School-based supplementation studies addressing anemia among adolescents in Indonesia
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Citation for published version (APA):

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CHAPTER 6

Effectiveness of weekly iron supplementation among adolescent boys and girls in East Java, Indonesia: compliance is an important determinant

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Submitted for publication
ABSTRACT

Background: Anemia prevalence was high and compliance with iron supplementation poor in earlier school-based interventions among adolescents in East Java, Indonesia.

Objective: To assess the effectiveness of iron supplementation with increased efforts to raise motivation among urban adolescents.

Design: A 19 weeks' double-blind placebo-controlled weekly iron supplementation (60 mg iron + 250 µg folic acid) with education effort was carried out among 908 adolescent girls and boys (13-17 y) in 16 schools in Surabaya, East Java, Indonesia.

Results: Hemoglobin increase among boys in the iron group (n=216) was 3.4 g/L (95% CI: 1.8-5.2) higher than in the placebo group (n=222), but no effect was found in girls. Under supervision, compliance rates as recorded by field workers were 87-98%, and lower in the iron group than in the placebo group (p<0.05). Without supervision, self-reported compliance decreased to around 50%, and in the iron group it was higher for girls than boys (48.2% vs 38.4%; p<0.01). In discussions, girls reported giving tablets to other family members even during period with supervised supplementation, and mentioned peer pressure and lack of authority of field workers as factors inducing poor compliance.

Conclusions: In fact, supplementation was only effective among boys, indicating higher compliance rates. Girls' compliance was negatively influenced by side effects. Boys' compliance can be improved with motivation and education. Investment in formative research, education and high quality supplements is necessary at the early stages of intervention programs. Research is needed into behavior of adolescents in relation to supplementation programs.
INTRODUCTION

The problem of iron deficiency and anemia in adolescence has long been neglected, although a considerable proportion of adolescents suffer from iron deficiency with its serious consequences. Even in non-anemic iron-deficient individuals, verbal learning and memory are compromised (1), and in subjects with anemia the capacity to perform even less-strenuous tasks is impaired (2,3). The economic implications of impaired capacity to learn and decreased work productivity are evident (4).

The main cause of iron deficiency anemia is inadequate intake of bio-available iron, in addition to other factors, such as other micronutrient deficiencies, especially vitamin A, infections and excessive blood loss. Rapid growth, such as occurs in childhood and pregnancy, but also in adolescence, highly increases the iron needs (5-7), which makes these groups especially vulnerable to iron deficiency.

Programs of iron supplementation in pregnancy have been implemented for several decades in many countries, but the effectiveness of such programs has been relatively low as illustrated by the lack of decline in anemia prevalence over the past decades (8). Factors reducing their effectiveness include logistic problems, like availability of supplements and coverage of maternal health care (9), as well as low compliance due to the bad taste and side effects of iron supplements (10-13), and poor knowledge and awareness regarding anemia and the importance of iron supplements (14,15).

These problems are not specific for pregnancy. In two earlier school-based intervention studies in East Javanese adolescents, the impact of weekly iron/folate and vitamin A for 14 and 22 weeks, respectively, with minimal supervision of supplement ingestion was less than expected (16,17). In both studies compliance was sub-optimal, in particular for iron tablets and was related to gastro-intestinal side effects and bad taste. Therefore, the goal of the present intervention was to assess the effect of increased education and motivation on compliance and thereby effectiveness of iron supplementation in urban adolescent boys and girls, who had participated in the two previous studies.

SUBJECTS AND METHODS

Subjects

The study presented in this paper was the third intervention implemented in Junior High Schools in East Java, Indonesia as part of the GIRLS (Gizi: Intervensi pada Remaja Lewat Sekolah or ‘Nutrition: Intervention among Adolescents through Schools’) project
It was carried out between November 1998 and April 1999, among the pupils in the third grade of 16 urban Junior High Schools who had also been involved in the two earlier studies when they were in grade 1 and 2, respectively.

Nine schools were general Junior High Schools (SMP = Sekolah Menengah Pertama), and seven were Islamic Junior High Schools (MTs = Madrasah Tsanawiyah). Pupils in all selected schools were of middle and low socio-economic class, of Javanese or Madurese ethnicity, and Muslim, except for one school, where the majority was Chinese and Christian.

All pupils in the third grade of these schools received the supplement, but data were collected only on those who had been enrolled in the earlier studies as described above, and who had written informed consent from their parents. The pupils were between 13 and 17 years old at the start of the intervention.

The intervention was conducted in collaboration with the Indonesian Ministries of Health and Education after approval from the Medical Ethical Committee of the Ministry of Health, Indonesia.

**Sample size**

In order to be able to detect a 50% reduction from the anemia prevalence of 30% (17) at $\alpha = 0.05$ and $\beta = 0.80$, and accounting for an expected drop-out rate of 20%, 148 subjects per intervention group were needed.

**Design**

The pupils in the third grade of the 16 schools were enrolled in a double-blind placebo-controlled intervention and received one red sugar-coated tablet once per week for five months (total: 19 tablets). The schools were randomly assigned to either the supplementation group (60 mg elemental iron (as ferrous sulphate) and 250 $\mu$g folate; 7 schools) or placebo group (9 schools) (figure 1). This randomization was independent of the previous study. Both iron and placebo tablets were produced by Kimia Farma, Jakarta, Indonesia and were the same as those used in the second intervention study. No deworming was given as the prevalence of helminthic infections was extremely low (unpublished data).

The supplements were taken at the schools under supervision of the field workers. At each visit, the pupils were reminded of the importance of taking the tablets. This information was given in the form of posters and quizzes. During the fasting month the supplements were distributed through the schools to be taken at home at the breaking of the fast (approximately at 6 p.m.). Tablets were also taken at home during holidays and when subjects had been absent from school at the day of supplement distribution. Compliance was recorded each week by the fieldworkers. The main difference between this study and the previous ones was that compliance was more closely supervised and documented by the field workers, and that
ongoing education about the importance of taking the iron tablets was given in a playful manner.

**Data collection**

Data were collected using standard questionnaires, before and after the intervention, unless stated otherwise, by trained fieldworkers who were either trained nutritionists, nurses or had a university degree, under supervision of a medical doctor (DS). Before each round of data-collection, the fieldworkers were re-trained.

This was the third in a series of studies in the same population, and data on socio-economic status collected at the baseline of the first study (October 1996-January 1997) (18) were used in this study as well and were not re-collected after the intervention. In April 1998, data on health status were collected on the pupils as part of the endline of the previous study (17) and these data were used as baseline data for this study. The actual intervention started in November 1998. Pubertal status was determined with the status quo method (19): each respondent was asked whether she or he had started menstruating or had experienced his first nocturnal emission, respectively.

Hemoglobin was determined with the HemoCue device (HemoCue™, Angelholm, Sweden) in peripheral blood obtained from the fingertip.

Compliance was monitored each week by the field workers who supervised the ingestion of the tablets. They recorded for each pupil, whether they received a tablet and whether they took it, as well as the reason in the case of non-compliance. If a pupil had been absent, or supplementation could not be supervised for other reasons (e.g., holidays or fasting month), supplements were provided by the teacher and the subjects recorded their compliance on specially provided compliance cards. The cards were returned at the next occasion and the field workers recorded self-reported compliance for the unsupervised supplement(s). In addition, at the end of the intervention, all pupils were asked how many tablets they had taken with and without supervision, reasons for non-compliance, as well as negative and positive effects of the supplements. The numbers of tablets to be taken with or without supervision were not the same for all pupils in all schools, and compliance is reported as percentage of tablets that should have been taken rather than absolute numbers.

After the end of the intervention, a discussion was held with a total of fifteen girls from eight schools to evaluate the supplementation. In particular they were asked about reasons for not complying. The discussion was moderated by two of the field workers. The reason for this discussion was the surprising lack of effect of the intervention. Due to sudden changes in the schools’ schedules caused by the volatile safety situation in the country, there was no opportunity to repeat this with boys.
Figure 1. Supplementation study design

Data analysis and statistics

Before data were analyzed, a weighted random sample of subjects in the placebo group was taken. This was necessary, because the distribution of the two types of school, religious and general, an important indicator of socio-economic status and related to Hb (18), was different in the two treatment groups. In addition, compliance differed slightly between the types of school. Therefore, this paper reports data on all boys and girls in the iron group, and on a random sample from the placebo group weighed for school type.

Values are expressed as mean±SD, median (25-75%) or proportions. Statistical tests used included analysis of variance (ANOVA) for the differences between iron and placebo group and logistic regression analysis (20). The computer program SPSS (SPSS 7.5 for Windows, SPSS Inc., Chicago, Illinois) was used for all statistical analyses. A p-value <0.05
was considered significant.

RESULTS

Data on 641 boys and 593 girls were collected in April 1998. In April 1999, follow-up data were collected on 576 of these boys and 553 of these girls. Drop-out was 8.3% and ranged from 6.3% among girls in the iron group to 11.1% among boys in the placebo group. The main reasons, as in the previous studies, were absenteeism on several days during the last data collection round and leaving school. Complete data are available on 574 boys and 547 girls. As mentioned in the methods section, data from all boys and girls in the iron group were included in the analyses, while a weighted random sample was taken from the placebo group (figure 1). Thus, data on 438 boys and 422 girls are reported on in this paper. Of these, 65.7% of girls and 57.3% of boys attended a religious school.

Of the girls, 94.8% had reached puberty, while among boys this was 77.4%. Girls in the iron group were slightly older (median age 14.7 vs. 14.4 years in placebo group; p<0.001) and had a higher mean BMI (18.5 vs. 17.9 kg/m² in the placebo group; p<0.05), but otherwise they were similar to the placebo group. Boys in the two groups were similar, except for maternal education (a proxy for socio-economic status), which was higher for boys in the placebo group (35.9% of mothers had more than primary education vs. 22.6% in iron group; p<0.01). However, all these differences are small and unlikely to have influenced the response to iron supplements.

Compliance is defined here as number of tablets taken divided by the number of tablets distributed (at least 15 tablets), and data were collected as described in the data collection section. Complete compliance data are available on 413 subjects in the iron group and 366 subjects in the placebo group. Figure 2 shows the percentage of subjects with at least 75% compliance. Compliance under supervision (9-13 tablets, median 10 tablets) was calculated from the results of the monitoring by the field workers, while compliance without supervision (6-10 tablets, median 9 tablets) was calculated from the reports of the subjects themselves as no direct monitoring was possible. Without supervision, compliance was about half of that under supervision, as could be expected. Compliance was lower in the iron group compared to the placebo group (38.4 vs. 49.3% in boys and 48.2 vs. 59.8% in girls; p<0.05 for both sexes), and lower among boys compared to girls (p<0.05 in both intervention groups). Under supervision, girls in the iron group had lower compliance rates compared to those in the placebo group (87.0 vs. 98.2%; p<0.001). Within the placebo group, girls were reported to have higher compliance rates than boys (98.2 vs. 91.9%; p<0.05). The total
number of tablets taken by subjects in the placebo group was slightly higher than of those in
the iron group (median intake boys 16 vs 15 tablets, p<0.05; median intake girls 17 vs 15
tablets, p<0.001).

Discussions with 15 girls from 8 schools revealed that – in contrast to both self-
reported and monitored compliance – girls in fact did not take many supplements. In front of
the field workers they either pretended to put the tablets in their mouth, but in fact hid them in
their desk, or they actually put the tablets in their mouths and pretended to swallow them but
later took them out and threw them away. Reasons they gave were side effects (which was
also reflected in the lower compliance rates in the iron compared to the placebo group), peer
pressure and wanting to give the tablets to their mothers. In addition, the fact that there was
no sanction to non-compliance and the field workers did not have authority over them,
reinforced their tendency to not comply.

The effect of the intervention, expressed as change of hemoglobin concentration, is
shown in table 1. Hemoglobin concentration at baseline was, for both sexes, not different
between the treatment groups, except in non-anemic boys (placebo group 134±9 vs 131±8 in
the iron group, p<0.005) There was no effect of iron supplementation in the girls, even when
other factors (pubertal state, initial anemia, compliance) were considered. The boys in the iron
<table>
<thead>
<tr>
<th></th>
<th>Placebo group</th>
<th>Iron group</th>
<th>p-value&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Baseline change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Baseline</td>
<td>Change</td>
<td>n</td>
</tr>
<tr>
<td>All</td>
<td>168</td>
<td>119.3 [117.7 to120.9]</td>
<td>0.6 [-1.2 to 2.3]</td>
<td>254</td>
</tr>
<tr>
<td>Hb&lt;120 g/L</td>
<td>81</td>
<td>111.0 [109.4 to112.5]</td>
<td>4.9 [2.4 to 7.3]</td>
<td>144</td>
</tr>
<tr>
<td>Hb ≥120 g/L</td>
<td>87</td>
<td>127.0 [125.7 to128.4]</td>
<td>-3.1 [-5.3 to -1.0]</td>
<td>110</td>
</tr>
<tr>
<td>Pub</td>
<td>159</td>
<td>119.3 [117.7 to120.9]</td>
<td>0.6 [-1.3 to 2.4]</td>
<td>241</td>
</tr>
<tr>
<td>Pre-pub</td>
<td>9</td>
<td>119.1 [113.3 to124.9]</td>
<td>1.1 [-5.9 to 8.1]</td>
<td>13</td>
</tr>
<tr>
<td>Compliance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under spv &lt;75%</td>
<td>5</td>
<td>120.2 [108.1 to132.3]</td>
<td>4.6 [-11.1 to 20.3]</td>
<td>33</td>
</tr>
<tr>
<td>Under spv ≥75%</td>
<td>163</td>
<td>119.3 [117.7 to120.9]</td>
<td>0.5 [-1.3 to 2.2]</td>
<td>220</td>
</tr>
<tr>
<td>No spv &lt;75%</td>
<td>74</td>
<td>122.0 [119.5 to124.5]</td>
<td>-0.5 [-3.2 to 2.2]</td>
<td>139</td>
</tr>
<tr>
<td>No spv ≥75%</td>
<td>94</td>
<td>117.2 [115.2 to119.1]</td>
<td>1.4 [-0.9 to 3.8]</td>
<td>114</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>222</td>
<td>128.2 [126.5 to129.8]</td>
<td>3.5 [1.8 to 5.2]</td>
<td>216</td>
</tr>
<tr>
<td>Hb&lt;120 g/L</td>
<td>59</td>
<td>112.1 [110.5 to113.8]</td>
<td>10.4 [7.3 to 13.5]</td>
<td>51</td>
</tr>
<tr>
<td>Hb ≥120 g/L</td>
<td>162</td>
<td>134.0 [132.6 to135.3]</td>
<td>1.0 [-0.9 to 2.9]</td>
<td>166</td>
</tr>
<tr>
<td>Pub</td>
<td>173</td>
<td>128.9 [127.0 to130.9]</td>
<td>3.0 [1.2 to 4.9]</td>
<td>166</td>
</tr>
<tr>
<td>Pre-pub</td>
<td>48</td>
<td>125.4 [122.1 to128.7]</td>
<td>5.1 [0.8 to 9.4]</td>
<td>51</td>
</tr>
<tr>
<td>Compliance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under spv &lt;75%</td>
<td>20</td>
<td>127.9 [121.9 to133.8]</td>
<td>3.5 [-2.0 to 8.9]</td>
<td>26</td>
</tr>
<tr>
<td>Under spv ≥75%</td>
<td>201</td>
<td>128.1 [126.4 to129.9]</td>
<td>3.5 [1.7 to 5.3]</td>
<td>190</td>
</tr>
<tr>
<td>No spv &lt;75%</td>
<td>121</td>
<td>128.9 [126.8 to131.1]</td>
<td>4.6 [2.3 to 7.0]</td>
<td>143</td>
</tr>
<tr>
<td>No spv ≥75%</td>
<td>100</td>
<td>127.1 [124.4 to129.8]</td>
<td>2.1 [-0.4 to 4.7]</td>
<td>73</td>
</tr>
</tbody>
</table>

<sup>1</sup> mean±SD;

<sup>2</sup> Compliance under supervision as recorded by the fieldworkers and without supervision as reported by the students;

<sup>3</sup> ANOVA
Table 2. Odds ratios [95% CI] for girls and boys to have a hemoglobin concentration <120 g/L post intervention¹.

<table>
<thead>
<tr>
<th></th>
<th>Girls (n=422)</th>
<th></th>
<th>Boys (n=438)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>[95% CI]</td>
<td>p-value</td>
<td>OR</td>
</tr>
<tr>
<td>Hb at baseline (g/L)</td>
<td>0.91</td>
<td>[0.89 - 0.93]</td>
<td>&lt;0.0001</td>
<td>0.93</td>
</tr>
<tr>
<td>Type of school: religious</td>
<td>1.00</td>
<td></td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>general</td>
<td>1.89</td>
<td>[1.19 – 2.98]</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Intervention group:</td>
<td></td>
<td></td>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Iron</td>
</tr>
</tbody>
</table>

¹ The logistic regression analysis was run for stepwise entrance into the model. P-value for entrance into the model was <0.10. Variables that were available, but did not enter either regression model were compliance, BMI, weight, height, age, puberty, maternal education level.

The group however, experienced a 6.2 g/L (95% CI: 4.5-7.9) increase of hemoglobin concentration compared to only 3.5 g/L (95% CI: 1.8-5.2) in the placebo group (p<0.05). Subgroups of boys benefiting from iron supplementation were anemic boys, pubertal boys and those with good compliance under supervision.

Baseline anemia prevalence of boys was similar in the two groups (26.6% in the placebo group vs 23.6% in the iron group) but after the intervention it was higher in the placebo group compared to the iron group (17.6% vs 9.7%, respectively; p<0.05). In particular anemia prevalence among pubertal boys was reduced by 60.5% in the iron group, compared to a reduction of 24.6% in the placebo group (p<0.05). Among girls, no difference was found between anemia prevalence in both groups either at baseline (48.2% in placebo group vs 56.7% in iron group) or after the intervention (50.0% in placebo group vs 57.9% in iron group).

Logistic regression analysis was performed to assess the risk of having a hemoglobin concentration <120 g/L after the intervention (table 2). For girls, this risk was higher when they attended a general school, as opposed to an Islamic school, and had a lower initial hemoglobin concentration. For boys, the risk to be anemic at the end of the intervention was higher if they received placebo, and had a lower initial hemoglobin concentration. Compliance did not enter either model.

**DISCUSSION**

This school-based iron/folate supplementation combined with nutrition education was the third study in these schools and found an increase in Hb among adolescent boys but not among girls. The previous studies were implemented in the same urban schools and 8 rural
schools. The first study (14 weeks of weekly supplementation with 60 mg iron + 250 µg folic acid and 10,000 IU vitamin A, either alone or in combination) found no impact of supplementation on Hb, while vitamin A supplementation increased serum retinol concentration in boys but not in girls (16). The second study (22 weeks of weekly supplementation in a double-blind placebo-controlled design with 2 sugar-coated tablets containing either 60 mg iron + 250 µg folic acid or placebo, and 20,000 IU vitamin A or placebo, respectively) found no impact in rural schools. Hemoglobin concentration of urban subjects decreased in all groups due to the economic crisis, but among girls Hb decreased less with any of the supplementation regimens (p<0.001) and in boys with vitamin A alone or with iron/folic acid (p<0.001). No effect of interventions was found on serum retinol concentration as assessed in a subsample (17).

The sex difference in impact of the iron supplementation in this study is striking, particularly in view of the effect found among girls in the previous study. In this age group, growth velocity of boys is approximately twice as high as among girls (21), increasing boys’ iron requirements to the level of requirements of pubertal girls (7,22). Although the girls experience menstrual iron losses, their growth spurt occurs some 2 years before that of boys, preceding menarche by about 1 year (23). The increase in testosterone levels which causes pubertal changes in boys also stimulates erythropoiesis (7). This explains the increasing hemoglobin concentrations and decreasing anemia prevalence among pubertal boys (18). Baseline anemia prevalence was twice as high among girls compared to boys, and their mean hemoglobin concentration was approximately 10 g/L lower. Because iron absorption is more efficient in iron deficient individuals (24), it was expected that the increase in hemoglobin concentration among girls would be higher than among boys. However, the opposite was true.

Other studies (25,26) have found that weekly supplementation with the same iron dose increased hemoglobin concentrations of adolescent girls. However, those were small, highly supervised efficacy trials, while this study aimed to assess the effectiveness of iron supplementation in a programmatic setting. The authors are not aware of well-designed studies on iron supplementation among boys.

Effectiveness of supplementation depends on the efficacy of the supplement, the efficiency of the intervention and compliance of the subjects. The tablets used in the first study were the same as are used in the Indonesian government’s supplementation programs, and those used in the second and third study had the same composition but were sugar coated. These ferrous sulphate tablets have been shown to have good relative bioavailability (27) and to be efficacious in increasing Hb in adolescent girls (25). The lack of effect among girls can not be explained by supplement mix-up as boys and girls were in the same class rooms and received supplements from the same bag.

Compliance can be determined by several factors (figure 3): factors related to
Figure 3. Problem analysis diagram of potential factors contributing to poor compliance among adolescents receiving supplements (adapted from Varkevisser et al, with permission (ref. 28))
services, including tablet availability, factors related to the disease and the treatment (including side effects), and subjects' understanding and appreciation of modern treatment. This latter can be determined by socio-cultural factors and the degree of social support.

Services factors that may have influenced compliance were the sex of the field workers (most of them being female) and the way they communicated, including the type of messages used. Anemia is a chronic condition and the symptoms are either not perceived at all or not perceived as serious, which negatively influences compliance. Lack of improvement of symptoms and/or experiencing side effects further decrease compliance (10,14,29). Although the relative role of side effects in decreasing compliance is disputed (15,30,31), effectiveness of supplements became much higher after the introduction of sugar coated iron tablets in the second study (17). However, this was less so among subjects who had also participated in the first study. The reason for this might have been a lack of understanding of the importance of iron supplementation or disbelief that the sugar coated tablets would not cause similar side effects to the previously used, non-sugar coated tablets.

To improve subjects' awareness, ongoing education about the importance of the iron supplements was given in this study. Effective communication has been shown to enhance the effectiveness of iron supplementation among urban Tanzanian adolescent schoolgirls (14). However, in our case the increased communication effort resulted in an increase of Hb only among boys but not among girls.

The support received by subjects from their families was not assessed but the discussion with some of the girls revealed that mothers accepted iron tablets from their daughters instead of urging them to take the tablets themselves. Peer pressure appeared to be very strong in some schools and mostly oriented towards non-compliance. The involvement of teachers was not quantified but was certainly suboptimal and this may have further decreased compliance as subjects indicated they respected and feared their teachers.

Supervision by field workers apparently improved compliance approximately two-fold. It is conceivable that the difference between compliance with and without supervision was even larger than reflected in our data, as self-reporting has been shown to overestimate compliance rates (11). The lack of impact among girls contrasted sharply with their higher apparent compliance compared to boys, both when monitored and self-reported. Thus, either there was an unexplained physiological (lack of) response among the girls, or there was a sex difference in compliance reporting and behavior towards supplementation. In view of the fact that almost all girls were post-menarcheal with high iron needs, and of the results of several other trials, including our previous study (17), the former is not likely. Thus, poor compliance among girls but not boys is the most plausible explanation of the lack of impact found among the girls.

In general, it was observed during all three studies, that boys were more overt in their
refusal to take the tablets, even to the extent of throwing them back in the faces of the fieldworkers. The girls, however, made the impression of complying (as reflected in the compliance monitored by the fieldworkers); while in fact they did not swallow the tablets, but hid them and later threw them away or gave them to their mothers.

The sex difference in compliance seen in this study could be partly caused by the messages used. These were very much focused on becoming healthier and achieving more and this might be more appealing to boys than to girls (Triwijati E 2002, Varkevisser C 2003; personal communications). It is possible that boredom set in during this third consecutive year of supplementation, which was lifted for the boys – but not the girls - by increased awareness of the risks of anemia and the benefits of supplementation.

Conclusions and recommendations

Several issues need to be taken into account when designing randomized controlled trials in program setting. The first is that previous experience with side effects of supplements can negatively influence compliance for a long time, even if the tablets are improved. The second is that more intensive supervision seems to increase compliance among adolescents. Thirdly, in order to improve compliance, information should be provided repeatedly in different formats and in a form that appeals to the audience. Providing once only information about anemia and the importance of taking the supplements did not lead to improved compliance, while continuing education did, at least among boys. Fourthly, there is culture-related gender-specific behavior regarding compliance and the degree in which non-compliance is forthright or hidden. Last, there is a need for gender-specific health messages. For boys, focus on health, productivity, (academic) achievement, as was used in this study, seems appropriate, while for girls probably beauty and potential to care for parents, husband and offspring are also important.

The high anemia prevalence among adolescent boys and girls warrants supplementation of all adolescents, not only those who are anemic. Randomized controlled trials of iron supplementation among adolescents should focus on effectiveness rather than merely on efficacy. As compliance to iron supplementation is negatively influenced by earlier experience, presumed side effects as well as current side effects, and positively influenced by expected desirable effects, supplementation programs should invest in high quality tablets with as few side effects as possible and include intensive education and motivation activities from the start, and in particular in long-term programs. A behavioral change component, based on timely formative research, should form an integral part of the intervention. All supplementation activities should be adequately monitored and evaluated to assess effectiveness and to identify the best communication strategies to achieve optimal compliance. Messages should be focused on the target group and this might mean gender-
specific messages are needed. The optimal communication strategies in mixed groups of adolescent girls and boys need to be determined in relation to the cultural context.

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