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The economics of iron deficiency

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Abstract

This paper examines the evidence for a causal relationship between iron deficiency and a variety of functional consequences with economic implications (motor and mental impairment in children and low work productivity in adults). To the extent that we can be confident that iron deficiency does cause a consequence with economic implications, this effect is quantified in economic terms. Illustrative calculations for 10 developing countries suggest that the median value of annual physical productivity losses due to iron deficiency is around $2.32 per capita, or 0.57% of GDP. Median total losses (physical and cognitive combined) are $16.78 per capita, 4.05% of GDP. Using a cost of $1.33 per case of anemia prevented, from one of the few effectiveness studies of national fortification, allows us to calculate the benefit-cost ratio for long-term iron fortification programs. The median value is 6:1 for the 10 countries examined and rises to 36:1 including the discounted future benefits attributable to cognitive improvements. This paper improves on previous work by including a much more thorough survey of the quantitative magnitudes involved, and by incorporating effects of iron deficiency on cognition. However, more research is needed to verify the accuracy of the assumptions needed for this type of analysis.

Keywords: Cost-benefit; Cost-effectiveness; Iron deficiency; Anaemia; Cognitive effects; Productivity effects; Micronutrients

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Introduction

Iron deficiency has earned distinction as the most common nutritional deficiency in the world today. Because iron is important for blood formation, iron deficiency often leads to anemia, defined as having a blood hemoglobin level below standard.[1] It is estimated that 1.7 bn people worldwide suffer from anemia, of which half is iron-deficiency anemia (IDA) (WHO, 1997), while iron deficiency (without anemia) is as widespread as IDA. Given the magnitude of the problem it is important to know how IDA actually affects the lives of these individuals. Many studies document the association of IDA with poor pregnancy outcome, poor motor and mental performance in children and low work productivity in adults. Studies also increasingly show that milder iron deficiency, unaccompanied by anemia, has negative outcomes.

This paper aims to make realistic quantitative estimates of the economic consequences of iron deficiency that can be defended on epidemiologic and economic grounds, and to use these to estimate population-wide benefit–cost ratios for iron fortification.

There are two broad areas in which iron deficiency is considered to have important functional impacts on humans, where economic consequences can be estimated: cognitive ability of children, and work capacity of adults. Although we also examined child growth, immune function and susceptibility to the toxic effects of heavy metals , there was insufficient consistent evidence to incorporate these into the analysis. Effects on pregnancy outcome are well documented, but insufficient cost data exist for developing countries to incorporate this into the economic analysis.

Our benefit–cost ratios can be compared to the few previous such estimates. Levin et al. (1994) using hypothetical data estimate this ratio as 84:1 for iron fortification interventions, and 28:1 for iron supplementation (with corresponding ratios ranging from 6:1 to 28:1 for iodine interventions, and 7:1 to 22:1 for vitamin A interventions). The present study benefits from more recent literature on the functional consequences of iron deficiency to refine previous estimates. We also allow for different consequences in light manual work, and heavy manual work, and include the cognitive effects on white-collar work, not previously considered.

Section 2 considers effects on children and Section 3 on adults. Section 4 estimates the costs of iron deficiency anemia for a selection of 10 countries, and uses the first effectiveness data available for a national iron fortification program in a developing

[1] Hemoglobin is an iron-containing component of red blood cells that is needed for oxygen transport. Its level in the blood normally varies according to age, sex and physiological state so standards also vary. The following hemoglobin (Hb) concentrations are used by the WHO (1997) to indicate cutoffs below which anemia may be present: children under 5 years: $<$110 g/dL; children 6–11 years: $<$115 g/L; children 12–14 years: $<$120 g/L; adult males: $<$130 g/L; adult females (non-pregnant): $<$120 g/L; adult females (pregnant): $<$110 g/L. The population can be divided into four groups depending on the presence of anemia and/or iron deficiency (based on iron stores). We are concerned here with iron deficiency. However, due to the lack of nationally representative data on iron deficiency we use the prevalence of anemia as a proxy for some of our estimates. This is appropriate when applying coefficients derived from studies of responses to iron supplementation among anemic subjects.

country (Venezuela) as a guideline to simulate cost–benefit ratios for national iron fortification programs in 10 selected countries. Section 5 concludes.

Lower future productivity of children

A biological mechanism

The biological basis for the effects of iron uses animal studies. There are high concentrations of iron in certain similar regions of both the rat and human brains, suggesting important roles for iron that could account for its importance in cognition. Evidence from iron-deficient rats suggests a permanent reduction in dopaminergic neurotransmission due to the failure to develop dopamine receptors early in life (Ben-Shachar et al., 1986; Yehuda et al., 1986). Dopamine is an important neurotransmitter in both rat and human brains. In rats, dopamine relies on an iron-dependent receptor to function normally. Unlike the permanent effects of early iron deficiency, iron deficient adult rats will recover dopamine receptor function if given iron.

The function of receptors for at least two other neurotransmitters, serotonin and GABA (γ-aminobutyric acid), are also compromised in iron-deficient rats, although these systems are less well understood. The amount of another neurotransmitter, norepinephrine is reduced in peripheral tissues in iron-deficient rats (Beard et al., 1993). Although these results do not provide conclusive evidence for a direct link between iron deficiency and cognitive effects in humans, they do provide a number of plausible biological mechanisms to support the epidemiological evidence that brain function is compromised in iron deficiency.

Evidence for an effect of iron deficiency on cognitive development in children under 2 years

The standard tests of development in infants, used in virtually all of the studies reviewed here, are the Bayley scales of infant development. These scales include both mental and motor development components, each standardized to have a mean of 100 and a standard deviation of 16 points. In addition, the Bayley scales include the Infant Behavior Record, designed to assess the infant's affective state such as responsiveness to the investigator, attention span, fear and other behavioral signs that might explain mental or motor test performance. The Bayley scales are not considered an intelligence test but a means of determining the stage of development of the infant in comparison with age-appropriate standards.

Observational studies of the relationship between iron deficiency anemia and mental test performance are remarkably consistent in finding that infants with moderate iron deficiency anemia have test scores that are 0.5 to 1.5 standard deviations lower than those of infants with sufficient iron stores (see reviews by Lozoff, 1988, and Pollitt, 1993). These differences are large enough to be of great concern, especially given the prevalence of child anemia in poor environments. However, there are confounding factors in observational studies, not all of which can be controlled. Many

of the developmental effects ascribed to protein-energy malnutrition (PEM) may in fact be due to iron deficiency (Pollitt, 1995).

The most conclusive evidence for the effect of iron deficiency on cognitive development comes from intervention studies. The results of the many iron intervention trials on children below 24 months so far published are summarized in Table 1. The ideal study design is a randomized, controlled, double-blind trial. However, because studies that withhold treatment from anemic subjects are hard to justify on ethical grounds, these have generally been restricted to very short periods of placebo-controlled interventions (Lozoff et al., 1982; Oski and Honig, 1978), sometimes followed by a longer period of universal coverage (Walter et al., 1989; Lozoff et al., 1987), or have been conducted in situations where the anticipated benefits of the intervention are uncertain because subjects are not generally anemic (Moffatt et al., 1994).

The short-term placebo-controlled studies have produced mixed results. A pioneering study (Oski and Honig, 1978) in the US found a statistically significant 7.5 point (approximately half a standard deviation) greater rise in mental scores of infants given an intramuscular injection of iron than of infants receiving a saline placebo. In Guatemala there was no effect of daily oral supplementation for 1 week on either motor or mental development scores of anemic infants 6–24 months old (Lozoff et al., 1982a; Lozoff et al., 1982b). Similarly, a replication of this study in Costa Rica found no effect of iron supplementation (Lozoff et al., 1987).

Only two placebo-controlled studies published to date have described the effects of long term iron therapy in a population of very young children with iron deficiency anemia. Aukett et al. (1986) found that 31% of 17–19-month-old anemic children receiving daily iron supplements versus only 12% of those receiving placebo attained an average rate of motor development over the 60-day intervention period, a difference that was statistically significant ($p < 0.05$). Idjradinata and Pollitt (1993) found that in Indonesia, both treatment and placebo groups improved their mental and motor scores over the course of the 4-month intervention. But the children receiving daily iron supplements improved their mental scores by 19 points more and their motor scores by 18 points (in both cases just over 1 S.D.) more than did the children receiving a placebo. These studies provide conclusive evidence for a causal link between iron deficiency and developmental delays that can be corrected by iron therapy.

Intervention studies in developed countries where anemia is less common, have found smaller effects. Moffatt et al. (1994) in a Canadian study found that infants fed fortified formula had higher motor development scores at 9 and 12 months (by 4.0 and 6.3 points, respectively) than infants who received a standard non-fortified formula, but by 15 months these differences were no longer apparent. Williams et al. (1999) studied 6–8-month-old infants from a ‘socially deprived’ inner city area of Birmingham, whose mothers had already decided to feed them unmodified cow’s milk, and who were randomly selected to receive iron-fortified formula or to continue on cow’s milk. By 18 months of age, infants receiving iron-fortified formula had lower prevalence of anemia (2% vs. 33%, $p < 0.001$) and although developmental scores (Griffths scales) declined in both treatment groups, the decline among infants on iron-fortified formula was less ($p < 0.02$) than that among infants on cow’s milk.

Table 1
Effects of iron therapy on cognitive and behavioral development in children younger than 24 months

Authors (date)	Location	age group (months)	Design	Treatment and dose	Period (days)	n	Definition of IDA	Test	Effect of treatment on IDA children	Effect of treatment on IDNA children
Lozoff et al. (1982a, 1982b, 1985)	Guatemala	6–24	randomized, placebo-controlled, double blind	10 mg Fe/kg/d orally as ferrous ascorbate in two doses	6–8	28 IDA, 40 non-anemic	Hb(105g/L	Bayley scales	none	na
Lozoff et al. (1987)	Costa Rica	12–23	randomized, placebo-controlled, double blind	10 mg Fe/kg/d orally as ferrous ascorbate in two oral doses *or* intramuscular injection	7	97 IDA, 94 non-anemic	Hb(105g/L	Bayley scales	mental: none, $p > 0.69$ motor: none $p > 0.80$	not different from IS at baseline
Lozoff et al. (1987)	Costa Rica	12-23	pre-post comparison with non-anemic controls	6 mg Fe/kg/d orally as ferrous ascorbate in two doses *or* intramuscular injection	90	17 mod IDA, 90 mild IDA or non-anemic	Hb(105g/L	Bayley scales	mental: none, $p = 0.76$ motor: 9.3 points, $p = .007$	not different from IS at baseline
Walter et al. (1983)	Chile	15	pre-post comparison with non-anemic controls	3-4 mg Fe/kg/d orally as ferrous sulphate	11	10 IDA, 12 IDNA, 15 IS	Hb < 110g/L	Bayley scales	mental: 10 points $p < 0.01$ motor: none	yes, 6 non-anemic children with ≥2 abnormal indices: mental: 10 points, $p < 0.01$

(*continued on next page*)

Table 1 (*continued*)

Authors (date)	Location	age group (months)	Design	Treatment and dose	Period (days)	n	Definition of IDA	Test	Effect of treatment on IDA children	Effect of treatment on IDNA children
Walter et al. (1989)	Chile	12	randomized, placebo-controlled, double blind	15 mg of Fe orally as ferrous sulphate 3 times/d	10	39 anemic, 127 IDNA, 30 IS	Hb < 110g/L + 2 abnormal biochemical measures	Bayley scales	mental: 1.9 points∗, ns motor: 1.6 points∗, ns	mental: 0.2 points∗, ns motor: 0.2 points∗, ns
Walter et al. (1989)	Chile	12	pre-post comparison with non-anemic controls	15 mg of Fe orally as ferrous sulphate 3 times/d	90	39 anemic, 127 IDNA, 30 IS	Hb < 110g/L + 2 abnormal biochemical measures	Bayley scales	mental: −0.2 points, ns motor: 1.9 points, ns	motor: 0.2 points, ns
Aukett et al. (1986)	UK	17–19	randomized, placebo-controlled, double blind	24 mg Fe/day orally as ferrous sulphate (parent administered at home)	60	110 anemic		Denver test	more attained average rate of development: 31% (treatment) vs. 12% (control), $p < 0.05$	na

Table 1 (*continued*)

Authors (date)	Location	age group (months)	Design	Treatment and dose	Period (days)	n	Definition of IDA	Test	Effect of treatment on IDA children	Effect of treatment on IDNA children
Idjradinata and Pollitt (1993)	Indonesia	12–18	randomized, placebo-controlled, double blind	3 mg/kg/d orally as ferrous sulphate	120	47 IDA, 28 IDNA, 44 IS	Hb < 105g/L; TS <10%; SF < 12 µg/L	Bayley scales	mental: 18.8 pts∗p < 0.001 motor: 18.4 pts∗p < 0.001	none
Moffatt et al. (1994)	Canada	neonates	randomized, placebo-controlled, double blind	iron fortified formula (12.8 mg Fe/l)	6, 9, 12, 15 months	225, 204, 186, 154 at each assessment, respectively	na	Bayley scales	mental: motor: 4 points at 9 and 6.3 points at 12 months $p <$ 0.001, no at 6 and 15 months $p > 0.05$	results include mostly non-anemic children (90% at 15 months)
Williams et al. (1999)	UK	6–8	randomized, double blind	iron fortified formula (12 mg Fe/l)	to 18 months	85	na	Griffiths scales	na: scores not analyzed by hematological status	5.4 point smaller decline $p <0.02$

∗, adjusted for response in controls receiving placebo; IDA, iron deficient anemic, IDNA, iron deficient non-anemic, IS, iron sufficient; na, not applicable; ns, not (statistically) significant; Hb, hemoglobin; MCV, mean corpuscular volume; SF, serum ferritin; SI, serum iron; TS, transferrin saturation; FEP, free erythrocyte protoporphyrin.

Although there are clearly other nutritional differences between formula and cow's milk, the strong effects on anemia prevalence strongly suggests that the mechanism for the developmental effects involves iron.

What are the functional implications of early developmental delays for the long-term cognitive abilities of these children and can they be corrected? Answers to these questions remain somewhat speculative because none of the intervention studies with anemic children had sufficiently long periods of follow-up. Mental development scores in infancy do not predict differences in intellectual function in later childhood (Idjradinata and Pollitt, 1993). Mental development of children on the Bayley scales is known to be poorly correlated with later intelligence. Motor scores, on the other hand, do predict cognitive test performance not only later in childhood but also at 18 years of age (Pollitt and Gorman, 1990), although in this case these were not attributed to or influenced by iron deficiency. However, if we separately take the improvement in motor performance in the Indonesia study as indicative of the magnitude of the motor delay due to deficiency, then we would expect motor scores in anemic infants to be reduced by approximately 18 points (or just over 1 S.D.). Furthermore, since this was the net correction observed in anemic children (anemia from all causes) after a placebo-controlled, randomized, double-blind intervention, we can attribute this reduction to iron deficiency with considerable confidence. Since the final motor scores were roughly the same as those of the non-anemic children, it appears that the motor impairment observed was completely reversed by 4 months of therapy.

Failure to reverse the mental and motor effects of anemia in previous placebo-controlled studies may therefore be attributed to the brief duration of therapy offered, or possibly that effects at certain ages are more reversible than others. Trials of longer therapy without placebo controls have also had mixed results. In Costa Rica, 90 days of oral iron therapy had no apparent effect on mental development scores but did appear to improve motor test performance by 9 points in anemic children 12–24 months old (Lozoff et al., 1987). In Chile, on the other hand, a similar regimen in 12-month-old infants had no effect on either mental or motor scores (Walter et al., 1989). However, since (for ethical reasons) the comparison groups in both of these trials were non-anemic children and therefore not strictly comparable, and since it is possible that the test performance without therapy could have worsened over this period, these results are inconclusive.

The evidence available satisfies all of the conditions needed to conclude that iron deficiency causes developmental delays and that these can be at least partially reversed by iron therapy. There is a strong association between iron deficiency anemia and cognitive and behavioral test performance that remains even after controlling for a wide variety of potential confounders. This has been confirmed in numerous studies in a wide variety of situations. Although there is still uncertainty about the biological basis for this effect, the importance of iron in several neurological processes suggests more than one plausible biological mechanism. The timing of iron deficiency relative to the developmental delays is difficult to demonstrate in infants because ethical considerations preclude the experimental induction of iron deficiency. However, in cross-sectional observational studies, since the developmental delays

appear at least to accompany the deficiency, there is no evidence to contradict the proposed chronology. Finally, the evidence from therapeutic trials suggests that this relationship is causal and that the observed delays may be corrected.[2]

Evidence for an effect of iron deficiency on cognitive development in children over 2 years

In children 2 years of age and older it is possible to measure intelligence using tests such as the Wechsler Intelligence Scales for Children and the Raven Progressive Matrices. It has been shown that iron deficient children score about half a standard deviation lower on these tests than do non-deficient controls (Pollitt, 1993). Although this association remains even after statistically adjusting for the effects of socioeconomic status, such adjustment cannot compensate for unrecognized, unmeasured or imperfectly measured factors. Verification through placebo-controlled interventions is therefore required to establish that the observed associations are causal. In reviewing the results of the several published clinical trials of the effects of iron therapy on cognitive performance and school achievement of children older than 24 months, Pollitt (1993) concluded that iron therapy lasting at least two months resulted in major improvement in IQ and that "iron deficiency anemia causes an alteration in cognitive function among preschool and school age children that is reversible following the repletion of iron stores".

The studies on which this conclusion is based are summarized in Table 2. The one study that provides a quantitative estimate of the size of this effect suggests a reversible IQ deficit in anemic 5–6-year-old Indian boys of 8 points or half a standard deviation (Seshadri and Golpadas, 1989). This deficit is similar in size to the difference in IQ between anemic and non-anemic children in observational studies.

Evidence for economic impact of cognitive deficits

There are a few studies of adults relating cognitive scores to wages in developing countries. For Colombia, a one-standard deviation improvement in cognitive scores was associated with a 7–9% increase in hourly earnings (Psacharopoulos and Velez, 1992). For employees in Nairobi, Kenya, a one-standard deviation improvement in cognitive score is associated with a 17% increase in hourly earnings for primary school leavers and a 23% increase for secondary school leavers. The corresponding figures for employees in Dar es Salaam, Tanzania, are 8% and 13% respectively

[2] In Costa Rica, Lozoff et al. (1991) retested, at age five, children who were the subjects of therapeutic trials as infants. Children who were anemic as infants scored significantly lower on intelligence tests than did those who were not iron deficient, even though the associated anemia had been entirely corrected and even though the investigators controlled for a variety of potential confounding factors. This seems to contradict the conclusion that deficits can be corrected. However, not all the predisposing factors originally contributing to the anemia could have been entirely controlled for. These are almost certain to include factors (such as poverty, poor caring practices or poor health) that might be expected independently to lead to lower performance on intelligence tests later in childhood.

Table 2
Effects of iron therapy on cognitive and behavioral development in older children

Authors (date)	Location	age group (years)	Design	Treatment and dose	Period (days)	N	Definition of IDA	Test	Effect of treatment on IDA children	Effect of treatment on IDNA children
Seshadri and Golpadas (1989)	India	5–6	randomized, placebo-controlled, double blind	40 mg Fe/day, + deworming and folate, placebo: deworming only	60 d	14 matched pairs	Hb < 105g/L	WISC	verbal: 5 points∗ Performance: 11 points∗ Total: 8 points∗	Na
Soewondo et al. (1989)	Indonesia	pre-school, mean: 4.5	randomized, placebo-controlled, double blind	50 mg Fe/day	8 weeks	49 IDA, 57 IDNA, 70 IS	Hb < 110g/L, 2 additional abnormal indices	Discrim-ination learning, oddity learning,	improvements in discrimination and oddity learning	not reported
Pollitt et al. (1989)	Thailand	9–11	randomized, placebo-controlled, double blind	2 mg Fe/kg/d for 2 weeks followed by 4 mg Fe/kg/d for 14 weeks + deworming, placebo: deworming only	16weeks	101 IDA, 47 IDNA, 1210 IS	Hb < 120g/L, 2 additional abnormal indices	RCPM; educational achievement test	none	none

∗, adjusted for response in controls receiving placebo; IDA, iron deficient anemic; IDNA, iron deficient non-anemic; IS, iron sufficient; WISC, Wechsler Intelligence Scale for Children; RCPM, Raven Colored Progressive Matrices; na, not applicable; ns, not (statistically) significant; Hb, hemoglobin concentration; TS, transferrin saturation.

(Boissiere et al., 1985). These studies control for schooling, and hence do not incorporate the indirect contribution of higher cognitive scores via increased schooling.

Two other studies in developing countries use more sophisticated econometric techniques to allow for issues of selectivity (the fact that wage workers are not a random sample of all workers) and simultaneity (whereby schooling, cognitive skills and work experience are determined jointly). For rural Pakistan, Alderman et al. (1996) found that a one-standard deviation improvement in cognitive scores (measured by specifically designed tests of literacy and numeracy) was associated with an increase in wages ranging from 10% (using ordinary least squares regression) to about 12% (allowing for selectivity and simultaneity). Finally, in Ghana reading and math scores had strong effects on wages (a one-standard deviation improvement in math scores was associated with a 22% increase in wages in the public sector, and a similar improvement in reading scores with a 33% in the private sector: Glewwe, 1996).

These studies confirm similar findings for industrial countries that higher cognitive scores are significantly associated with earnings and income (Hause, 1972; Hauser and Sewell, 1986; Wise, 1975). Although these observational studies do not allow us to attribute higher earnings to better cognitive ability with absolute certainty, the consistency of this evidence across many studies and the obvious plausibility of the cause-and-effect argument convince us that this relationship is causal.

Productivity implications of iron deficiency in childhood

Based on the studies discussed in Section 2.4, a reasonable estimate is that one-half of a standard deviation decrease in scores on various tests of cognitive achievement is associated with a 4% decrease in hourly earnings. This may be conservative, since it is likely that cognitive achievement has additional indirect effects through greater schooling, and the studies cited control for schooling. In turn, half of a standard deviation decline in IQ/cognitive test performance is a reasonable estimate of the effect of iron deficiency anemia in childhood, as discussed in Section 2.3.

We do not have data as to how much of the difference observed for anemic children persists until adulthood (although ongoing longitudinal studies may be able to provide evidence: Lozoff, pers. comm.) One of the few longitudinal studies available (where children received supplements containing energy, protein and a range of micronutrients) suggests that improved childhood nutrition is associated with modest but significant improvements on a wide range of cognitive measures, which persisted into adolescence (Pollitt et al., 1995). The intercorrelation between IQ scores at age 6 to 8 with those at age 17 is between 0.62–0.65 (Jensen, 1980).[3] We do not have data as to how all the measures of ability in the studies discussed in Section 2.4 are correlated with childhood IQ, and the productivity studies did not typically use IQ as

[3] The predicted IQ on retest at an older age, Pred(IQt) = r12 (IQ0–IQm) + IQm, where r12 is the intercorrelation coefficient, IQ0 is the individual's earlier score, and IQm is the population mean at both times (Jensen, 1980).

the cognitive measure. We make the strong assumption that the measures of literacy, numeracy, and cognitive ability used in these studies are perfectly correlated with IQ. Thus we assume that childhood anemia is associated with a drop in wages in adulthood of 2.5% (4%×0.62).

We assume that this 2.5% loss of earnings is also applicable to self-employment earnings, where ability is likely to have, if anything, a stronger effect on earnings than for wage-earning employees because the full cost of any productivity decrease is borne by the worker. We conservatively assume that the effect on earnings represents decreased labour productivity, with no effect on the productivity of other factors. Hence the annual loss of per capita productivity for a child currently aged *j*, assuming he/she survives to age *k* in the future, due to childhood IDA, is: Cog loss(k) = 2.5% × WS × GDP/cap(k) × Pr(child), where: Cog loss is the annual productivity losses per child due to lower cognitive scores related to childhood IDA; Pr(child) is the prevalence of anemia in children (We use the prevalence of anemia rather than IDA because the 0.5 standard deviation improvement in cognitive test scores reported for Indonesia by Seshadri and Gopaldas, 1989, was the average observed among treated anemic children, not just among those with IDA.); WS is the share of wages (labor) in GDP measured at factor cost; GDP/cap(k) is the per capita GDP in year k

We make the simplifying assumption that there is no growth in per capita GDP (for sub-Saharan Africa and many Latin American countries this is consistent with experience between 1970 and 2000, and is a little conservative for the South Asian countries). We therefore use 1994 per capita GDP throughout, and GDP/cap(k) becomes GDP/cap, and Cog loss(k) becomes Cog loss.

Note that we use WS∗GDP/cap instead of average wages (which are not readily available for all countries), assuming implicitly that those who work in the labour market earn WS∗GDP/cap∗LFPR, where LFPR is the labour force participation rate expressed as a proportion of the entire population of all ages.

We next find the present value of the future productivity stream associated with improved iron status. Future productivity is less valuable, first because it has to be discounted, and second because not all children survive to age 65. The present value for the entire loss of future productivity associated with anemia for a child currently age j, PV loss(j) is: Cog loss × $_{k = 15,65}$ 3 p(survive k|j)]/$(1 + r)^{k - j}$, where p(survive k|j) denotes the probability that a child currently age *j* years will survive to age *k*, and r represents the social discount rate. Let $_{k = 15,65}$ 3 p(survive k|j)/$(1 + r)^{k - j}$ = LDF(j), where LDF(j) equals the 'lifetime discounting factor' for future earnings, for a child currently aged *j*, where the discounting also takes account of survival probability.

We make one more simplifying assumption, namely that the improvement in cognition associated with iron status requires maintenance of iron status throughout the first 15 years of life. More specifically, each year in which the child is not anemic 'locks in' one-fifteenth of the value of Cog Loss. It is quite possible that anemia is more critical at certain ages than others. However the assumption is not particularly restrictive, except in so far as it has a small effect on the discount factor, since we are evaluating a population-wide iron fortification program. If anemia at preschool

ages is the most critical, this would imply we should discount future labour productivity by slightly more than is done here, for example. We do not have good enough data to improve this assumption: we would need longitudinal (panel) data on children throughout childhood, associated either with cognitive score data at age 15, or adult productivity data.

Hence the discount factor to apply to future earnings for all current children is taken to be: LDF(1 - 15) = $1/15\ _{m=1,15}\ 3$ LDF(m). Hence the present value of lifetime earnings loss associated with one additional year of the current level of iron deficiency, per child, is Cog loss∗LDF(1 - 15) and the corresponding value per capita is: Cog loss∗LDF(1 - 15)∗1/p(child) where p(child) is the proportion of the population in the under-15 age group.

Example

In Bangladesh, anemia prevalence in children (Pr(child)) is 73%, per capita GDP is $220 US, and wage share in GDP is assumed to be 40%. Hence annual loss per child (Cog loss) is: Cog loss = $0.025 \times 0.40 \times 220 \times 0.73$ or $1.61 per capita

Given Bangladesh's infant mortality rate (79 per 1000), under-5 mortality rate (106 per 1000) and life expectancy at birth (58 years), combined with a social discount rate of 3% (the rate recommended by the World Bank for social investments), gives LDF(1-15) for Bangladesh is 17.307. Thus for Bangladesh the present value of the loss of lifetime earnings per child associated with a 73% rate of childhood anemia maintained over 1 year, is: Cog loss × LDF(1 - 15) = $1.61 × 17.307 = $27.80 per child. Since the proportion of under-16s in the population is 46.7%, then the corresponding present value of the per capita loss is $12.98. In Section 4, we will compare this with the cost of a program which can reduce anemia by a specified amount.

Lower current productivity of adults

Evidence of effects of iron deficiency/anemia

It has long been observed that the symptoms of iron deficiency anemia include tiredness, lethargy and fatigue. The biological basis for these effects almost certainly includes the role of hemoglobin as an iron-containing transport protein needed to move oxygen from the lungs to the muscles, brain and other tissues of the body. Anemic individuals are therefore unable to transport enough oxygen to support strenuous activity of long duration. It is likely that iron deficiency affects several other metabolic systems such as neurotransmission; myoglobin, needed for oxygen transport and storage within muscles; and a number of cytochromes essential for the electron transport system in energy metabolism. Evidence for a direct role of these systems in the reduction of physical capacity in iron deficiency is not as clear as that involving anemia directly. However, there is evidence from some physical capacity and productivity studies that functional improvements following therapy are seen prior to or in the absence of improvements in hemoglobin (Ohira et al., 1979)

and that even non-strenuous physical activities are affected (Li et al., 1994). These findings suggest that anemia is not the sole mechanism for the effect of iron deficiency on productivity and that subclinical deficiencies also matter.

Laboratory studies have found that anemia is associated with a more rapid heart rate during exercise (Davies et al., 1973; Nelson et al., 1994). A more informative approach is to examine changes in physical capacity and work productivity in response to iron therapy. Table 3 summarizes the results of a number of such studies published to date.

Laboratory studies find that iron interventions are associated with decreased heart rates during exercise. There are also at least three randomised, placebo-controlled field trials involving iron supplementation. Only a modest increase in productivity was found to be associated with a daily iron supplement for female plantation workers in Sri Lanka (1.2%: Edgerton et al., 1979). However, the lack of an economic incentive to pick more tea was likely a factor. Work productivity of supplemented anemic rubber tappers in Indonesia increased 17% more than in a control group of anemic workers receiving a placebo (a difference similar to the baseline difference observed between anemic and non-anemic workers: Basta et al., 1979). A productivity increase of 5% for supplemented female cotton mill workers in China was observed, a surprisingly large effect given that the relatively light nature of work (Li et al, 1994, in a randomized, placebo-controlled trial). In these circumstances, the positive effect of the iron is likely not operating through maximal work capacity, but rather through endurance and similar mechanisms. A similar magnitude of effect was observed in a cross-sectional study of female loom operators and female cigarette-rollers in Indonesia (Scholz et al., 1997; Untoro et al., 1998)

Productivity implications of iron deficiency in adults

To be conservative, we assume that iron therapy in anemic adults is associated with a 5% increase in labor productivity in all blue-collar work except heavy manual labor, where we assume that the increase in productivity is 17%, using the results summarized in Table 3. We estimate the output loss associated with lower productivity in heavy manual labor, assuming that manual labor accounts for one half of the output of agriculture and construction, but none of the output of other industries (manufacturing, utilities, services, commerce, etc.). We further assume that output in construction is 15% of output in agriculture, since disaggregated data on output are not readily available. Note that the productivity loss we use is more conservative than Levin et al, (1994), who assume a 20% productivity impairment for all adult wage employees, almost certainly an overestimate of the physical losses.

Hence the annual per capita loss associated with adult anemia (via lower physical productivity of adults) is estimated as: $(5\% \times \text{WS} \times \text{BC Share} \times \text{GDP/cap} \times \text{Pr(adult)}) + (12\% \times \text{WS} \times \text{HML} \times \text{GDP/cap} \times \text{Pr(adult)})$ where: WS is the wage share in GDP (measured at factor cost); HML is the heavy manual labor share in GDP (measured as 50% of the value of output in agriculture and construction); BC Share is the share of blue-collar employment in total employment (share of output attributable to blue-collar workers in GDP would be preferable, but not available); Pr(adult) is the preva-

Table 3
Studies of the effects of iron therapy on physical capacity and work productivity

Authors (date)	Location	Subjects	age group (years)	Design	Treatment and dose	Period (days)	N	Definition of IDA	Outcome	Effect of treatment on iron status	Effect of treatment on productivity
Gardner et al. (1975)	Venezuela Lab	rural residents	17–46	placebo-controlled	Intra-muscular iron dextran, vermifuge	84	29 anemic, 10 control	<13.9 g/100ml women, <14.3 men	Hb, heart rate	Hb increased from 7.7 to 12.4 women, 7.1 to 14.0 men	Peak heart rate fell 21–27%, blood lacate sign if higher in placebo.
Ohira et al. (1979)	Sri Lanka Lab	hospital patients	21–72	placebo-controlled	Single IV infusion of 30-50 ml iron dextran	3, 4, 8, 12 and 16 d	20	'hemato-logical test'	Hb, max workload, heart rate response to exercise	increase in Hb from 66 to 84 g/L (27%) in 16 d;	increase in max work load by about 70%; reduction in heart rate for a given work load by about 25%.*

(*continued on next page*)

Table 3 (*continued*)

Authors (date)	Location	Subjects	age group (years)	Design	Treatment and dose	Period (days)	N	Definition of IDA	Outcome	Effect of treatment on iron status	Effect of treatment on productivity
Ohira et al. (1981)	Sri Lanka Lab	hospital patients	group means: 40–55	pre-post comparison with non-anemic controls	Single IV infusion of 30–50 ml iron dextran	7–8	11 anemic, 12 marginal, 22 normal	<130 g/L (marginal); <100 g/L (low), also SI <44 µg/dL	Hb, max exercise time, heart rate response to exercise	slight increase in Hb in anemic groups, ns	Increase in max exercise time by 46-59% in anemic groups, reduction in heart rate in heavy work by ca 20% in anemic and and low serum iron groups
Zhu and Haas (1998)	USA Lab	active healthy females	19–36	placebo-controlled, double-blind	45 mg Fe/day	56	43	Hb>120g/L and SF <16µg/L	level of exertion for a fixed work load	significant increase in serum ferritin concentration relative to baseline and placebo group ($p<0.005$) and decrease in serum tranferin receptor relative to placebo ($p<0.05$)	5.1% lower exertion (as % of maximum oxygen consumption) after controlling for baseline levels ($p=0.016$)

Table 3 (*continued*)

Authors (date)	Location	Subjects	age group (years)	Design	Treatment and dose	Period (days)	N	Definition of IDA	Outcome	Effect of treatment on iron status	Effect of treatment on productivity
Basta et al. (1979)	Indonesia Field	male rubber plantation workers	16–40	placebo-controlled, double-blind	100 mg ferrous sulphate /day	60	152 anemic, 150 non-anemic	Hematocrit <38%	Harvard step test (HST), labor productivity	Significant improvement in Hb (and 4 other indices) over intial values and placebo control	No effect on HST, 17% increase in weight of latex collected, no effect on weeding productivity
Li et al. (1994)	China Field	female textile factory workers	19–44	placebo-controlled, double-blind	60 or 120 mg Fe/day	84	80	Hb<120g/L and *either* SF<12μg/L *or* FEP>0.62 μmol/L	heart rate, productivity, production efficiency (pay/energy expenditure)	Significant improvement in Hb from 114 to 127 g/L ($p<0.001$), serum ferritin, and FEP	5% decrease in HR at work, 5% increase in productivity, 17% increase in production efficiency

IDA, iron deficient anemic; IDNA, iron deficient non-anemic; IS, iron sufficient; WISC, Weschler Intelligence Scale for Children; na, not applicable; ns, not (statistically) significant; Hb, hemoglobin concentration; SF, serum ferritin; SI, serum iron; FEP, free erythrocyte protoporphyrin.

lence of anemia in adults (weighted average of male and female rates, using relative shares in labour force as weights). (We use the prevalence of anemia rather than IDA because the estimates of the consequences of IDA in the studies in Table 3 are the average response to therapy among anemic workers rather than only those with confirmed IDA.)

Example

For Bangladesh, the share of blue-collar work in GDP is taken as 70%, the prevalence of anemia in the labor force as 65.9% (based on a prevalence of 74% for women and 60% for men, and a female share of the labour force of 42%). Per capita GDP is $220 as before, and the wage share is 40% as before. Thus the loss of productivity in blue-collar work (BC loss) is: $0.05 \times WS \times BC\ Share \times GDP/cap \times Pr(adult) = \times 0.05 \times 0.4 \times 0.7 \times \$220 \times 0.659$, or $2.03 per capita, which amounts to 0.9% of GDP.

A further loss is expected in heavy manual labour, which is a subset of blue-collar work. The share of heavy manual labour in GDP is estimated as 57.5% of the share of agriculture in GDP (assuming that half of labour in agriculture and construction is heavy labour, and that construction is 15% of the size of the agriculture sector). In Bangladesh, the share of agriculture in GDP is 30%. Thus the additional loss in heavy manual labour (HML loss) is: $0.12 \times WS \times HML \times GDP/cap \times Pr(adult)$, i.e. $0.12 \times 0.4 \times 0.575 \times 0.3 \times \$220 \times 0.659$,or $1.20 per capita, which amounts to 0.5% of GDP.

Total loss due to lower physical productivity is therefore the sum of BC loss, plus HML loss, or $3.23 per capita in Bangladesh, which amounts to 1.47% of per capita GDP.

Country examples

Table 4 contains some results of calculations of the labor productivity effects (using the methodology described in Sections 2 and 3) for ten selected countries.[4] Some of the underlying data are given in Table A.1. These results suggest that in dollar terms, productivity losses are larger in richer countries, since we have assumed a constant percentage loss of productivity. This is only partially offset by the fact that IDA is lower in richer countries, and that blue-collar work and heavy manual labor are less important. The dominant effect is the loss associated with cognitive effects on children. Although the losses in heavy manual labor may be overestimates in labor surplus countries, this is less likely to be the case for the losses associated with cognitive skills.

The results suggest that the losses are very large. The physical productivity losses

[4] Note that for most countries in Table 4, we do not have data on the prevalence of anemia among adult males. For these countries we assume that the prevalence of anemia among men is 85% of female prevalence (the average for countries for which we have data).

Table 4
Calculations of the economic consequences of iron deficiency anemia for selected countries

Country	Pr(child)%	Pr(male)%*	Pr(fem)%	GDP/cap$	Physical loss $/cap	PV of Cog loss$/capita	PV Total loss $/capita	PV Total loss % of GDP	Simulation I $/capita	Simulation II $/capita
Bangladesh	73	60	74	220	3.23	12.98	16.21	7.9	0.44	2.04
India[a]	66	(50)	59	320	3.78	15.50	19.28	6.0	0.54	2.65
Pakistan[a]	47	(31)	37	430	2.97	19.44	22.41	5.2	0.81	4.53
Mali	28	33	27	250	1.92	6.98	8.90	4.2	0.58	2.82
Tanzania	25	15	15	140	0.62	3.17	3.79	2.7	0.37	1.51
Egypt[a]	25.2	(14)	17	720	1.92	15.46	17.38	2.4	1.14	6.70
Oman	60	14	32	5140	9.09	359.41	368.50	7.2	5.01	58.92
Bolivia[a]	35	(14)	16	770	2.08	28.14	30.22	3.9	1.29	8.53
Honduras[a]	17.5	(12)	14.3	600	1.49	10.92	12.41	2.0	1.05	6.67
Nicaragua[a]	28	(31)	36	340	2.56	10.33	12.89	3.8	0.71	4.03

Pr(child), prevalence of anemia in children; source: MI web page (http://www.micronutrient.org); Pr(male), prevalence of anemia in adult males; source: MI web page; Pr(fem), prevalence of anemia in adult females (non-pregnant, non-lactating); source: MI web page; GDP/cap, Per capita GDP; source: World Bank World Development Report, Washington DC, 1996. PVCog loss, Present value of productivity loss due to cognitive losses associated with current anemia levels in childhood persisting for one year, calculated in Section 2.5 of the text. Physical loss, productivity loss associated with lower physical productivity of anemic adults in blue-collar occupations and heavy manual occupations, calculated in Section 3 of the text. PVTotal loss, present value of total loss: PVCog loss+Physical loss, expressed both as 1994 US $ per capita and as % of per capita GDP.Simulation I estimates the effect on the economy of a 9 percentage point decrease in the level of anemia for all age and sex groups, including only the physical productivity benefits.Simulation II estimates the effect on the economy of a 9 percentage point decrease in the level of anemia for all age and sex groups for a period of 1 year, including both physical productivity and present value of cognitive benefits.

[a] For some countries in Table 4, we do not have data on the prevalence of anemia among adult males. For these countries we conservatively assume that the prevalence of anemia among men 85% of that in women, the median value for those countries where data are available both for men and women.

range from $0.62 per capita (in Tanzania, where anemia rates are in the medium range and wages are low) to $9.09 per capita in Oman where anemia rates are similar but wages are relatively high. When results are expressed as a percentage of GDP, the physical productivity losses are highest in the poorest countries, where anemia rates and heavy manual labour are highest: these losses are 1.47% of GDP in Bangladesh and 1.18% in India. In absolute dollar terms, the losses in South Asia are staggering: close to $4.2 bn annually in Bangladesh, India and Pakistan.

The present value of cognitive losses associated with current levels of anemia in children are calculated. These losses are a factor of 5–6 higher than the physical productivity losses in the poorest countries, and higher still in the richer countries. The present value of total losses is $3.79 in Tanzania (the lowest value), with a median value of $16.78 per capita.

We can also compare these losses with the costs of one intervention. We use an example of a national fortification program, for which program data on hemoglobin levels are available before and after the program intervention (albeit with no control group). We use this rather than supplementation programs. Previous studies have estimated the cost-benefit of iron supplementation based on field trials (e.g. Basta et al., 1979). However, we are not aware of any studies of the cost–benefit of supplementation programs, perhaps because large-scale supplementation programs typically do not lead to significant reductions in the prevalence of anemia, even in targeted subgroups (Gillespie, 1998).

National fortification of maize and wheat flour began in Venezuela in 1993, following a severe economic downturn which adversely affected nutrition. Flour was fortified with iron and vitamin A (maize flour only), and enriched with B vitamins. A survey of children aged 7, 11 and 15 in Caracas found that the prevalence of iron deficiency (as measured by serum ferritin concentration) was reduced from 37% in 1992 to 15% in 1994, and the prevalence of anemia from 19% to 10% (Layrisse et al., 1996). The cost per person was $0.12 annually (Mannar, 2000).[5] There was no control group.

A recent well-controlled field trial for Morocco suggests that it may be possible to obtain similar results to those in Venezuela in other settings (Zimmermann et al., in press). In Morocco, double-fortified salt (iron and iodine) was used, with a higher concentration of the iron fortificant than in Venezuela. The cost was approximately $0.22 per capita, and iron-deficiency anemia fell in children 6–14 by 22 percentage points more in the intervention than the control group.

We cannot be sure that similar fortification programs in other countries would be equally effective. Effectiveness varies according to patterns of consumption of the fortification vehicle, consumption of inhibitory as well as complementary factors in the diet, and the distribution of anemia in the population (both mean level of hemog-

[5] The cost per case of anemia averted would therefore be $0.12/0.09 or $1.33, and the cost per case of iron deficiency averted would be $0.12/0.22 or $0.55).

lobin as well as variance). There are also no data on the effect of fortification on anemia levels in adults in Venezuela.

Likewise, fortification costs are likely to vary between countries, depending on factors such as the food vehicle chosen for fortification, the degree of dispersion of processing facilities, country size (scale economies), etc.

However, if anemia can be reduced in children by 9 percentage points after 1 year of intervention, in a country with lower anemia rates than all except one of the countries in Table 4, it seems reasonable to undertake a simulation using a 9 percentage point reduction. The simulated effects on present value of productivity improvements are also given in Table 4, with the first column for physical productivity effects alone, and the second for the present value of total productivity effects associated with 1 year of fortification. (What is modelled is a 1-year improvement in adult productivity in physical labor, and the present value of a future stream of benefits due to cognitive improvements in children).

Assuming that annual fortification costs are the same as in Venezuela ($0.12 per capita), the benefit–cost ratio for physical productivity has a median value of 6.3:1. Benefits exceed costs in all 10 countries. When discounted cognitive benefits are also added, the benefit cost ratio rises to 35.7:1. These data provide strong support for public investments in fortification. Once the public sector has undertaken the initial investments and the co-ordination required, it is likely that consumers can pay the recurrent costs, and the state's role can become a monitoring and quality assurance one.

Conclusions

We have tried to calculate and substantiate some of the economic losses due to iron deficiency. These include the cognitive losses due to childhood iron deficiency (Section 2), and the loss due to lower productivity in manual occupations for adults (Section 3). The cognitive losses are large and increase faster with development, although these losses have been less widely recognized in previous literature. We do not attempt to estimate the economic costs associated with the social cost of the estimated 20% of maternal deaths in Africa and 23% in Asia, attributable to maternal iron-deficiency anemia, nor the cost of prematurity and other health impacts to the health system.

Our country examples (Section 4) suggest that the median value of per capita physical productivity losses is around $2.32, and the median physical productivity loss is 0.57% of GDP. The absolute dollar value of losses is particularly large in South Asia, where losses are close to $4.2 billion annually, for physical productivity losses alone. The cognitive losses require more assumptions but raise the estimated losses markedly. Including cognitive losses, the present value of the median loss increases to $16.78 per capita, or 4.05% of present GDP.

These figures on losses are sensitive to the many assumptions made. In particular, the productivity effects rely on the few well-controlled studies. If productivity effects were for example only half as large, then the benefits would be correspondingly lower. If the cognitive effects were half as large, this would reduce the benefits in all countries, but relatively more in the middle income countries (the values in columns 6 and 7 of Table 4 would change, which would then change the values in columns 8 through 11 correspondingly).

We conduct some simulations. In one, we compare the current costs of a national fortification program (based on one example from Venezuela), with the projected benefits, if the reduction in anemia were of the same magnitude as observed in Venezuela. I.e. we compare the benefits implied if anemia rates declined throughout the population by 9 percentage points, with the annual costs of $0.12 per capita. The benefits in terms of physical productivity are 6.3 times as large as the costs (median value for the 10 countries), and if cognitive benefits are included, total benefits are 35.7 times costs (again, median value).

These results have to be treated very cautiously. The simulations give estimates of the relative orders of magnitude potentially involved, but are not definitive. Further work is needed to strengthen and refine the estimates. Effectiveness studies of interventions such as national fortification are needed (the results for Venezuela rely only on effects on children, and only in one city where distribution of fortified flour is likely to be good). Not all populations can be reached by iron fortification, and iron supplementation is more costly.

Additional studies substantiating the predicted productivity benefits of improved cognition would be useful, especially those shedding light on the age-specificity and reversibility of these effects. We also need to understand the more subtle and widespread effects of ID without anemia, especially on the less strenuous tasks, since these make up the greater, and increasing, share of output. Finally, we need to develop some consensus on how to translate physical capacity measures or cognitive scores into economic productivity and other consequences with direct public policy significance.

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Appendix

Table A.1
Underlying data for Table 4

Country	F labforce%	Ag share%	BC share%	<16 share %	LDF
Bangladesh	42	30	70	46.7	17.31
India	32	30	70	39.8	18.44
Pakistan	28	25	70	50.9	18.93
Mali	51	42	70	56.8	17.57
Tanzania	49	57	70	57.2	15.83
Egypt	30	20	60	43.8	19.45
Oman	13	3	50	56.3	20.70
Bolivia	37	24	60	45.9	22.75
Honduras	28	20	70	50.9	20.43
Nicaragua	36	33	70	55.3	19.63

F labforce, % of labour force which is female in 1994 (% of labour force is used rather than % of marketed output which is produced by women, since the latter is not available); source: World Bank (1996). Ag share, % share of agriculture in GDP in 1994; Source: World Bank (1996). BC share, % share of blue-collar work in total employment (it would be preferable to use % of output which is attributable to blue collar workers, but this is not available); source: interpolated using International Labour Organization (1994); figures used were 70% for low-income countries, 60% for lower-middle-income countries including Egypt, and 50% for upper-middle-income countries. HML share, % share of heavy manual work in total employment, taken as 50% of employment in agriculture and construction combined, which is turn taken as 57.5% of work in agriculture (construction is assumed to be 15% of employment in agriculture): data from World Bank (1996). <16 share, % share of under 16's in the total population: data from UNICEF, 1993. LDF, Lifetime discount factor, averaged over 1 through 15 year olds (LDF(1-15)), discussed in section 2.5. Represents lifetime earnings as a multiple of annual earnings, discounted at 3% and reduced by the relevant survival probability.

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