Current evidence suggests that food fortification is a cost-effective means of addressing iron deficiency at the population level, particularly in infants and young children.

Key insights
Iron deficiency anemia has a profound impact on human health and productivity, with especially pronounced and long-lasting effects in the first 1,000 days of life. The use of fortified foods is a cost-effective tool for addressing iron deficiency in infants and young children in the Philippines. There are three categories of the most commonly used food vehicles employed for this purpose: staple food items (rice, oils and wheat), condiments (fish sauce, soy sauce and sugar) and processed commercial food items (infant complementary foods, dairy products and noodles). For infants and young children, the use of fortified complementary foods has been shown to be safer and more effective compared to supplements.

Current knowledge
In the Philippines, a large percentage of the population suffers from one or more forms of malnutrition including micronutrient deficiencies. The most common form of malnutrition in the Filipino population is iron deficiency, particularly amongst children. Iron deficiency is frequently manifested as iron deficiency anemia. Given the pervasive effects of iron deficiency on all aspects of an individual’s health and throughout the life span, iron is a key target for optimizing health, physical and cognitive potential and economic productivity.

Practical implications
The feasibility and cost-effectiveness of using fortified powdered milk to increase micronutrient intake amongst children were estimated based on a consumer survey of 1,800 Filipino households. Powdered milk was found to be an appropriate vehicle, since it is a widely used food item for children in the Philippines. Not surprisingly, poorer households were more price sensitive, indicating that they would buy more milk if the price was lower. Altogether, the most cost-effective interventions which would result in the greatest health and economic benefits are those targeting the poorest 20% of the population.

Recommended reading
Food Fortification for Addressing Iron Deficiency in Filipino Children: Benefits and Cost-Effectiveness

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Key Messages

- In the Philippines, a large percentage of the population suffers from one or more forms of malnutrition including micronutrient deficiencies.
- Iron deficiency (manifested as iron deficiency anemia) is the most common form of malnutrition in the Filipino population, especially in children.
- Ensuring adequate iron status will enhance individual health, with a positive impact on physical and cognitive productivity: this will increase the individual's ability to contribute socially and economically.
- The fortification of commonly consumed food items presents an opportunity to increase the nutrient intake of a population, thereby improving nutritional status.
- Safety and compliance aspects indicate that fortification is superior to supplementation.
- Impacts of iron deficiency are measured in health-care costs, productivity losses and disability-adjusted life years.
- The estimated consequences of these deficiencies in childhood throughout the lifetime of the individual, using a health-economic model, are large and significant and vary substantially between socioeconomic strata.

- The feasibility and cost-effectiveness of using fortified powdered milk to increase micronutrient intake amongst children were estimated based on a consumer survey of 1,800 Filipino households.
- The most cost-effective interventions are those targeting the poorest 20% of the population, since the costs of intervention increase more rapidly relative to the additional disability-adjusted life year gains if the intervention is extended to the wealthier segments of the population.

Key Words

Micronutrient deficiencies · First 1,000 days · Food fortification · Burden of disease · Cost of illness · Cost-effectiveness analysis · Philippines

Abstract

Iron deficiency is one of the most widespread nutritional disorders in both developing and industrialized countries, making it a global public health concern. Anemia, mainly due to iron deficiency, affects one third of the world’s population and is concentrated in women and children below 5 years of age. Iron deficiency anemia has a profound impact on human health and productivity, and the effects of iron deficiency are especially pronounced in the first 1,000 days of life.
Introduction

The past few decades have witnessed tremendous socioeconomic growth in the Asia Pacific region [1]. Yet, despite these advances, the benefits of development have not reached all sectors of society. Undernutrition in women and children is still widespread in the Asia Pacific region, and the ongoing cycle of malnutrition, underweight and malnourishment in girls gives rise to a generation of undernourished mothers of underweight babies [2–4]. Early malnutrition affects physical and cognitive health in later life, with far-reaching effects on personal well-being and the economic potential of the future generation [4, 5].

Iron Deficiency: Effects on Health

Iron is an essential micronutrient as it plays key roles in many metabolic processes, such as oxygen transport, DNA synthesis, neurotransmitter synthesis, energy metabolism, cell growth and differentiation and electron transport [11, 12]. Due to its essential role in so many physiological functions, iron homeostasis is tightly regulated. Since the human body lacks specific mechanisms for active iron excretion, iron balance is regulated largely at the level of absorption [11]. In general, iron is conserved in the body and is not readily lost. However, an increased demand occurs during childhood growth and pregnancy and in cases of bleeding or menstruation. The average adult stores between 1–3 g of iron in the body [11].

Iron deficiency occurs when iron supply or absorption are not sufficient to compensate for the individual’s iron requirements and losses [13]. Those with particularly high iron requirements, including pregnant women, infants, young children and adolescents, have a greater risk of being iron deficient [13–17]. The condition of iron deficiency is defined as the state in which no mobilizable iron stores are available in the body, resulting in a compromised iron supply to tissues. Iron deficiency can exist with or without the development of anemia. Anemia is defined as the condition in which the number of red blood cells is low, or if they contain less than the normal amount of hemoglobin [18]. Anemia affects an estimated one third of the world’s population, especially children below 5 years of age and women [2, 3], making it a global public health concern. Half of all anemias is related to iron deficiency [19]. In developing countries, the main cause of iron deficiency is the low iron bioavailability of the diet due to the concomitant presence of substances (such as through prescriptions for iron supplements), rather than through preventive strategies that can be influenced through population awareness and public policy [10].

The purpose of this review is to examine food fortification as a means of addressing iron deficiency in the Philippines. The first part of this review covers the effects of iron on health and the effectiveness of food fortification when used to ameliorate iron status at the population level. This is followed by a discussion of the economic burden related to iron deficiency and the cost-effectiveness of food fortification as a tool for addressing iron deficiency in the Philippines, particularly in infants and young children.
like phytate or polyphenols that limit iron absorption [13].

The physiological consequences of iron deficiency affect the individual at many levels (table 1). Iron deficiency has a direct effect on cognitive function [20]. A deficiency in iron during the neonatal period and in early childhood is an important factor in perturbing cognitive development [21, 22]. Depending on the duration and severity of the iron deficiency, these cognitive deficits may be irreversible. The well-known effects of iron deficiency on memory, intelligence and sensory perception have a direct impact on school performance, later translating into decreased economic productivity and earning potential [21, 22]. Iron deficiency also impairs immune function, increasing an individual’s susceptibility to infections [23, 24]. In pregnancy, iron deficiency can cause irreversible changes to fetal biochemical and cellular processes, for example, affecting kidney and neuronal development in the fetus [25, 26].

In the Philippines, the highest prevalence of iron deficiency anemia is seen in infants aged 6–11 months (56.5%), followed by children aged 12–23 months (41%) [6, 27]. The proportion of children up to 5 years of age with iron deficiency anemia remains high, ranging from 20 to 50% depending on the region [7]. Similarly, around half of pregnant women in the Philippines are anemic, a factor which may contribute to the infant mortality rate, one of the highest in Southeast Asia [8]. Not surprisingly, a high incidence of low birth weight and prematurity has also been reported in the Philippines [8]. Studies in birth cohorts from low- to middle-income countries (including the Philippines) have shown that preterm or term small-for-gestational-age birth was associated with deficits in adult height and reduced schooling attainment and that this pattern was consistent across all birth cohorts [28, 29].

Therefore, multiple arguments support the investment for improving iron status. Ensuring adequate iron status will enhance individual health, with a positive impact on physical and cognitive productivity [9]. In turn, this will increase the individual’s ability to contribute socially and economically. The key window of intervention lies during the first 1,000 days of life. This is the critical period of brain development when adequate iron status is crucial for ensuring the optimal morphologic, cellular and biochemical processes that modulate brain function [20, 28]. Addressing the iron status of children will have effects that cascade throughout later life, improving the rates of illness and school dropouts (reducing public expenditure in health and education) and strengthening their long-term economic prospects [9]. The additional benefit of targeting children and pregnant mothers is that this can compensate for cultural biases against girls and facilitate optimal health for both genders [9].

### Table 1. Consequences of iron deficiency [12, 20]

<table>
<thead>
<tr>
<th>Impairments in metabolic and immune functions</th>
<th>Maximum aerobic capacity</th>
<th>Endurance</th>
<th>Work capacity</th>
<th>Temperature regulation</th>
<th>Immunity (increased risk of infections)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy, growth and development</td>
<td>Increased risk of complications in pregnancy (premature birth, fetal growth retardation)</td>
<td>Growth retardation, leading to small-for-gestational-age birth</td>
<td></td>
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</tr>
<tr>
<td>Cognitive function impairment</td>
<td>Memory</td>
<td>Attention span</td>
<td>Intelligence</td>
<td>Sensory perception</td>
<td>School performance</td>
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## Food Fortification as a Tool for Addressing Micronutrient Deficiency

The fortification of commonly consumed food items presents an opportunity to increase the nutrient intake of a population, thereby improving nutritional status [30]. In developed countries, iron fortification of staple food items has long been used to increase the iron intake of the population [31]. There are three categories of the most commonly used food vehicles employed for this purpose: staple food items (rice, oils and wheat), condiments (fish sauce, soy sauce and sugar) and processed commercial food items (infant complementary foods, dairy products and noodles) [32]. The effectiveness of any intervention that seeks to improve the nutritional status of a target population depends upon several factors, including the delivery system, the recipients’ compliance and the perceived benefits [33, 34]. Iron fortification of different food vehicles has been successfully used to deliver iron to large segments of the population, including flours (in Venezuela), fish sauce (in Vietnam), soy sauce (in China) and rice (in the Philippines) [31].

However, these foods are suitable for older children and adults, but targeting infants and young children poses several challenges. This target population requires spe-
The use of fortified milk and cereal-based products was more effective in reducing anemia in young children in developing countries compared to nonfortified products.

In infants and young children, the use of fortified complementary foods has been shown to be more effective compared to supplements [35]. Three large trials in children between 1 month and 4 years of age in Nepal, India and Africa demonstrated that children who received additional iron/folic acid plus zinc in the form of supplements experienced more adverse effects compared to those who received only placebo, raising concerns on potential negative zinc-iron interactions and questioning the safety of this strategy [36–39]. In contrast, no safety issues were raised when iron and zinc were delivered through food, suggesting that these adverse interactions are minimized with this strategy [39, 40]. Another issue that has been raised is compliance, a factor which may have affected the safety outcomes in the iron/folic acid and zinc supplementation trials [40]. A study in northern India evaluated user compliance for two home-based fortification strategies for providing iron and zinc: a rice-based fortified complementary food versus a sprinkle delivered in sachets in children aged 6–24 months [40]. The authors found that the use of the fortified complementary food for 6 months resulted in a significant increase in mean hemoglobin levels and that it had a higher compliance than the use of sprinkles [40]. These findings have been supported by a number of other studies, indicating the advantages of using fortified foods over micronutrient supplements, particularly for infants and young children [41, 42].

Fortified complementary foods for infants older than 6 months typically consist of milk or cereal-based products to be used in combination with continued breastfeeding. One of the problems is that these food items are often excluded from national programs that provide fortified foods for the general population [43]. In comparison to the efficacy of other types of fortified foods, there are relatively little data on the effects of fortified milk and cereals in children. A recent meta-analysis compared the impact of micronutrient-fortified milk and cereal-based products versus similar nonfortified items in children between 6 months and 5 years of age [43]. This analysis included 18 randomized controlled trials and 5,468 children. The study concluded that the use of fortified milk and cereal-based products was more effective in reducing anemia in young children in developing countries compared to nonfortified products. Blood hemoglobin was significantly increased by 6.2 g/l and the risk of anemia was 50% lower in children receiving the fortified milk or infant cereals. Furthermore, results from the study revealed that fortification with iron plus multiple micronutrients was more effective than iron fortification alone for improving hematological parameters [43].

The benefits of fortified complementary foods for reducing iron deficiency have also been demonstrated by several independent groups. One study illustrated the effectiveness of fortified milk and noodles in reducing anemia in Indonesian children aged 6–59 months from a large sample of families (total of 81,885) living in rural and urban slum areas [44]. In this population, consumption of fortified milk and noodles was associated with a significant decrease in the odds of childhood anemia [44] and stunting [45]. A double-blind group-randomized trial assessed the effectiveness of a large-scale iron-fortified subsidized milk program in reducing the rates of anemia and iron deficiency in Mexican children between 12 and 30 months of age [46]. This trial showed a significant reduction in anemia in the study population after 6 and 12 months of the fortified subsidized milk distribution program. Importantly, these effects were biologically significant and were reflected by improved serum levels of ferritin and soluble transferrin receptor, two biomarkers of body iron stores [46]. Similar findings have been reported in a systematic review on the use of iron supplements (including iron-fortified formula) in low-birth-weight infants [47].

Taken together, these data support the benefits and feasibility of using fortified milk and complementary foods to address iron deficiency in infants and young children.

The Economic Impact of Iron Deficiency

There are two ways of expressing the economic impact of a disease (including iron deficiency). First, this may be captured in terms of the ‘cost of illness’, focusing on the health-care costs and productivity losses for the affected individual. Second, the impact of a disease may be expressed in terms of ‘burden of the disease’, which identifies the impact on the affected individual in terms of years lived with disability (disability-adjusted life years; DALYs) and years of life lost [48]. The costs of illness and burden of disease are often used as indicators to reflect the impact
of a disease and thus categorize the importance of addressing each disease for policy makers.

In a study that evaluated the causal relationship between iron deficiency and functional consequences in economic terms for 10 developing countries, the median value of annual losses due to decreased physical productivity was found to be USD 2.32 per capita (0.57% of the gross domestic product) [49]. The median total losses (physical and cognitive losses combined) were USD 16.78 per capita or 4.05% of the gross domestic product. Assuming a cost of USD 1.33 per case of anemia prevented, the authors calculated the benefit-cost ratio for long-term iron fortification programs. The median benefit-cost ratio value was 6:1 for the 10 countries examined, increasing to 36:1 when potential future benefits due to cognitive improvements were included in the estimate [49]. The Asian Development Bank estimated that productivity losses due to iron deficiency anemia in manual laborers are 17% for workers who perform heavy physical labor and 5% for blue-collar workers [50]. In children, decreased cognitive performance due to iron deficiency was associated with a 4% decrease in hourly earnings in later life [50].

A recent study by Wieser et al. [48] used a health-economic model that simulated the consequences of micronutrient deficiencies (specifically iron, vitamin A and zinc) in Filipino children aged 6–23 and 24–59 months. The authors designed a model that enabled them to extrapolate the consequences of these deficiencies in childhood throughout the lifetime of the individual (fig. 1). The total lifetime costs were reflected in the following three parameters: medical costs, which amounted to USD 30 million, production losses of USD 618 million and other intangible costs of 122,138 DALYs [48]. The bulk of the costs incurred were due to projected lifetime costs, resulting from impaired mental and physical development and the costs of premature deaths. Furthermore, the authors revealed that the burden of micronutrient deficiencies varied substantially between socioeconomic strata: the costs were 5 times higher in the poorest third of the households compared to the wealthiest third. The conclusions from this study are two-fold. First, the results underscore the importance of addressing micronutrient deficiencies in infants and young children in the Philippines. Second, this study confirms that the target population at highest risk consists of children in the very poorest households (fig. 2). This latter finding has important implications when determining the strategy for targeting this population. Not only should the food vehicle be suitable for children, but the means of delivery has to be accessible to families in the lowest socioeconomic strata in the Philippines [48].

**Cost Savings Associated with Food Fortification**

While there is evidence to support the cost-effectiveness of food fortification strategies in general, there is relatively little information on the cost-effectiveness in preschool children. Extending on the findings of previous work on the effectiveness of milk and cereal fortification...
in infants and young children [43] and on the cost burden of iron deficiency in the Philippines [48], Wieser et al. [51] evaluated the feasibility and cost-effectiveness of using fortified powdered milk in 1,800 Filipino households. The authors designed different price-based interventions with fortified powdered milk in order to assess the effectiveness and cost-effectiveness of each intervention in the reduction of iron and vitamin A deficiencies in Filipino children aged 6–23 months. Powdered milk was selected as the most appropriate vehicle, since it is a widely used food item for this age group in the Philippines and is well integrated into the local dietary habits. Using a questionnaire designed for a household survey, the authors obtained results from 1,800 low- to middle-income households with at least one child aged 6–23 months. In these households, the target respondents were mothers who were also the primary decision makers regarding food purchased for the child [51].

The findings from this study have several implications. First, the authors found that a large proportion of the households (32% in the lowest and 83% in the highest socioeconomic quintile) are already using fortified powdered milk on a regular basis. This strengthens the case for using fortified powdered milk as a vehicle for intervention. Second, and not surprisingly, the poorer households were more price sensitive, meaning that they would buy more milk if the price was lower. Third, the authors observed that the nutritional knowledge of the mothers (awareness) had no impact on the demand for fortified powdered milk, that these products were widely available (availability) and that product price was one of the main drivers of demand (affordability). Taken together, these findings suggest that in order to ameliorate nutritional deficiencies using fortified powdered milk, the child’s family must first be in a position to purchase the product. One of the mechanisms by which this can be brought about is through lowering the price of the product [51]. The poorest households also exhibit a greater price elasticity, where a small change in price can effect a larger change in demand, compared to wealthier households. The authors concluded that the most cost-effective interventions are those targeting the poorest 20% of the population, since the costs of intervention increase more rapidly relative to the additional DALY gains if the intervention is extended to the wealthier segments of the population [51].

Other studies have also demonstrated that, in general, cost is a significant factor influencing the purchase of food items, particularly in poorer households. A study in South Africa showed that purchasing healthier food items resulted in 69% higher daily costs and that these cost increases represent a high proportion of the total income for much of the population [52]. A Chinese study found that, in rural populations, food fortification was a cost-effective strategy. The authors compared the costs of supplementation, food fortification and dietary diversifica-

Fig. 2. Prevalence of micronutrient deficiencies by socioeconomic class and age group (adapted from the National Nutrition Survey 2008 [27] and the National Demographic and Health Survey [57]). IDA = Iron deficiency anemia; ZnD = zinc deficiency; VAD = vitamin A deficiency.
tion per DALY [53]. The results indicated that for iron deficiency, food fortification was the most cost-effective method (expressed in international dollars; $I$) with a cost of $I$ 66 per DALY, whereas supplementation and dietary diversification had estimated costs of $I$ 179 and 103 per DALY, respectively. The authors concluded that food fortification is one of the more effective strategies for targeting rural populations [53]. It is important to note that when designing intervention programs that target a specific population, cost may not be the only factor to consider, as consumers are also sensitive to the taste [54], color [55] and texture [56] of the food items involved, showing that acceptance of the fortified product is key.

Conclusions

The effectiveness of any intervention which aims at improving the nutritional status of a population depends on a number of variables, including the delivery system, the recipients' compliance, as well as the characteristics of the target population [34]. Food fortification remains a promising means of addressing micronutrient deficiencies, particularly for infants and young children. The ideal characteristics of a food vehicle for fortification include the following: (1) it enables the intervention to reach the target population, using existing or improved food delivery systems; (2) it does not require major changes in a population’s dietary patterns, and (3) regular consumption of the fortified item enables the individual to maintain steady body stores of the nutrient in question [32]. Current evidence suggests that food fortification is a cost-effective means of addressing iron deficiency at the population level, particularly in infants and young children.

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