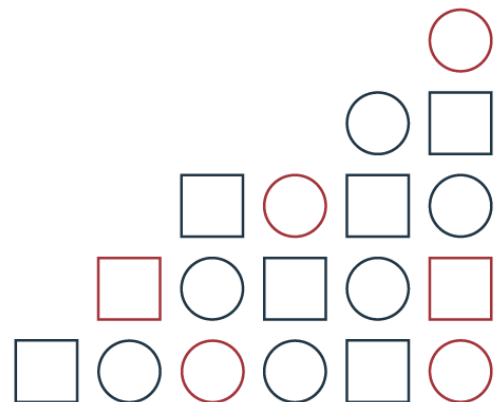


# Frequently Asked Questions

## Weekly Iron Folic Acid Supplementation (WIFAS) for Adolescents



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## Section 1: Intervention overview

### 1. What are WIFAS?

Weekly Iron and Folic Acid Supplements, or WIFAS, are oral supplements that consist of 60 mg of elemental iron and 0.4mg of folic acid, or, where available, they may consist of the World Health Organization (WHO) recommended dose of 2.8 mg of folic acid<sup>1</sup>. They are recommended by the WHO as a preventative public health intervention for adolescent girls and menstruating women living in areas where the prevalence of anaemia in adolescent girls and women of reproductive age (WRA;15-49 years of age) is 20% or greater. The current guidelines for intermittent iron and folic acid supplementation state that the supplement should be taken at minimum once weekly, usually on a predetermined day and time for a period of three months, followed by a three-month period with no supplementation for a total of 6 months per year. After this, supplementation should restart<sup>1</sup>. Alternatively, if feasible, supplements can be given throughout the school calendar year and a break from supplements aligned with school vacations. For adolescents, it is recommended for girls from 10-19 years of age.

### 2. Why is the supplement taken weekly?

WIFAS has been proposed as an alternative to daily supplementation for: 1) efficiency of absorption; and 2) increased adherence. Intestinal cells turnover every 5-6 days, and thus have limited absorptive potential. However, intermittent supplementation would expose only new cells with iron, which could increase absorption<sup>2,3</sup>. It is also thought that intermittent supplementation can reduce oxidative stress, minimize absorptive competition between iron and other minerals, and reduce some of the unpleasant reported side effects associated with daily supplementation<sup>4,5</sup>. Additionally, intermittent supplementation programs have been shown to increase adherence and acceptability among participants, making it a cost efficient option for anaemia reduction.<sup>6,7</sup>

### 3. Why is IFA important for adolescent girls?

Adolescence is the period with the second highest rate of growth in a person's life, second only to infancy<sup>8</sup>. Since this period of growth is longer than that of infancy, adolescents have greater nutritional needs during puberty than any other period of life<sup>8</sup>. Adolescents have increased needs of certain nutrients to support their rapid growth. One such nutrient is iron, which is important for adolescents' expanding blood volume, development of lean body mass, as well as counteracting menstrual blood loss in females<sup>8</sup>.

Due to their increased need for iron, and often low dietary intake of iron, many adolescents in low and middle income countries (LMIC) are at an increased risk of having iron deficiency anaemia. In fact, iron deficiency anaemia is currently the leading cause of years lived with disability in adolescent girls 10-19 and boys 10-14, as measured by DALYs (Disability Adjusted Life Years)<sup>9</sup>. This is further exacerbated in females, as the beginning of menstruation increases their iron needs and additionally girls have lower iron stores than boys<sup>8</sup>. Due to this, and social risks for lower dietary iron intake, adolescent girls are at an increased risk of anaemia and its negative

consequences, which can include reduced physical work capacity, fatigue, and reduced cognitive ability, which can directly affect their school performance. For adolescents who do become pregnant there are also increased risks for negative birth outcomes for the mother and infant.

Once weekly supplementation with IFA is a cost-effective method for reducing anaemia where it is of public health concern and delivery platforms to reach girls are available.

#### 4. Why are WIFAS programs often only for girls 10-19 years old?

Adolescent Nutrition programs often target adolescents, who are defined by WHO as people between 10-19 years of age<sup>10</sup>. It has been found that accessing adolescent girls through the health system can be unfeasible, as they often are among the least likely to access health facilities for preventative health services. Thus, the best way to reach them is through already existing platforms, often beyond health<sup>11</sup>. In contexts where school attendance is high, schools are the most cost effective delivery platform, with Ministry of Education as a key partner. Out of school girls are among the most vulnerable and different strategies are needed to reach them.

While adolescent nutrition programs typically target girls 10-19 years old, WIFAS programs have been shown to be effective for girls 10-19 years of age, as well as women 20-49 years of age<sup>11,12</sup>. In fact, WIFAS should ideally be given to all menstruating adolescent girls and adult women in populations where the prevalence of anaemia in non-pregnant (females 15-49 years of age) is greater than 20%. Thus, supplements should be taken from the time of menarche through to menopause<sup>1</sup>. However, in practice it is not necessary or practical to confirm menarche, as the intervention prevents anaemia.

Therefore, it should be noted that if there are female students in schools older than 19 years, they should be encouraged to continue to be part of the program and take the supplements as well. Additionally, the WHO guidelines recommend women of reproductive age older than 19 years of age would also benefit from WIFAS. However, different delivery platforms and partnerships would be required for programs for delivering WIFAS to women of reproductive age (20-49 years).

#### 5. Why are boys not included in most WIFAS programs?

Adolescent males do not receive WIFAS supplementation in many contexts because their physiological iron needs are not as high as those of adolescent females<sup>13</sup>. For example, males do not need to account for menstrual losses in their iron needs. They also generally have larger iron stores in their bodies than females. However, adolescent boys may receive WIFAS in contexts where their anaemia rates are high. For instance, currently, NI's program in India does include supplementation for boys. The anaemia prevalence in women of reproductive age is often higher than that of adolescent girls, as risk for anaemia increases. In some contexts anaemia is

higher in adolescent males than in adult men, suggesting that the future risks of anaemia may decrease for boys.

## 6. What are alternatives to WIFAS for reducing anaemia in adolescent girls?

Interventions that have been implemented in order to improve adolescent nutrition have included efforts such as promotion of healthy diets and eating practices, fortification of staple foods, and promotion of physical activity, among others. However, while intervention efforts have existed, implementation has been limited, and there is very little evidence of their effectiveness as a public health approaches.

WIFAS is one of the limited examples of nutrition interventions with proven effectiveness to impact adolescent girls' nutritional status, as evidenced through previous anaemia reduction programs in the Asia region. The 2011 Cochrane review, which informed the WHO guidance, found that intermittent iron supplementation in girls and women (6-49 years), alone or with other vitamins and minerals, reduced the risk of anaemia by 27%<sup>12</sup>.

IFA supplementation and iron supplementation have both been found to be effective at reducing the prevalence of anaemia and increasing haemoglobin concentrations<sup>14</sup>. Multiple micronutrient supplementation has also been found to significantly improve haemoglobin concentrations in adolescents<sup>14</sup>. However, it should be noted that daily iron supplementation programs have not been effective as a public health approach for adolescent girls and women in practice due to low coverage rates, insufficient tablet distribution, and low adherence due to reported unwanted side effects (e.g. constipation, dark stools, and metallic taste)<sup>15</sup>. It has been suggested that weekly intermittent regimes may be more acceptable to participants and increase adherence<sup>1</sup>.

While food fortification interventions, such as those for industrially processed flour, maize or corn meal, when appropriately implemented, are an efficient, inexpensive strategy for supplying vitamins and minerals to the diets of large segments of the population, this is a much longer-term strategy. An intervention like WIFAS supports anaemia reduction efforts in the short term and by targeting a vulnerable group, such as adolescent girls, which can be concurrent to broader, often national initiatives like food fortification.

Promotion of dietary diversity and interventions for dietary modification can increase dietary iron intake by promoting increased consumption of iron-rich foods. They may also increase the absorption of iron through foods through processing techniques that reduce inhibitors (such as phytates) or increase enhancers (such as ascorbic acid (vitamin C)) for non-heme iron absorption. However, these interventions do not have evidence as a scalable public health approach, as food insecurity, including limited access to iron-rich, and especially animal source foods, is often a barrier to increasing dietary consumption of iron. Food based approaches can be complementary to supplementation<sup>10</sup>.

## Section 2: WIFAS and Anaemia

### 7. Is WIFAS for treating anaemia? What is the dose for treating anaemia?

No, WIFAS programs are not for treating anaemia, rather WIFAS is a public health intervention for anaemia prevention in adolescents and non-pregnant WRA<sup>1</sup>. To treat severe anaemia in adolescents (defined as hemoglobin levels <7 g/dL or hematocrit below 20%), daily supplementation with 120 mg iron and 0.4 mg folic acid should occur for a period of 3 months<sup>16</sup>. Following this, if haemoglobin concentrations return to normal, a preventative regimen, such as WIFAS, should commence.

### 8. What are the signs and symptoms of anaemia?

Anaemia can range from mild to severe with a range of signs and symptoms. Some common signs and symptoms of anaemia include: fatigue, weakness, difficulty concentrating, brittle or spooned nails, pale skin, cracks at the sides of the mouth, coldness in the feet and hands, pica, shortness of breath, and, in severe cases, irregular heartbeat<sup>17</sup>.

### 9. Should we screen for anaemia before starting WIFAS?

Because WIFAS is not a targeted program and it is preventative, screening is not done as it is not cost-effective where anaemia in women of reproductive age is >20%. Therefore, girls are not tested for anaemia through this program prior to receiving weekly supplements. However, should a girl present with signs and symptoms of anaemia, such as those mentioned above, she should be referred to a local health center for follow-up, to be assessed and given treatment as appropriate.

## Section 3: Benefits of WIFAS

### 10. What are the benefits of WIFAS to prevent anaemia?

WIFAS prevents and reduces anaemia in the population. There is lost potential from anaemia in adolescent girls and women. This includes decreased school performance, loss of productivity, and has negative reproductive outcomes for the adolescent mother and her infant.

WIFAS have been found to reduce the risk of anaemia and improve concentrations of haemoglobin and ferritin<sup>12</sup>. This improvement in haemoglobin and possible reduction in anaemia could lead to improvements in brain function and subsequent school performance<sup>11,18</sup>. Girls could

also find that they feel more energized and have an improved capacity for physical activity and exercise<sup>19</sup>.

Adolescent girls who took WIFAS regularly qualitatively described a positive impact on “enhanced skin glow and improved appearance”, which could result from an improvement in haemoglobin concentrations<sup>11</sup>; however, there is no available evidence to support this or other claims related to beauty. WIFAS can be positioned as a product for girls to feel strong and beautiful, but it is important not to make false claims about WIFAS improving beauty.

## 11. How do WIFAS affect school performance?

A 2010 review of 14 trials examined the effects of oral iron supplementation on cognitive performance in older children and adults (children aged 6+, adolescents, and women)<sup>20</sup>. The trials included providing daily iron supplementation ranging from 17mg/day to 260mg/day. Two trials provided iron supplementation at a dose of 2mg/kg/day, and one provided a dose of 4mg/kg/day. In addition to daily iron supplementation, one trial also included a group that received a weekly iron dose of 60mg. This review found that iron supplementation, independent of baseline iron status improved attention and concentration<sup>20</sup>. In participants with anaemia, supplementation significantly improved their IQ score, but this effect was not seen in non-anaemic participants<sup>20</sup>. Additionally, a 2013 review of oral iron supplementation in primary school-aged children found that supplementation improved global cognitive scores, IQ scores in anaemic children, and measures of concentration and attention<sup>21</sup>. There is no direct evidence assessing the effectiveness of WIFAS in adolescents 10-19 years of age and the benefits on school performance or dimensions of learning.

## 12. What happens if a girl does not take IFA?

Many girls with mild anaemia may be unaware that they have anaemia. Girls do not need to be or appear sick in order to take WIFAS, as it is not a treatment for anaemia. All girls without other medical contraindications are recommended to take WIFAS as a preventative measure against anaemia and its negative consequences. While taking WIFAS is of course strongly recommended, remember that it is completely voluntary. However, if a girl chooses not to take the supplement she may be at higher risk of anaemia and its consequences, such as fatigue, reduced physical work capacity, and reduced cognitive function.

## 13. To maximize benefit, how can we increase adherence and increase consumption of WIFAS?



In order to ensure adherence and consumption, the girls must receive the supplements. For example in a school-based program this means they need to be at school on WIFAS day, supplies need to be available at schools, and teachers need to feel motivated and confident to give out supplements to their students.

There is a clear link between school attendance and program adherence. Thus, one of the best long-term strategies to ensuring that supplements are consumed will be to break down barriers that students face in attending school. A fixed day approach can also be part of ensuring supplements are given out on the day when the most girls will be at school<sup>22</sup>.

Being prepared to support girls in the early weeks of supplementation, such as at the beginning of the school semester is critical, as this is when side effects are most likely to occur. While they will likely lessen over time, support in preventing or managing side effects can influence a girl's willingness to keep taking a supplement<sup>23</sup>. Availability of clean water and timing the supplement consumption to be closest to a meal or snack can reduce side effects (see Question 21).

Strategies to increase adherence for girls who are at school can include individual cards held by the participants; the cards engage girls in the intervention, and serve as a reminder of the benefits of using WIFAS regularly and to consume the supplement on a specific day<sup>11</sup>.

#### 14. What are best practices for monitoring coverage and adherence?

Proper monitoring can help program managers track the coverage of programs, identify and reduce dropouts, and develop strategies to increase adherence<sup>11</sup>.

Monitoring registers at the class or school level, where a teacher enters information each week, have been found to be practical, simple, and acceptable by teachers<sup>11</sup>. Such registers can be modeled after existing attendance forms and can record information on side effects and discontinuation of WIFAS, which is useful for following up on low adherence cases and arranging subsequent counselling sessions. As WIFAS are a health intervention often delivered at schools, harmonization and collaboration between education and health partners are essential for developing forms and data that work for both sectors. Digital platforms may be an option in some settings where digital health and/or education strategies are in place. Ideally, WIFAS can be integrated and included into HMIS.

### Section 4: Safety considerations

#### 15. Is it safe to consume WIFAS?

Yes, WIFAS are safe to take once a week. The current WHO formulation is well below the weekly upper limit for both folic acid (7 mg/week) and iron (280-315 mg/week) set by the Institutes of

Medicine<sup>13</sup>. Thus, if only *one supplement* is taken per week as recommended, it will be safe and will not be possible to overdose.

## 16. Is it safe to consume WIFAS over long time periods?

Yes, it is safe to consume WIFAS over long and/or multiple time periods as the current weekly formulation is well below the weekly upper limits set by the Institutes of Medicine<sup>13,24</sup>. A recent study showed sustained effectiveness of WIFAS over six years, which also indicates that it is safe to take for multiple years<sup>25</sup>. Additionally, as mentioned in Question 4, the current WHO guideline recommends WIFAS for all menstruating adolescent girls and adult women<sup>1</sup>. Females have higher iron needs until they reach menopause, thus consuming WIFAS from the time of menarche through to menopause will help them to meet their physiological iron needs while also reducing the risk of anaemia (33% of women of reproductive age are anaemic globally)<sup>26</sup>. Any side effects associated with WIFAS usually occur early on in the supplementation regime and normally decrease over time<sup>11</sup>.

## 17. Are there any girls who should be excluded from taking WIFAS?

It should be noted that girls who are diagnosed as having anaemia are not recommended to take WIFAS. Instead, anaemic girls should be treated using her country's clinical guidelines. WHO recommends that if anaemia is diagnosed, the girl should be treated with daily iron (120 mg of elemental iron) and folic acid (0.4 mg) supplementation until her haemoglobin concentrations rise to normal levels. Following this, she can take WIFAS to prevent the anaemia from returning<sup>1</sup>.

Additionally, pregnant adolescent girls should not consume WIFAS. They should be supported to receive Ante Natal Care (ANC) from trained providers and they should receive daily iron folic acid supplements as their iron needs are much higher than that of non-pregnant adolescent girls. Current WHO guidelines recommend 60 mg iron with 0.4 mg folic daily during pregnancy and 3 months post-partum<sup>27,28</sup>. WHO recommends that WIFAS are formulated to supply a weekly dose of 60 mg iron and 2.8 mg folic acid, but this formulation is not readily available<sup>1</sup>. The WIFAS will not harm a pregnant woman or pregnant adolescent; however, her iron needs are greater and folic acid is proven effective for prevention of neural tube defects (NTD) with the daily dose. Should an adolescent girl or woman determine she is pregnant while on WIFAS, she should discontinue her use of the weekly supplement when she is able to begin consuming the WHO recommended daily supplement.

In the case of illness, including malaria or other acute infections, healthcare providers may recommend suspending WIFAS until the course of treatment is complete (see Questions 22 and 23).

## 18. Is it safe for teachers to administer WIFAS?

Yes, it is safe for teachers to administer WIFAS. As the best method for implementing WIFAS is through utilizing existing school structures it is also helpful to have the support of the teachers. In prior experience implementing WIFAS in the Asia region, teachers were found to be effective distributors and monitors of the WIFAS supplements<sup>11</sup>. Additionally, they are trusted and considered credible by the girls, which can also help to boost acceptance and success of the program<sup>11</sup>.

## 19. Is it safe to supplement throughout the school calendar year?

Yes. There are no safety concerns associated with giving WIFAS throughout the school calendar year. The most important aspect is that the girls take the WIFAS for at least 6 months of the year as this is typically the amount of time iron therapy is needed to have the desired positive effect on their haemoglobin levels, as well as to increase the body's iron stores<sup>29</sup>.

In considering aiming for at least a minimum of 6 months of supplementation in a year, the WHO guideline recommends a three-months on followed by three-months off regimen, after which supplementation should resume with another three-months, and so on. The guideline also suggests aligning with the school calendar year, as an option. However, this is only a suggestion, and there is no concern with aligning WIFAS supplementation in a way that is more convenient for those delivering the programs, such as aligning with ongoing program delivery through other platforms.

## 20. Are there side effects associated with WIFAS?

There are some side effects associated with taking WIFAS, which can include: black stools, nausea, constipation, abdominal cramping, and vomiting. However, these side effects are typically reported only in the first few weeks of use and normally decrease over time<sup>11</sup>. It is very important to inform everyone participating in the program of the possible side effects, and note that they are normally mild and transient.

## 21. How can the side effects be managed?

Side effects have been most commonly associated with taking the supplement on an empty stomach. Thus, to reduce the chance of side effects, it is best to take the supplement within two hours of consuming a meal<sup>11</sup>. Each program can assess what might be optimal timing, for example, in some countries girls eat before coming to school. However, if food is unavailable, or if schools do not provide any food, it is still safe to consume the supplement without a meal. WIFAS will still be effective as the iron and folic acid can be absorbed without the presence of food.

If this is the case, it is recommended that the girls take their WIFAS with water. Schools can recommend girls to bring a bottle/canteen of water with them from home on assigned WIFAS days. There may also be seasonal considerations, such as those for areas that observe Ramadan. During this season, WIFAS supplements could still be sent home with the girls so that they can take them with water and food once they break fast.

## 22. Can WIFAS be administered in areas with haemoglobinopathies?

In areas where haemoglobinopathies (e.g. sickle cell disease and thalassemias) are endemic, a screening program is recommended before commencing an iron supplementation program. This is because iron deficiency may not be the cause of anaemia, and supplementation will therefore not be an effective anaemia reduction strategy<sup>30</sup>.

## 23. Can WIFAS be administered in areas with malaria?

It is safe to take weekly iron folic acid supplementation in malaria endemic areas. In these areas, the provision of weekly iron and folic acid supplements should be implemented in conjunction with adequate measures to prevent, diagnose and treat malaria<sup>1</sup>.

Recent evidence suggests that iron and folic acid supplements consumed once, twice or three times a week on non-consecutive days by adolescents and women of reproductive age are an effective, safe and more acceptable alternative to daily iron supplements, including in settings where malaria is endemic<sup>31</sup>.

As a precaution, in a case where a girl is infected by malaria and is taking treatment for it, a healthcare provider may recommend that she not take WIFAS while she is being treated. She may resume taking WIFAS once the course of malaria treatment is complete, upon healthcare provider guidance.

## Section 5: WIFAS and reproductive health

### 24. Are WIFAS a contraceptive?

No, this nutritional supplement is not a contraceptive. The formulation contains iron and folic acid which are not contraceptive agents. A girl can still become pregnant while taking WIFAS supplements as it is neither a reproductive tool nor a family planning method.

Pregnancy in adolescence is associated with higher risks for negative health outcomes for both the adolescent mother and the baby. For example, adolescent mothers are at higher risk of

eclampsia and systemic infections than mothers aged 20-24 years, while newborns born to young mothers are at increased risk of low birthweight, preterm delivery, and other severe neonatal conditions<sup>32</sup>. In programs, it must be emphasized that if a girl has sex without effective contraception, she may still become pregnant, as WIFAS is not a contraceptive.

*In many cases there is stigma with girls accessing contraceptives. It may be important for parents to know that WIFAS are not contraceptives, in order to support their adolescent girls' consumption and participation in the adolescent nutrition program. Broader adolescent nutrition strategies can consider that delaying pregnancy beyond adolescence and reducing number of pregnancies before the age of 18 can have nutritional and health benefits for adolescents, and accessing contraceptives or information about sexual and reproductive health may be part of this.*

## 25. Do WIFAS help regulate menstruation?

Girls who are underweight and gain weight may experience increased regularity in menstruation, or return of menstruation, if periods were absent. There is currently no evidence that links iron supplementation with improving or influencing menstruation. WIFAS contain iron and folic acid (vitamins and minerals), which do not provide calories and are therefore unable to improve upon the chronic negative energy balance that causes menstrual irregularity or nutritional amenorrhea<sup>33</sup>.

As these are not targeted programs and WIFAS is a preventative intervention, it is not necessary to confirm a girl's menstrual status. In many settings it may not be appropriate for teachers to ask a girl about menarche as part of the Adolescent Nutrition programs, especially if a teacher is male.

## Section 6: WHO-recommended formulation

### 26. What should a country do when the WHO formulation is not available?

Currently, the formulation of WIFAS outlined in the WHO guideline (60 mg elemental iron and 2.8 mg folic acid) is not included on the 20<sup>th</sup> WHO Model List of Essential Medicines<sup>34</sup>. As this is what many countries base their national model lists on, this formulation is unlikely to be on national essential medicines lists, which guide a country's procurement and supply of medicines.

In addition, a recent scoping found that there is only one manufacturer globally that is currently making the WHO recommended supplement (60 mg iron and 2.8 mg folic acid), while a couple of others have expressed interest in future production. While efforts progress to make the supplement more globally and commercially available, programs are recommended to use the same supplement as that used in many contexts for daily IFA supplementation in pregnant women (60 mg iron and 0.4 mg folic acid). The prenatal dose with 60mg iron and 0.4 mg folic acid is safe to use for adolescents once weekly as it does not exceed the weekly upper limits for both folic acid (7 mg/week) or iron (280-315 mg/week) set by the Institutes of Medicine<sup>13,24</sup>.

This supplement is being used because it has the same weekly iron dose (60 mg) that is recommended for anaemia reduction<sup>1</sup>. The dose of folic acid is lower than that recommended by WHO for potential NTD prevention; however, there is currently no evidence for NTD prevention with a once weekly dose of 2.8mg folic acid. Additionally, this supplement is used instead of the one for anaemia treatment in a clinical setting because the dose of 120 mg of iron would be too high for weekly prevention, side effects would be higher with this dose, and adherence could be negatively impacted.

## 27. How can I differentiate the IFA for pregnant women from the IFA for adolescent girls?

The WHO-recommended weekly dose for adolescent girls (60 mg iron and 2.8 mg folic acid) is not the same as the daily dose for pregnant women (60 mg iron and 0.4 mg folic acid)<sup>1,27</sup>. However, as market scoping to date has found limited manufacturers that currently produce the WHO formulation of WIFAS, it is recommended that the daily dose for pregnant women be used for WIFAS programs until the commercial availability and affordability of the 60 mg iron and 2.8 mg folic acid formulation is increased. Once the WIFAS formulation is readily available and accessible, it will likely have a different colour, shape, and package than the prenatal formulation for pregnant women, which will make it easy and clear to differentiate between the two supplements.

## 28. Will using the same IFA supplements for pregnant women in WIFAS programs result in stockouts?

As in many settings both adolescent programs and maternal health programs are currently using the same supplement (60mg iron + 0.4mg folic acid), there is valid concern that either or both programs will face stockouts due to drainage of one's supply for the other.

In order to ensure this does not happen, concerted and collaborative effort will be required from both programs. Mitigating strategies should include joint forecasting, and procurement and supply management plans, considering the needs and requirements of both populations. Including these details in one clear plan will facilitate adequate supply is available for both programs, and that pregnant women and adolescent girls will benefit from anaemia reduction efforts. The forecasting exercises will likely require collaboration of education and other sectors, where schools and/or social welfare programs are involved in the delivery to adolescents.



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