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Effect of a Community Health Worker–Delivered Parental Education and Counseling Intervention on Anemia Cure Rates in Rural Indian Children

A Pragmatic Cluster Randomized Clinical Trial

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Additional Information: Supply of iron and folic acid: iron and folic acid tablets containing 20 mg of elemental iron and 1 mg of folic acid were provided to the community health worker through the state government apparatus as usual.

Data Sharing Statement: See Supplement 3.

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Key Points

Question

Is community health worker–delivered parental education/counseling combined with ferrous sulfate treatment more effective at curing childhood anemia than ferrous sulfate alone?

Findings

In this pragmatic cluster randomized effectiveness trial, children with anemia exposed to parental education/counseling had a 37% relative risk difference of being cured of anemia compared with those exposed to usual treatment. Children in the intervention group consumed more ferrous sulfate tablets than in the usual treatment group.

Meaning

Parental education/counseling by a community health worker improves anemia cure rates in preschool-aged children, probably through improved adherence to treatment.

Abstract

Importance

Iron deficiency anemia, the largest cause of anemia worldwide, adversely affects cognitive development in children. Moreover, the imperceptible childhood anemia prevalence reduction in response to anemia control measures is associated with tremendous social and economic cost.

Objective

To evaluate the effects of community-based parental education/counseling when combined with usual treatment on children's anemia cure rate.

Design, Setting, and Participants

A pragmatic cluster randomized clinical trial in children aged 12 to 59 months from 55 villages from the rural Chamrajnagar district in southern India was conducted between November 2014 and July 2015; 6-month follow-up ended in January 2016. Villages were randomly assigned to either usual treatment (n = 27) or to the intervention (n = 28). Among 1144 participating children, 534 were diagnosed as having anemia (hemoglobin levels <11 g/dL and >7.9 g/dL; to convert to grams per liter, multiply by 10) and constituted the study sample in this analysis. Data were analyzed between July 2016 and September 2017.

Interventions

Iron and folic acid (IFA), 20 mg/d, 5 times daily per week, for 5 months (usual treatment) or health worker–delivered education/counseling combined with usual treatment (intervention).

Main Outcomes and Measures

The primary outcome was anemia cure rate defined as hemoglobin level at or greater than 11 g/dL during follow-up.

Results

Of the children included in the study, the mean age was 30 months, with a slightly higher ratio of boys to girls. Of 534 children with anemia (intervention n = 303; usual treatment n = 231), 517 were reassessed after 6 months (intervention n = 298; usual treatment n = 219) while 17 were lost to follow-up (intervention n = 5 and usual treatment n = 12). Anemia cure rate was higher in children in the intervention group compared with children receiving usual treatment (55.7% [n = 166 of 298] vs 41.4% [n = 90 of 219]). The risk ratio derived through multilevel logistic regression was 1.37 (95% CI, 1.04-1.70); the model-estimated risk difference was 15.1% (95% CI, 3.9-26.3). Intervention-group children demonstrated larger mean hemoglobin increments (difference, intervention vs control: 0.25 g/dL; 95% CI, 0.07-0.44 g/dL) and improved IFA adherence (61.7%; 95% CI, 56.2-67.3 vs 48.4%; 95% CI, 41.7-55.1 consumed >75% of tablets provided). Adverse events were mild (intervention: 26.8%; 95% CI, 21.8-31.9 vs usual treatment: 21%; 95% CI, 15.6-26.4). To cure 1 child with anemia, 7 mothers needed to be counseled (number needed to treat: 7; 95% CI, 4-26).

Conclusions and Relevance

Parental education and counseling by a community health worker achieved perceivable gains in curing childhood anemia. Policy makers should consider this approach to enhance population level anemia control.

Trial Registration

ISRCTN identifier: ISRCTN68413407

This randomized clinical trial evaluates the effects of community-based parental education/counseling when combined with usual treatment on children's anemia cure rate in rural southern India.

Introduction

Nutritional iron deficiency leading to iron deficiency anemia (IDA) is the largest cause of anemia worldwide.[1,2] Iron deficiency anemia has morbidity and mortality consequences[3,4,5,6] predominantly affecting young children and premenopausal women living in sub-Saharan Africa and South Asia.[2,7,8,9] The decline of childhood anemia prevalence worldwide is imperceptible (<0.2% per year) and is accompanied by profound socioeconomic consequences that unfavorably affect low-income to middle-income countries.[3,8]

Iron is critical for the developing brain, and IDA in preschool-aged children leads to cognitive and psychomotor delays that are only partly reversible by treatment with iron, emphasizing the urgency for early detection and rapid treatment.[3,10,11,12,13] Insufficient maternal iron stores and low dietary iron intake are important contributors to the development of childhood IDA.[14,15] Additionally, socioeconomic status, genetic factors, infectious diseases, intestinal parasites, lack of education, and environmental factors (hygiene and sanitation) influence childhood anemia prevalence.[1,16,17,18]

Iron deficiency anemia is highly prevalent in India,[19,20,21] and iron deficiency prevention is among the most cost-effective of public health interventions, yet anemia control efforts have yielded a lower-than-expected rate of anemia decline.[22,23,24,25] Control measures for anemia in India have been suboptimal largely owing to implementation challenges (stocking/procurement of iron and insufficient funding),[23,25,26] limited maternal awareness of anemia,[27,28] and poor adherence to iron supplementation.[29,30,31] Moreover, whereas community-based education interventions targeting anemia are effective, their effects have not been rigorously evaluated in children from this setting.[32,33,34] To address this gap, we developed a health worker–led intervention targeted to families of children with anemia that consisted of 5 monthly education sessions covering (1) maternal anemia awareness, (2) adherence to medicinal iron, (3) dietary modification and diversification to include iron rich foods, and (4) hygiene and sanitation.[35] We tested the hypothesis that among children with anemia, anemia cure rate would be higher in those receiving the intervention in addition to iron treatment compared with those receiving iron treatment alone. Owing to the pragmatic nature of the intervention, we used a cluster randomized design to evaluate its effectiveness in improving anemia cure rates in children aged 12 to 59 months.

Methods

Study Design

The study was a pragmatic cluster randomized controlled effectiveness trial,[36,37] a complete protocol of which has been published.[35] A cluster (randomization unit) was defined as a village from the Chamarajnagar subdistrict together with its Anganwadi Daycare Centre (ADC) and the corresponding lay health worker (LHW) in charge of the ADC. Ethical clearance was obtained from the institutional ethics committee of St Johns Medical College and Hospital, and parents/caregivers of all participants in both the intervention and usual treatment groups provided written informed consent. The formal trial protocols can be found in Supplement 1.

Study Area and Participants

The study was conducted in Chamarajnagar district, Karnataka, South India. In this area, children are fed a millet-based or rice-based diet mixed with lentils; breastfeeding is prolonged beyond age 1 year. Childhood malnutrition is widespread but hemoglobinopathy, malaria, and hookworm prevalence is low.[19] All children aged 12 to 59 months residing in the village and registered in the ADC were eligible to participate in the trial. Exclusion criteria were temperature greater than 38.33°C; hemoglobin level 7.9 g/dL or less (to convert to grams per liter, multiply by 10); and blood transfusion within 3 months of enrollment.

Randomization

A random sample of eligible villages (60 of 270) was drawn using a computerized algorithm and subsequently stratified into 2 groups based on the resident number of children younger than 6 years (2 strata: ≤50 and >50 children). Thereafter, villages were randomly allocated to intervention and usual treatment groups using a 1 to 1 ratio within each stratum. The randomization procedure was performed by a researcher with no direct involvement in this trial. Group assignment was disclosed to the LHWs after randomization, and the participants were

not aware of the village treatment group assignment while obtaining consent. The random assignment was done simultaneously for all villages prior to the field activities to recruit the LHW and the population participants.

Procedures

Recruitment of Clusters and Participants

The flow of recruitment of villages and participants is shown in the Figure. After randomization, 2 LHWs from each treatment group refused to participate, resulting in the exclusion of 4 villages. Additionally, mothers/caregivers in 1 village refused to participate en masse, citing lack of prior spousal permission for blood sampling in their children. Thus, 55 of 60 initially randomized villages were retained in the study (intervention n = 28; usual treatment n = 27).

Recruitment began in November 2014, simultaneously to both groups, and was completed in July 2015. Chance inclusion of smaller villages and overestimation of children in the ADC registry yielded a smaller than anticipated number of eligible children (n = 1860 vs n = 2400). Moreover, the combined effects of cluster dropout (4 clusters; n = 155) and nonparticipation owing to the family's physical absence during recruitment (traveling n = 341; migrated/untraced n = 80) further reduced the population screened at baseline (n = 1284) (Figure). Exclusion either for severe anemia (intervention n = 26; usual treatment n = 22) and fever (intervention n = 1; usual treatment n = 1) or inability to participate for other reasons resulted in enrollment of 1144 participants at baseline (intervention n = 608 and usual treatment n = 536) (Figure).

Participants With Anemia for Primary Outcome

The baseline population of 1144 participants encompassed 534 children with anemia (intervention n = 303; usual treatment n = 231; Figure). This resultant sample of children with anemia constituted the population for study of the primary outcome of the intervention. At the end of 6-month follow-up, 517 of these children were reassessed (intervention n = 298 and usual treatment n = 219). Loss to follow-up (n = 17; intervention n = 5 and usual treatment n = 12) included those who had migrated with their family (n = 7), withdrawn parental consent (n = 5), or failed phlebotomy attempts (n = 5), resulting in 3% attrition (Figure).

Data Collection and Samples

Baseline information concerning demographic, socioeconomic (demographic and heath survey wealth index), dietary intake (24-hour diet recall; eMethods in Supplement 2), anthropometric measurements, and venous blood was collected from all participants as previously described.[19,35] Plasma hemoglobin was measured within 6 hours of blood collection by automated hemocytometry (Sysmex XP-100; Sysmex Corporation). Serum samples prepared in the field and stored at −80°C were used to measure ferritin by electro chemiluminescent immunoassay (Access 2; Beckmann Coulter Inc). In pilot studies, we confirmed that preanalytical sample collection and processing variables did not influence hemoglobin and ferritin values. Accuracy of measurements was ensured by routinely calibrating instruments with manufacturer standards.

Intervention and Comparator

All children with anemia received medicinal iron treatment as usual, based on international consensus statements, in a dosing schedule modified to enhance adherence (iron [ferrous sulfate] and folic acid [IFA] tablets, containing 20 mg of elemental iron and 1 mg of folic acid each, 20 tablets/mo for 5 months).[1,25,38,39,40] In the intervention group, in addition to usual iron treatment, a trained LHW provided a total of 5 education/counseling sessions (once a month for 5 months) to the mother/caregivers of children with anemia and monitored the child's monthly IFA treatment adherence. The intervention began in January 2015 and ended in February 2016, after children belonging to the final recruited village completed their 6-month follow-up visit. At the end of 6 months, venous blood, anthropometric measurements, 24-hour dietary recall, and adherence/adverse effects to IFA in the previous 30 days were obtained for all participants. A field research team ensured smooth intervention implementation by providing telephone support to LHWs in both treatment groups.[35]

Outcomes

The primary outcome was anemia cure rate at 6-month follow-up, and the effect measure was the risk ratio (RR), intervention relative to control. Anemia was defined as a plasma hemoglobin value of less than 11 g/dL.[41] Therefore, a cured case of anemia for the primary outcome was a child with baseline anemia whose hemoglobin level at follow-up was at or greater than the threshold of 11 g/dL. Secondary outcomes were (1) net hemoglobin change, measured as the difference in children's mean hemoglobin level between baseline and follow-up, (2) adverse effects to IFA, and (3) adherence to IFA during month 6,[35] the latter measured by returned medication pill counts as:

([Total Prescribed IFA Tablet Number for 30 Days − Total IFA Tablets Number Remaining]/Total Prescribed IFA Tablet Number for 30 Days) × 100

Statistical Methods

On the basis of published studies of clinical anemia treatment, a minimum difference of 12% in anemia cure rate between the 2 experimental groups was judged to be clinically important.[32,42,43] Further, we hypothesized that this difference would occur owing to a cure rate of 30% in the usual treatment group and 42% in the intervention group. The required sample size to detect this difference was 1220 children with anemia ($\alpha = .05$ and power [$1-\beta = 0.80$] design effect of 2.2, with expected loss to follow-up of 10%).[35] Our pretrial anemia prevalence estimates indicated that enrolling 2400 participants would achieve this sample size.[19] Data entry and analyses were blinded. Data were entered manually by 2 coworkers and cross-checked. The primary analysis was done on an intention-to-treat basis based on all available cases, ie, participants lost to follow-up were excluded. The intervention's effect was expressed as RR with the corresponding 95% confidence interval of being nonanemic at follow-up in the intervention group relative to usual treatment. The inference on RR was derived from the outcome predicted probabilities estimated through logistic regression models, with village-level random intercepts. The corresponding 95% CIs were calculated with the Δ method. The intraclass correlation coefficient was used to measure the cluster effect.[44] We used linear regression with village-level random intercepts to study the interventions effect concerning net hemoglobin change as a function of the intervention. The conventional threshold of *P* less than .05 was used for statements about statistical significance, and all *P* values were 2-sided. The num-

ber needed to treat was calculated as 1 divided by absolute risk reduction (model-derived absolute risk reduction). We conducted analyses without adjusting for baseline covariates because differences were very small and likely owing to chance.[45,46] Statistical analyses were performed using Stata, version 15.0 (StataCorp) and SAS, version 9.3 (SAS Institute Inc).

Results

Baseline Characteristics of Children With Anemia

Nonparticipants had similar baseline characteristics to study participants (eTable 1 in Supplement 2). Both usual treatment and intervention groups appeared well balanced, and very minor differences were observed (Table 1). In particular, absolute differences in variables that may represent predictors of outcome were of very small magnitude: mean hemoglobin level (0.13 g/dL); median ferritin level (1 ng/mL; to convert to picomoles per nanograms per milliliter, multiply by 2.247); median iron intake (4%); child's mean weight (0.1 kg); and percentage of mothers with less than seventh-grade education (5.2%). Because differences of this nature are likely to occur by chance in a randomized study, we did not adjust for them. Nutritional status was generally poor, as indicated by the high overall prevalence of malnutrition (Table 1). In both groups, iron intake estimated from the 24-hour dietary recall was less than the recommended daily allowance, and measures of body iron stores obtained from serum ferritin were consistent with IDA (Table 1).[15,19,47]

Anemia Cure Rate

In an intention-to-treat analysis (ie, considering children with anemia as they fully received the assigned intervention) and using all available cases, the anemia cure rate, ie, recovery from anemia at the end of 6-month follow-up, was significantly higher among intervention-group children compared with usual treatment (55.7%; 95% CI, 50.0-61.3 vs 41.1%; 95% CI, 34.5-47.6) (Table 2). The effects of clustering at the village level accounted for 7% of the variability in anemia cure rates (intraclass correlation coefficient, 0.068; 95% CI, 0.02-0.19). After adjusting for the effect of clustering, the RR of anemia cure for intervention vs control was 1.37 (95% CI, 1.04-1.70) (Table 2). Adjustment for differences in hemoglobin and maternal education observed at baseline between the groups attenuated the RR estimate by 11% (1.33; 95% CI, 1.01-1.65; eTable 2 in Supplement 2). The model-estimated risk difference of 15.1% (95% CI, 3.9-26.3) was larger than the minimally important clinical difference of 12%. For a case of childhood anemia to be cured, the number needed to treat or the number of mothers who needed to be educated and counseled was about 7 (number needed to treat, 6.6; 95% CI, 3.8-25.9).

Net Hemoglobin Change

The analysis of hemoglobin change between baseline and follow-up revealed a mean (SD) increase of 1.087 (0.103) g/dL among children in the intervention group and of 0.829 (0.106) g/dL in the usual treatment group, ie, a between-group mean difference of 0.257 g/dL (95% CI, 0.07-0.44). The intraclass correlation coefficient for hemoglobin change was small (0.086), indicating that less than 9% variability in net hemoglobin change was accounted for by clustering. In a linear mixed-effects model adjusted for clustering, the mean hemoglobin difference was 0.244 g/dL (Table 2).

Adherence to IFA and Adverse Events

During study month 6, intervention-group children consumed more IFA tablets than children with anemia in the usual treatment group (the proportions of children with >75% adherence to IFA tablets were 61.7% [n = 184 of 298] vs 48.4% [n = 106 of 219]) (Table 3). Moreover, both the 50th and the 75th quartiles for percentage adherence revealed a higher proportion of children in the intervention group compared with the usual treatment group (Table 3). Adverse events ascribed to IFA assessed during study month 6 in both treatment groups were similar (intervention n = 80 of 298 [26.8%]; usual treatment n = 46 of 219 [21%]) (Table 3) and were relatively minor (eTable 3 in Supplement 2).

Discussion

We found that this intervention seeking to improve maternal awareness about anemia and children's adherence to medicinal iron significantly improved the child's anemia cure rate after 6 months when compared with usual treatment alone. After taking into account the effects of clustering, participants exposed to the intervention had a 37% higher risk difference for anemia cure compared with participants exposed to usual treatment. The results also suggested that 7 mothers of children with anemia need to be exposed to the intervention to revert the hemoglobin in 1 child with anemia to nonanemic levels, a rather modest number considering the global health importance of this problem. The findings also indicated that greater adherence to medicinal iron and possibly heightened maternal awareness of their child's anemia ultimately led to improved anemia cure. This trial demonstrates that maternal/caregiver education and counseling enhances the effectiveness of medicinal iron prescribed for anemia treatment. The pragmatic design ensures that information derived from the trial is directly relevant to support decision-makers in making choices regarding anemia control activities in India. In this context, LHW salaries and IFA are health system costs that are already accounted for, and the only additional intervention-related expenditure incurred was for LHW training, suggesting that the intervention would be cost-effective. The results are generalizable to individuals with anemia living in similar agrarian parts of India and possibly other similar regions of the world.

Community interventions, particularly those involving LHWs, have improved child health outcomes in a variety of geographic settings.[33,43,48,49,50,51,52] Although studies combining iron supplementation with education/counseling have examined hemoglobin outcomes,[34,42,53,54,55,56] to our knowledge, the combined effect of medicinal iron with parental education/counseling on curing childhood anemia has not been previously evaluated. Consequently, to our knowledge, this is the first randomized clinical trial to demonstrate that a simple and scalable LHW-led education intervention improves anemia cure rate in rural anemic preschool-aged children more than the effect of medicinal iron. In a previously published qualitative study,[57] we reported that LHWs found the intervention acceptable and feasible to perform. The finding that this LHW-based intervention increased the effectiveness of medicinal iron for childhood anemia treatment adds to the accumulated evidence of LHW interventions demonstrating improved child health outcomes.[33,34,51,58,59] Childhood anemia prevalence in India is unacceptably high despite global and local recommendations for its control and widespread availability of medicinal iron.[25,38,39] This trial provides relevant contextual evidence for enhanced childhood anemia control.

The superior adherence to iron treatment observed in this study was possibly mediated by a combination of trial participation, improved maternal anemia awareness, and close LHW follow-up. Studies in children with IDA and women with iron deficiency provide scientific evidence that a flexible dosing schedule (daily or every-other-day iron therapy) reduces adverse events and improves adherence.[60,61] Both incomplete adherence to medicinal iron and multifactorial causation of anemia may explain why only 41% to 55% of the anemia cases in both groups were completely cured. Nonetheless, the cure rate for anemia observed in this study was analogous to rates obtained in comparable field trials that used a less rigorous anemia cure definition (ie, hemoglobin level of 10 g/dL).[40,62,63] Adverse events to treatment doses of iron were noticeably mild and occurred with a slightly higher incidence in children exposed to the intervention, in line with the higher adherence.

Strengths and Limitations

The strengths of this trial rest on its randomized design and rigorous methods. Although the obtained sample size was smaller than intended, the sizes of the 2 trial arms were numerically well balanced, while the greater than expected effect size and minimal loss to follow-up compensated for the low initial recruitment.[64,65] Randomization ensured that all baseline factors among the 2 study groups were balanced, and any possible differences were likely owing to chance. Loss to follow-up was small and relatively well balanced, indicating that the estimated proportions using the available cases were not importantly affected by attrition. Owing to the pragmatic design of the trial, collection of venous blood to define plasma hemoglobin instead of capillary blood by finger prick would be a limitation in some settings. Moreover, loss of 4 clusters prior to enrollment owing to LHW nonparticipation implies the possibility of suboptimal intervention delivery by less-motivated LHWs during wider implementation. Additional research is required to address the sustainability of the intervention's effect beyond 6 months, ie, whether continued parental education/counseling by the LHW is required to prevent anemia recurrence.

Conclusions

In conclusion, this pragmatic trial of an innovative LHW intervention for mild to moderate anemia in children demonstrated improvement in anemia cure greater than that expected by standard treatment with medicinal iron alone. Implementation of this public health intervention statewide and perhaps nationally has the potential to reduce the prevalence of IDA in Indian children.

Notes

Supplement 1.

Trial Protocol

Supplement 2.

eMethods. 24 hr Dietary Recall

eTable 1. Characteristics of Nonparticipants Compared With Recruited Baseline Participants Enrolled in the KAP 2 Study, Chamarajnagar District, Karnataka.

eTable 2. Sensitivity Analysis Reporting Estimates of Risk Ratio and Corresponding Confidence Intervals After Adjusting For Selected Predictors of outcome With Minor Imbalance Between the Experimental Groups

eTable 3. Summary of Adverse Drug Reactions Reported by Mothers/Caregivers of Anemic Children Receiving Iron and Folic Acid Treatment in Both Study Groups

eReferences

Supplement 3.

Data Sharing Statement.

References

1. Camaschella C. Iron-deficiency anemia. *N Engl J Med*. 2015;372(19):1832-1843. doi: 10.1056/NEJMra1401038 [PubMed: 25946282] [CrossRef: 10.1056/NEJMra1401038]

2. Kassebaum NJ, Jasrasaria R, Naghavi M, et al.. A systematic analysis of global anemia burden from 1990 to 2010. *Blood*. 2014;123(5):615-624. doi: 10.1182/blood-2013-06-508325 [PMCID: PMC3907750] [PubMed: 24297872] [CrossRef: 10.1182/blood-2013-06-508325]

3. Plessow R, Arora NK, Brunner B, et al.. Social costs of iron deficiency anemia in 6-59-month-old children in India. *PLoS One*. 2015;10(8):e0136581. doi: 10.1371/journal.pone.0136581 [PMCID: PMC4552473] [PubMed: 26313356] [CrossRef: 10.1371/journal.pone.0136581]

4. Bailey RL, West KP Jr, Black RE. The epidemiology of global micronutrient deficiencies. *Ann Nutr Metab*. 2015;66(suppl 2):22-33. doi: 10.1159/000371618 [PubMed: 26045325] [CrossRef: 10.1159/000371618]

5. Murray CJ, Barber RM, Foreman KJ, et al.; GBD 2013 DALYs and HALE Collaborators . Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet*. 2015;386(10009):2145-2191. doi: 10.1016/S0140-6736(15)61340-X [PMCID: PMC4673910] [PubMed: 26321261] [CrossRef: 10.1016/S0140-6736(15)61340-X]

6. Scott SP, Chen-Edinboro LP, Caulfield LE, Murray-Kolb LE. The impact of anemia on child mortality: an updated review. *Nutrients*. 2014;6(12):5915-5932. doi: 10.3390/nu6125915 [PMCID: PMC4277007] [PubMed: 25533005] [CrossRef: 10.3390/nu6125915]

7. McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anaemia: WHO Vitamin and Mineral Nutrition Information System, 1993-2005. *Public Health Nutr*. 2009;12(4):444-454. doi: 10.1017/S1368980008002401 [PubMed: 18498676] [CrossRef: 10.1017/S1368980008002401]

8. Stevens GA, Finucane MM, De-Regil LM, et al.; Nutrition Impact Model Study Group (Anaemia) . Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. *Lancet Glob Health*. 2013;1(1):e16-e25. doi: 10.1016/S2214-109X(13)70001-9 [PMCID: PMC4547326] [PubMed: 25103581] [CrossRef: 10.1016/S2214-109X(13)70001-9]

9. Balarajan Y, Ramakrishnan U, Ozaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. *Lancet*. 2011;378(9809):2123-2135. doi: 10.1016/S0140-6736(10)62304-5 [PubMed: 21813172] [CrossRef: 10.1016/S0140-6736(10)62304-5]

10. Lozoff B, Jimenez E, Wolf AW. Long-term developmental outcome of infants with iron deficiency. *N Engl J Med*. 1991;325(10):687-694. doi: 10.1056/NEJM199109053251004 [PubMed: 1870641] [CrossRef: 10.1056/NEJM199109053251004]

11. Iannotti LL, Tielsch JM, Black MM, Black RE. Iron supplementation in early childhood: health benefits and risks. *Am J Clin Nutr*. 2006;84(6):1261-1276. doi: 10.1093/ajcn/84.6.1261 [PMCID: PMC3311916] [PubMed: 17158406] [CrossRef: 10.1093/ajcn/84.6.1261]

12. Lozoff B, Wolf AW, Jimenez E. Iron-deficiency anemia and infant development: effects of extended oral iron therapy. *J Pediatr*. 1996;129(3):382-389. doi: 10.1016/S0022-3476(96)70070-7 [PubMed: 8804327] [CrossRef: 10.1016/S0022-3476(96)70070-7]

13. Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics*. 2000;105(4):E51. doi: 10.1542/peds.105.4.e51 [PubMed: 10742372] [CrossRef: 10.1542/peds.105.4.e51]

14. Lozoff B, Kaciroti N, Walter T. Iron deficiency in infancy: applying a physiologic framework for prediction. *Am J Clin Nutr*. 2006;84(6):1412-1421. doi: 10.1093/ajcn/84.6.1412 [PMCID: PMC1892813] [PubMed: 17158425] [CrossRef: 10.1093/ajcn/84.6.1412]

15. Nair KM, Iyengar V. Iron content, bioavailability and factors affecting iron status of Indians. *Indian J Med Res*. 2009;130(5):634-645. [PubMed: 20090120]

16. Balarajan YS, Fawzi WW, Subramanian SV. Changing patterns of social inequalities in anaemia among women in India: cross-sectional study using nationally representative data. *BMJ Open*. 2013;3(3):e002233. doi: 10.1136/bmjopen-2012-002233 [PMCID: PMC3612779] [PubMed: 23516270] [CrossRef: 10.1136/bmjopen-2012-002233]

17. Baranwal A, Baranwal A, Roy N. Association of household environment and prevalence of anemia among children under-5 in India. *Front Public Health*. 2014;2:196. doi: 10.3389/fpubh.2014.00196 [PMCID: PMC4202784] [PubMed: 25368862] [CrossRef: 10.3389/fpubh.2014.00196]

18. Calis JC, Phiri KS, Faragher EB, et al.. Severe anemia in Malawian children. *N Engl J Med*. 2008;358(9):888-899. doi: 10.1056/NEJMoa072727 [PubMed: 18305266] [CrossRef: 10.1056/NEJMoa072727]

19. Pasricha SR, Black J, Muthayya S, et al.. Determinants of anemia among young children in rural India. *Pediatrics*. 2010;126(1):e140-e149. doi: 10.1542/peds.2009-3108 [PubMed: 20547647] [CrossRef: 10.1542/peds.2009-3108]

20. is Nair KM, Fernandez-Rao S, Nagalla B, et al.. Characterisation of anaemia and associated factors among infants and pre-schoolers from rural India. *Public Health Nutr*. 2016;19(5):861-871. [PMCID: PMC10271129] [PubMed: 26139153]

21. Kumar T, Taneja S, Yajnik CS, Bhandari N, Strand TA; Study Group . Prevalence and predictors of anemia in a population of North Indian children. *Nutrition*. 2014;30(5):531-537. doi: 10.1016/j.nut.2013.09.015 [PubMed: 24560137] [CrossRef: 10.1016/j.nut.2013.09.015]

22. Vijayaraghavan K, Brahmam GN, Nair KM, Akbar D, Rao NP. Evaluation of national nutritional anemia prophylaxis programme. *Indian J Pediatr*. 1990;57(2):183-190. doi: 10.1007/BF02722084 [PubMed: 2246014] [CrossRef: 10.1007/BF02722084]

23. Kumar A. National nutritional anaemia control programme in India. *Indian J Public Health*. 1999;43(1):3-5, 16. [PubMed: 11243085]

24. Lahariya C, Khandekar J. How the findings of national family health survey-3 can act as a trigger for improving the status of anemic mothers and undernourished children in India: a review. *Indian J Med Sci*. 2007;61(9):535-544. doi: 10.4103/0019-5359.34525 [PubMed: 17785892] [CrossRef: 10.4103/0019-5359.34525]

25. Sachdev HP, Gera T. Preventing childhood anemia in India: iron supplementation and beyond. *Eur J Clin Nutr*. 2013;67(5):475-480. doi: 10.1038/ejcn.2012.212 [PubMed: 23388662] [CrossRef: 10.1038/ejcn.2012.212]

26. Vijayaraghavan K. Control of micronutrient deficiencies in India: obstacles and strategies. *Nutr Rev*. 2002;60(5 Pt 2):S73-S76. doi: 10.1301/00296640260130786 [PubMed: 12035864] [CrossRef: 10.1301/00296640260130786]

27. Galloway R, Dusch E, Elder L, et al.. Women's perceptions of iron deficiency and anemia prevention and control in eight developing countries. *Soc Sci Med*. 2002;55(4):529-544. doi: 10.1016/S0277-9536(01)00185-X [PubMed: 12188461] [CrossRef: 10.1016/S0277-9536(01)00185-X]

28. Kwon HJ, Ramasamy R, Morgan A. "How often? How much? Where from?" knowledge, attitudes, and practices of mothers and health workers to iron supplementation program for children under five in rural Tamil Nadu, south India. *Asia Pac J Public Health*. 2014;26(4):378-389. doi: 10.1177/1010539513514435 [PubMed: 24357609] [CrossRef: 10.1177/1010539513514435]

29. Galloway R, McGuire J. Determinants of compliance with iron supplementation: supplies, side effects, or psychology? *Soc Sci Med*. 1994;39(3):381-390. doi: 10.1016/0277-9536(94)90135-X [PubMed: 7939855] [CrossRef: 10.1016/0277-9536(94)90135-X]

30. López-Flores F, Neufeld LM, Sotres-Álvarez D, García-Guerra A, Ramakrishnan U. Compliance to micronutrient supplementation in children 3 to 24 months of age from a semi-rural community in Mexico. *Salud Publica Mex*. 2012;54(5):470-478. doi: 10.1590/S0036-36342012000500003 [PubMed: 23011498] [CrossRef: 10.1590/S0036-36342012000500003]

31. Christensen L, Sguassero Y, Cuesta CB. Anemia and compliance to oral iron supplementation in a sample of children attending the public health network of Rosario, Santa Fe. *Arch Argent Pediatr*. 2013;111(4):288-294. [PubMed: 23912285]

32. Bharti S, Bharti B, Naseem S, Attri SV. A community-based cluster randomized controlled trial of "directly observed home-based daily iron therapy" in lowering prevalence of anemia in rural women and adolescent girls. *Asia Pac J Public Health*. 2015;27(2):NP1333-NP1344. doi: 10.1177/1010539513486176 [PubMed: 23666832] [CrossRef: 10.1177/1010539513486176]

33. Shankar AV, Asrilla Z, Kadha JK, et al.; SUMMIT Study Group . Programmatic effects of a large-scale multiple-micronutrient supplementation trial in Indonesia: using community facilitators as intermediaries for behavior change. *Food Nutr Bull*. 2009;30(2)(suppl):S207-S214. doi: 10.1177/15648265090302S204 [PubMed: 20496613] [CrossRef: 10.1177/15648265090302S204]

34. Palupi L, Schultink W, Achadi E, Gross R. Effective community intervention to improve hemoglobin status in preschoolers receiving once-weekly iron supplementation. *Am J Clin Nutr*. 1997;65(4):1057-1061. doi: 10.1093/ajcn/65.4.1057 [PubMed: 9094893] [CrossRef: 10.1093/ajcn/65.4.1057]

35. Shet AS, Zwarenstein M, Mascarenhas M, et al.. The Karnataka Anemia Project 2: design and evaluation of a community-based parental intervention to improve childhood anemia cure rates: study protocol for a cluster randomized controlled trial. *Trials*. 2015;16(1):599. doi: 10.1186/s13063-015-1135-x [PMCID: PMC4697328] [PubMed: 26718897] [CrossRef: 10.1186/s13063-015-1135-x]

36. Ford I, Norrie J. Pragmatic trials. *N Engl J Med*. 2016;375(5):454-463. doi: 10.1056/NEJMra1510059 [PubMed: 27518663] [CrossRef: 10.1056/NEJMra1510059]

37. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ*. 2015;350:h2147. doi: 10.1136/bmj.h2147 [PubMed: 25956159] [CrossRef: 10.1136/bmj.h2147]

38. National iron + initiative: Ministry of Health and Family Welfare, Government of India website. http://www.pbnrhm.org/docs/iron_plus_guidelines.pdf. Published 2013. Accessed March 26, 2015.

39. Pasricha SR, Drakesmith H, Black J, Hipgrave D, Biggs BA. Control of iron deficiency anemia in low- and middle-income countries. *Blood*. 2013;121(14):2607-2617. doi: 10.1182/blood-2012-09-453522 [PubMed: 23355536] [CrossRef: 10.1182/blood-2012-09-453522]

40. Ip H, Hyder SM, Haseen F, Rahman M, Zlotkin SH. Improved adherence and anaemia cure rates with flexible administration of micronutrient Sprinkles: a new public health approach to anaemia control. *Eur J Clin Nutr*. 2009;63(2):165-172. doi: 10.1038/sj.ejcn.1602917 [PubMed: 17895911] [CrossRef: 10.1038/sj.ejcn.1602917]

41. World Health Organization *Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity* Geneva, Switzerland: World Health Organization; 2011.

42. Jack SJ, Ou K, Chea M, et al.. Effect of micronutrient sprinkles on reducing anemia: a cluster-randomized effectiveness trial. *Arch Pediatr Adolesc Med*. 2012;166(9):842-850. doi: 10.1001/archpediatrics.2012.1003 [PubMed: 22801933] [CrossRef: 10.1001/archpediatrics.2012.1003]

43. Rivera JA, Sotres-Alvarez D, Habicht JP, Shamah T, Villalpando S. Impact of the Mexican program for education, health, and nutrition (Progresa) on rates of growth and anemia in infants and young children: a randomized effectiveness study. *JAMA*. 2004;291(21):2563-2570. doi: 10.1001/jama.291.21.2563 [PubMed: 15173147] [CrossRef: 10.1001/jama.291.21.2563]

44. Wu S, Crespi CM, Wong WK. Comparison of methods for estimating the intraclass correlation coefficient for binary responses in cancer prevention cluster randomized trials. *Contemp Clin Trials*. 2012;33(5):869-880. doi: 10.1016/j.cct.2012.05.004 [PMCID: PMC3426610] [PubMed: 22627076] [CrossRef: 10.1016/j.cct.2012.05.004]

45. Austin PC, Manca A, Zwarenstein M, Juurlink DN, Stanbrook MB. A substantial and confusing variation exists in handling of baseline covariates in randomized controlled trials: a review of trials published in leading medical journals. *J Clin Epidemiol*. 2010;63(2):142-153. doi: 10.1016/j.jclinepi.2009.06.002 [PubMed: 19716262] [CrossRef: 10.1016/j.jclinepi.2009.06.002]

46. Stang A, Baethge C. Imbalance *p* values for baseline covariates in randomized controlled trials: a last resort for the use of *p* values? a pro and contra debate. *Clin Epidemiol*. 2018;10:531-535. doi: 10.2147/CLEP.S161508 [PMCID: PMC5947842] [PubMed: 29773956] [CrossRef: 10.2147/CLEP.S161508]

47. World Health Organization *Assessing the Iron Status of Populations: Report of a Joint World Health Organization/ Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level*. Geneva, Switzerland: World Health Organization; 2004.

48. Black MM, Cutts DB, Frank DA, et al.; Children's Sentinel Nutritional Assessment Program Study Group . Special Supplemental Nutrition Program for Women, Infants, and Children participation and infants' growth and health: a multisite surveillance study. *Pediatrics*. 2004;114(1):169-176. doi: 10.1542/peds.114.1.169 [PubMed: 15231924] [CrossRef: 10.1542/peds.114.1.169]

49. Tandon BN. Nutritional interventions through primary health care: impact of the ICDS projects in India. *Bull World Health Organ*. 1989;67(1):77-80. [PMCID: PMC2491220] [PubMed: 2706729]

50. Varma JL, Das S, Sankar R, Mannar MG, Levinson FJ, Hamer DH. Community-level micronutrient fortification of a food supplement in India: a controlled trial in preschool children aged 36-66 mo. *Am J Clin Nutr*. 2007;85(4):1127-1133. doi: 10.1093/ajcn/85.4.1127 [PubMed: 17413115] [CrossRef: 10.1093/ajcn/85.4.1127]

51. Lassi ZS, Bhutta ZA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. *Cochrane Database Syst Rev*. 2015;3(3):CD007754. [PMCID: PMC8498021] [PubMed: 25803792]

52. Vazir S, Engle P, Balakrishna N, et al.. Cluster-randomized trial on complementary and responsive feeding education to caregivers found improved dietary intake, growth and development among rural Indian toddlers. *Matern Child Nutr*. 2013;9(1):99-117. doi: 10.1111/j.1740-8709.2012.00413.x [PMCID: PMC3434308] [PubMed: 22625182] [CrossRef: 10.1111/j.1740-8709.2012.00413.x]

53. Osei A, Pandey P, Nielsen J, et al.. Combining home garden, poultry, and nutrition education program targeted to families with young children improved anemia among children and anemia and underweight among nonpregnant women in Nepal. *Food Nutr Bull*. 2017;38(1):49-64. [PubMed: 27837036]

54. Kapur D, Sharma S, Agarwal KN. Effectiveness of nutrition education, iron supplementation or both on iron status in children. *Indian Pediatr*. 2003;40(12):1131-1144. [PubMed: 14722364]

55. Dongre AR, Deshmukh PR, Garg BS. Community-led initiative for control of anemia among children 6 to 35 months of age and unmarried adolescent girls in rural Wardha, India. *Food Nutr Bull*. 2011;32(4):315-323. doi: 10.1177/156482651103200402 [PubMed: 22590964] [CrossRef: 10.1177/156482651103200402]

56. Haldar D, Chatterjee T, Sarkar AP, Das SK, Mallik S. A study on the role of parental involvement in control of nutritional anemia among children of free primary schools in a rural area of West Bengal. *Indian J Public Health*. 2011;55(4):332-335. doi: 10.4103/0019-557X.92420 [PubMed: 22298147] [CrossRef: 10.4103/0019-557X.92420]

57. Shet AS, Rao A, Jebaraj P, et al.. Lay health workers perceptions of an anemia control intervention in Karnataka, India: a qualitative study. *BMC Public Health*. 2017;17(1):720. doi: 10.1186/s12889-017-4758-x [PMCID: PMC5604152] [PubMed: 28923041] [CrossRef: 10.1186/s12889-017-4758-x]

58. Bhutta ZA, Soofi S, Cousens S, et al.. Improvement of perinatal and newborn care in rural Pakistan through community-based strategies: a cluster-randomised effectiveness trial. *Lancet*. 2011;377(9763):403-412. doi: 10.1016/S0140-6736(10)62274-X [PubMed: 21239052] [CrossRef: 10.1016/S0140-6736(10)62274-X]

59. Black RE, Victora CG, Walker SP, et al.; Maternal and Child Nutrition Study Group . Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet*. 2013;382(9890):427-451. doi: 10.1016/S0140-6736(13)60937-X [PubMed: 23746772] [CrossRef: 10.1016/S0140-6736(13)60937-X]

60. Powers JM, Buchanan GR, Adix L, Zhang S, Gao A, McCavit TL. Effect of low-dose ferrous sulfate vs iron polysaccharide complex on hemoglobin concentration in young children with nutritional iron-deficiency anemia: a randomized clinical trial. *JAMA*. 2017;317(22):2297-2304. doi: 10.1001/jama.2017.6846 [PMCID: PMC5815003] [PubMed: 28609534] [CrossRef: 10.1001/jama.2017.6846]

61. Stoffel NU, Cercamondi CI, Brittenham G, et al.. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. *Lancet Haematol*. 2017;4(11):e524-e533. doi: 10.1016/S2352-3026(17)30182-5 [PubMed: 29032957] [CrossRef: 10.1016/S2352-3026(17)30182-5]

62. Zlotkin S, Arthur P, Antwi KY, Yeung G. Randomized, controlled trial of single versus 3-times-daily ferrous sulfate drops for treatment of anemia. *Pediatrics*. 2001;108(3):613-616. doi: 10.1542/peds.108.3.613 [PubMed: 11533326] [CrossRef: 10.1542/peds.108.3.613]

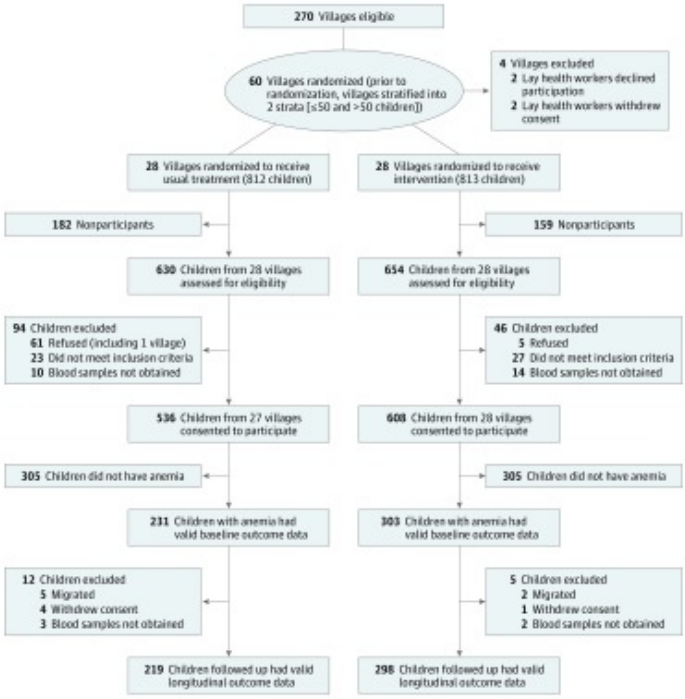
63. Bhutta Z, Klemm R, Shahid F, Rizvi A, Rah JH, Christian P. Treatment response to iron and folic acid alone is the same as with multivitamins and/or anthelminthics in severely anemic 6- to 24-month-old children. *J Nutr*. 2009;139(8):1568-1574. doi: 10.3945/jn.108.103507 [PubMed: 19535425] [CrossRef: 10.3945/jn.108.103507]

64. Bacchetti P. Peer review of statistics in medical research: the other problem. *BMJ*. 2002;324(7348):1271-1273. doi: 10.1136/bmj.324.7348.1271 [PMCID: PMC1123222] [PubMed: 12028986] [CrossRef: 10.1136/bmj.324.7348.1271]

65. Zwarenstein M. Peer review of statistics in medical research: journal reviewers are even more baffled by sample size issues than grant proposal reviewers. *BMJ*. 2002;325(7362):491. doi: 10.1136/bmj.325.7362.491/a [PMCID: PMC1124007] [PubMed: 12202336] [CrossRef: 10.1136/bmj.325.7362.491/a]

Figures and Tables

Figure.



Flow Diagram of the Karnataka Anemia Project 2 Study From Recruitment to Analysis

Sixty clusters were randomly assigned to the intervention and to usual treatment. Lay health workers in the intervention arm were trained to deliver the intervention. After obtaining informed consent from a parent, eligible participants were recruited and enrolled. Parents/guardians were surveyed on socioeconomic and demographic characteristics and anemia risk factors at baseline, and children were followed up at 2 times (at baseline and after 6 months at the end of the trial) for measurements of hemoglobin, ferritin, prior 24-hour dietary recall, and anthropometry. Adherence to iron tablets and adverse events in the last 30 days were recorded at 6 months when the trial concluded. Anemia cure rate, postintervention hemoglobin change, and adherence among children with anemia in both intervention and usual treatment groups were compared. To convert hemoglobin to grams per liter, multiply by 10.

Table 1.

Baseline Characteristics of Children With Anemia in the KAP 2 Study by Trial Group

Sociodemographic Characteristics[a]	No. (%)	
	Usual Treatment[b]	Intervention[b]
	Children With Anemia (n = 231)	Children With Anemia (n = 303)
Child's age, mean (SD), mo	30.1 (12.3)	30.6 (11.9)
12-23	82 (35.5)	104 (34.3)
24-35	82 (35.5)	100 (33.0)
36-47	38 (16.4)	64 (21.1)
48-59	29 (12.6)	35 (11.6)
Sex		
Male	127 (55.0)	156 (51.5)
Female	104 (45.0)	147 (48.5)
Birth order		
Firstborn	103 (44.6)	133 (43.9)
Secondborn	102 (44.2)	138 (45.5)
Thirdborn/higher order	26 (11.3)	32 (10.6)
Mothers' age, mean (SD), y[c]	25.1 (3.7)	24.4 (3.2)
<20	2 (0.9)	3 (1.0)
20-25	142 (62.6)	200 (66.2)
>25	83 (36.6)	99 (32.8)
Pregnancies, No.		
Primigravida	52 (22.5)	71 (23.4)
2	118 (51.1)	131 (43.2)
3	35 (15.1)	59 (19.5)
≥4	26 (11.3)	42 (13.9)
Maternal education, y		
0	39 (16.9)	43 (14.2)
1-6	13 (5.6)	41 (13.5)
7-12	171 (74.0)	214 (70.6)
>12	8 (3.5)	5 (1.7)
DHS wealth score, median (IQR)	38 (31-47)	40 (31-47)
Poorest quartile	71 (30.7)	80 (26.4)

Abbreviations: DHS, demographic and health survey; IQR, Interquartile range; KAP, Karnataka Anemia Project; RDA, recommended daily allowance; WHO, World Health Organization.

[a]Quartiles represent within-study population comparisons.

[b]The usual treatment group comprised 27 villages, and the intervention group comprised 28 villages.

[c]Usual treatment n = 227; intervention n = 302.

[d]Obtained from child's immunization record; usual treatment n = 213; intervention n = 287.

[e]Usual treatment n = 230; intervention n = 300.

[f]Underweight was defined as weight for age less than −2 SD of the WHO growth standards median.

[g]Stunting was defined as height for age less than −2 SD of the WHO growth standards median.

[h]Wasting was defined as weight for height less than −2 SD of the WHO growth standards median.

[i]Usual treatment n = 231; intervention n = 302.

[j]Usual treatment n = 222; intervention n = 296.

Table 2.

Group Comparison on Outcome Variables

Variable	Usual Treatment (n = 219)	Intervention (n = 298)	Risk Ratio (95% CI)[a]	Risk Difference (95% CI)[a]
Primary outcome				
Anemia cure rate at follow-up, %	41.1	55.7	1.37 (1.04-1.70)	15.1 (3.9-26.3)
Secondary outcomes				
Postintervention Hb change, g/dL	0.83	1.09	0.244 (0.00005-0.49)[b]	NA
Mean Hb following intervention, g/dL	10.7	11.07	NA	NA

Abbreviations: Hb, hemoglobin; NA, not applicable.

SI conversion factor: To convert hemoglobin to grams per liter, multiply by 10.

[a]Estimated using logistic regression in mixed models with random effects at the village level.

[b]Between-group mean difference using linear regression in mixed models with random effects at the village level.

Table 3.

Adherence to Iron Treatment and Adverse Events Reported by Mothers of Children With Anemia by Experimental Group

Variable	No. (%)	
	Usual Treatment (n = 219)	Intervention (n = 298)
Proportion with adherence to IFA		
0%-25%	70 (32.0)	43 (14.4)
26%-50%	27 (12.3)	27 (9.1)
51%-75%	16 (7.3)	44 (14.8)
>75%	106 (48.4)	184 (61.7)
Reporting adverse events, No.[a]	46 (21.0)	80 (26.8)

Abbreviation: IFA, iron and folic acid.

[a]Detailed adverse event information provided in eTable 2 in Supplement 2.