aged between 4.5 and 5.5 years from 99 study clusters across the four survey rounds, which were conducted between December 2018 and June 2021. A total of 1,089 children were included in the baseline survey, 1,004 in round two, 906 in round three, and 859 in the endline survey. **Table 1** presents characteristics of children in the baseline pre-intervention survey stratified by the steps by which villages clusters were randomized to receive the LEAPS intervention. The baseline characteristics of children were similar for villages randomized to receive LEAPS in the first, second or third step in terms of the child's mean age, gender, birth order, parents, household characteristics and anthropometric measures at baseline. The coverage of the LEAPS intervention among surveyed children in which the intervention was to be implemented was 78% (248 out of 320) in round two, 59% (343 out of 518) in round three, and 72% (613 out of 857) in the endline survey (**Supplemental Table 2**). The distribution of anthropometric measures among intervention and control children by survey rounds is presented in **Supplemental Table 3**.

Table 2 shows the effect of the LEAPS intervention on children's anthropometric measures. The LEAPS intervention had a positive effect on linear growth and increased HAZ by 0.13 z-scores (95% CI: 0.02, 0.24). However, there were significant negative effects on BMIZ, WHZ, and MUACZ, with mean differences of -0.13 z-scores (95% CI: -0.23, -0.03), -0.29 z-scores (95% CI: -0.42, -0.15), and -0.16 z-scores (95% CI: -0.25, -0.05), respectively. There was no statistically significant effect of LEAPS on WAZ, HCZ, or the risk of stunting, wasting, and underweight (p-values > 0.05).

Per-protocol analyses which included 91 clusters, showed similar results as our primary ITT analysis (**Supplemental Table 4**). An as-treated analysis that analyzed children who attended LEAPS preschools in the intervention clusters compared to control children showed similar direction, but generally larger effect sizes compared to our primary ITT analysis (**Supplemental Table 5**). The negative effect of LEAPS on WHZ increased, with a mean difference of -0.35 z scores (95% CI: -0.50, -0.20) in the as-treated analysis.. All sensitivity analyses that assessed different modeling assumptions were also generally consistent with results from the primary ITT analyses (**Supplemental Tables 6-14**). However, there was a statistically significant negative effect of the LEAPS intervention on wasting in the GEE model sensitivity analysis (odds ratio: 1.31; 95% CI: 0.99-1.74; p-value: 0.04).

We also conducted an exploratory analysis to examine the potential of effect modification of the LEAPS intervention on nutritional status by the COVID-19 lockdown. Overall, we found that the negative effect of the LEAPS intervention on acute undernutrition indicators appeared to be stronger during the COVID-19 lockdown (**Table 3**). Before COVID, in survey round two the effect of the LEAPS intervention on BMIZ was 0.07 (95% CI: -0.07, 0.02), but during the COVID-19 lockdown in survey round three the effect was -0.33 (95% CI: -0.47, -0.19) (p-value for interaction <0.001). Similarly, the effect of LEAPS on WHZ and WAZ was more negative during the COVID lockdown period compared to before COVID (p-values for interaction <0.05). We also observed that the effect of LEAPS on the risk of being underweight was higher during the COVID lockdown (OR: 1.53; 95% CI: 1.05, 2.23) than before COVID (OR: 0.95; 95% CI: 0.66, 1.35; p-value for interaction 0.05). We did not observe evidence of effect modification on HAZ, MUACZ, HCZ, stunting, or wasting by the COVID lockdown period.

Exploratory subgroup analyses showed significant effect modification of the effect of the LEAPS intervention on some anthropometric measures by child sex, age group, household socioeconomic status, and household food insecurity status (**Supplemental Table 15-18**). We found larger positive effects of LEAPS on stunting and HCZ among males as compared to female children (p-values for effect modification < 0.05). In contrast, the negative effect of LEAPS on MUACZ appeared to be stronger among females as compared to male children (p-value < 0.05). We also found greater improvement in HAZ and an effect on stunting among under-five children as compared to children older than five years (p-values < 0.05). The negative effect of LEAPS on BMIZ was also more pronounced among children under five as compared to those over five (p-value 0.001). Additionally, the negative effect of LEAPS on wasting appeared to be stronger among children from high-income households compared to children from low-income households (p-value: 0.03). We also observed a stronger positive effect of LEAPS on HCZ indicator among children from food-insecure households compared to children from food-secure households (p-value: 0.01))

Discussion

Our study examined the effect of LEAPS, a center-based ECCE intervention, on the nutritional status of children aged 4.5 to 5.5 years in rural Pakistan. We found a positive impact of the LEAPS intervention on child HAZ, a marker of linear growth generally reflective of long-term nutrition status. However, we also observed a significant negative effect on weight-based anthropometric indicators, including WHZ, MUACZ, and BMIZ. Further, our exploratory analyses indicated that the negative effect of the LEAPS intervention on weight-based indicators appeared to be more pronounced during the COVID-19 lockdown period.

In this study, we found contrasting effects of LEAPS intervention on child anthropometric outcomes with positive effects on linear growth but negative effects on multiple weight-based indicators. Prior research has also shown mixed results on the effectiveness of center-based ECCE programs on child anthropometry outcomes (10, 12, 23-25). The complex relationship between linear and ponderal (weight) growth involves shared risk factors, but the response of linear growth and weight to these risk factors may differ (26-28). On an individual level, reductions in WHZ or BMIZ among children are often considered a short-term response to inadequate dietary intake or infection and are generally characterized to precede linear growth faltering (26). However, catch-up linear growth can occur, particularly among preschool-aged children. In this study, we did not follow up with the same cohort of children over time. Therefore, we cannot evaluate the effect of the intervention effect on individual growth trajectories. Nevertheless, based on the Leroy et al framework, each of the components that positively or negatively affect growth may differentially affect a child’s height and weight at the population level(9, 13). For example, weight-based indicators may be more sensitive to infections through cleanliness, hygiene, and exposure pathways, while height/length-based indicators may be more sensitive to long-term changes in child's diet through school meal or feeding, health and care practices at home through nutrition education targeted towards caregivers or social interaction.

There are multiple pathways through which ECCE interventions may have a positive effect on linear growth (9). Studies conducted in Colombia (10) and Guatemala (29) demonstrated that providing school meals can have a direct positive effect on children's dietary intake and linear growth. Unlike these programs, the LEAPS intervention did not provide school meals but instead may have indirectly improved child’s linear growth through changes in the home environment. At LEAPS preschools, children received a few short lessons on a healthy diet and good hygiene practices in school; however, it seems unlikely due to the low intensity and lack of direct communication with the caregivers that this component of LEAPS resulted in significant behavior change and contributed to effects on nutritional status. However, our qualitative interviews with caregivers of the preschool children revealed that many mothers interacted with other mothers and teachers for the first time outside their homes when their children began attending LEAPS preschools and expressed greater aspirations for improving their children's health and development. Prior literature also supports that mother’s social networks can positively impact their children's nutrition status through changes in caregiving practices by health knowledge and resource sharing (30, 31). Therefore, while ECCE programs are generally focused on promoting development outcomes and readiness for primary school, they may also indirectly support health and growth of children through effects on caregivers’ practices or directly through school lunch or supplementation interventions. Research in LMICs should evaluate the effectiveness of ECCE programs as a platform for interventions to promote broader health, nutrition, and development of preschool children.

On the other hand, the negative effects of the LEAPS intervention on weight-based anthropometry indicators, such as WHZ and BMIZ, could be either due to short-term changes in the child's diet or increased infectious disease morbidities (9). We do not anticipate any acute change in child diet within LEAPS preschools as children only stayed at school for 2 hours during the school days, while increased morbidities in the preschools are possible considering increased risks of infection among children at this age as well as the increased risk of transmission of infectious diseases in group settings. Unfortunately, in our study, we did not collect data on morbidity or infections in the population-based surveys. Nevertheless, multiple studies have found that children attending center-based ECCE programs have two to three times higher risk of infections, especially respiratory tract infections, otitis media, and diarrhea, as compared to children receiving home-based care (25, 32-36). There is a well-documented cyclical link between nutrition and infection in children; importantly, infection can lead to undernutrition through reduced nutrient intake and absorption, increased metabolism, and greater energy expenditure (37-39). Moreover, in rural Pakistan, children under five are particularly vulnerable to the infection-malnutrition cycle due to multiple existing risk factors such as high level of food insecurity, infectious diseases burden, and low vaccination coverage (17, 36). Therefore, when implementing center-based ECCE programs in contexts where food insecurity and infections are prevalent, it seems important to consider and evaluate school-based nutrition interventions such as school meals and nutrition education as well as supplemental infection control strategies, such as immunization, standard infection control protocols, illness notification, isolation of sick children, disinfection of surface areas (36, 40-42). The LEAPS program did not specifically include these components. Most infection control guidelines for preschools have been developed and evaluated in high-income settings, and therefore, research is necessary to adapt and evaluate tailored infection control strategies for contexts in LMICs (40-42).

In an exploratory analysis, we also found that the negative effects of LEAPS appeared to be stronger on weight-based anthropometry indicators in the survey conducted during the COVID-19 lockdown period. Despite the closure of preschools, children in the LEAPS intervention group continued to gather informally to support learning, which potentially increased their exposure to and transmission of infections compared to children who stayed at home (43). In contrast, the lockdown and restricted movement may have further reduced the risk of infection transmission among the children in the control areas during COVID lockdown. Therefore, the relative difference in infectious disease risk between children in LEAPS intervention and control villages may have been greater during the COVID-19 lockdown period. A population-based observation study in the UK found lower incidence and hospitalization rates for common childhood infections such as influenza, pneumonia, meningitis, mumps, and measles during the period of COVID lockdowns, school closures, and restricted travel (44). Further, COVID-19 had a negative impact on food security during lockdown periods and increased food insecurity was associated with increased wasting among children in Pakistan where there was low social support and safety net programs (45, 46). As a result, increased nutritional vulnerability during the COVID-19 lockdown, in combination with the cyclical relationship with infection, may have contributed to a stronger negative effect on acute undernutrition (37-39).

A major strength of our study was the use of a randomized design that allowed for the determination of the causal effect of LEAPS intervention on the nutritional status of the children. However, our study also had several limitations. First, inherent in the stepped wedge randomized control trial design, more clusters were exposed to the intervention towards the end of the study than in its early stages which may have confounded the effect of the intervention with any underlying temporal trend (47). To address this potential issue, we used a random effect for the cluster to account for inter- and intra-cluster correlation and fixed effects for stratified randomization by strata and survey rounds in our primary ITT analysis. We also conducted a sensitivity analysis using random effect interaction between cluster and times and random effect interaction between treatment and cluster, which yielded consistent estimates with our primary ITT analysis. As a result, there is limited potential for temporal trends to impact our study findings. Second, the evaluation used population-based cross-sectional surveys that included children who did not attend the LEAPS preschool (22% in round 2, 41% in round three, and 29% in the end line); we likely underestimated the magnitude of the effect of the LEAPS intervention on nutritional outcomes if all children in village clusters had, in fact, attended the LEAPS program. Third, we did not collect morbidity and dietary data, and therefore, we were not able to evaluate mediation pathways through which LEAPS may have impacted the nutritional status of preschool children. Of note, the LEAPS program evaluation included four cross-sectional surveys, and therefore, morbidity data would have been limited to a short duration maternal morbidity symptom recall, which would not adequately capture the incidence of infection during the LEAPS program. As a result, cohort evaluation of ECCE programs that include data on morbidity incidence, diet changes, and other potential mediators noted by Leroy, et al. should be conducted. Fourth, while LEAPS effects on continuous HAZ, WHZ, and BMI were found, there was no statistically significant effect on the binomial outcomes of stunting, wasting, and underweight, although the measures of effect were in the same direction as the continuous outcomes. This difference was likely due to reduced statistical power for binomial as compared to continuous outcomes. However, these findings are important considering the linear relationship of child HAZ with child developmental outcomes (48, 49). Lastly, our study was conducted in rural Pakistan where the burden of infectious disease and food insecurity is high. Therefore, our findings may not be fully generalizable to other settings and to center-based ECCE programs that include supplementary nutrition or infection control interventions.

Overall, center-based ECCE programs play an important role in promoting early child development and school readiness; however, these programs may also have unintended positive or negative effects on child nutrition status. In our study, we found that the LEAPS intervention had positive effects on linear growth but negative effects on weight-based anthropometric measures. Based on these findings, implementation research should be conducted to evaluate integrated strategies including infection control measures, provision of nutritious meals, and engagement of caregivers in diet counseling to promote health and good nutrition in center-based ECCE programs in LMIC settings. Finally, ECCE programs should not only be considered as an intervention to promote development and school readiness, but also as a potential platform to promote the broader health, nutrition, and well-being of preschool children.

Conflicts of interest

The authors declare no conflict of interest.

Contributors

AKY conceptualized the study. AYK, CRS, SS, and SB developed study design, implementation strategies, and data collection materials. SS coordinated the implementation of the study, training, data collection, and quality assurance. NBA conducted the formal analysis and wrote the paper. CRS and AKY supervised manuscript development, data analysis and contributed to the revisions. NBA had the primary responsibility for the final content. All authors reviewed and approved the final manuscript.

Data Sharing

Data described in the manuscript, code book, and analytic code may be made available upon reasonable request to the study principal investigator, Aisha K. Yousafzai (email: ayousafzai@hsph.harvard.edu).

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Figure 1. Study flowchart

Table 1. Baseline **c**haracteristics of the study participants who were randomized to receive LEAPS intervention in three steps, rural Sindh, Pakistan

	Baseline		
	Clusters randomized to receive LEAPS intervention in Step 1	Clusters randomized to receive LEAPS intervention in Step 2	Clusters randomized to receive LEAPS intervention in Step 3
Cluster characteristics			
Number of clusters (n)	33	33	33
Child Characteristics			
Number of children (n)	361	366	362
Female (n, %)	182 (50.4%)	188 (51.4%)	156 (43.1%)
Age in years (mean, SD)	5.0 (0.4)	5.0 (0.4)	5.1 (0.4)
Birth order (mean, SD)	3.6 (2.3)	3.9 (2.6)	3.7 (2.4)
Child nutritional statuses			
Height-for-age z score	-1.55(1.28)	-1.36(1.03)	-1.34(1.05)
Weight-for-height z score	-0.61(0.96)	-0.71(1.09)	-0.69(0.86)
Weight-for-age z score	-1.45(0.91)	-1.38(0.88)	-1.30(0.85)
BMI-for-age z score	-0.65(0.95)	-0.77(1.09)	-0.65(0.86)
MUAC-for age z score	-0.93(0.80)	-0.99(0.78)	-0.96(0.77)
Head circumference z scores	-1.31(1.10)	-1.14(0.94)	-1.04(1.13)
Mother's Characteristics			
Mother is the primary caregiver (n, %)	357 (98.9%)	361 (98.6%)	355 (98.1%)
Mother's age (mean, SD)	33.4 (6.6)	34.0 (6.5)	33.6 (6.5)
Mother's education level			
No formal schooling (n, %)	302 (83.7%)	309 (84.4%)	296 (81.8%)
Some primary school (n, %)	19 (5.3%)	17 (4.6%)	18 (5.0%)
Completed primary school (Grade 5) (n, %)	40 (11.1%)	40 (10.9%)	48 (13.3%)
Mother's primary occupation			
Housewife (n, %)	286 (79.2%)	280 (76.5%)	288 (76.5%)

	Baseline		
	Clusters randomized to receive LEAPS intervention in Step 1	Clusters randomized to receive LEAPS intervention in Step 2	Clusters randomized to receive LEAPS intervention in Step 3
Handicraft (n, %)	56 (15.5%)	57 (15.6%)	57 (15.6%)
Daily paid worker (n, %)	12 (3.3%)	21 (5.7%)	21 (5.7%)
Father's Characteristics			
Father is the primary provider (n, %)	354 (98.1%)	361 (98.6%)	354 (97.8%)
Father's education level			
No formal schooling (n, %)	160 (44.3%)	169 (46.2%)	162 (44.8%)
Completed primary school (Grade 5) (n, %)	66 (18.3%)	52 (14.2%)	67 (18.5%)
Completed middle school (Grade 8) (n, %)	19 (5.3%)	29 (7.9%)	10 (2.8%)
Completed lower secondary school (Grade 10) (n, %)	97 (26.9%)	88 (24.0%)	100 (27.6%)
Father's primary occupation			
Farmer (n, %)	112 (31.0%)	106 (29.0%)	108 (29.8%)
Daily paid worker (n, %)	71 (19.7%)	79 (21.6%)	87 (24.0%)
Industrial worker (n, %)	81 (22.4%)	69 (18.9%)	47 (13.0%)
Household Characteristics			
Family size (mean, SD)	10.7 (5.2)	10.6 (6.3)	12.3 (9.2)
Number of children in household (mean, SD)	5.0 (2.3)	5.2 (2.5)	5.0 (2.3)
Joint /extended family (n, %)	244 (67.6%)	220 (60.1%)	240 (66.3%)
Nuclear family (n, %)	117 (32.4%)	146 (39.9%)	122 (33.7%)
Household wealth quintiles (mean, SD)	2.9 (1.3)	3.1 (1.5)	3.0 (1.5)
Households having private, reliable source of drinking water (n, %)	348 (96.4%)	352 (96.2%)	344 (95.0%)
Households having latrine with flush system (n, %)	97 (26.9%)	126 (34.4%)	142 (39.2%)
Food secure household (n, %)	175 (48.5%)	183 (50.0%)	172 (47.5%)
Mild to moderate food insecure household (n, %)	125 (34.6%)	139 (38.0%)	145 (40.1%)
Severely food insecure household (n, %)	61 (16.9%)	44 (12.0%)	45 (12.4%)

Table 2. Intention-to-treat (ITT) effect of LEAPS intervention on anthropometric indicators for children aged 4.5-5.5 years in rural Sindh, Pakistan (N=3843)

Outcome	LEAPS intervention effect	P value	ICC*
Continuous outcomes	**Mean Difference (95% Confidence Interval)**		
Height-for-age z score (HAZ)	0.13 (0.02, 0.24)	<0.05	0.07
BMI-for-age z score (BMIZ)	-0.13 (-0.23, -0.03)	<0.01	0.06
Weight-for-age z score (WAZ)	-0.00 (-0.09, 0.09)	0.96	0.07
Weight-for-height z score (WHZ)	-0.29 (-0.42, -0.15)	<0.001	0.06
MUAC-for age z score (MUACZ)	-0.16 (-0.25, -0.05)	<0.01	0.06
Head circumference z scores(HCZ)	0.08 (-0.06, 0.22)	0.24	0.07
Binary outcomes	**Odds Ratio (95% Confidence Interval)**		
Stunted (HAZ< -2)	0.93 (0.73, 1.18)	0.54	0.07
Wasted (WHZ < -2 / BMI Z < -2)	1.34 (0.94, 1.91)	0.11	0.10
Underweight (WAZ < -2)	1.06 (0.83, 1.36)	0.62	0.06

*ICC= Intra cluster correlation coefficient

Table 3. Effect of LEAPS intervention on children's nutrition statuses before COVID, during COVID lockdown and effect modification by COVID 19 lockdown period

Outcome	Effect of LEAPS before COVID in Round 2	Effect of LEAPS during COVID lockdown in Round 3	Effect modification by COVID 19 lockdown period [Interaction term Intervention x Round]	P value for effect modification
Continuous outcomes	**Mean Difference (95% Confidence Interval)**			
Height-for-age z score (HAZ)	0.00 (-0.16, 0.17)	0.10 (-0.07, 0.26)	0.09 (-0.07, 0.26)	0.37
BMI-for-age z score (BMIZ)	0.07 (-0.07, 0.20)	-0.33 (-0.47, -0.19)	-0.40 (-0.57, -0.22)	<0.001
Weight-for-age z score (WAZ)	0.05 (-0.09, 0.18)	-0.16 (-0.30, -0.03)	-0.21 (-0.37, -0.04)	<0.05
Weight-for-height z score (WHZ)	-0.09 (-0.29, 0.11)	-0.48 (-0.66, -0.30)	-0.39 (-0.64, -0.14)	<0.01
MUAC-for age z score (MUACZ)	-0.15 (-0.30, -0.01)	-0.19 (-0.33, -0.06)	-0.04 (-0.23, 0.15)	0.65
Head circumference z scores (HCZ)	-0.11 (-0.31, 0.09)	0.11 (-0.08,0.30)	0.22 (-0.03, 0.48)	0.08
Binary outcomes	**Odds Ratio (95% Confidence Interval)**			
Stunted (HAZ< -2)	1.22 (0.86, 1.73)	0.85 (0.60, 1.21)	0.69 (0.44, 1.09)	0.12
Wasted (WHZ < -2 / BMI Z < -2)	1.22 (0.76, 1.95)	1.76 (1.02, 3.05)	1.45 (0.73, 2.85)	0.29
Underweight (WAZ < -2)	0.95 (0.66, 1.35)	1.53 (1.05, 2.23)	1.62 (1.01, 2.59)	0.05