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The Rang-Din Nutrition Study in Rural Bangladesh: The Costs and Cost-Effectiveness of Programmatic Interventions to Improve Linear Growth at Birth and 18 Months, and the Costs of These Interventions at 24 Months

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Abbreviations and Acronyms

CF	community facilitator
CHDP	Community Health and Development Program
CHW	community health worker
DALY	disability-adjusted life year
FANTA	Food and Nutrition Technical Assistance III Project
FC	field coordinator
IFA	iron/folic acid
kg	kilogram(s)
MNP	micronutrient powder(s)
NGO	nongovernmental organization
PLW	pregnant and lactating women
RDNS	Rang-Din Nutrition Study
SDU	safe delivery unit
LAZ	length-for-age z-score
LNS	lipid-based nutrient supplement(s)
LNS-C	lipid-based nutrient supplement(s) for children
LNS-PLW	lipid-based nutrient supplement(s) for pregnant and lactating women
UCD	University of California, Davis
USAID	U.S. Agency for International Development
VHV	village health volunteer
WFP	World Food Programme

Glossary of Selected Economic Terms Relevant to the RDNS Project

Incremental Cost: The *additional* amounts of cash, time, or value of the use of physical infrastructure associated with the planning, management, or monitoring/evaluation of the distribution of the products, services, and messages delivered in the context of the RDNS trial, *regardless* of the economic agents called on to contribute the cash, time, or infrastructure.

Incremental Cost-Effectiveness: The ratio of the total incremental costs associated with the products/ services distributed to individuals in a specific arm of the RDNS trial to the incremental measured outcomes that accrued to these individuals. In this document, the measured outcome is cases of newborn stunting averted.

1 Introduction

The prevalence of newborn stunting, defined as a newborn with a length-for-age z-score (LAZ) < −2 (Prendergast and Humphrey 2014), is high in many developing countries (Martorell and Young 2012). This is especially true in Bangladesh, where 20 percent of infants were born stunted in 2015 (National Institute of Population Research and Training, Mitra and Associates, and ICF International 2015). Newborn stunting is associated with poor subsequent growth, a greater vulnerability to certain chronic diseases, and reduced cognitive ability in adulthood (Victora et al. 2008). While numerous factors can result in poor birth outcomes, maternal undernutrition is one of the most significant contributors (Abu-Saad and Fraser 2010).

A potential means of preventing poor maternal nutritional status is through the provision of micronutrient supplements to pregnant women at risk of dietary insufficiency of one or more micronutrients. One such product is a small-quantity lipid-based nutrient supplement (LNS).

In an effort to measure the effectiveness of LNS for improving birth outcomes and child development and growth, the Rang-Din Nutrition Study (RDNS) was undertaken in rural Bangladesh from 2011 to 2015. The RDNS was a cluster-randomized trial designed to test the effectiveness of two LNS products, one developed specifically for women during pregnancy and the first 6 months postpartum (LNS for pregnant and lactating women [LNS-PLW]) and another developed for children aged 6–24 months (LNS-C), in reducing maternal and child undernutrition during the “1,000 day window,” the period of time from conception through a child’s second birthday, and hence improving selected indicators of maternal and child health and development. This report focuses on one birth outcome, i.e., newborn stunting, and a second measure of child growth, i.e., stunting at 18 months of age.

Analysis of the RDNS birth outcome data shows that maternal consumption of LNS-PLW reduces the risk of newborn stunting and small head circumference (head circumference-for-age z-score < −2) (Mridha et al. 2016). Additionally, Dewey et al. (2017) found that at 18 months of age, children in the group that received LNS-C and whose mothers received LNS-PLW demonstrated a lower stunting prevalence than children receiving micronutrient powder (MNP). However, those charged with managing society’s scarce resources need to know (even if it’s only imperfectly) the efficiency with which alternative investments can help achieve agreed-on objectives. Additionally, cost-effectiveness measures can provide decision makers with information that can be useful in assessing the feasibility and sustainability of scaling up small interventions that have proven to be effective (Bhutta et al. 2013). Despite the fundamental importance of cost-effectiveness measures, there is a paucity of cost-effectiveness analyses related to early childhood outcomes. Batura et al. (2015) highlight this gap, citing mostly evidence from the developed world. The research reported here begins to fill this important information gap in the context of a set of nutrition interventions targeted at pregnant women and their children, in a rural area in northern Bangladesh.

The paper proceeds as follows. Section 2 provides background information on the RDNS project. Section 3 discusses the motivation of collecting and analyzing cost and cost-effectiveness data. Section 4 provides an overview of methods used to calculate intervention and *adjusted* intervention costs, and Section 5 provides an overview of estimates of those costs from enrollment to birth. Section 6 reports on the effects and several measures of cost-effectiveness of the LNS-PLW intervention on newborn stunting. Section 7 presents both the intervention and *adjusted* intervention costs of distributing supplements and information about them to participating RDNS women until their children reached 18 months of age. Section 8 reports both the effects and cost-effectiveness of LNS relative to MNP at 18 months of age.

Section 9 provides estimates of the RDNS interventions and adjusted intervention costs to mother-child pairs up to the point that treated children reached 24 months of age. Section 10 discusses the strengths and limitations of the data and the methodology used and the results of the cost-effectiveness analysis.

2 Background[1]

The RDNS is a collaborative effort of the U.S. Agency for International Development Agency (USAID)-funded Food and Nutrition Technical Assistance III Project (FANTA); the University of California, Davis (UCD); icddr,b; and the LAMB Project (formally known as Lutheran Aid to Medicine in Bangladesh).

The objective of the RDNS is to evaluate the effects of LNS and other interventions on nutrition and health outcomes of pregnant women and their children through a cluster-randomized effectiveness trial.

2.1 Research Design

The RDNS cluster-randomized design consisted of four randomized trial arms.

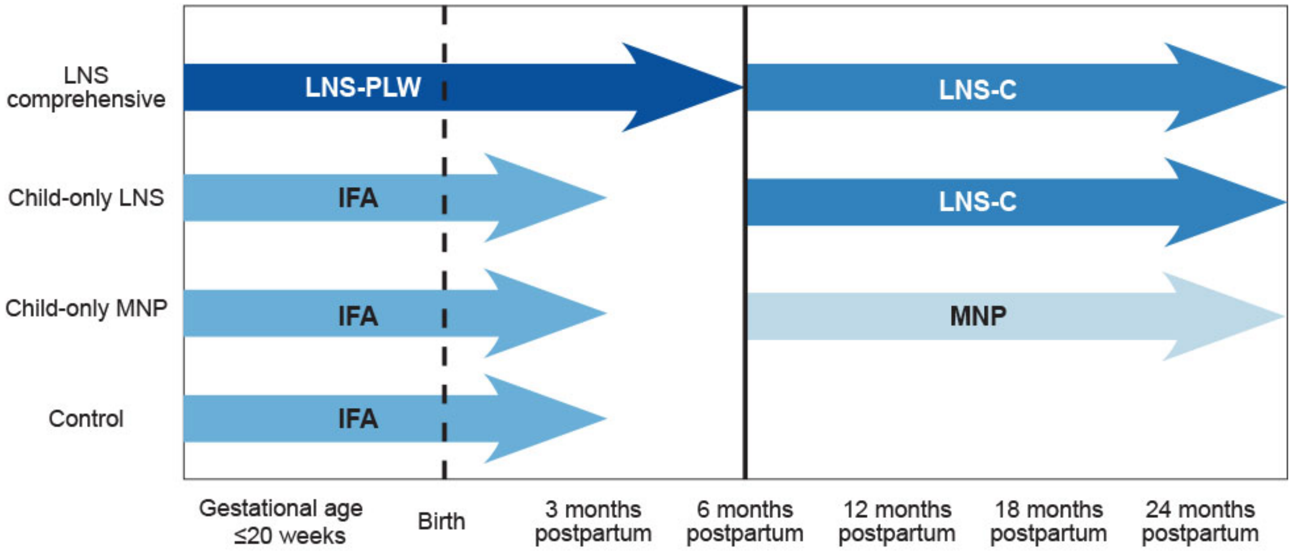
1. Comprehensive LNS (LNS-LNS): Women received LNS-PLW daily during pregnancy and for the first 6 months postpartum. Their children then received LNS-C daily from 6 to 24 months of age.
2. Child-only LNS (IFA-LNS): Women received iron/folic acid (IFA) daily during pregnancy and on an every-other-day basis during the first 3 months postpartum. Their children received LNS-C daily beginning at 6 months of age and continuing until 24 months of age.
3. Child-only MNP (IFA-MNP): Women received IFA daily during pregnancy and every other day for the first 3 months postpartum. Their children then received multiple MNP daily from 6 months to 24 months of age.
4. Control: Women received IFA daily during pregnancy and on an every-other-day basis during the first 3 months postpartum. No additional supplements were provided to their children.[2]

Figure 1 depicts the various arms of the RDNS trial. This figure foreshadows some of the dissimilarities between calculating cost at birth and at 24 months. More specifically, for assessing the effects of these interventions at birth, the child-only LNS (IFA-LNS), the child-only MNP (IFA-MNP), and the control arms are combined into a composite control arm and compared with the results for the comprehensive LNS (LNS-LNS) arm.

[1] Much of the information in this section is taken from Harding et al. (2017).

[2] While the distribution of IFA tablets to pregnant women is the suggested standard of care in Bangladesh, in practice, IFA tablets are not distributed at no cost to women, but rather are made available for purchase at safe delivery units(SDUs). Hence, the RDNS “control” group is not representative of the current standard of care.

Figure 1. Arms of the RDNS



2.2 The LAMB Project

The LAMB Project provides an ideal programmatic context in which to test these interventions, as it provides services to tens of thousands of people in northern Bangladesh with a staff of more than 1,000 individuals engaged in multifaceted health and development activities, such as primary health care and poverty alleviation, but with special focus on maternal and child health/welfare.[3]

Within the LAMB Project, the Community Health and Development Program (CHDP) served as the platform for RDNS product and information delivery. The CHDP provides a host of services to the community, including maternity services at the home and at safe delivery units (SDUs) and behavior change communication sessions on a wide variety of health topics. Among the numerous CHDP staff, those fundamental to the RDNS include community facilitators (CFs), field coordinators (FCs), community health workers (CHWs), and village health volunteers (VHVs).

2.3 Trial Area

The RDNS used a longitudinal, cluster-randomized design. In this design, clusters were defined as the duty areas of individual CHWs. CHWs visit each household within their cluster on a monthly basis, delivering supplements and information to mothers; VHVs are responsible for the majority of the direct interaction with study participants. Consequently, RDNS clustering and randomization was by CHW cluster, and not at the level of households or caregivers within them. These clusters span a broad area within rural northwest Bangladesh.

Bangladesh is divided into seven administrative divisions, which are further divided into 64 districts. Each district is further divided into subdistricts (*upazilas* or *thanas*); there are a total of 507 subdistricts across the country. The rural areas of subdistricts are divided into approximately 7–10 unions, with each union consisting of multiple villages and roughly 30,000 people. Unions are the lowest administrative units in the rural areas of Bangladesh.

[3] http://www.lambproject.org/.

The RDNS trial was implemented in six unions (Auliapukur, Fateajangpur, Nasratpur, Saintara, Satnala, and Tentulia) of the Chirirbandar subdistrict (**Figure 2**) of the Dinajpur district (**Figure 3**) and five unions (Bishnupur, Damodorpur, Lohanipara, Madhupur, and Ramnathpur) of the Badarganj subdistrict (**Figure 4**) of the Rangpur district in northwest Bangladesh (**Figure 5**). The LAMB Project and the RDNS offices are located in the Rajabashor union of the Parbatipur subdistrict of the Dinajpur district (**Figure 3**).

Figure 2. Map of Chirirbandar Subdistrict

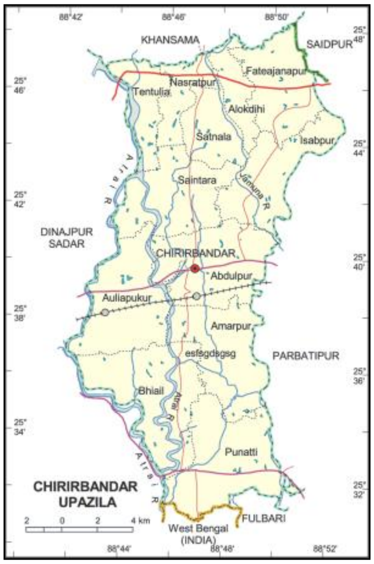
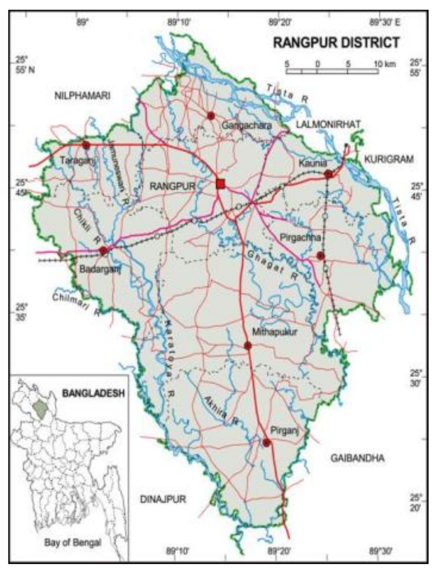


Figure 3. Map of Dinajpur District

Figure 4. Map of Badarganj Subdistrict

Figure 5. Map of Rangpur District



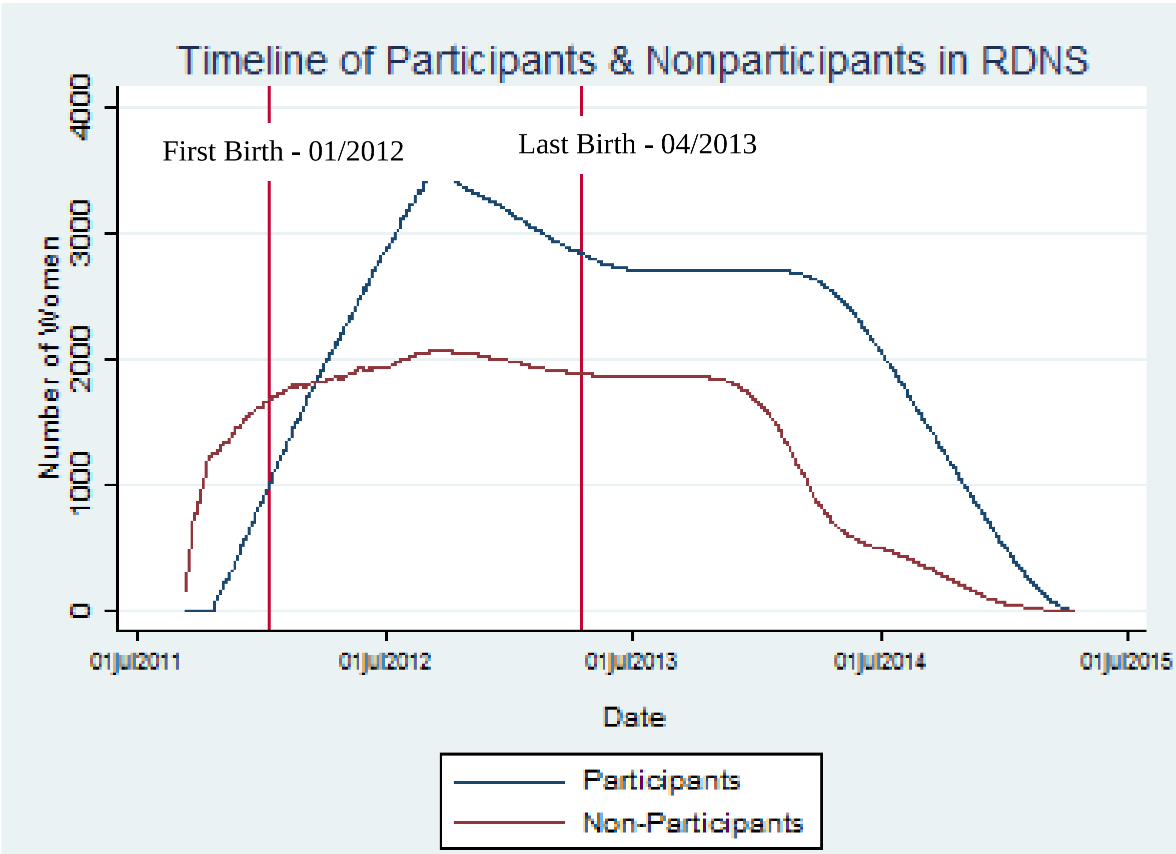
2.4 Enrollment

Before enrollment began in late October 2011, CHWs and VHVs identified pregnant women within their clusters. Women were then divided into two groups: participants and nonparticipants. Women beyond the 20th week of gestation at enrollment or who planned to move out of the area within the next 3 years were assigned to the *non*participant group, along with women who did not provide written consent. Consenting women who were no more than 20 weeks of gestation and did not plan to move out of the area within the next 3 years (the trial's inclusion criteria) were included in the study *participant* group. Both groups of women received supplements as dictated by the arm into which they were randomly assigned, because it was deemed logistically and ethically infeasible to withhold supplements from pregnant women in any of the intervention or control villages who did not meet the inclusion criteria. However, the RDNS research staff visited and collected data only from study participants. Consequently, effectiveness measures, such as anthropometric outcomes, are available only for the participant subgroup. This complicates the cost calculations, as will be seen below.

Figure 6 displays the numbers of participants and nonparticipants over the course of the RDNS. The vertical lines represent the first participant births in January 2012 and the last participant births in April 2013. The numbers of nonparticipants and participants follow two different trajectories: Both groups received arm-specific treatment, but we are interested only in the costs (and the outcomes) associated with the participants. The sample of participants was a rolling sample, so the number of participants slowly built to a peak (in about August of 2012), before it began declining as participants in the control arm ceased to receive supplements (for cost accounting purposes) and graduated out of the trial (for outcome measurement purposes). The vast majority of *non*participants, on the other hand, were identified and began to receive supplements at the onset of the RDNS project. After this initial wave of nonparticipants was introduced into the project, the number of *new* nonparticipants rapidly declined. The remaining (small) growth in the number of nonparticipants consisted mainly of two types of women: those who were not present[4] during enrollment and had passed the 20th week of gestation when they were revisited, and those who met the gestational age inclusion criterion, but could not be reached by RDNS research personnel or planned to move out of the area within the next 3 years.

[4] Women were not present during enrollment for many reasons, e.g., some were not home during the first visit by RDNS research staff, others recently moved into the region.

Figure 6. Number of Participants and Nonparticipants in RDNS Project, Over Time



3 Motivation for Collecting and Analyzing Cost Data

Decision makers are charged with allocating scarce resources across various activities, programs, and investments (we refer to these collectively as "interventions"), both within and across sectors. An array of political and other factors influence their choices; economic efficiency is one key factor. Introducing economic efficiency into decision-making processes requires intervention-specific estimates of outcomes and costs, and methods for combining the two to identify the most efficient intervention options.

At the economy-wide level, cost/benefit and related tools are used to compare among alternative interventions in health, education, infrastructure, etc. (e.g., Copenhagen Consensus Center 2017, Belli 1996). Within the health sector, Drummond et al. (2015) provide a framework for evaluating and choosing among alternative interventions for achieving specific outcomes, based on economic efficiency. More narrowly, Walker et al. (2013) provide a tool for estimating the effects of alternative health and nutrition interventions on child mortality; the tool now contains a cost submodule that allows for comparing outcomes and costs of alternative interventions. Even more narrowly, Shekar et al. (2016) provide an economic optimization tool to inform country-level discussions related to alternative interventions for achieving four of the World Health Assembly targets. Still more narrowly, Vosti et al. (2015) provide a subnational bio-economic optimization tool to design and manage more-efficient micronutrient intervention programs. All of these tools are designed to address specific policy questions at specific levels of spatial and socioeconomic aggregation.

This report borrows the framework of Drummond et al. (2015) to address the more granular question of site-specific choices among alternative products for improving child growth and development. More specifically, we measure the incremental costs and the incremental outcomes in terms of linear growth (only) in young children of providing two alternative nutritional supplements—MNP and LNS—in the context of the RDNS trial.

It is important to note that in many cases there is no *single* outcome associated with a given intervention, but rather an array of expected outcomes. Cases involving multiple expected outcomes that are hard to value are particularly challenging, especially when the outcomes accrue over time and perhaps to different stakeholders. Many examples exist, e.g., national parks provide an array of ecosystem services, now and into the foreseeable future, but putting values on these outcomes is quite challenging, and hence aggregation to a single, comparable outcome measure is challenging (see, e.g., Keohane and Olmstead 2007). Some investments in education (e.g., improving the quality of teachers) face the same issues. Similar examples exist in the context of health investments (Johns et al. 2003).

The nutrition interventions examined in the context of the RDNS fall essentially into this final category: Improving the nutritional status of pregnant women and their children is expected to generate a vector of positive outcomes, including, but not limited to, reduced prevalence of stunting, accelerated linear growth, accelerated child development, and reductions in morbidity and mortality. Each of these outcomes has some value to society, but there are no social value weights (or market prices) that can easily be associated with any of these expected outcomes. In some cases, subsets of these outcomes can be aggregated into a common metric of societal concern, e.g., child mortality (Walker et al. 2013), but in other cases the scientific evidence for doing so is deficient.

Therefore, it is common practice to select a trial's primary outcome (the outcome to which the trial has been powered to undertake statistically valid cross-arm tests) and use it as *the* indicator of success, understanding that in most cases the cost-effectiveness estimates that emerge will be underestimates of the total value to society of all of the benefits associated with a given intervention. The extent to which single-outcome measures of cost-effectiveness underestimate the total value to society of given interventions is a very important policy issue, since known or measurable resources (all with opportunity costs) will need to be expended to carry out proposed interventions.

Although researchers face challenges associated with generating comprehensive estimates of the costs and (especially) the cost-effectiveness of nutrition interventions, the information that emerges is important to decision makers within and outside the public sector.

Finally, there are essentially two types of costs to consider in the RDNS context: the costs associated with adding *any* additional intervention to an existing health care product/information distribution system (such as the LAMB system), and the product-specific costs of the *chosen* intervention. Clearly, the former need to be paid regardless of intervention chosen, but separating the two for cost-effectiveness analyses can provide a more precise assessment of the efficiency of alternative interventions. This will be addressed in greater depth below.

4 Intervention Costs: Enrollment to Birth

The goal of the intervention cost calculations is to identify and to sum up the costs incurred by the RDNS project that were *directly related to* the procurement and distribution of different supplements and information associated with them to caregivers (e.g., planning, procurement, transport, personnel, equipment, and training costs). The focus of this section is on the cost incurred from enrollment of pregnant women until they gave birth. (Section 7 examines the costs incurred from enrollment until the participating children reached 24 months of age.) The incremental costs actually faced by the RDNS project need not reflect those that an implementing nongovernmental organization (NGO), for example, would reasonably expect to face if it chose to replicate the RDNS interventions; these *adjusted* intervention costs are discussed in Section 5.

4.1 Methods for Collecting and Processing Cost Data

Costs are broken down into five categories: product procurement, product transport, personnel, equipment,[5] and training. Many of these cost categories (e.g., product procurement and transport) are straightforward to calculate, and estimates are based solely on available in-depth accounting data maintained by the RDNS project and the suppliers and the transportation firms engaged by the project. All non-labor costs were estimated based on original receipts for LNS-PLW products procured and shipped and for the equipment (e.g., laptop computers, bicycles, motorcycles, and storage bins for LNS product) purchased. The same is true for IFA tablets. Training and village-level meeting costs were estimated based on the LAMB Project and RDNS accounting sheets that report the numbers of individuals trained or visited, transportation cost reimbursements provided, and meals and supplies purchased/provided.

Estimating personnel, some equipment, and training costs can be challenging, in part because the RDNS project utilized the existing infrastructure of the LAMB Project to deliver supplements and information. From a technical perspective, some of the costs of the RDNS project and those of LAMB Project activities were interwoven. For example, CHWs have numerous responsibilities, of which only a few were directly related to the RDNS project. In our cost calculations, we include *only* those personnel and other costs that were directly associated with *adding* the distribution of supplements and related information to pregnant women and/or children participating in the RDNS project to the *existing* LAMB Project platform. Personnel costs associated with the distribution of LNS-PLW and IFA products and information were estimated using time-and-motion studies, with careful attention paid to identifying and including in cost calculations only those activities that were directly related to the LNS intervention.[6]

Equally challenging is the need to separate the product and information delivery costs from the research costs of the RDNS project. An effort was made to include *only* those RDNS costs that were directly associated with the distribution of supplements and information about them.

4.2 Flows of Costs over Time

Attributing these costs over time to specific trial participants was challenging, especially for large outlays that occurred at specific periods of time, e.g., training, capital purchases, or storage rental facilities that are paid for at the project's outset, but that provide flows of services over the entire RDNS project cycle.

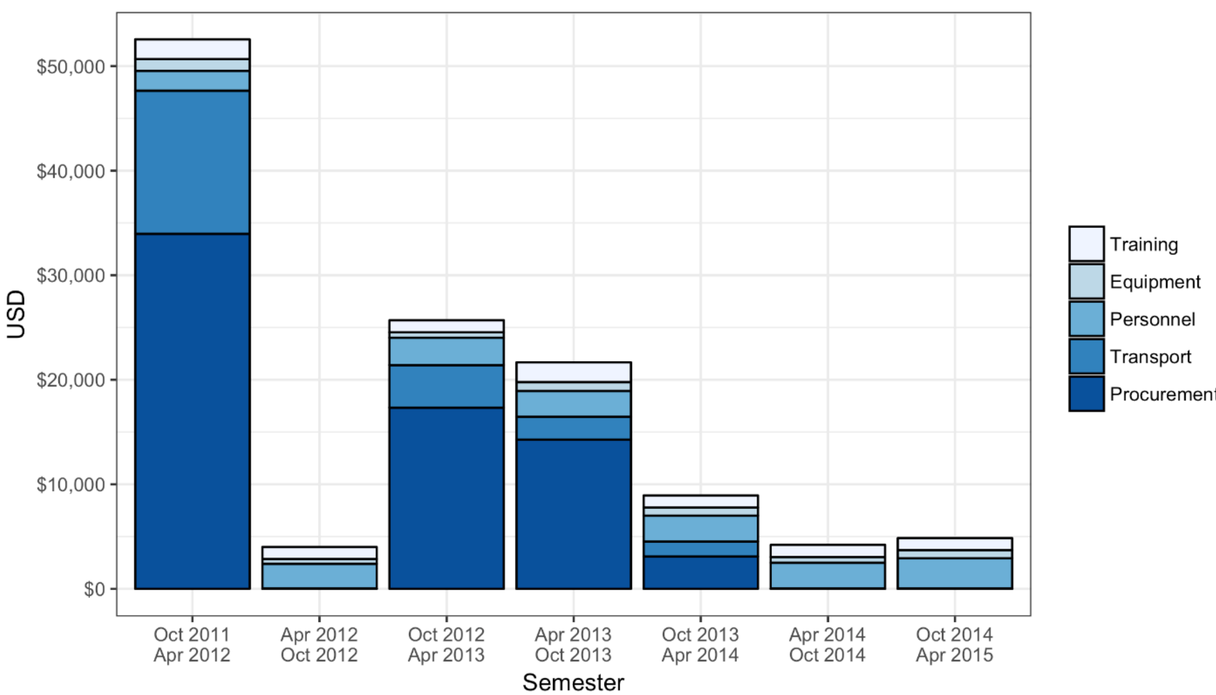
[5] Product storage costs were included in the equipment cost category.

[6] For details, see Humber and Vosti (2016).

Constructing cost estimates associated with delivering supplements and information that could affect health outcomes *at birth* requires that these costs be separated from those associated with distributing supplements and information to postpartum mothers and their infants. Isolating the cost of delivering supplements to pregnant mothers, however, is not straightforward. Two issues complicate this task: the RDNS's rolling enrollment process and the perennial challenge of temporally allocating large, up-front costs.

To deal with these issues, we subdivided costs into seven 6-month time periods ("semesters"), thereby allowing us to track costs over time. **Figure 7** depicts the incremental costs[7] incurred in each of the seven semesters, by cost category. Note that equipment costs, while never large, are concentrated in the first semester. Note also that procurement and training costs are distributed over time in highly non-uniform ways. Finally, recall that the training, equipment, and personnel costs associated with adding the distribution of LNS-PLW would have to be paid, regardless of product chosen for delivery.[8]

Figure 7. Total Incremental Costs over Time



As discussed above, the RDNS sample is composed of both participant and nonparticipant groups; outcome and other data were collected from the former, but not from the latter. In what follows, we calculate the cost of distributing supplements and information *only* to pregnant women in the subsample of participating women. Calculating costs for this participant subsample presents obstacles for several cost categories. For example, LAMB Project personnel distributed supplements to nonparticipants; hence, it is necessary to adjust the procurement, personnel, and other costs to "remove" the costs directly

[7] These incremental costs represent the costs of adding the LNS-PLW distribution program to an *existing* LAMB Project-managed program.

[8] There may be slight differences between, e.g., the personnel, equipment, and training costs associated with delivering IFA tablets, on one hand, and the costs of delivering LNS-PLW or multiple MNP, on the other. The former is a better-known product with simple consumption recommendations (and hence relatively cheaper to distribute), while the latter are new products with more-complex consumption recommendations.

associated with the nonparticipant subgroup. To address this issue, we developed a cost scaling parameter (which we labeled a "part-ratio")—essentially, the proportion of all treated women receiving the intervention who were participants, and therefore from whom we collected data, at any given point in time. **Table 1** presents seven different part-ratios, one for each semester of the RDNS; note that the part-ratio is quite small for the first semester, when all pregnant women (regardless of gestational age) received the intervention; more than doubles in the second semester; and then remains nearly constant until the final semester of the trial. To calculate only those costs directly related to the participant subgroup of interest for the cost-effectiveness analysis, we scale the cost calculation within each semester by its respective part-ratio. **Table 2** reports summary part-ratios for two periods: enrollment-to-birth and enrollment-to-24 months.

Table 1. Average Part-Ratios for the RDNS Project, by Cost Semester

	10/2011-4/2012	4/2012-10/2012	10/2012-4/2013	4/2013-10/2013	10/2013-4/2014	4/2014-10/2014	10/2014-4/2015
Average Part-Ratio	0.29	0.60	0.61	0.60	0.60	0.60	0.76

Table 2. Average Part-Ratios for the RDNS Project, for Birth Outcomes and at 24 Months of Age

	Birth Outcomes	24 Months
Average Part-Ratio	.50	0.58

Finally, regarding factors that complicated cost calculations, in February 2012, the World Food Programme (WFP) announced new standards for *Cronobacter sakazakii*, an opportunistic pathogen present in many foods (U.S. Centers for Disease Control and Prevention 2015). To adhere to these new standards, the distribution of LNS-PLW was halted at the RDNS site, supplies of LNS-PLW were tested, and products suspected of containing *Cronobacter sakazakii* were destroyed. This caused a delay in the delivery of LNS-PLW to women in the LNS-LNS arm of the trial from August 8 to October 16, 2012. During this period, all participants in the LNS-LNS arm received IFA, the recommended standard of care in Bangladesh. The RDNS project was reimbursed for all destroyed LNS-PLW; hence, product replacement costs are not included in our calculations. That said, this disruption did cause a change in the treatment effect, which is addressed in our cost-effectiveness estimates below.

4.3 Summary of RDNS LNS-PLW Intervention Costs: Enrollment to Birth

Table 3 presents the total and average incremental costs of LNS-PLW intervention from enrollment until delivery for trial participants. Note that this and subsequent tables report incremental costs, i.e., the costs of adding the delivery of LNS-PLW and product information to the existing suite of products and services that the LAMB Project already provided to pregnant women. These additional costs are reported in two ways in the following tables: the total incremental cost of adding the products/services associated with a given trial arm and the average incremental cost per treated woman. To calculate the average incremental cost, we use the total number of pregnant women enrolled in the selected trial arm.[9] Intervention average treatment costs were approximately US$28/treated woman in the LNS-PLW study arm. Table 3 also reports total and average costs by cost category to identify the personnel, equipment, and training costs that would have to be paid by any organization intending to add any product/information project to an

[9] Given sample attrition, this method understates average costs.

existing delivery platform, such as the LAMB Project platform; and to highlight the large procurement and transport costs associated with the LNS-PLW intervention. Finally, Table 3 also reports the costs associated with the IFA intervention that all of the women in the composite control arm received.[10] Note that in the case of the IFA intervention, the costs of procuring and transporting the product were very small in absolute terms, and especially relative to the personnel, training, and equipment costs that were faced.

Table 3. Costs of LNS-PLW Intervention,[11] Enrollment to Birth[a]

Cost Category	Total Intervention Cost	Average Intervention Cost Per Treated Woman
LNS-LNS Arm (N = 1047)		
Procurement Cost	$11,851	$11.32
Transport Cost	$6,894	$6.35
Personnel Cost	$6,878	$6.57
Equipment Cost	$2,804	$2.67
Training Cost	$1,136	$1.09
Total	***$29,318***	***$28.00***
Composite Control Arm (N = 2964)		
Procurement Cost	$1,785	$0.63
Transport Cost	$79	$0.03
Personnel Cost	$19,471	$6.57
Equipment Cost	$7,938	$2.67
Training Cost	$3,216	$1.09
Total	***$32,489***	***$10.96***

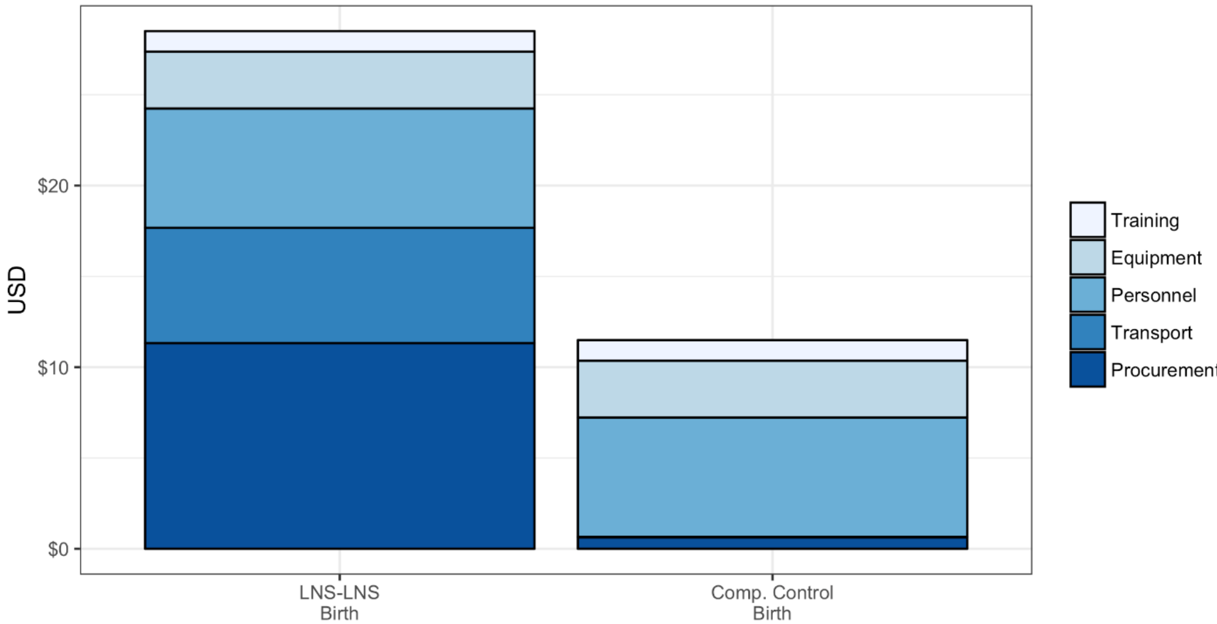
[a] All numbers are in US$.

The breakdown across cost categories of the intervention's average incremental cost for trial participants enrolled into the LNS-LNS and composite control trial arms is presented in **Figure 8**. Clearly, a large proportion of the intervention costs are attributable to LNS-PLW procurement and transportation; these costs are pivotal in understanding the cost-effectiveness of this particular intervention.

[10] Recall that the suggested protocol for pregnant women (IFA throughout pregnancy) is not generally followed in Bangladesh, but was followed in the context of the RDNS trial. The RDNS trial cannot estimate the reductions in newborn stunting attributable to the comprehensive IFA treatment to all women in the control arm, but we can "deduct" from the LNS-LNS treatment arm the cost of the IFA tablets (procurement and transport). There is more on this subject later in the report.

[11] All cost estimates presented in this paper should be interpreted as the incremental intervention costs, i.e., the costs of adding an intervention to an existing program (with the LAMB Project's history and reach) that provides information and services to women of reproductive age and to their children.

Figure 8. Composition of Average Intervention Costs for the LNS-PLW and Composite Control Arms



5 Adjusted LNS-PLW Intervention Costs: Enrollment to Birth

In this section, we report estimates of the *adjusted* incremental LNS-PLW intervention costs and some of the key assumptions made to calculate them. Recall that *adjusted* intervention costs represent those that would likely be faced by an entity, such as an NGO, that sought to replicate the pregnancy detection and intervention activities associated with specific arms of the RDNS. Recall also that all cost figures contain the incremental personnel, training, and equipment costs of adding the LNS-PLW intervention, or any other intervention, to the *existing* LAMB Project.

5.1 Key Assumptions

Below, we list the important assumptions that differentiate the intervention cost calculations from those undertaken to arrive at *adjusted* intervention costs.

- *Cronobacter Incident Eliminated*: As discussed above, in February 2012, WFP introduced new standards regarding *Cronobacter sakazakii*. For the *adjusted* intervention, we assume that this change in standards did not occur. Consequently, all costs borne by the RDNS as a result of the change in standards are omitted from the *adjusted* intervention cost calculations.
- *Higher Cost of LNS-PLW*: Nutriset sold the LNS-PLW product to the RDNS team at a discounted price of €3/kg. The price for LNS-PLW that is included in the *adjusted* intervention calculations is €5/kg.
- *Maritime Transport*: In the *adjusted* intervention cost calculations, Nutriset remains the supplier, but all shipments arrive by sea, rather than by a mixture of air and sea shipments, which was the case in the RDNS.

Since the RDNS was an effectiveness trial, supplement distribution mimicked a real-world distribution mechanism. Therefore, most of the supplement distribution, personnel, storage, equipment, and training costs associated with the intervention cost calculations were retained in the adjusted intervention cost calculations.

5.2 Summary of Adjusted LNS-PLW Intervention Costs: Enrollment to Birth

Table 4 presents the *adjusted* total and average intervention costs for treatment for the LNS-LNS arm from enrollment until birth for trial participants. Again, the table reports two sets of costs in two ways: total incremental cost of providing LNS-PLW and product information to pregnant women in the LNS-LNS arm and the average incremental cost per treated woman for that study arm, and the same sets of costs for the composite control arm that received comprehensive IFA treatment. To obtain the average cost, we utilize the total number of participating women enrolled. The reader will note that the adjusted intervention cost estimates are higher than those for the intervention (US$34 versus US$28): The combined “savings” associated with more-efficient shipping and the elimination of the *Cronobacter* incident were smaller than procurement cost increases associated with the higher cost of the LNS-PLW product. Again, the cost categories are included to aid in the identification of the “fixed” costs of adding any intervention to the existing LAMB system and to identify the intervention costs specific to the LNS-PLW product. Note again that the product procurement and transport costs for the control arm were very small.

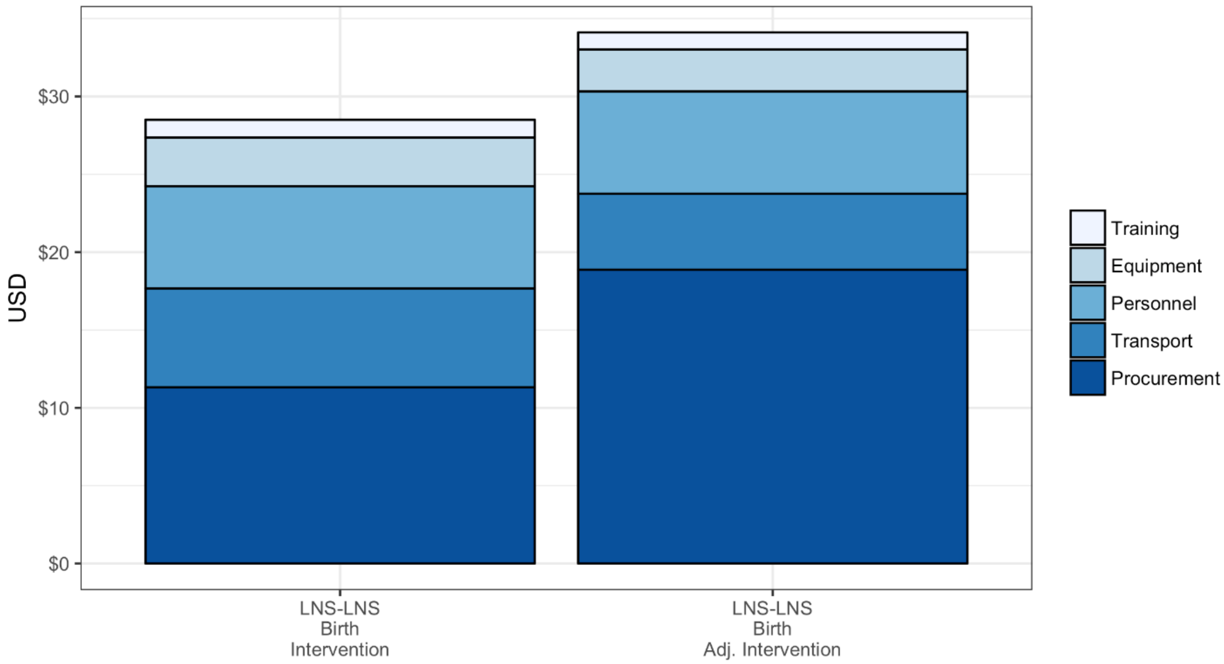
Table 4. *Adjusted* Cost of the LNS-PLW Intervention, Enrollment to Birth[a]

Cost Category	Total Intervention Cost	Average Intervention Cost Per Treated Woman
LNS-LNS Arm (N = 1047)		
Procurement Cost	$19,752	$18.87
Transport Cost	$5,111	$4.88
Personnel Cost	$6,878	$6.57
Equipment Cost	$2,804	$2.67
Training Cost	$1,136	$1.09
Total	***$35,681***	***$34.08***
Composite Control Arm (N = 2964)		
Procurement Cost	$1,785	$0.60
Transport Cost	$79	$0.03
Personnel Cost	$19,471	$6.57
Equipment Cost	$7,938	$2.67
Training Cost	$3,215	$1.09
Total	***$32,758***	***$11.05***

[a] All numbers are in US$.

Figure 9 depicts the breakdown, by cost category, of average intervention costs and *adjusted* intervention costs, enrollment to birth, for RDNS participants. Not surprisingly, given the product price assumption noted above, procurement costs comprise an even larger proportion of average total cost in the *adjusted* intervention case than in the intervention case. In contrast, the transport costs corresponding to the *adjusted* intervention have decreased relative to the intervention case.

Figure 9. Average Intervention and Average *Adjusted* Intervention Costs of LNS-PLW Treatment, Enrollment to Birth, by Cost Category



6 Effects and Cost-Effectiveness of LNS-PLW Intervention in Reducing Newborn Stunting

The RDNS intervention resulted in improvements in a range of newborn health outcomes (Mridha et al. 2016), all of which may have value to society. The cost-effectiveness measures reported here focus exclusively on reductions in newborn stunting, and hence likely understate the total benefits of the intervention, but the extent of that understatement is not known. **Table 5** (final column) reports on the changes in the prevalence of stunting in the LNS-LNS trial arm relative to the control arm[12] (our measure of the outcome of the intervention). Two sets of results are reported: those for the entire sample of RDNS participants in the LNS-LNS trial arm and those for the subsample of participants who did *not* experience the disruption in the distribution of LNS-PLW associated with *Cronobacter sakazakii*. Although the number of participants in the 'No Disruption' subgroup within the LNS-LNS trial arm is < 1,200, the reduction in stunting relative to the control group was greater, −7.17 versus −3.99 percentage points, than in the entire sample of women in the LNS-LNS arm of the trial.

Table 5. LNS-PLW Intervention Effects: Newborn Stunting Averted

	Number of Enrolled Participants	Number of Enrolled Participants in the LNS-LNS Arm	Number of Cases of Newborn Stunting Averted	Prevalence of Newborn Stunting Relative to the Control Arm (percentage point difference)
Entire Sample	3446	1047	42	−3.99[a] (−6.63, −1.34)
No Disruption	1194	336	27	−7.17[a] (−12.13, −2.22)

[a] Significant at the 5% level; 95% confidence intervals in parentheses.
Source: RDNS biostatistics team.

To calculate the cost-effectiveness of the LNS-PLW intervention at birth in the context of this single-outcome measure (cases of newborn stunting averted, compared to the composite control arm), we divide the incremental cost per participant by the incremental change in the prevalence of newborn stunting.[13] (See **Table 6**.) As expected, cost-effectiveness estimates based on intervention costs are substantially different from those based on *adjusted* intervention costs; again, this is primarily attributable to the increase in LNS-PLW product price (vis-à-vis the research project discounted price) that a government or NGO would likely pay. Additionally, the cost-effectiveness estimates are substantially lower for the subgroup that did not experience a disruption in LNS-PLW product distribution.

[12] Recall that the treatment actually received by all women in the RDNS's IFA arms is the recommended standard of care, but not the implemented standard of care, in Bangladesh.

[13] For example, for the entire sample and based on *adjusted* intervention costs, (US$34 − US$11) ÷ .0399 = US$576.44. Differences that appear in Table 6 are due to rounding errors.

Table 6. Product-Only Cost per Case of Newborn Stunting Averted by the LNS-PLW Intervention, Using Intervention Costs and *Adjusted* Intervention Costs, for the Entire Sample and for the No-Disruption Subgroup[14]

	Intervention (2014 US$)	***Adj.* Intervention** (2014 US$)
Entire Sample	$427	$579
No Disruption	$238	$323

[14] Note that this measure of cost-effectiveness includes only the costs of purchasing the LNS-PLW product and transporting it to the RDNS site; personnel, equipment, and training costs associated with distributing the product or information associated with it are ignored in this calculation because they are assumed to be the same as in the control arm.

7 Intervention and Adjusted Intervention Costs at 18 Months

Recall (see **Figure 1**) that when the children born to RDNS participants reached 6 months of age, the interventions changed and with those changes came additional complexities associated with calculating intervention costs. More specifically, the "combined" control group for cost estimates up to birth (which included the IFA-LNS, IFA-MNP, and control study arms) had to be separated and the costs of each arm tracked from that point forward.

This section reports the costs of purchasing, transporting, and distributing supplements and information about them to all participating RDNS women until their children reached 18 months of age.

To generate estimates of all costs directly related to the distribution of supplements and information from enrollment until the children of the RDNS women reached 18 months of age, we invoked many of the same assumptions discussed previously regarding, e.g., the allocation of large establishment and initial training costs over time and the underlying assumptions that distinguish the intervention from the *adjusted* intervention cost estimates. However, to ensure that the cost estimates accurately reflect only those costs associated with distributing supplements and information about them to caregivers of study child until 18 months of age, we separated the total cost of the RDNS intervention into seven 6-month semesters. Children received supplements until 24 months of age. Consequently, to obtain the costs of providing supplements and information to caregivers of children up to 18 months of age, the last semester is excluded from the total cost calculations.

Table 7 reports intervention and *adjusted* intervention total and average cost estimates at 18 months for children born to women participating in the RDNS, by trial arm and cost category. As with all other tables, average cost calculations are based on the total number of women enrolled in each study arm.[15] Unlike costs from enrollment to birth, which focused exclusively on the pregnant women participating in the RDNS and hence were reported on a per-treated-woman basis,[16] cost estimates below are reported for treated woman-child pairs. Costs associated with the control group are also presented.

Table 7. Cost of RDNS Interventions, Enrollment to 18 Months of Age, by Trial Arm and Cost Category

Cost Category	Total Cost		Average Cost Per Woman-Child Pair	
	Intervention Cost	*Adjusted* Intervention Cost	Intervention Cost	*Adjusted* Intervention Cost
LNS-LNS Arm (N = 1047)				
Procurement Cost	$59,835	$100,159	$57.15	$95.66
Transport Cost	$14,298	$10,176	$13.66	$9.72
Personnel Cost	$14,312	$14,312	$13.67	$13.67
Equipment Cost	$1,731	$1,731	$1.65	$1.65
Training Cost	$2,373	$2,373	$2.27	$2.27
Total	***$92,548***	***$128,751***	***$88.39***	***$122.97***
IFA-LNS Arm (N = 930)				
Procurement Cost	$28,221	$46,204	$30.35	$49.68
Transport Cost	$4,605	$4,206	$4.95	$4.52

[15] Again, given attrition of women and children from the sample, this method underestimates average intervention costs.

[16] Where "treatment" refers to intention-to-treat.

Personnel Cost	$12,713	$12,713	$13.67	$13.67
Equipment Cost	$1,538	$1,538	$1.65	$1.65
Training Cost	$2,108	$2,108	$2.27	$2.27
Total	***$49,184***	***$66,767***	***$52.89***	***$71.79***
IFA-MNP Arm (N = 1052)				
Procurement Cost	$12,369	$12,369	$11.76	$11.76
Transport Cost	$122	$122	$0.12	$0.12
Personnel Cost	$14,380	$14,380	$13.67	$13.67
Equipment Cost	$1,739	$1,739	$1.65	$1.65
Training Cost	$2,384	$2,384	$2.27	$2.27
Total	***$30,995***	***$30,995***	***$29.46***	***$29.46***
Control Arm (N = 980)				
Procurement Cost	$595	$595	$0.61	$0.61
Transport Cost	$16	$16	$0.02	$0.02
Personnel Cost	$13,424	$13,424	$13.67	$13.67
Equipment Cost	$1,624	$1,624	$1.65	$1.65
Training Cost	$2,226	$2,226	$2.27	$2.27
Total	***$17,884***	***$17,884***	***$18.22***	***$18.22***

[a] All numbers are in US$.

Figure 10 and **Figure 11** provide estimates of average total intervention costs, by cost category and treatment arm, for the intervention and *adjusted* intervention cases. Procurement and transport costs represent the key cost drivers and explain why the LNS-LNS arm is more costly than both the IFA-LNS and IFA-MNP interventions. The cost of LNS in the intervention and *adjusted* intervention are, respectively, US$.07 and US$.11 per sachet. MNP and IFA are significantly less expensive to procure (US$.03 per sachet and US$.003 per tablet, respectively) and lighter and hence cheaper to transport. In contrast to the LNS product that is produced in Normandy, France, and shipped to Bangladesh, IFA and MNP are produced in Bangladesh, resulting in significantly lower transport costs.[17]

[17] It may be possible to lower LNS procurement and transportation costs via national production, especially if new formulas made intensive use of cheaper, locally available agricultural products as key ingredients (see Ryan et al. 2014).

Figure 10. Average Intervention Costs, by Trial Arm and Cost Category

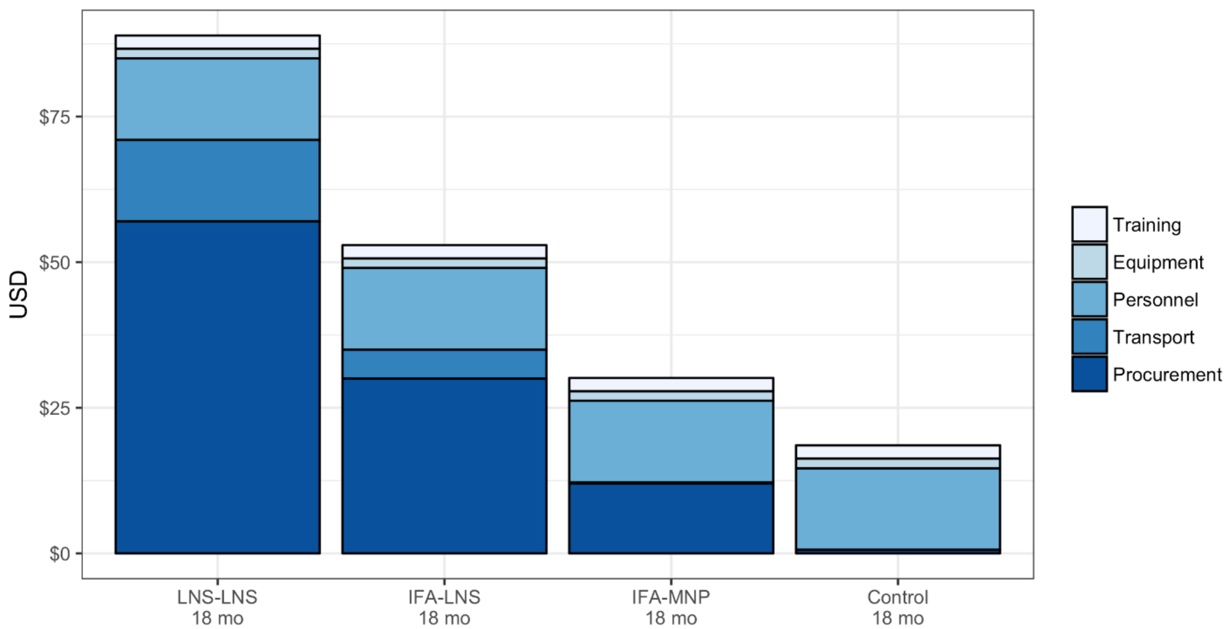
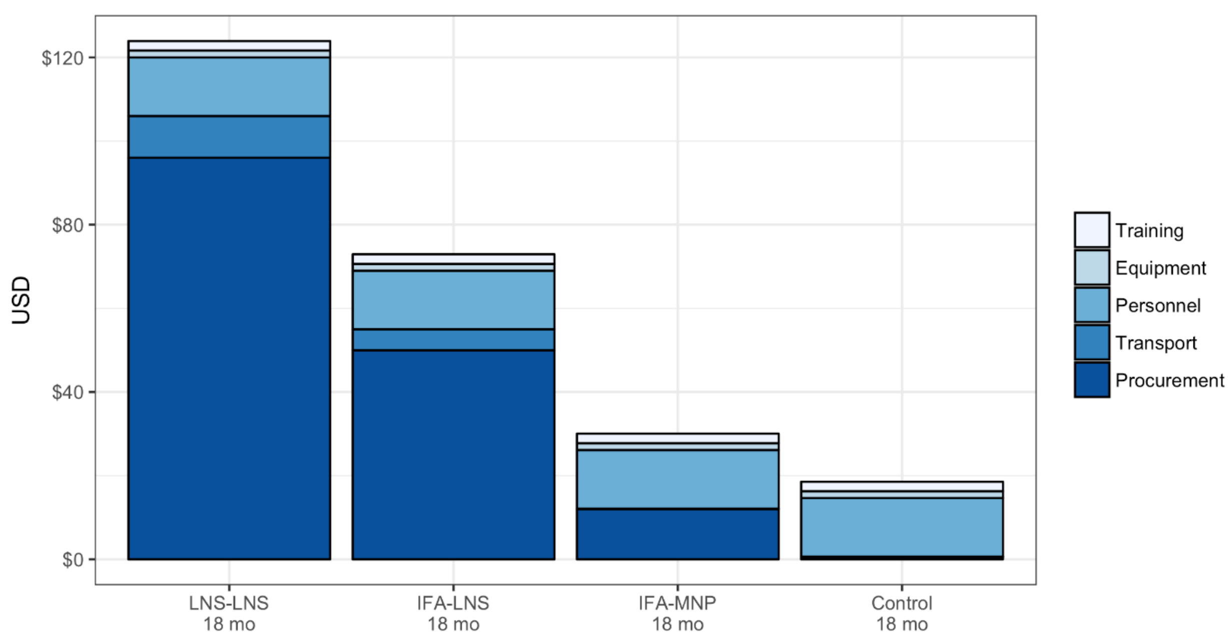


Figure 11. Average *Adjusted* Intervention Costs, by Trial Arm and Cost Category



8 Effects and Cost-Effectiveness of the LNS Intervention in Reducing Stunting at 18 Months

In this section, we shift the focus to 18 months of age of the index children, the point in the child growth cycle at which children in the LNS-LNS group experienced statistically significantly lower rates of stunting than those in the IFA-MNP group. The LNS products used in the RDNS trial (Arimond et al. 2015) included energy, essential fatty acids, and seven additional micronutrients that were not contained in the MNP; these additional ingredients may play important roles in enhancing birth outcomes. **Table 8** reports on the differences in the prevalence of stunting in the LNS-LNS trial arm relative to the IFA-MNP, IFA-LNS, and control arms. Note that the prevalence of stunting at 18 months was statistically significantly lower for the LNS-LNS arm only from that of the IFA-MNP study arm (−8.05 percentage points). We calculate the incremental cost-effectiveness only for trial arms for which the prevalence rates of stunting are statistically different.

Table 8. Stunting Averted in the LNS-LNS Study Arm at 18 Months Relative to Other Study Arms

Selected RDNS Study Arms	Prevalence of Stunting at 18 months (percentage point difference compared to LNS-LNS study arm)
IFA-MNP	−8.05[a] (−12.66, −3.44)
IFA-LNS	−3.40 (−8.11, 1.34)
Control	−4.21 (−8.90, 0.48)

[a] Significant at the 5% level; 95% confidence intervals in parentheses.
Source: RDNS biostatistics team.

To calculate the cost-effectiveness of the LNS-LNS intervention relative to the IFA-MNP intervention at 18 months, we divide the incremental cost per participant by the incremental change in the prevalence of stunting at 18 months. Results are reported in **Table 9.** The difference between intervention and *adjusted* intervention cost-effectiveness estimates is attributed to the higher cost of both the LNS-PLW and LNS-C products.

Table 9. Product-Only Cost per Case of Stunting Averted, LNS-LNS versus IFA-MNP Arm, Using Intervention and *Adjusted* Intervention Costs at 18 Months[18]

	Intervention (2014 US$)	*Adj.* Intervention (2014 US$)
Entire Sample	$732	$1161

[18] Note that this measure of cost-effectiveness includes only the costs of purchasing the LNS products and transporting them to the RDNS site; personnel, equipment, and training costs associated with distributing the products or information associated with them are ignored in this calculation, because they are assumed to be the same as in the IFA-MNP arm.

9 Intervention Costs and Adjusted Intervention Costs at 24 Months

Finally, in this section we report on the costs to the endpoint of the trial, i.e., to 24 months of age for the children of all participating RDNS women. Calculating costs at the endpoint of the trial is reasonably straightforward compared to generating cost estimates at 18 months.

Table 10 reports on intervention and *adjusted* intervention total and average cost estimates at 24 months for children born to women participating in the RDNS, by trial arm and cost category. As with all other tables, average cost calculations are based on the total number of women enrolled in each study arm.[19]

Table 10. Cost of RDNS Interventions, Enrollment to 24 Months of Age, by Trial Arm and Cost Category

	Total Cost		Average Cost Per Woman-Child Pair	
Cost Category	Intervention Cost	*Adjusted* Intervention Cost	Intervention Cost	*Adjusted* Intervention Cost
LNS-LNS Arm (N = 1047)				
Procurement Cost	$75,385	$126,294	$72.00	$120.62
Transport Cost	$21,682	$15,510	$20.71	$14.81
Personnel Cost	$17,215	$17,215	$16.44	$16.44
Equipment Cost	$2180	$2180	$2.08	$2.08
Training Cost	$2,513	$2,513	$2.40	$2.40
Total	***$118,049***	***$163,711***	***$112.75***	***$156.36***
IFA-LNS Arm (N = 930)				
Procurement Cost	$42,034	$69,008	$45.20	$74.20
Transport Cost	$7,118	$6,503	$7.65	$6.99
Personnel Cost	$15,291	$15,291	$16.44	$16.44
Equipment Cost	$1,936	$1,936	$2.08	$2.08
Training Cost	$2,232	$2,232	$2.40	$2.40
Total	***$68,612***	***$94,970***	***$73.78***	***$102.12***
IFA-MNP Arm (N = 1052)				
Procurement Cost	$18,256	$18,256	$17.35	$17.35
Transport Cost	$395	$406	$0.38	$0.39
Personnel Cost	$17,297	$17,297	$16.44	$16.44
Equipment Cost	$2,188	$2,188	$2.08	$2.08
Training Cost	$2,525	$2,525	$2.40	$2.40
Total	***$40,661***	***$40,672***	***$38.65***	***$38.66***
Control Arm (N = 980)				
Procurement Cost	$595	$595	$0.63	$0.63
Transport Cost	$27	$27	$0.03	$0.03
Personnel Cost	$16,111	$16,111	$16.44	$16.44
Equipment Cost	$2,038	$2,038	$2.08	$2.08
Training Cost	$2,352	$2,352	$2.40	$2.40
Total	***$21,123***	***$21,123***	***$21.55***	***$21.55***

[a] All numbers are in US$.

[19] Again, given attrition of women and children from the sample, this method underestimates average intervention costs.

Figure 12 and **Figure 13** provide estimates of average total intervention costs, by cost category and treatment arm, for the intervention and *adjusted* intervention cases. Again, procurement and transport costs represent the key cost drivers and explain why the LNS-LNS arm is more costly than both the IFA-LNS and IFA-MNP interventions.

Figure 12. Average Intervention Costs, by Trial Arm and Cost Category

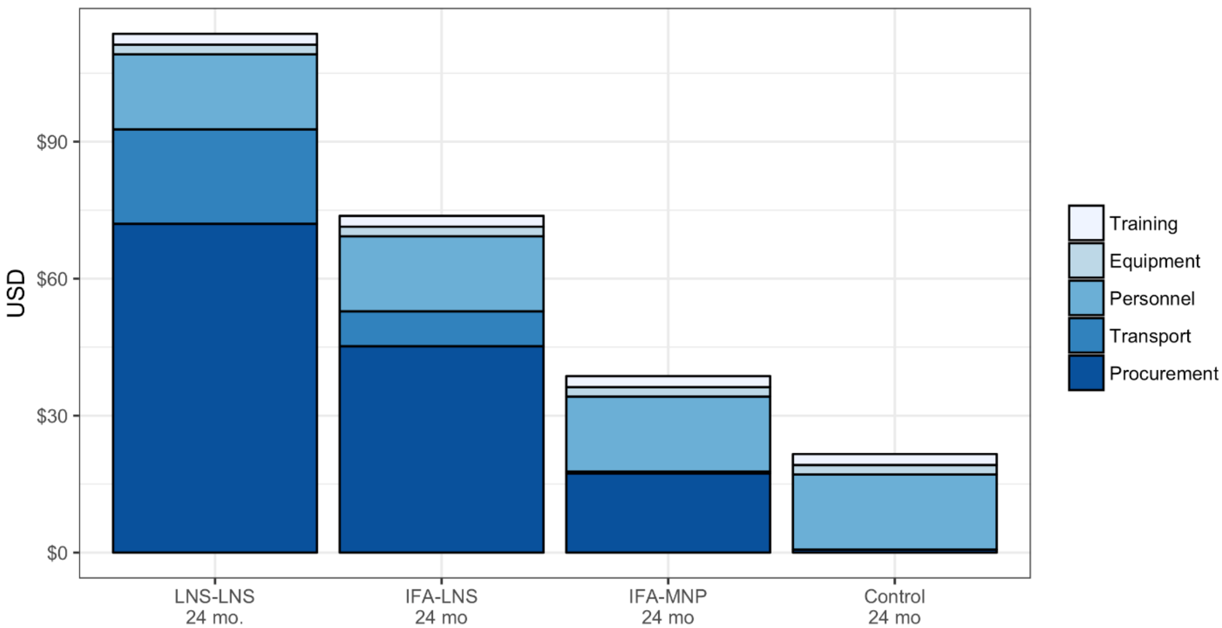
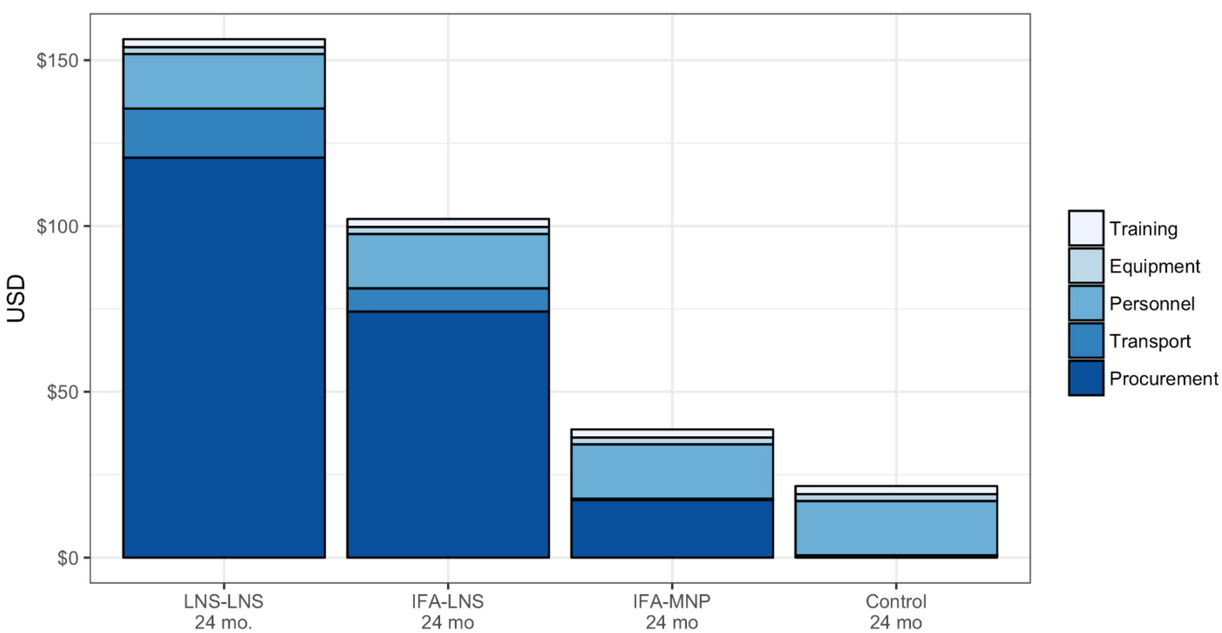
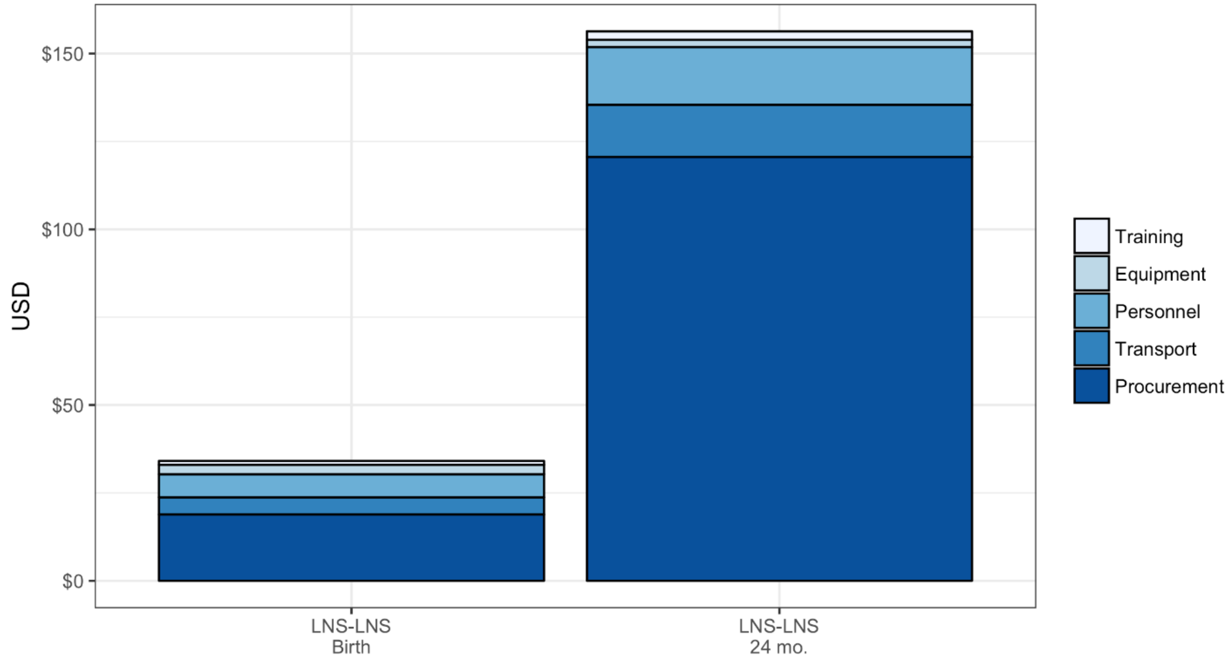


Figure 13. Average *Adjusted* Intervention Costs, by Trial Arm and Cost Category



Finally, **Figure 14** brings together the average cost estimates for the LNS-LNS arm of the RDNS trial, at birth and at 24 months of age. Not surprisingly, the cost of providing LNS-PLW and LNS-C on a daily basis to participating women (during pregnancy) and children (6–24 months of age) was substantially higher than that of providing LNS-PLW on a daily basis only to their mothers during pregnancy. Future work will assess the incremental cost-effectiveness of the LNS-C intervention.

Figure 14. Average *Adjusted* LNS Intervention Costs, Enrollment to Birth and Enrollment to 24 Months of Age, by Cost Category



10 Discussion

This report presents the first set of results of the cost analyses undertaken as part of the RDNS project in northern Bangladesh. Estimates of intervention costs from enrollment to birth, from enrollment to 18 months of age, and from enrollment to 24 months of age for children born to participating women are reported, by trial arm. We estimate the cost-effectiveness of the LNS-PLW provided to participating women in reducing newborn stunting. Finally, we estimate the cost-effectiveness estimates of providing women with LNS-PLW and their children with LNS-C (compared to providing IFA to women and MNP to children) on stunting rates at 18 months of age.

The average *adjusted* intervention cost per treated woman of the LNS-PLW, including all procurement, transportation, personnel, equipment, and training costs, was about US$34 from enrollment to birth. Focusing only on LNS-PLW procurement and transportation costs, estimates of the average cost per case of newborn stunting averted vis-à-vis the composite IFA control group at the RDNS site ranged from US$323 to US$579. The average *adjusted* intervention cost of providing LNS to women *and* their children, from enrollment to 18 months, was approximately US$123. The average cost per case of stunting averted at 18 months in the LNS-LNS arm was US$1,161. These results contribute to the growing literature on the cost-effectiveness of alternative interventions for improving the nutritional status of pregnant women and the growth and development of their young children, with particular focus on the first 1,000 days.

Regardless of the cost metrics chosen, one of the lingering challenges for these analyses is to establish the proper context in which to interpret the results. An array of lenses exists for doing so. One can look to the literature on the cost and cost-effectiveness of health expenditures on young children to begin to establish benchmarks. For example, vaccination of children in Bangladesh costs approximately US$5/child and, depending on various assumptions, costs approximately US$29,365 per death averted (Troeger et al. 2014). Measles vaccinations in Bangladesh cost approximately US$1.04 per child and, again depending on numerous programmatic objectives and other assumptions, can cost an estimated −US$19.20 to US$85.30 per disability-adjusted life year (DALY) averted (Bishai et al. 2010). Through the education expenditure lens in Bangladesh, we see that *annual* outlays for primary school in 2011 were approximately US$23/student (Steer et al. 2014). There are many investments being undertaken to save the lives of and to improve the health and development of young children in the developing world. How to make the cost-effectiveness results from the RDNS compatible with those associated with other human capital investments is an ongoing research task, but an essential one if we are to assist decision makers.

This research has several strengths. First, the analyses are based on careful and complete accounting for all the costs (including personnel costs) associated with adding new products and their associated messages to an existing maternal and infant health and care program (in this case, the LAMB Project), regardless of which organizations or individuals bore the burden of these costs. Second, preliminary assessments of costs were adjusted to reflect the research-focused nature of the RDNS and some of the unusual circumstances under which it was undertaken. Preliminary cost assessments reflecting those faced by the research project were labeled *intervention* costs. The costs that we believe an NGO or government seeking to replicate the RDNS interventions would expect to face in the geographic, socioeconomic, and institutional setting in which the RDNS took place were labeled *adjusted* intervention costs. These costs likely represent the real-world costs and we recommend using them in discussions related to the design and management of nutrition intervention programs. Third, most important and by design, intervention costs can be set alongside measured benefits, thereby generating credible estimates of cost-effectiveness. Fourth, one of the unexpected strengths of this research is that it provides one of the few estimates of the declines in measured benefits of LNS products if they are not consumed per protocol. The (unfortunate) natural experiment demonstrated that the "effectiveness" of the LNS product at birth was much higher in the "No Disruption during Pregnancy" group than in the entire sample (both relative to the control group, respectively, −7.17 versus −3.99 percentage point reductions in newborn stunting). The approximately 9-week interruption in an intervention period of approximately 26 weeks (about 35% of the average intervention pregnancy period for women) brought about an approximately 44% decline in the percentage reduction in newborn stunting. The most important implication of this result is the need to provide and promote the consumption of LNS products during the pregnancy period. This result also provides some solace for those designing and implementing supplementation programs in the challenging contexts of rural areas in developing countries—even substantial deviations from per-protocol consumption of LNS during pregnancy will not likely completely erase the benefits at birth.

As with all studies of this type, there are shortcomings. First, and perhaps most important, the cost-effectiveness results presented here focus on two birth outcomes: the number of cases of newborn stunting averted and the number of cases of stunting averted at 18 months. There are other benefits at birth and at 18 months, and there may be many other benefits up to and well beyond the 24-month endpoint of the RDNS interventions. None of these other benefits are included in the "effects" calculations, in part because methods for simultaneously assessing multiple birth and later-life outcomes are not available.[20] Future work will focus on identifying the multiple benefits that the RDNS interventions brought about and the correlations among them, and on identifying a set of value weights that may allow researchers to move from single-outcome to multiple-outcome indicators of cost-effectiveness, perhaps following the DALY approach.

Second, as always, there is scientific uncertainty regarding some measures of costs and effects that can influence cost-effectiveness estimates. For example, attrition among women and children from the RDNS sample population was low, but not zero. Depending on how these attriters are dealt with both in the cost calculations and in the estimates of effects, average cost-effectiveness measures will vary. In the results reported here on birth outcomes, attriters (257 in the composite control and 90 in the LNS arm) were included in the cost calculations to reflect normal programmatic circumstances, but no "benefits" are attributed to them. Regarding costs, self-reported estimates by village health workers of time that they spent distributing LNS and MNP products and the information associated with these products may be biased (though the direction of bias, which may vary by study arm, is challenging to predict), and these biases may influence cost estimates.

Third, there are several very important cost parameters in the *adjusted* intervention cost analyses that are challenging to predict. For example, prices paid for and shipping costs associated with LNS products will greatly influence cost-effectiveness measures. Prices paid may hinge on governments' or NGOs' abilities to negotiate with producers and import taxes, and shipping costs will be influenced by the location of production. These will be the focus of future sensitivity analyses.

Fourth, given the context in which the RDNS study was undertaken, the results presented here should be interpreted with care. More specifically, we report the costs and cost-effectiveness of adding interventions (once the decision has been made to add an intervention) to a long-established, well-performing program (the LAMB Project) with exceptional reach. Few, if any, developing countries have similar systems in place.

[20] For example, what value weights to use for each outcome? If multiple outcomes are all highly correlated with one another and all lead to long-term outcomes, such as labor market performance, should they be weighted separately in cost analyses?

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