

Economic Gains of a Home Fortification Program

Evaluation of “Sprinkles” from the Provider’s Perspective

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ABSTRACT

Introduction: This paper models the effects of a home-fortification program (using Sprinkles which contain zinc and iron and other micronutrients), in Pakistan, a country with high levels of infant mortality, anemia, and diarrhea. It uses the results of randomized trials of the effect of Sprinkles on anemia and on longitudinal prevalence of diarrhea.

Methods: Based on previous literature, the effect of Sprinkles on intermediate outcomes (diarrhea and anemia) is linked to longer-term outcomes (infant and young child mortality, and cognitive achievement and hence adult wages). Three different measures of cost effectiveness are presented: the cost per death averted (effect via zinc supplementation on reduction of longitudinal prevalence of diarrhea); the cost per ‘disability adjusted life year’ (DALY) saved (same modality); and the gain in earnings due to higher cognitive functioning for each dollar spent (effect via iron supplementation on reduced anemia).

Results: We estimated that the cost per death averted is \$406 (\$273-\$3248), the cost per DALY saved is \$12.2 (\$8-\$97) and the present value of the gain in earnings is \$37 (\$18-\$51) for each dollar spent on the Sprinkles program. These estimates were developed for a low-income country (GDP per capita = \$417) with a high infant mortality rate (IMR = 83/1000), high prevalence of anemia (93%), and high mean longitudinal prevalence of diarrhea (17%).

Discussion: These outcomes are particularly favourable in Pakistan. The outcomes are more favourable when used with children 6-12 months. Further longer-run field trials of Sprinkles with larger populations would be helpful.

MeSH terms: Home fortification; zinc deficiency; iron deficiency; anemia; diarrhea; cost-effectiveness; Sprinkles

La traduction du résumé se trouve à la fin de l'article.

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In developing countries, micronutrient deficiencies in weaning-age children are a serious problem. As much as 80% of infant mortality is attributed to diarrhea-related illnesses¹ while most of the remaining 20% is due to acute respiratory infections (ARIs). Nutritional status in general (including zinc status) is a significant risk factor.²⁻⁵

These same children are also at increased risk of developing iron deficiency anemia by the age of 6 months; the prevalence of anemia among children 6-24 months of age is between 60-90% in the worst-affected region, South Asia.⁶ Anemia is associated with cognitive impairment^{7,8} which in turn is correlated with lower school attendance and lower earnings in adult life. The first 24 months of life are considered to be a critical period or a ‘window of opportunity’ to optimize brain development, with iron playing an important role.

Reaching weaning-age children with iron and zinc interventions is challenging. Fortification of common staples (e.g., wheat flour) is unlikely to provide enough micronutrients at this critical age. ‘Sprinkles’ single-dose sachets were developed as an alternative at the Research Institute of the Hospital for Sick Children, one of the affiliated teaching hospitals of the University of Toronto (Toronto, Canada). These single-dose sachets contain micronutrients in a powder form which are easily sprinkled onto any foods prepared in the household (this practice is referred to as ‘home fortification’). The iron (ferrous fumarate) is encapsulated with a thin lipid layer to prevent the iron from interacting with food so that there are minimal changes to the taste, colour or texture of the food; other micronutrients, including zinc, iodine, vitamins C, D and A, and folic acid, are added.

The use of Sprinkles in a randomized clinical trial (RCT) in Ghana (a malaria-endemic area) was associated with a 58% cure rate among anemic infants.⁹ Several other trials done elsewhere produced similar results, although in non-malaria areas, the cure rate was higher (up to 92%). An RCT in Pakistan in children with recent history of diarrhea found an 11% reduction in the longitudinal prevalence of diarrhea among children 6-12 months of age in the Sprinkles group compared to the placebo group.¹⁰ Longitudinal prevalence of diarrhea is defined as number of days of diarrhea per observed child days. It is a predictor of mortality.¹¹

This paper models the cost-effectiveness and cost-benefit of an intervention whereby 60 Sprinkles sachets are provided to households with young children (predominantly in the 6-12 month age group), to be consumed by those young children over a period of 2-4 months.

METHODS

We modelled two fictitious communities representative of the Pakistani population, each having a total population of 200,000. According to 2002 estimates, Pakistan has a population of about 150 million, the birth rate is 30.4/1000, infant mortality rate (IMR) is 83/1000, under-five mortality rate is 107/1000, and the annual per capita gross domestic product (GDP) is US\$ 417. Children (6-24 months old) make up 6% of the population.

The model assumes an intervention whereby children in the 6-24 month age group receive 60 Sprinkles sachets over a period of 4 months. We assume that there is imperfect coverage (95% of the children in the appropriate age group are reached initially). However, children who miss being covered receive the intervention at a later age. Children who received 60 sachets once are not eligible to re-enter the program.

The production cost for a pilot distribution of Sprinkles sachets to approximately 100,000 children is estimated at \$0.015 (US dollars) per sachet, plus \$0.005 per sachet for distribution and overhead, for a total cost per sachet of \$0.02. Thus, cost per child is estimated to be \$1.20. The cost is likely to be lower for a larger volume.

Estimation of cost per death averted

There is strong evidence that zinc supplementation is associated with reduction in morbidity and mortality from diarrhea and ARI.¹² We used longitudinal prevalence of diarrhea to measure burden of diarrhea in children and its subsequent effect on mortality; however, as direct evidence on mortality from a Sprinkles study is lacking, we extrapolated evidence from literature as follows.

Longitudinal Prevalence of Diarrhea: Control Group

Shah and colleagues reported that at the time of conducting their survey in Pakistan, 51% of children had diarrhea in the preceding 2 weeks.¹³ Two RCTs in

TABLE I

Projected Number of Deaths During the First Five Years of the Sprinkles Program in a Community Compared to a Control Group

	Mean Longitudinal Prevalence of Diarrhea %		Projected Number of Deaths			
	Control	Sprinkles	Control		Sprinkles	
			<12 months n = 31,896	≥12 months n = 6000	<12 months n = 31,896	≥12 months n = 6000
Base case	17	11	638	12	528	10
Sensitivity analyses						
	10	5.8	512	10	449	8
	10	9.2	512	10	499	9
	20	11.6	701	13	538	10
	20	18.4	701	13	667	12

Karachi, Pakistan found longitudinal prevalence of diarrhea was 26% in children who had a recent history of diarrhea at time of enrolment in the study,¹⁰ and 7.6% in children with no recent history,¹⁴ yielding an overall mean of longitudinal prevalence of diarrhea (control group) of 17%.

Longitudinal Prevalence of Diarrhea: Sprinkles Group

Sharieff et al.'s study of young children found that the Sprinkles intervention was associated with a decrease in longitudinal prevalence of diarrhea (in children with a recent diarrhea history) from 26% to 15%. If we make the conservative assumption that Sprinkles does not reduce longitudinal prevalence of diarrhea in children with no recent diarrhea history (these children are less likely to be zinc-deficient), then the overall mean of longitudinal prevalence of diarrhea (Sprinkles group) is 11%; thus, the absolute reduction in longitudinal prevalence of diarrhea would be 6%.

Probability of Death: Control Group

To model the mortality rate in narrow age brackets, we assumed an exponential survival curve and estimated that 50 out of 83 would die before reaching 6 months of age (IMR=83 per 1000). Hence, the probability of dying between 6-12 months given that an infant was alive at 6 months of age is 3.4% (33/950). 950 represents the number of live infants at 6 months taken from the IMR which is expressed per 1000 live births and 33 represents the number who would die between 6 and 12 months given an IMR of 83/1000 live births.

Similarly, the probability of dying between 12-60 months of age given a child is alive at 12 months is 2.6% (24/917). Thus, in the control group, the probability of dying in the 4-month supplementation

period for a 6-12 month old child would be 2% (3.4/1.5) and for a 12-24 month old child, would be 0.2% (2.6/12).

Probability of Death: Sprinkles Group

Morris et al. studied 6-23 month old children and, using conditional logistic regression, estimated that a 5% increase in longitudinal prevalence of diarrhea corresponded to a 17% increased risk of mortality (β coefficient = 3.14).¹¹ Thus, a 6% decrease in longitudinal prevalence of diarrhea would reduce the risk of mortality by 18% ($1/e^{3.14 \times 0.06} = 0.82$). Hence, in the Sprinkles group, the probability of dying in 4 months (duration of supplementation) for a 6-12 month old child would be 1.64% (2x0.82) and for a 12-24 month old child, this probability would be 0.164% (0.2x0.82).

Estimation of cost per 'disability adjusted life year' (DALY) saved

As in Baltussen et al.,¹⁵ we restricted DALY calculations to mortality as the outcome; this was because translation of anemia-induced cognitive impairment into DALYs is problematic. Using the methods described by Homedes,¹⁶ we calculated DALYs per infant death as 33.1 (age 9 months) and per child death as 33.7 (age 18 months).

Estimation of gain in earnings via improvement in cognitive development, per dollar spent (benefit: cost ratio)

Using the human capital approach, we used intervention trials where Sprinkles raised Hb concentrations, and linked those with studies where reduction in anemia has been associated with raised IQ, and higher IQ with higher earnings. For the base case, we estimated that the mean Hb in the control group was 95 g/L (SD = 10 g/L) corre-

TABLE II
Effect of Sprinkles on Annual Earnings (E) via Improvement in Hemoglobin (Hb) Concentrations and IQ Scores

Control Group Hemoglobin g/L *	Sprinkles Hemoglobin g/L *	Mean Difference (Sprinkles – control) Hb	IQ	Discounted Average Gain in Cumulative Earnings \$‡
Base case 95 (93)	107 (62)	12	2.1	44
Sensitivity analyses				
85 (99)	102 (78)	17	2.9	61
90 (97)	105 (69)	15	2.6	55
100 (84)	110 (50)	10	1.75	36
105 (64)	113 (38)	8	1.4	29
110 (50)	116 (27)	6	1.05	22

* At 9 months of age.

† % < 110 g/L computed using the cumulative distribution function (standard deviation = 10 g/L).

‡ Assuming no effect on earnings of individuals who received Sprinkles after 9 months of age.

sponding to anemia prevalence (Hb < 110 g/L) of 93%.^{17,18}

Effect of Sprinkles on Hb

We used the following model whose development and validation has been described elsewhere¹⁹ to estimate Hb in the Sprinkles group in relation to Hb in the control group:

$$Hb(S) = e^{4.2 + 0.005xHb(C)}$$

where Hb(S) and Hb(C) are the means of Hb in the Sprinkles and control groups, respectively.

Effect of Hb on IQ

We estimated the effect of Hb on IQ on the basis of results from a cohort study by Palti and colleagues.²⁰ Palti et al. followed a cohort from 9 months of age to 5 years of age and observed that children who had higher Hb concentrations at 9 months of age had higher IQ scores at 5 years of age compared to their counterparts (a 10 g/L increment in Hb concentration at 9 months of age corresponded to an increment of 1.75 IQ points at 5 years of age after adjusting for other covariates, including mother's education). Lozoff and colleagues observed similar findings after as long as 15 years of follow up.²¹ These IQ scores (Wechsler scale) are likely to persist until past childhood²² and may have an impact on work productivity.

Effect of IQ on Earnings

We estimated the effect of IQ on earnings based on Salkever's model.²³ Salkever estimated that each IQ point increment corresponds to an increment of 0.0123 units in earnings (log-scale) after controlling for other factors, including parents' and individual's education and ethnicity.

We assume that individuals will enter the labour force at age 18 and retire at age 55. Conservatively, we assume no growth in GDP per capita over time, and assume a wage share of 40% in GDP.²⁴ Then expected annual earnings (E) are \$167 (\$417 x 0.4) for the control group.

A child in the intervention group would have 2.1 points higher IQ than the child in the control group and an E of \$171 ($167 e^{0.0123 \times 2.1}$). This difference of \$4 at age 18 would correspond to a present value of \$2.33 after discounting at a 3% annual rate ($4 e^{-0.03 \times 18}$). Therefore, the cumulative difference in earnings up to 55 years of age would be \$54 ($4 e^{-0.03 \times 18} + 4 e^{-0.03 \times 19} + \dots + 4 e^{-0.03 \times 55}$).

The gain in earnings was restricted to 6-8 month old children who had received the intervention prior to 9 months of age because it was assumed that a rise in Hb after 9 months would not affect IQ.²⁰ This is conservative; there may be gains at later ages.

Sensitivity analyses

To account for the uncertainty in the means of longitudinal prevalence of diarrhea and Hb, and the effect of Sprinkles on longitudinal prevalence of diarrhea, we carried out sensitivity analyses over a range of plausible values.

For cost per death averted, we varied the mean of longitudinal prevalence of diarrhea in the control group using a lower bound of 10% and an upper bound of 20%.²⁵ Next we varied the β coefficient for mortality and used the lower and upper bounds of the 95% confidence interval (CI); the mean was -0.43 (95% CI = -0.096, -0.76). Finally, we varied the mean

of Hb in the control group and estimated the effect of Sprinkles in relation to each of these values (85, 90, 100, 105 and 110 g/L as compared to the base case of 95 g/L).

RESULTS

Over five years, 37,896 children were covered by the program in the community. In the 6-8 month age group, there were 28,500 children; 8-10 months, 2,342; 10-12 months, 1,054; and 12-24 months, 6,000 children. A detailed spreadsheet is available from the corresponding author.

Table I shows the longitudinal prevalence of diarrhea and the corresponding number of projected deaths in the Sprinkles and control groups. 112 deaths were averted with the use of Sprinkles, with a **cost per death averted** of \$406 (range is \$273-\$3248 based on sensitivity analyses). This corresponds to a **cost per DALY saved** of \$12.2 (range is \$8-\$97 based on sensitivity analyses).

Table II shows the mean Hb in the Sprinkles group corresponding to a range of values for the mean Hb in the control group, as well as the corresponding differences in IQ scores. For each dollar spent (**benefit:cost**) the return was \$37 (range is \$18-51 based on sensitivity analyses).

DISCUSSION

The results reported here support the Copenhagen Consensus view, which ranked interventions to increase the availability of micronutrients as the second highest priority in advancing 'the lives of people living in developing countries'.²⁶ Our estimates are comparable to other primary health care prevention programs: the cost per death averted is estimated to be: \$67.2 for vitamin A supplementation in children between 6-59 months of age in the Philippines,²⁷ and \$327 in Nepal;²⁸ \$115-\$919 for breastfeeding promotion in young infants in Central and South America;²⁹ and for diarrhea control in young children in developing countries, \$333 for rotavirus immunization, \$3025 for cholera immunization and \$3405 for oral rehydration therapy.³⁰ Similarly, home-based care for HIV/AIDS varies from \$100 to \$1000 per DALY saved.³¹ Thus, a short-term intervention with Sprinkles appears cost effective. Likewise the benefit:cost ratio is extremely favourable

(benefit:cost ratios are not widely available for primary health care interventions).

Our estimates are extremely conservative. We assumed no effect on longitudinal prevalence of diarrhea in 49% of the children who received the intervention; no effect on mortality after children had stopped using Sprinkles (post 4 months); and no effect on cognition in children who were older than 9 months.

The major limitations in the development of the model were lack of direct evidence from Sprinkles studies to support the effects on mortality, IQ and earnings. Therefore, our estimates should be used in the context of these limitations. Since we have reported a range of values for relevant population parameters (means for longitudinal prevalence of diarrhea and Hb, prevalence of anemia), the use of Pakistan as a country example should not limit the generalizability of our results to other countries, although in Pakistan (an environment with high levels of mortality, diarrhea, and anemia), the intervention is particularly favourable.

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RÉSUMÉ

Introduction : Un modèle a été utilisé pour évaluer l'effet d'un programme pour enrichir les aliments à domicile (en utilisant les suppléments Sprinkles contenant du zinc et du fer, ainsi que d'autres micronutriments) au Pakistan, un pays où les taux de mortalité infantile, d'anémie et de diarrhée sont élevés. Le modèle comprend les résultats d'essais cliniques randomisés de l'effet des Sprinkles sur l'anémie et sur la prévalence longitudinale de la diarrhée.

Méthode : La documentation existante suggère que les effets des Sprinkles à moyen terme (sur la diarrhée et l'anémie) sont liés à certains effets à plus long terme (baisse de la mortalité infantile et post-infantile, meilleur développement cognitif, et donc revenus plus élevés à l'âge adulte). Nous présentons trois mesures différentes de l'efficacité par rapport au coût : le coût par décès évité (en réduisant la prévalence longitudinale de la diarrhée grâce à la supplémentation en zinc); le coût par « année de vie épargnée pondérée par l'invalidité » (DALY) (toujours grâce à la supplémentation en zinc); et le gain de revenus dû à un fonctionnement cognitif supérieur pour chaque dollar dépensé (en réduisant la prévalence de l'anémie grâce à la supplémentation en fer).

Résultats : Nous avons estimé que, pour chaque dollar dépensé sur le programme Sprinkles, le coût par décès évité est de 406 \$ (273 \$-3 248 \$), le coût par DALY épargnée est de 12,20 \$ (8 \$-97 \$), et le gain de revenus actuel est de 37 \$ (18 \$-51 \$). Ces estimations ont été élaborées pour un pays à faible revenu (PNB par habitant = 417 \$) avec un taux élevé de mortalité infantile (TMI = 83/1 000), une prévalence élevée d'anémie (93 %) et une prévalence longitudinale moyennement élevée de diarrhée (17 %).

Discussion : Ces résultats sont particulièrement favorables dans un environnement aux taux élevés de mortalité infantile, d'anémie et de diarrhée comme le Pakistan. Les résultats sont plus favorables chez les enfants âgés de 6 à 12 mois. Il serait utile de mener d'autres essais avec les suppléments Sprinkles, sur le terrain, à plus long terme et avec un plus grand nombre de participants.