

Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Lucas Gosdin

Date

Iron and folic acid supplementation for the control of anemia among adolescent girls: Schools as delivery platforms

By

Lucas Gosdin
Doctor of Philosophy

Nutrition and Health Sciences

Yaw Addo, MS/PhD
Advisor

Reynaldo Martorell, PhD
Advisor

Maria Elena Jefferds, PhD
Committee Member

Usha Ramakrishnan, PhD
Committee Member

Andrea J. Sharma, PhD MPH
Committee Member

Accepted:

Lisa A. Tedesco, Ph.D.
Dean of the James T. Laney School of Graduate Studies

Date

Iron and folic acid supplementation for the control of anemia among adolescent girls: Schools as
delivery platforms

By

Lucas Gosdin

MPH, Emory University, 2017

BA, Auburn University, 2012

Advisors: Yaw Addo, MS/PhD & Reynaldo Martorell, PhD

An abstract of

A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy
in Nutrition and Health Sciences

2020

Anemia remains a problem of moderate public health significance among adolescent girls in Ghana. In response, the Girls' Iron-Folic acid Tablet Supplementation (GIFTS) program was implemented in October 2017. We aimed to identify predictors of anemia among adolescents in Ghanaian schools, evaluate the effectiveness of school-based weekly iron-folic acid (IFA) supplementation after one school year, and examine the barriers and facilitators to the program during its first two years. Among 2,948 girls and 609 boys (10-19 years) randomly selected from 115 schools within 8 regions of Ghana, the prevalence of anemia was 24% and 13% respectively. Predictors of anemia and hemoglobin concentration (Hb) among girls included age, geophagy, malaria, diet, and body mass index (BMI). Predictors of anemia among boys included age, malaria, diet, and BMI. Age and BMI each had opposite associations with anemia among boys and girls. Our longitudinal, cohort study with 1,387 adolescent girls from 60 secondary schools found that anemia declined from 25.1% to 19.6% after 8 months. Cumulative weekly IFA tablets consumed (mean 16.4, range: 0-36) was positively associated Hb and negatively associated with anemia. IFA supplementation had a curvilinear dose-response relationship with Hb. Next, we derived a cut-point for the minimum effective number of tablets over one school year reflective of adequacy of Hb: 26.3 tablets. While 90% of schoolgirls received at least one IFA tablet over the first school year, 76% had not consumed the minimum effective number of tablets. School-level represented 75% of the variance in IFA consumption. The ability to make up missed doses, school level, educators' program-related training and experiences, and educator perceptions on difficulty of implementation and time burden were associated with cumulative IFA consumption. Finally, at 16 schools, we conducted 77 semi-structured key informant interviews with educators and parent leaders. The results indicated that, after two years of implementation, schools had adapted the program, and widespread changes in attitudes and beliefs about the IFA tablets had improved their acceptability. However, limitations remained including supply chain, program ownership, communication, training, motivation, and resources. These results may be used to improve Ghana's IFA program and have applications for similar programs.

Iron and folic acid supplementation for the control of anemia among adolescent girls: Schools as
delivery platforms

By

Lucas Gosdin

MPH, Emory University, 2017

BA, Auburn University, 2012

Advisors: Yaw Addo, MS/PhD & Reynaldo Martorell, PhD

A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy
in Nutrition and Health Sciences

2020

Acknowledgements

We are grateful to the hundreds of students and teachers who gave their time and attention to this study. This research was only possible because of their participation. We also recognize the personnel of the Ghana Health Service (GHS), Ghana Education Service (GES), and UNICEF-Ghana that are responsible for the functioning of the Girls Iron-Folic acid Tablet Supplementation (GIFTS) program throughout the studied regions and beyond. We also offer our thanks to the dedicated survey staff, many of whom returned time-after-time to help us gather the highest quality data possible. Their performance reflected a commitment to public health and their fellow Ghanaians.

The GIFTS program was initiated by a group of enthusiastic public health professionals in Ghana and their international collaborators. Members of this team included Esi Foriwa Amoafu, Kate Quarshie, Mutala Abdulai, Gifty Ampah (GHS), Lilian Selenje, Abraham Mahama, Porbilla Ofosu-Apea (UNICEF-Ghana), Katie Tripp, and Yaw Addo (CDC).

Collaborating partners for the GIFTS program included GHS, GES, UNICEF-Ghana, Korean International Cooperation Agency (KOICA), Emory Global Health Institute (EGHI), and the Centers for Disease Control and Prevention (CDC). The study was funded by UNICEF-Ghana, CDC, and EGHI. I received funding support from the Emory University Laney Graduate School, EGHI, UNICEF-Ghana, and CDC through the Oakridge Associated Universities. I also want to thank the incredible team of researchers with whom I am privileged to work at the CDC and who have read and revised each of the manuscripts that follow.

I also wish to thank the overwhelming support of the Nutrition and Health Sciences program. My advisors and committee members, listed above, have volunteered many hours reviewing and revising this research with me and have made immeasurable contributions to my training and growth as a researcher. In particular, I wish to thank Yaw Addo for his patience, kindness, and dedication to my success over the past three years. There is no doubt I would not be at this critical milestone without him. Other key NHS faculty members including Melissa Young and Amy Webb-Girard have given me additional opportunities to develop my research and teaching skills and supported me throughout my doctoral training.

I am also extremely thankful for the support of my family. I am especially indebted to my parents who pushed me to become the first in my family to attend college and now the first to obtain a doctoral degree. Finally, I must thank my best friend and partner Justin for supporting me through my studies. He spent many hours listening and helping me cope with the stress of a doctoral program. I could not have done it without him, and I know he will celebrate this as much as I do.

Contents

Acknowledgements.....	vi
List of Figures	ix
List of Tables	x
Research in Context	xi
Chapter 1: Introduction	1
Chapter 2: Overview of Methods.....	4
2.1: Setting	4
2.2: Program, Training, and Oversight	4
2.3: Program Evaluation Study Design and Sampling Frame	6
2.4: Data Collection and Data Management.....	8
2.5: Statistical Methods and Data Analysis.....	10
2.6: Alternate Study Designs and Analytic Strategies	13
References (Chapters 1 and 2).....	18
Chapter 3: Predictors of Anemia among Adolescent Schoolchildren of Ghana	20
3.1: Introduction	22
3.2: Methods.....	23
3.3: Results.....	27
3.4: Discussion	29
3.5: Figures and Tables	34
References (Chapter 3)	41
Chapter 4: A School-Based Weekly Iron and Folic Acid Supplementation Program is Effective at Reducing Anemia in a Prospective Cohort of Ghanaian Adolescent Girls.....	43
4.1: Background	45
4.2: Methods.....	47
4.3: Results.....	51
4.4: Discussion	54
4.5: Conclusion.....	56
4.6: Figures and Tables	58
References (Chapter 4)	66
Chapter 5: Barriers and Facilitators of Iron and Folic Acid Supplementation within a School-based Integrated Nutrition and Health Promotion Program among Ghanaian Adolescent Girls.....	68
5.1: Background	70

5.2: Methods.....	72
5.3: Results.....	75
5.4: Discussion	79
5.5: Figures and Tables	84
References (Chapter 5)	95
Chapter 6: A Qualitative Analysis of Program Fidelity, Innovation, and Perspectives of Educators and Parents after Two Years of the Girls’ Iron-Folic acid Tablet Supplementation (GIFTS) Program	97
6.1: Introduction	99
6.2: Methods.....	101
6.3: Results.....	104
6.4: Discussion	123
6.5: Figures and Tables	127
References (Chapter 6)	135
Chapter 7: Expanded Discussion.....	136
7.1: Summary of Findings.....	136
7.2: Comparison of Findings to Similar Studies	137
7.3: Study Strengths and Limitations	141
7.4: Remaining Research Gaps and Next Steps	144
7.5: Conclusions	145
References (Chapter 7)	147
Appendices.....	149
Appendix 1: Key Informant Interview Guides.....	149
Appendix 2: Distribution of Hemoglobin Concentration at the Baseline and Follow-on Surveys of the Phase I Evaluation of the GIFTS Program.....	158

List of Figures

Figure 2.2.1: Map of the Phased Rollout of the GIFTS Program, Ghana

Figure 2.2.2: GIFTS Program Schema

Figure 2.3.1: GIFTS Program Evaluation Timeline

Figure 3.5.1: Characteristics of Adolescent Girls and Boys in Ghanaian Schools in Upper West, Western, and Western North Regions

Figure 3.5.2: Distribution of Hemoglobin Concentration among Adolescent Girls and Boys in Ghanaian Schools by Region (n=2,948)

Figure 3.5.3: Unadjusted Prevalence of Anemia among Adolescent Girls and Boys in Ghanaian Schools by Malaria, Geophagy, and Selected Dietary Variables, Northern, Upper West, Volta, Western, and Western North Regions (n=2,948)

Figure 4.6.1: Participant Flow Chart for Baseline and Follow-on Surveys of Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Figure 4.6.2: Iron-folic Acid (IFA) Tablets Consumed among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana over One School Year by Term

Figure 4.6.3: The Relationship between the Cumulative Iron-folic Acid (IFA) Tablets Consumed and the Change in Hemoglobin Concentration over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Figure 4.6.4: Adjusted Change in Anemia Prevalence Difference by Cumulative IFA Tablets Consumed over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Figure 4.6.5: Adjusted Change in Mean Hemoglobin Difference by Cumulative IFA Tablets Consumed over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Figure 5.5.1: Conceptual Framework of the Barriers and Facilitators of School-based Iron and Folic Acid (IFA) Supplementation

Figure 5.5.2: Levels of Iron and Folic Acid (IFA) Supplementation Coverage and Bottlenecks among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions

Figure 5.5.3: Total Iron and Folic Acid Tablets Consumed Over One School Year by Basic Participant and School Characteristics among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,307)

Figure 6.5.1: Conceptual Framework of the Barriers and Facilitators of a School-based Adolescent Anemia Control Program with Iron-Folic acid Supplementation

Figure 6.5.2: Regional Map of Ghana, GIFTS Program Phases, and Study Sites

Figure 6.5.3: Primary Distributor of IFA Tablets in 16 Schools in Ghana

Figure 6.5.4: Reported Time Devoted to Girls Iron-Folic acid Tablet Supplementation (GIFTS) Program in 16 Schools on Distribution Day by Respondent Role

List of Tables

- Table 3.5.1: Characteristics of Adolescent Girls in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions
- Table 3.5.2: Adjusted Model of the Predictors of Hemoglobin Concentration among Adolescent Girls and Boys in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions
- Table 3.5.3: Adjusted Model of the Predictors of Anemia among Adolescent Girls and Boys in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions
- Table 4.6.1: Demographic Characteristics of Participants in the Baseline Survey of Adolescent Schoolgirls in the Northern and Volta Regions of Ghana
- Table 4.6.2: Health and Dietary Characteristics at Baseline and Follow-on and the Population Average Changes over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana
- Table 4.6.3: Iron-folic Acid (IFA) Tablets Consumed among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana over One School Year and Anemia Prevalence at Follow-on
- Supplemental Table 4.6.1: Adjusted Change in Anemia Prevalence Difference and Hemoglobin Concentration Mean Difference from Baseline to Follow-on among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana by Participant Characteristics
- Table 4.6.4: Adjusted Model of Anemia at Follow-on among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana
- Table 5.5.1: Student Characteristics by Self-reported Consumption of Iron-folic Acid (IFA) Tablets Over One School Year among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions
- Table 5.5.2: School-level Characteristics by Self-reported Consumption of Iron-folic Acid (IFA) Tablets Over One School Year among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions
- Table 5.5.3: Predictors of the Total Number of Iron and Folic Acid (IFA) Tablets Consumed Over One School Year, Among Consumers of IFA among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,231)
- Table 5.5.4: Predictors of the Total Number of Iron and Folic Acid (IFA) Tablets Consumed Over One School Year, Among all participants among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,298)
- Table 6.5.1: Summary Findings from Interviews with 77 Educators and PTA/SMC Chairpersons in 16 Ghanaian Schools

Research in Context

Evidence before this research

The complexity and population-specific nature of anemia etiology is well known. Yet, most anemia research is focused on young children and women of reproductive age, and little is known about anemia among younger adolescents. The principal anemia control strategy recommended by the World Health Organization for adolescent girls is iron and folic acid (IFA) supplementation. This strategy has been shown efficacious in studies of school-based IFA distribution, but results are mixed for community-based supplementation. There are few countries with high anemia burdens that have active IFA supplementation for adolescent girls, and they are all in Asia. Program impact evaluations are needed to determine the effectiveness of IFA supplementation for adolescent girls within other regions.

Added value of this research

This dissertation examined the context-specific drivers of anemia among adolescent girls and boys, both younger and older. It also demonstrates the effectiveness of school-based IFA supplementation under real-world conditions and in the sub-Saharan African context. This is the first study to our knowledge to provide a data-driven cut-point for minimum effective number of IFA tablets for achieving adequacy of hemoglobin concentration (as defined by anemia cut-offs) among a population of adolescents. Our work also identified school- and individual-level barriers and facilitators to IFA tablet intake adherence and identified bottlenecks to program coverage and adherence. Lastly, this dissertation examines program fidelity, evolution of beliefs and practices, perceptions of the program, and motivations of program implementers after two years of the intervention.

Implications of all available research

Adolescent girls are an appropriate target of anemia control measures, and anemia control programs in Ghana should be integrated into education and health system. They should include malaria prevention and behavior change strategies related to nutrition. School-based IFA supplementation is effective in reducing the prevalence of anemia among Ghanaian adolescents; however, IFA intake adherence could be improved by addressing barriers at the school-level. Strong cross-sectoral collaborations, training, resources, motivation, monitoring, and a healthy supply chain are necessary components for program fidelity and adherence.

Chapter 1: Introduction

Globally, iron deficiency anemia is a leading cause of morbidity and mortality among adolescent girls 10-19 years of age.⁽¹⁾ It is responsible for a loss of an estimated 1,001 disability-adjusted life-years per 100,000 adolescent girls.⁽¹⁾ Anemia is typically diagnosed by a low circulating hemoglobin concentration (Hb),⁽²⁾ a protein critical to the transport of oxygen.⁽³⁾

Anemia has a complex etiology that can differ among and between populations.^(4,5) Because anemia is a condition defined by the quantity or quality of erythrocytes in circulation rather than a deficiency of a specific nutrient, its root causes can be varied and numerous.⁽⁶⁾ Broadly, proximal causes of anemia include nutrient deficiencies, infection or illness, blood loss, and blood disorders.⁽⁷⁾ Deficiencies of iron, folate, vitamin B12, and vitamin A are commonly associated with anemia.⁽⁸⁾ Infections and illnesses such as malaria that alter erythrocyte vitality or production can induce anemia.⁽⁹⁾ Hemorrhage, menstruation, and other forms of blood loss can substantially lower Hb and lead to anemia.⁽⁶⁾ Blood disorders such as thalassemia and sickle cell disorder may lead to chronic anemia in persons with these disorders.⁽¹⁰⁾

The pathophysiology of anemia and low Hb stems from reduced oxygen transport to cells.⁽⁶⁾ Immediate effects may include poor immune function,^(11,12) reduced aerobic capacity,⁽¹³⁾ and poor oxidative and nuclear metabolism.⁽¹⁴⁾ These effects may lead to lethargy, fatigue, and lack of concentration.⁽⁷⁾ Lower total body Hb even without anemia is associated with decreased maximal oxygen uptake (VO₂Max), and consequently, reduced work capacity.⁽¹⁵⁾ Anemia is also associated with reduced work capacity⁽¹⁶⁾ and cognition.^(7,17,18) Nutrition-related anemia can be transient but its consequences longer lasting^(19,20) such as lost academic potential⁽²¹⁾ and reduced human capital.⁽⁷⁾ Anemia during pregnancy can lead to poor outcomes such as hemorrhage, preterm birth, low birth weight, perinatal mortality, and neonatal mortality.^(22,23)

Treatment of anemia depends on its etiology, and treatments are specific to the underlying causes of the condition. When the prevalence of anemia is high within a population, supplementation with iron and folic acid (IFA) may be warranted for anemia prevention because nutritional anemias are thought to be the main causes. For example, the World Health Organization recommends IFA supplementation to all non-pregnant women and adolescent girls of reproductive age (15-49 years) and to preschool and school-aged children (2-12 years) where the prevalence of anemia exceeds 20% and in conjunction with malaria prevention and treatment in malaria endemic regions.^(24,25) This guideline recommends 3 months of weekly supplementation with 60 mg of elemental iron and 2800 µg of folic acid followed by a 3-month break or a strategy that follows the academic calendar. The basis for weekly supplementation was the 5-6 day turnover of intestinal cells, reduced side-effects, and improved acceptability as compared to a daily supplement with similar effects on hemoglobin concentration. The 3-month schedule was chosen because this duration was common in the reviewed literature and had no differences in its effect when compared to schedules of shorter or longer duration.⁽²⁴⁾

In a meta-analysis of experimental trials, school-based IFA supplementation reduced the prevalence of anemia among adolescents, but results were mixed for community-based supplementation.⁽²⁶⁾

Adolescent nutrition has received little research attention in low- and middle-income countries, and few programs target adolescent nutrition outside of the context of childbearing, despite evidence that adolescence is a critical period of growth and development during which nutritional needs are greater.^(27,28) Health behaviors and dietary patterns that are established during this period often track into adulthood.^(29,30) Calls for increased efforts focused on adolescent nutrition are receiving global attention.⁽³¹⁾

Ghanaian adolescents carry a high burden of micronutrient deficiencies. For example in the 2017 national micronutrient survey, 26.4% of girls 15-19 years old were anemic, 14.5% had iron deficiency anemia, and 57.3% had folate deficiency.⁽³²⁾ Malaria, another seasonal risk factor for anemia, affects a

larger proportion of school-age adolescents than adults in Ghana.^(32,33) The prevalence of anemia in adolescents 15-19 years has been consistently high. According to Demographic and Health Surveys, the prevalence of anemia in 2003 was 46%, 63% in 2008, and 48% in 2014.⁽³⁴⁾ Based on recommendations from international partners⁽³⁵⁾ and with their financial and technical support, an anemia control program with IFA supplementation was added to the national anemia reduction strategy for Ghana in 2016.

Previous studies had focused on older adolescents, no data existed on anemia among adolescent boys, and the drivers of anemia among adolescents in Ghana were still unclear. An integrated approach to anemia control with IFA supplementation had only been implemented in a small number of countries with high anemia burdens, none of which were in sub-Saharan Africa.⁽³⁶⁾ Though lessons shared by other implementing countries were utilized in the design of the program, it was unclear how effective it might be or the context-specific barriers that might be faced in Ghana.

This dissertation had four aims: 1) to identify key determinants of anemia among adolescents, which might be applied to tailor the intervention components for the population, 2) to evaluate the effectiveness of school-based weekly IFA supplementation on anemia prevalence and hemoglobin concentrations and establish a minimum effective number of weekly doses over the school year for prevention of anemia in a prospective cohort of Ghanaian adolescent schoolgirls, 3) to determine the barriers and facilitators of program fidelity and adherence of a school-based integrated nutrition and health promotion program with IFA supplementation, and 4) to describe potential operational and socio-ecological drivers of intake adherence and program fidelity, explain how these factors influence the success of the program, and understand how they might be modified to improve it. As the first adolescent supplementation program in sub-Saharan Africa, evidence from the evaluation of this program has the potential to influence not only the improvement of the program in Ghana but also its implementation within other countries in the region.

Chapter 2: Overview of Methods

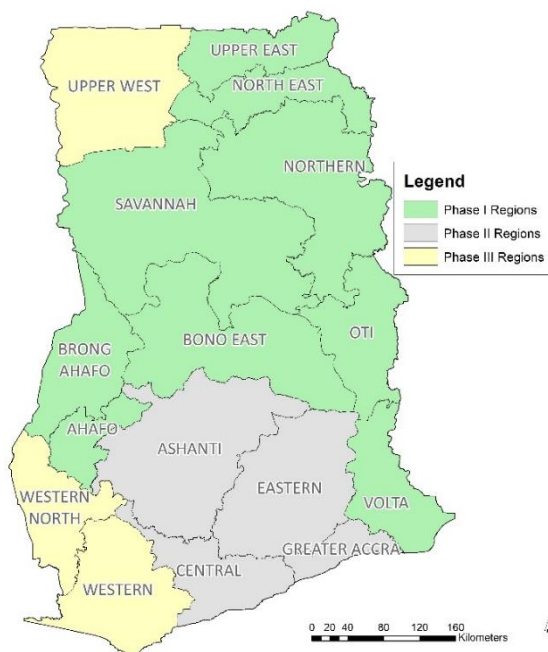
2.1: Setting

Ghana is a lower-middle income country located in coastal West Africa.⁽³⁷⁾ It has a fast-growing population of nearly 30 million people and an adolescent fertility rate of 66 per thousand.⁽³⁸⁾ Ghana has regions that are coastal, savannah, and forested. The country has three main seasons: hot, rainy, and dry. The country is divided into 18 administrative regions (up from 10 in 2018). The school year in Ghana runs from late September through July. Primary school enrollment is high (86%), but enrollment in secondary schools is lower (57%). However, the introduction of free senior secondary school in 2017 has been associated with an increase in enrollment, especially of girls.⁽³⁹⁾

2.2: Program, Training, and Oversight

The Girls' Iron-Folic acid Tablet Supplementation (GIFTS) program was rolled out in three phases beginning in the northern- and eastern-most regions in 2017. The second phase expanded the program to the central-south portion of the country, and the third phase included the remaining western regions.

Figure 2.2.1: Map of the Phased Rollout of the GIFTS Program, Ghana



The GIFTS program was designed as a collaboration between the health and education sectors to reach all adolescent girls ages 10-19 years through school-based and health center-based delivery. In schools, all adolescents, including boys, received regular health and nutrition education aimed at improving knowledge, attitudes, and practices related to anemia and promote behavior change. Behavior change messages targeted consumption of a diverse and iron-rich diet; water, sanitation, and hygiene; malaria

prevention; and menstruation. Educators provided weekly IFA tablets with 60 mg of elemental iron as ferrous fumarate and 400 µg of folic acid via directly observed therapy to adolescent girls throughout the school year. School-based delivery was limited to secondary and vocational schools during the first year but subsequently expanded to include girls in the target age range enrolled in primary schools within this scheme. Through local health centers, adolescent girls not enrolled in schools (and adolescents in primary schools during the first year) consumed one tablet each month by directly observed therapy and received three additional tablets to consume for the subsequent three weeks at home. Parents were often included in these community-based distributions and were oriented to the IFA tablets by health workers. In schools, parents were informed of the program through parent-teacher associations or school management committees. Pregnant adolescents were referred to antenatal care and received IFA supplementation through the existing health center-based program for pregnant women.

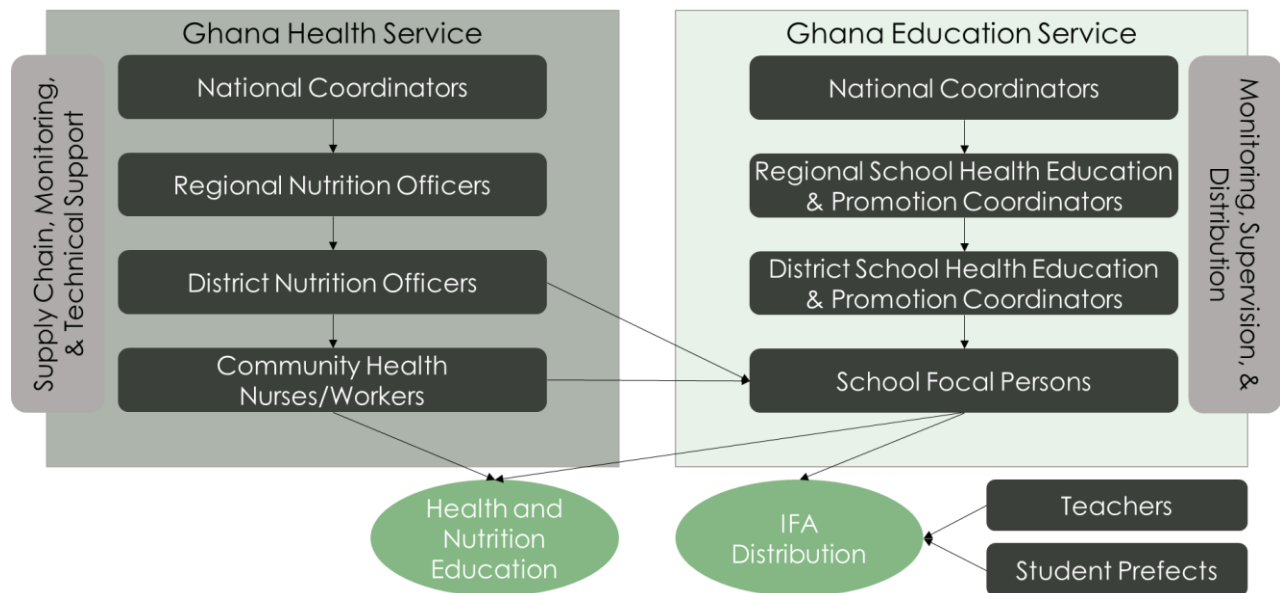
A cascade training was conducted prior to the rollout of the program. Regional health and education staff were trained by the national team at a central location. Those trained then assisted in the training of their district health/nutrition and education officers. District health/nutrition and education officers helped train a focal person in each school, and focal persons oriented other educators (teachers and head teachers) in their schools to the program.

Educators and health workers were trained on proper administration of IFA tablets including requiring the tablet be taken with water, not on an empty stomach, and not by girls suffering from sickle cell disease. They were also instructed to give tablets to female teachers to serve as role models. An IFA distribution protocol and educational materials developed by the Ministry of Health were given to program focal persons at the end of the training with first consignment of IFA tablets and program registers for each school. Program registers are paper booklets used to track individual dosage within schools.

Community sensitization activities were designed to promote awareness and knowledge of the benefits of IFA tablets for girls. The sensitization activities were rolled out before the program began and after it was underway. These activities included radio advertisements, local festivals, meetings with parents and community leaders, and promotional materials such as posters.

Supervision, monitoring, distribution, and supply of IFA tablets was integrated into existing structures with the Ghana Health Service and Ghana Education Service (Figure 2.2.2). The supply of IFA tablets passed from the health sector to the school focal person through either the District Nutrition Officer, community health workers, or District School Health Education and Promotion (SHEP) Coordinator. Educators were also given a handbook for education on anemia and IFA. Schools also utilized local health workers for leading health and nutrition education sessions.

Figure 2.2.2: GIFTS Program Schema

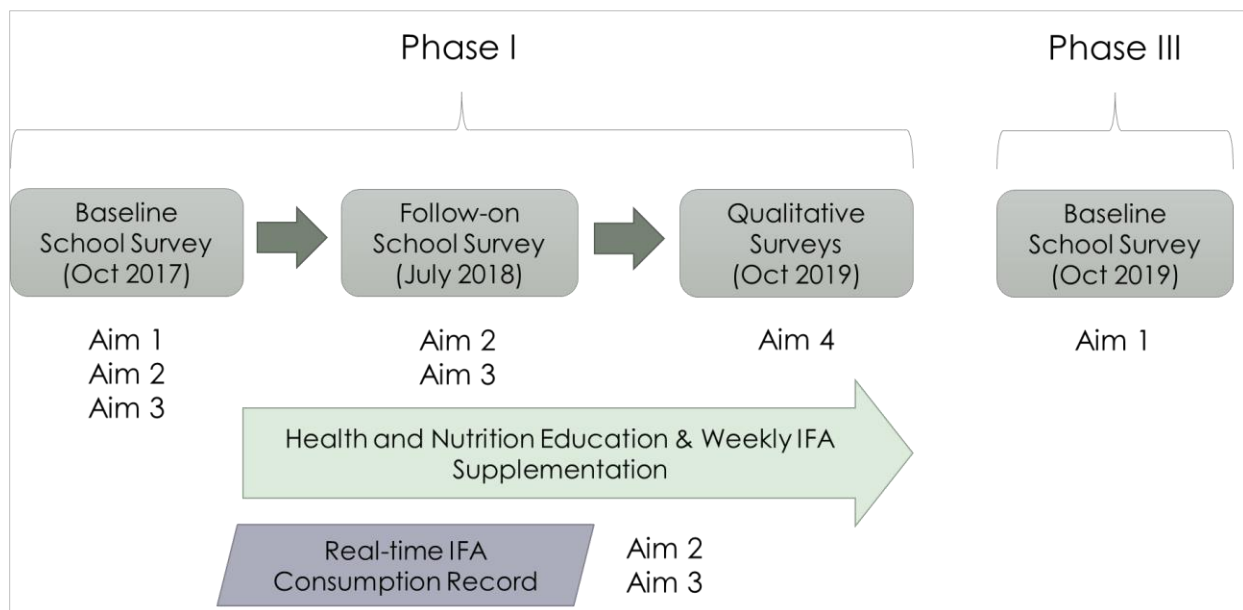


2.3: Program Evaluation Study Design and Sampling Frame

This dissertation is comprised of data from three quantitative surveys over two years and one qualitative study. Chapter 3 utilizes data from baseline quantitative surveys of Phases I and III conducted at the

beginning of the school year in 2017 and 2019, respectively. Chapters 4 and 5 utilize baseline and follow-on quantitative data from Phase I collected in 2017 and 2018. The qualitative study in Chapter 6 was conducted at the beginning of the school year in 2019.

Figure 2.3.1: GIFTS Program Evaluation Timeline



The Phase I, Year 1 evaluation was designed as a longitudinal cohort evaluation over one school year. Two regions, Northern (now Northern, Savannah, and North-East) and Volta (now Volta and Oti) were purposively selected by the Ministry of Health for their unique demographic and geographic characteristics. Within each region, schools were stratified into junior high schools (JHS) and senior high schools (SHS) or vocational schools, and 15 of each type were selected by probability proportion to size (enrollment of girls). Within each selected school, 29 girls from forms 1 and 2 (grades 7, 8, 10, and 11 in the North American system) were selected using simple random sampling. The resulting sample size was 1,521 girls ages 10-19 years. After approximately 8 months of program implementation, at the end of the school year in 2018, we were able to collect follow-up data prospectively from 1,387 of the girls.

Individual consumption of IFA tablets was recorded in classroom-level program registers each week of the school year. An educator focal person was surveyed on behalf of each school.

In 2019, Phase III was implemented bringing the GIFTS program nationwide by including the remaining three regions of Ghana: Western, Western North, and Upper West. The Phase III baseline survey, included in Chapter 3 of this dissertation, selected 55 schools using probability proportional to size. Thirty-one girls and 13 boys were selected from forms 1 and 2 of each school within the three regions. The resulting sample size was 1,437 girls and 618 boys.

In 2019, after two years of the program in Phase I regions and the national scale-up, a qualitative follow-up was conducted in 16 schools purposively selected from the schools evaluated in Year 1. Eight schools were selected from each of the Phase I regions (Northern and Volta) after stratifying by school level, size, geographic location (rural vs. urban), and average total number of IFA tablets consumed over Year 1 (underperforming vs. top performing). For each school, five stakeholders were interviewed: the district SHEP coordinator, the head teacher, the GIFTS program focal person in the school, a non-health teacher, and the Parent-Teacher Association (PTA) or School Management Committee (SMC) chairperson. Selection preference was given to a non-health teacher that had been at the school since the beginning of the GIFTS program.

2.4: Data Collection and Data Management

In the collection of quantitative data, questionnaires were interviewer administered using Android™-based computer tablets. The girls' questionnaire included demographic information; knowledge, attitudes, and practices (KAP) related to anemia; KAP related to IFA tablets; malaria-related practices; an iron-focused food frequency questionnaire; and health and nutrition education sessions. The school survey included the teacher's KAP related to anemia and IFA tablets, anemia-related activities within the school, school meals, and enrollment. The follow-on questionnaires also included information related to

experiences with the GIFTS program and IFA tablets. During the follow-on survey, individual IFA consumption data were also abstracted from the GIFTS registers.

Height was assessed by trained and standardized anthropometrists using a stadiometer (Shorrboard[®], Maryland, USA)⁽⁴⁰⁾ and weight with a lightweight electronic digital scale (SECA, Hamburg, Germany).

Twelve anthropometrists were used during the Phase I baseline survey, and 18 were used during the Phase I follow-on and Phase III baseline surveys. Standard anthropometric protocols were used which included the proper placement and calibration of equipment, positioning of students, and reading of the equipment. Shoes and unnecessary clothing were removed and pockets were emptied. Hairstyles that were not easily flattened were taken down as possible and appropriate. Provisions were made to measure the additional height given by hairstyles that could not be flattened using a ruler; however, no utilization of this method was required.

A field laboratory technician tested Hb using the HemoCue[®] 301 (Ängelholm, Sweden) and malaria using CareStart[™] Rapid Diagnostic Test (AccessBio, New Jersey, USA). Collection procedures are fully described in Chapter 3.

In the qualitative analysis, semi-structured key informant interviews were conducted using interview guides tailored to the role of the respondent. Interviews were recorded and summaries were developed by interviewers. All interviewers had prior interviewing experience and training. Teams were trained on qualitative interviewing techniques, goals of the study, ethics protocols, use of interview guides, use of recording devices, and summarizing interviews. During the training, interview guides were reviewed for clarity and revised as needed. Interviewers practiced in pairs including effective probing and writing interview summaries. A pilot and pre-test of interview guides was conducted in three schools during the training week prior to the start of data collection. Following the pilot, interview guides were further

refined and interviewer practiced with the final interview guides. Teams of three traveled to each region. Data collection occurred over nine days at the start of the 2019-2020 school year.

Semi-structured key informant interviews were used to collect information from respondents. Interview guides were developed based on deductive themes around the distribution of IFA tablets, sensitization and beliefs, health and nutrition education, and acceptability of purchasing. Four separate interview guides were created for each respondent category (Appendix I). Interviewers used the same guide with head teachers and GIFTS focal persons. Interview guides were designed to assist interviewers in using open-ended questions, covering the topics of deductive themes, and using effective probing questions when necessary. Interviews were designed to be conducted in English, the *lingua franca* of Ghana. Since formal education is done in English, we anticipated that educator interviews would be completed in English but that some PTA/SMC chairperson interviews may be conducted in local languages.

Individually, interviewers conducted interviews in a private location and recorded then using stereo digital recording devices. Educator interviews lasted an average of approximately 45 minutes, and PTA/SMC interviews lasted approximately 10-15 minutes. After each, interviewers completed a summary consisting of at least three paragraphs covering their overall impressions of the interview, interesting findings, and outstanding questions that were unanswered in the interview. These summaries were included with each interview. Data were stored on password-protected devices.

Informed consent was obtained from all parents and participants. The study protocol was approved by the Ghana Health Service Ethics Committee and exempted from review by the Emory University Institutional Review Board. The Centers for Disease Control and Prevention determined its role to be public health practice.

2.5: Statistical Methods and Data Analysis

Analytic methods are described in detail within each manuscript (Chapters 3-6). For the main analyses of the first manuscript (Chapter 3), we utilized multivariable Poisson and linear regression to model the

predictors of anemia and Hb controlling for potential confounders. Multivariable regression models were most suitable for quantifying the relationships between the outcomes and multiple exposures within the cross-sectional data. Poisson regression was employed when the outcome was anemia because of its utility in modeling prevalence ratios, and linear regression was used when continuous Hb was the outcome. Survey procedures were employed because of the clustering of the data at the school level. We created separate models for boys and girls. This was done primarily because of biological differences by sex that become more prominent during adolescence including the onset of menstruation and other sex dimorphisms such as the distribution of adipose tissue and growth trajectories. Secondly, sociocultural differences between genders may influence the relationships between behavioral predictors and anemia.

In the second manuscript (Chapter 4), we utilized generalized linear mixed models (GLMM) to quantify the change in anemia prevalence difference and mean Hb difference associated with total IFA consumption as a categorical variable. The GLMMs were most appropriate for repeated measures of the outcomes and covariates, treating time as a random effect. The GLMMs also accounted for the clustering of the data by nesting individuals within schools. We also examined dose-response with a restricted cubic spline (RCS), modeling the linear and non-linear association between the change in Hb and total IFA consumption as a continuous variable. Dose-response is an essential feature of such an intervention because it shows that stronger adherence yields improved results, adding credibility to causal inference and highlighting potential threshold effects. An initial look at the scatter plot of the crude relationship between Hb and IFA showed a high level of noise. Smoothing techniques including Loess and B-spline did not adequately capture the curvilinear relationship. The RCS model allowed modelling of the linear and non-linear portions of this relationship without having to categorize the number of IFA tablets, smoothing the outcome variable (IFA). The RCS model applies locally weighted cubic spline smoothing of averaging IFA doses consumed by each student and removes the discreteness

of the number of IFA tablets. This provides a biologic continuum of supplementation for capturing corresponding changes in hemoglobin concentration which is also continuous. Four knots at the fifth, thirty-fifth, sixty-fifth, and ninety-fifth percentiles were automatically chosen. The number of knots was based on literature suggesting that four knots provides the RCS model with enough flexibility to represent the relationship without overfitting.⁽⁴¹⁾ Still, the smoothness of models with three and five knots were compared before settling on the 4-knot model. Finally, we calculated a cut-point for the minimum effective number of IFA tablets associated with anemia reduction over one school year using a receiver operating characteristic (ROC) curve analysis. The GIFTS program protocol was based on strong guidance from the WHO; however, logistical, socio-ecological, and financial barriers often prevent complete intake adherence in real-world settings. Additionally, the context-specific etiology of anemia means that some countries, namely those with high prevalence of iron and folic acid deficiencies and lower mean Hb, might have greater benefit from IFA tablets. For these reasons, a population-specific cut-point was needed as a benchmark for minimum effective adherence to IFA consumption. This cut-point would be useful to program implementers and policy makers for measuring effectiveness coverage, creating budgets, and planning logistics. The ROC-curve analysis required a theory-based logistic regression model of anemia that was solved for the number of IFA tablets at the point of minimum misclassification. We used a bootstrapped resampling approach with 1,000 iterations to derive this estimate and its percentile-based confidence limits. We chose the bootstrapped approach because it allowed a check of the stability of our estimates in the absence of a separate test sample. For the third manuscript (Chapter 5), we conducted a bottleneck analysis, examining the levels of program coverage and adherence to identify potential program barriers to complete coverage. This helped categorize the areas that may have had downstream effects on adherence to IFA consumption. Addressing bottlenecks is necessary for the full benefit of the program to reach the targeted adolescent girls. We also implemented GLMMs to quantify the difference in the total number of IFA tablets

consumed over one school year associated with school-level and individual-level predictors that were considered barriers or facilitators. Schools were modeled as random effects. The barriers and facilitators identified were specific factors on which to improve the program. Modeling these factors hierarchically enabled an examination of the factors at the school and individual levels, which may have unique advantages and disadvantages. School-level factors may be addressed by targeting specific types of schools, while individual-level factors may require different approaches to address.

Post stratification weighting was used in quantitative analyses based on the enrollment of girls in each school during the corresponding school year. Analyses accounted for the sampling design and adjusted for clustering of the data at the school level. Quantitative analyses were performed in SAS 9.4 (SAS Institute, Cary, NC) and R version 3.5.1. Qualitative analyses were conducted in MAXQDA 2018 (VERBI Software, Berlin).

For the fourth manuscript (Chapter 6), we designed a study to examine further the operational and socioecological features of the program to provide additional data for improving the function of the program nationwide. We conducted a thematic/code-based analysis following pre-specified (deductive) and spontaneous (inductive) themes. This analysis was an iterative process involving listening to recordings, reading transcripts, creating a coding scheme, coding transcripts, altering the coding scheme, coding remaining transcripts, and organizing and summarizing themes. A qualitative approach was chosen for its dual advantages of allowing a deeper and more nuanced understanding of an issue while also eliminating the need for tailored and validated questionnaires for hard to measure phenomenon such as perceptions, attitudes, and beliefs.

2.6: Alternate Study Designs and Analytic Strategies

Each study design and analytic strategy comes with strengths and limitations. Often study designs are chosen based on logistical or financial constraints while maximizing the statistical power and potential

for causal inference. With this in mind, it is important to compare the strengths and limitations of our own study with that of potential alternate study designs and analytic strategies.

Aim 1: To quantify the burden and predictors of anemia among adolescent schoolchildren in Ghana

Plausibility of causal relationships between determinants and anemia would have been enhanced if a longitudinal cohort of healthy girls could have been followed from childhood through adolescence to determine which factors induced anemia. This was not a feasible study design due to the time and resources required, which would not produce timely information for decision making. Making use of the available data, an alternate analytic strategy was to examine the predictors of change in anemia and Hb; however, the study period was short and many of the hypothesized predictors of anemia would not have changed such as socio-economic status, body mass index, or even age. Additionally, the GIFTS program would have influenced the determinants of anemia by the follow-on survey of Phase I. An alternate analysis of the cross-sectional data may have been to combine the boys and girls data. This would have enabled a formal test for interaction by gender. However, because of sufficient biological evidence of sex differences, we hypothesized that the predictors of anemia would be distinct, such as menarche among girls, and built separate models for each.

Aim 2: To measure the impact of weekly IFA supplementation on anemia status and hemoglobin concentrations and quantify the minimum effective number of IFA tablets over one school year for achieving adequacy of hemoglobin concentration in a prospective cohort of Ghanaian adolescent schoolgirls

To evaluate the impact of the program, prospective data was used; however, there was no separate control group. A randomized placebo-controlled trial with a contemporaneous control group randomized at the individual level with an intent-to-treat analysis would have improved causal inference. However, the results would have been tainted because school-level elements of the program

would have contaminated the control group. It would not have not been an effectiveness trial because of special procedures outside of the normal program functioning that would be needed to provide the intervention to some and not others. Similar issues arise with randomization at the school or district level as the goal of this program effectiveness was to evaluate potential impact under real-world conditions. Ethical and governmental considerations also limited the ability to have a control group.

Using the employed cohort design, we could have chosen a one-year follow-up to eliminate the confounding effects of seasonality, but that choice presented several challenges. The first was students transferring schools or terminating their schooling, leading to loss to follow-up (was minimal in this cohort) . This challenge might have been mitigated by serial cross-sectional surveys rather than longitudinal follow-up of the same girls; however, this would have inhibited the ability to conduct analyses of individual change and dose-response, which is most needed in demonstrating biological impact in this population. Secondly, conducting a follow-on survey after the break between school years may have diluted results because the intervention would not be fresh on the minds of respondents.

With the present data, we could have chosen to model the difference in Hb at follow-on rather than a repeated measures model; however, such a simple difference model would not have accounted for changes with covariates. Another alternative GLMM analysis could have used total IFA tablets consumed as a continuous variable with a squared (quadratic) term to account for non-linearity, similar to the model used for the ROC analysis. We felt this model would have been more difficult to interpret because of the complexity of accounting for a squared term in the interpretation of beta values.

For calculation of the minimum effective number of IFA tablets, one could have categorized consumption of IFA into small categories, calculated kappa scores for the ability of each category to classify anemia, and chosen the category with the best kappa score or used another discriminant test such as maximizing sensitivity or specificity.⁽⁴²⁾ The primary limitations of this analytic strategy are its

inability to adjust for potential confounders and dependence on the population prevalence of anemia. The precision of this method would be also limited by the categories chosen and the sample sizes therein.

Aim 3: To determine the barriers and facilitators of uptake and intake adherence of IFA tablets within a school-based integrated nutrition and health promotion program

An alternate analytical method for the barriers and facilitators aim was to examine their relative importance using standardizing regression coefficients. This approach has the advantage of placing measures of association on the same unit-less scale for comparison; however, our approach has the advantage of interpretability as the coefficients are expressed in the number of IFA tablets consumed as well as quantifying the independent nested of a student-within-a school vs. school only effects.

Aim 4: To characterize educators' and parents' perspectives on program uptake and adherence and understand how these factors might be modified to improve the program and promote its sustainability at schools with high compared to low intake adherence during year one and changes over the first two years of the program

For the qualitative analysis, students' perspectives are not first-hand. Though their perspectives were not the primary objective of the study, a useful alternative would have included some primary information from students during the start of Year 3. However, analyses of Year 1 data suggested that school-level factors would be of greater interest for improving adherence, and quantitative data was already collected from students during Year 1. An alternative approach to summarizing the qualitative data would have been a case-based analysis rather than thematic analysis. This approach would make simultaneous use of all the different characteristics of an interviewee while describing his or her views. This approach, however, would make interpretation of the interviews difficult because of their quantity and patterns would be more difficult to identify. Most importantly, our thematic analysis provides useful

operational data for understanding issues, strengths, limitations, and potential solutions that can be used by the Ghana Health Service and Ghana Education Service to improve the program.

References (Chapters 1 and 2)

1. WHO (2017) *Global Accelerated Action for the Health of Adolescents (AA-HA!)*,. no. Licence: CC BY-NC-SA 3.0 IGO. Geneva: World Health Organization.
2. WHO (2001) *Iron deficiency anaemia assessment, prevention, and control: A guide for programme managers*. Geneva: World Health Organization, UNICEF, UNU.
3. Stipanuk MH, Caudill MA (editors) (2013) *Biochemical, physiological, and molecular aspects of human nutrition*, 3rd ed. St. Louis, Missouri: Saunders, an imprint of Elsevier Inc.
4. Wirth JP, Woodruff BA, Engle-Stone R *et al.* (2017) Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr* **106**, 416S-427S.
5. Nguyen PH, Gonzalez-Casanova I, Nguyen H *et al.* (2015) Multicausal etiology of anemia among women of reproductive age in Vietnam. *Eur J Clin Nutr* **69**, 107-113.
6. Chaparro CM, Suchdev PS (2019) Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. *Annals of the New York Academy of Sciences* **1450**, 15-31.
7. Balarajan Y, Ramakrishnan U, Ozaltin E *et al.* (2011) Anaemia in low-income and middle-income countries. *Lancet* **378**, 2123-2135.
8. Kraemer K, Zimmermann MB (editors) (2007) *Nutritional Anemia*. Switzerland: Slight and Life Press.
9. Abdulkareem BO, Adam AO, Ahmed AO *et al.* (2017) Malaria-induced anaemia and serum micronutrients in asymptomatic Plasmodium falciparum infected patients. *Journal of parasitic diseases : official organ of the Indian Society for Parasitology* **41**, 1093-1097.
10. Weatherall DJ (2010) The inherited diseases of hemoglobin are an emerging global health burden. *Blood* **115**, 4331-4336.
11. Hassan TH, Badr MA, Karam NA *et al.* (2016) Impact of iron deficiency anemia on the function of the immune system in children. *Medicine (Baltimore)* **95**, e5395.
12. Ekiz C, Agaoglu L, Karakas Z *et al.* (2005) The effect of iron deficiency anemia on the function of the immune system. *Hematol J* **5**, 579-583.
13. Dawson H, Piñero DJ, Beard JL (1996) Iron metabolism: A comprehensive review. *Nutr Rev* **54**, 295-317.
14. Beard JL (2000) Iron requirements in adolescent females. *J Nutr* **130**, 440S-442S.
15. Otto JM, Montgomery HE, Richards T (2013) Haemoglobin concentration and mass as determinants of exercise performance and of surgical outcome. *Extrem Physiol Med* **2**, 33-33.
16. Haas JD, Brownlie Tt (2001) Iron deficiency and reduced work capacity: A critical review of the research to determine a causal relationship. *J Nutr* **131**, 676S-688S; discussion 688S-690S.
17. Sive A, Berg A, Perez EM *et al.* (2005) Maternal iron deficiency anemia affects postpartum emotions and cognition. *J Nutr* **135**, 267-272.
18. Carter RC, Jacobson JL, Burden MJ *et al.* (2010) Iron Deficiency Anemia and Cognitive Function in Infancy. *Pediatrics* **126**, e427-e434.
19. Kassebaum NJ, Jasrasaria R, Naghavi M *et al.* (2014) A systematic analysis of global anemia burden from 1990 to 2010. *Blood* **123**, 615-624.
20. Lozoff B (2007) Iron deficiency and child development. *Food Nutr Bull* **28**, S560-571.
21. Halterman JS, Kaczorowski JM, Aligne CA *et al.* (2001) Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics* **107**, 1381-1386.
22. Rahman MM, Abe SK, Rahman MS *et al.* (2016) Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr* **103**, 495-504.
23. Townsley DM (2013) Hematologic complications of pregnancy. *Semin Hematol* **50**, 222-231.

24. WHO (2011) *Guideline: Intermittent iron and folic acid supplementation in menstruating women*. no. 9789241502023. Geneva: World Health Organization (WHO).
25. WHO (2011) *Guideline: Intermittent iron supplementation in preschool and school-age children*. Geneva: World Health Organization.
26. Salam RA, Hooda M, Das JK *et al.* (2016) Interventions to improve adolescent nutrition: A systematic review and meta-analysis. *J Adolesc Health* **59**, S29-S39.
27. Das JK, Salam RA, Thornburg KL *et al.* (2017) Nutrition in adolescents: physiology, metabolism, and nutritional needs. *Ann N Y Acad Sci* **1393**, 21-33.
28. Christian P, Smith ER (2018) Adolescent Undernutrition: Global Burden, Physiology, and Nutritional Risks. *Annals of Nutrition and Metabolism* **72**, 316-328.
29. Schneider BC, Dumith Sde C, Lopes C *et al.* (2016) How Do Tracking and Changes in Dietary Pattern during Adolescence Relate to the Amount of Body Fat in Early Adulthood? *PLoS One* **11**, e0149299.
30. Movassagh EZ, Baxter-Jones ADG, Kontulainen S *et al.* (2017) Tracking Dietary Patterns over 20 Years from Childhood through Adolescence into Young Adulthood: The Saskatchewan Pediatric Bone Mineral Accrual Study. *Nutrients* **9**.
31. Bhutta ZA, Lassi ZS, Bergeron G *et al.* (2017) Delivering an action agenda for nutrition interventions addressing adolescent girls and young women: priorities for implementation and research. *Ann N Y Acad Sci* **1393**, 61-71.
32. University of Ghana, GroundWork, University of Wisconsin-Madison *et al.* (2017) *Ghana micronutrient survey 2017*. Accra, Ghana.
33. U.S. Agency for International Development (2018) *Malaria Operational Plan FY 2018. President's Malaria Initiative*. Washington, D.C.: USAID.
34. Ghana Statistical Service - GSS, Ghana Health Service - GHS, ICF International (2015) *Ghana Demographic and Health Survey 2014*. Rockville, Maryland, USA: GSS, GHS, and ICF International.
35. Abdul-Kahad A, Moorthy D, Murphy H (2017) *Reducing Anemia in Ghana: The SPRING approach and lessons learned. Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING) project*. Washington, D.C.: U.S. Agency for International Development (USAID).
36. Global Database on the Implementation of Nutrition Action. Geneva, Switzerland: World Health Organization.
37. World Bank (2020) World Bank Country and Lending Groups. <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups> (accessed April 21, 2020)
38. World Bank (2020) World Development Indicators. https://databank.worldbank.org/views/reports/reportwidget.aspx?Report_Name=CountryProfile&Id=b450fd57&tbar=y&dd=y&inf=n&zm=n&country=GHA (accessed April 21, 2020)
39. UNESCO Institute for Statistics (2019) Enrolment ratios: United Nations Education Scientific and Cultural Organization.
40. Lohman TG, Roche AF, Martorell R (1991) *Anthropometric standardization reference manual*. Abridged ed. Champaign, Ill.: Human Kinetics Books.
41. Harrell Jr FE (2015) *Regression modeling strategies: with applications to linear models, logistic and ordinal regression, and survival analysis*: Springer.
42. Greiner M, Pfeiffer D, Smith RD (2000) Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. *Prev Vet Med* **45**, 23-41.

Chapter 3: Predictors of Anemia among Adolescent Schoolchildren of Ghana

Lucas Gosdin, MPH¹, Katie Tripp, MSc², Abraham B Mahama, MPH³, Kate Quarshie⁴, Esi Foriwa Amoafu⁴, Lilian Selenje, MSc³, Deepika Sharma, MPH⁵, Maria Elena Jefferds, PhD², Andrea J Sharma, PhD^{2,6}, Ralph D Whitehead, Jr., PhD², Parminder S Suchdev, MD^{1,2,8}, Usha Ramakrishnan, PhD^{1,7}, Reynaldo Martorell, PhD^{1,7}, and Yaw Addo, PhD^{1,2†,8}

¹Nutrition and Health Sciences, Laney Graduate School, Emory University; ²Nutrition Branch, Centers for Disease Control and Prevention; ³UNICEF-Ghana; ⁴Ghana Health Service of Ministry of Health, Accra, Ghana; ⁵UNICEF-Headquarters, New York, NY, USA; ⁶U.S. Public Health Service Commissioned Corps, Atlanta, GA; ⁷Hubert Department of Global Health, Rollins School of Public Health, Emory University; ⁸Emory Global Health Institute, Atlanta, GA USA;

Abstract

Anemia is a public health problem in Ghana. We sought to identify factors associated with hemoglobin concentration (Hb) and anemia among school-attending adolescents. We analyzed data from 2,948 adolescent girls and 609 boys (10-19 years) selected from 115 schools from 8 regions of Ghana as a secondary analysis of a program evaluation. We measured Hb, malaria from capillary blood, anthropometry, and used a modified food frequency questionnaire to assess diet. Adjusted multivariable analysis was used to identify predictors of Hb and anemia. The prevalence of anemia, malaria, and geophagy was 24%, 25%, and 24%, respectively, among girls and 13%, 27%, and 6%, respectively, among boys. Girls engaging in geophagy had 53% higher adjusted prevalence of anemia and 0.39 g/dL lower Hb. There were similar results among those who tested positive for malaria (+52% anemia; -0.42 g/dL). Among girls, lower anemia prevalence and higher Hb was associated with consumption of foods rich in heme iron (-22%; +0.18 g/dL), consumption of iron-fortified cereal and beverages consumed with citrus (-50% anemia; +0.37 g/dL), and being overweight (-22% anemia; +0.22 g/dL). Age was positively associated with anemia among girls, but negatively associated among boys. Boys who tested positive for malaria had 0.31 g/dL lower Hb. Boys who were overweight or had obesity and consumed flour products were also more likely to be anemic (119% and 56%, respectively). Factors associated with Hb and anemia may inform anemia reduction interventions among school-going adolescents in Ghana and suggest the need to tailor them uniquely for boys and girls.

Keywords: adolescent nutrition; anemia; gender differences in anemia; determinants of anemia; malaria; geophagy; pica

3.1: Introduction

Adolescence is a period of physiological and psychosocial change during which nutritional needs are changing and new roles and responsibilities are established ^(1,2). Puberty increases nutritional requirements due to accelerated growth and sexual maturation ⁽³⁾. This period of increasing independence and maturity presents an excellent opportunity for intervention to improve nutritional status and establish lasting, positive dietary and health practices ^(2,4,5).

The 2017 Ghana Micronutrient Survey estimated the national prevalence of anemia to be 26.4% among non-pregnant adolescent girls ages 15-19 years, constituting a problem of moderate public health significance ⁽⁶⁾. There are no nationally-representative estimates of anemia prevalence among adolescent boys. There are multiple causes of anemia including micronutrient deficiencies, infection, blood loss, genetic disorders, and malaria ^(7,8). Malaria is linked to anemia by the destruction of erythrocytes and decreased erythropoiesis caused by the malaria parasite ⁽⁹⁾. Monotonous, micronutrient-poor diets are commonly consumed in low- and middle-income countries and also contribute to the burden of anemia ⁽⁸⁾. In Ghana, the practice of pica (consumption of non-food substances) has been widely observed among young women mainly in the form of geophagy, eating soil or clay ^(10,11,12). While the causal direction of the association has not been established, there is a strong association between pica and anemia ^(12,13).

The etiology of anemia is complex and varies widely across populations ^(14,15). We aimed to identify context-specific predictors of hemoglobin concentration (Hb) and anemia among adolescent girls and boys in Ghanaian schools ⁽¹⁶⁾. In September 2017, a baseline survey was conducted at the beginning of the school year in Northern and Volta regions as part of an impact evaluation of Phase I of Girls' Iron-Folic acid Tablet Supplementation (GIFTS) Program ⁽¹⁷⁾. The GIFTS Program is an adolescent health and nutrition education program for adolescent boys and girls, with weekly iron and folic acid supplementation targeting adolescent girls (10-19 years) in Ghana. It is primarily carried out through

schools but also includes health center-based implementation. The national scale-up was carried out in three phases, of which the school-based portions of Phases I and III were evaluated. During the program scale-up, a second baseline was conducted in Upper West, Western, and Western-North regions in September 2019. Data from the two baseline surveys are used in this study to identify key factors associated with anemia among adolescents, which might be applied to tailor the intervention components for the population.

3.2: Methods

Sampling

Phase I was implemented in four of Ghana's ten regions¹ (Brong Ahafo, Northern, Upper East, and Volta). Two of the four Phase I regions (Northern and Volta) were purposively selected. Schools within each of the regions were selected by stratified probability proportional to size sampling⁽¹⁷⁾. Stratified sampling between junior high schools (JHS) and senior high schools (SHS) or equivalent was conducted from each region. Schools were treated as clusters and their size was estimated from the previous year's enrollment. The total primary sampling units (schools) were 837 JHS and 68 SHS in Northern region and 1,225 JHS and 104 SHS in Volta region. Sixty schools were selected: 30 from each region, 15 from each stratum (JHS/SHS). Simple random sampling was then followed to select 29 girls from forms 1 and 2 within each school (equivalent to grades 7, 8, 10, and 11 in the North American system). Phase III was implemented in Upper West, Western, and Western-North regions. Schools from each region were sampled following the same methodology as Phase I. Within these three regions, the total primary sampling units (schools) were 2,131 JHS and 180 SHS; 55 schools (29 JHS and 26 SHS) were selected. Within each school, 31 girls and 13 boys in forms 1 and 2 were randomly selected.

¹ In December 2018, Ghana's ten regions were divided into 16. Northern became Savannah, Northern, and North East. Volta became Volta and Oti.

Data Collection

Trained interviewers administered a tablet-based electronic questionnaire to each participant. Survey questions pertaining to this analysis included socio-demographic characteristics, anemia knowledge and practices, menarche, iron supplementation, geophagy, and diet.

A mobile laboratory at each school tested Hb using the HemoCue® 301 (Ängelholm, Sweden) and malaria using CareStart™ Rapid Diagnostic Test (AccessBio, New Jersey, USA). From the finger of each participant, capillary blood was collected. The first drop was wiped clean. During Phase I, the subsequent 2-3 drops of blood were collected onto parafilm. The first portion of the sample was analyzed immediately for Hb (within 30 seconds of the finger stick), and the malaria diagnostic was performed using the remaining blood. During Phase III, 1 mL of capillary blood was collected into a Microtainer® tube containing an anticoagulant and samples were drawn from the tube for immediate analysis of Hb and malaria infection as described for Phase I. Students testing positive for malaria and those with moderate or severe anemia were referred for treatment.

Standardized anthropometric protocols were used to measure height with a stadiometer (Shorrboard®, Maryland, USA) ⁽¹⁸⁾ and weight with a lightweight electronic digital scale (SECA, Hamburg, Germany).

The Ghana Health Service ethical review board in the Ministry of Health approved this project. The study was exempted by the Emory University Institutional Review Board. CDC determined its role was public health practice. A de-identified dataset was used for this secondary analysis.

Variable Definitions

The main outcomes of this analysis were Hb and anemia. Anemia was defined using age- and gender-specific Hb cut-off values (Children 10-11 years: Hb <11.5 g/dL; Girls ≥ 12 years and boys 12-14 years: Hb <12 g/dL; Boys ≥ 15 years: Hb <13 g/dL) ⁽¹⁹⁾. Hb was not adjusted for altitude or smoking status as no

adjustment is needed for populations living below 1000 meters above sea level ⁽¹⁹⁾, and smoking is rare among adolescents in Ghana ⁽²⁰⁾. Body mass index (BMI)-for-age z-scores (BAZ) were calculated based on the International Obesity Taskforce reference parameters, and cut-offs for thinness, overweight, and obesity were applied (thinness: BAZ <-2, overweight: BAZ >+1, and obesity: BAZ >+2) ^(21,22). Normal weight and thin categories were subsequently combined for all students due to prevalence of thinness <1%, and for boys, overweight and obesity were also combined due to prevalence of obesity <1%. Wealth tertiles were calculated following principal components analysis of household possessions ⁽²³⁾. Age in years, reached menarche (yes/no), consumption of an iron-containing supplement (iron, iron and folic acid, or multiple micronutrient supplement) in the previous 7 days (yes/no), and “sometimes” eating soil or clay (geophagy; yes/no) were self-reported. We divided respondents into 3 categories based on their anemia knowledge: 1) never heard of anemia, 2) only heard of anemia but no knowledge of causes, prevention, or symptoms, and 3) heard of anemia, and knowledge of any causes, prevention, or symptoms.

Dietary intake was assessed using a modified food frequency questionnaire with a 24-hour recall period. Grouping of foods was done based on iron content and bioavailability ⁽²⁴⁾. Rich sources of heme iron included red meats and organ meats. Fair sources of heme iron included white meats/poultry, eggs, and fish. Non-heme iron sources included dark green leafy vegetables, legumes, and seeds. We created a separate category for fortified cereals and beverages, and another category for wheat flour products. Fortified cereals and beverages included commonly sold products with an iron fortificant on the nutrition label. Although mandatory, wheat flour fortification is poor; only 13% of samples in a 2011 survey were fortified to the required standard.⁽²⁵⁾ Accordingly, we did not group wheat flour products with fortified foods and beverages. The two final categories considered were tea and citrus fruits.

Analytical methods

Means, proportions, and their 95% confidence intervals (95% CI) were calculated as descriptive statistics. Rao-Scott chi-square test and ANOVA with Taylor series variance were used to test for differences in characteristics between girls across the five regions and between boys and girls within Upper West, Western, and Western-North regions. Rao-Scott chi-square tests were used to assess bivariate differences in anemia prevalence by malaria status, geophagy, and key dietary variables, stratified by gender.

We assessed associations between Hb and adolescent-level factors such as malaria and dietary practices with multivariable linear regression models. Separate models were built for boys and girls. A priori selection of model covariates was based on theoretical considerations. These variables were age, BMI, menarche (for girls), iron supplementation, socioeconomic status, diet, malaria, and geophagy^(12,15,26,27). We also quantified associations at the lower tail of Hb distributions by examining anemia prevalence. Poisson models with a log link function were used to estimate adjusted prevalence ratios (PR, 95%CI) by the predictors of anemia. Inhibitors and enhancers of non-heme iron absorption are found in tea and citrus fruits, respectively⁽²⁸⁾. We therefore examined how same day tea and citrus consumption could modify the associations between non-heme and fortified foods with Hb. We also examined the interactions between geophagy with diet, region with all variables, and socioeconomic status with diet and geophagy. Only significant interaction terms were retained in the multivariable models.

For all analyses, post-stratification weighting was applied using the school-level enrollment of girls and boys. We used complex survey procedures in all analyses and Taylor series variance estimation was followed. Statistical significance was set at alpha 0.05. All analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC).

3.3: Results

In total, 2,983 girls participated, with an overall response rate of 95.6%. Thirty-five girls older than 19 years were removed from the current analysis. The analytical sample was 2,948 girls, 10 to 19 years of age. The mean age was 14.2 years for JHS girls and 16.8 years among SHS girls, and 93.8% had reached menarche. About 64% of girls had heard of anemia and had knowledge of its causes, prevention, or symptoms; this was highest in Volta and lowest in Northern region. About 5% of girls reported consuming iron-containing supplements. Nearly one quarter of girls reported engaging in geophagy. Most reported that they had eaten a fair source of heme iron (68.5%), a source of non-heme iron (68.3%), and/or a wheat flour product (59.6%) in the previous 24 hours. Dietary variables differed significantly across the surveyed regions. The prevalence of malaria and anemia were nearly equivalent, 24.6% and 23.5%, respectively, although their co-occurrence was only 7.6%. The highest prevalence of malaria was in Northern region (29.6%), while the lowest prevalence was in Western region (15.0%). The prevalence of anemia was not significantly different between any two regions; however, Hb differed significantly by region, being lowest in Volta and Western regions (Table 3.5.1). In total, 615 boys participated in Upper West, Western, and Western-North regions with a response rate of 95.5%. Six were removed for age older than 19 years. The analytical sample was 609 boys, 11 to 19 years of age. Mean age was 14.2 years for JHS boys and 16.9 years for SHS boys. Nearly 62% had heard of anemia and had knowledge of its causes, prevention, or symptoms.

Compared to the 1,427 girls assessed in the same three regions, a lower proportion of boys (13.1%) than girls (21.5%) had anemia ($p < .01$), but boys had a similar prevalence of malaria (26.8%) as girls (22.8%) ($p = 0.27$). More girls engaged in geophagy than boys (19.8% vs. 6.3%, respectively; $p < .01$). Ninety percent of boys were normal weight, while 77.3% of girls were normal weight ($p < .01$). The composition of the diets of boys and girls was similar, except that rich sources of heme iron were consumed by more girls (21.7%) than boys (17.4%) (Figure 3.5.1). Mean Hb was significantly higher among boys than girls

overall in these three regions (boys 14.2 g/dL vs. girls 12.7 g/dL; $p < .01$) and within each of the regions where both genders were surveyed (Figure 3.5.2).

Figure 3.5.3 shows the unadjusted prevalence of anemia according to malaria status, geophagy, and indicators of dietary iron intake. The prevalence of anemia was 9.7 percentage points ($p < .01$) higher among girls with a positive malaria test (30.8% vs 21.1%). Similarly, anemia was 11.4 percentage points ($p < .01$) higher among girls who engaged in geophagy (32.2% vs 20.8%). The prevalence of anemia was 5.5 percentage points ($p = 0.02$) lower among girls who consumed a rich source of heme iron (19.1% vs. 24.6%). Prevalence of anemia among girls did not differ by any other dietary iron intake factors, nor did it vary by other potential confounders including menarche, body mass index, and reported consumption of iron containing supplements in the past week (not shown). Prevalence of anemia also varied by wealth among girls: highest wealth tertile 26.6%, middle 20.1%, and lowest 22.9% ($p = 0.04$; Data not shown). None of these variables were associated with the prevalence of anemia among boys in unadjusted analyses.

Results of a multivariable model examining predictors of Hb are shown in Table 3.5.2. Geophagy was inversely associated with Hb such that girls who reported engaging in the practice had on average 0.39 g/dL lower Hb relative to their peers who do not practice geophagy. Similarly, positive malaria infection status was negatively associated with Hb ($\beta = -0.42$ g/dL). Reported consumption of a rich source of heme iron was associated with higher Hb ($\beta = +0.18$ g/dL) as was reported consumption of an iron-fortified food or beverage with a citrus fruit within 24 hours ($\beta = +0.37$ g/dL); there was a significant interaction between the two foods. Girls who were overweight, relative to those with normal weight or thinness had a higher Hb ($\beta = +0.22$ g/dL). Positive malaria infection status was negatively associated with Hb among boys ($\beta = -0.31$ g/dL). Hb increased 0.35 g/dL for each additional year of age in boys.

Results of a multivariable model examining predictors of anemia are shown in Table 3.5.3. Geophagy was positively associated with anemia such that the prevalence of anemia was 53% higher (Adjusted Prevalence Ratio (aPR) = 1.53) among girls who engaged in the practice. Positive malaria infection status was also associated with anemia (aPR= 1.52). Reported consumption of a rich source of heme iron and an iron-fortified food or beverage with a citrus fruit were respectively associated with a 22% (aPR= 0.78) and 50% (aPR= 0.50) lower prevalence of anemia. Girls who were overweight had a 22% (aPR= 0.78) lower prevalence of anemia relative to girls with normal weight or thinness. There was an average 9% (aPR=1.09) higher prevalence of anemia for each addition year of age, and girls from the highest wealth tertile had a 33% (aPR=1.33) higher prevalence of anemia relative to girls from the lowest wealth tertile. Among boys, only consumption of wheat flour products, body mass index, and age were associated with anemia, controlling for potential confounders. Boys who consumed flour products had a 56% (aPR=1.56) higher prevalence of anemia. Boys who were overweight or had obesity relative to normal weight or thin had a 119% (aPR=2.19) higher prevalence of anemia. There was an average 16% (aPR=0.84) lower prevalence of anemia for each year older a group of boys was.

3.4: Discussion

In Northern, Upper West, Volta, Western, and Western-North regions of Ghana, adolescent schoolgirls have a moderate burden of anemia, above 20% but below 40% ⁽¹⁹⁾. The burden of anemia is somewhat lower among boys but remains a mild public health problem, above 5% but below 20%, in the surveyed regions. Previous population-based surveys had not included boys, girls in early adolescence, or explored predictors of anemia in the secondary school context. However, our findings for girls align with previous analyses of the predictors of anemia among women of reproductive age ⁽²⁹⁾, although the emergence of geophagy as a prevalent predictor of anemia in girls is notable. Since none of the predictors are unique to school-going adolescent girls, these results may be applicable to other adolescents in Ghana. However, our results underscore the need to examine the context-specific

predictors of anemia, since they differed by gender even within the same setting. The significant predictors of mean Hb were also associated with anemia suggesting that these predictors act on the entire distribution rather than only those with already low Hb.

Our results show that nearly 40% of students had no knowledge of the causes, prevention, or symptoms of anemia. While knowledge of anemia did not predict Hb or anemia in this study, it is part of the hypothesized pathway to improved anemia prevention practices, and it highlights the gap in health and nutrition education. Only 5% of girls had taken an iron-containing supplement in the previous 7 days, another opportunity for intervention given the WHO recommendations for supplementation ⁽³⁰⁾.

We also found that diet was associated with Hb and anemia among girls. We chose to separate animal source foods into rich and fair sources of heme iron because of their marked differences in content of highly bioavailable iron ⁽²⁴⁾. Fair sources of heme iron were more commonly eaten, but rich sources of heme iron were associated with improved Hb and anemia status. Because consumption of rich sources of heme iron is low, increased consumption of foods such as red and organ meat may affect Hb and anemia, recognizing access may be a limitation. A difference in the effect of iron-fortified products by same-day consumption of citrus fruits was also observed. Ascorbic acid, found in citrus fruits, reduces iron from its ferric to ferrous form making it an enhancer of non-heme iron absorption ⁽³¹⁾. Given the large proportion of girls and boys who consumed fortified cereals and beverages, promotion of the consumption of citrus may increase the bioavailability of iron in the established diets of Ghanaian schoolchildren.

Although wheat flour fortification policies are in place, reported consumption of wheat flour was not associated with Hb or anemia among girls. It is not likely that they are consuming too little of the wheat flour products as they are common in Ghana – 60% of study participants had consumed them in the previous day. Challenges with adequate fortification of wheat flour may be the reason for this lack of

association as evaluations have shown that most wheat flour in Ghana is not adequately fortified ^(6,25).

Among boys, however, there was significant positive association between consumption of flour products and anemia. Indicators of body mass also had opposite relationships with anemia among girls and boys. Among boys, we hypothesize that increased consumption of nutrient-poor calorie-dense foods such as the breads and pies (categorized as flour products) might be associated with overweight/obesity and displaces better sources of iron and other micronutrients in the diets of boys. We are unsure of the reasons for the observed protective effect of overweight on anemia among girls. Wealth among girls was positively associated with anemia. As a social determinant of health, wealth is often protective; however, wealth may also increase access to packaged foods that are poor sources of micronutrients. Age also had opposite effects on anemia by gender, likely due to the differential effects of puberty on blood loss and testosterone production ⁽³²⁾.

Geophagy presents another potential opportunity for intervention. Approximately one quarter of schoolgirls engaged in geophagy, and this did not differ by school level, region, or socioeconomic status. It did differ significantly by gender with a higher proportion of girls engaging in geophagy than boys. Geophagy, a subset of the practice of pica, is not well understood, and the causal direction of its relationship to anemia has not been established ⁽¹²⁾. It is widely observed among pregnant women in Ghana but less-often studied among adolescents, and its relationship with anemia warrants further study ⁽¹⁰⁾.

Malaria infection was associated with Hb and anemia among girls and with Hb among boys. Ghana is a malaria-endemic country, and the surveys were conducted during September, the peak transmission season ⁽³³⁾. This finding underscores that malaria prevention is an essential part of anemia control in Ghana ⁽³⁴⁾. However, the low co-occurrence of the two conditions indicates that malaria may not be the only driver of anemia in the population, though the anemia may be persist after recovering from malaria.

This study has several strengths. The surveys are representative of adolescents attending school in both late and early adolescence within five regions, and inclusive of students of both genders within three regions. The relatively large sample of girls improves the precision of estimates, and high participation rates reduce the potential for selection bias. This study advances knowledge within an understudied population that is receiving increasing attention concerning health and nutrition ^(3,35).

The study limitations include the cross-sectional design, which hinders the ability to make causal inferences. Due to time and cost constraints, we used an imprecise measure (relative to a 24hr dietary recall or weighted food record) of diet that paid special attention to sources of iron. The method used may not reflect usual dietary intake within the individual ⁽³⁶⁾. We are not able to determine the level of parasitemia load from the malaria rapid diagnostic test nor do we have information about recent treatment, which would have improved the sensitivity of this measure. The present study is also missing potentially important predictors of anemia such as micronutrient deficiencies, inflammation, illness, other parasitic infections and diseases, and blood disorders ^(15,26), which would contribute to a fuller picture of the drivers of anemia in the population. Finally, the present study did not assess out-of-school adolescents. Further investigation is needed to understand if the predictors of anemia and hemoglobin differ for these populations.

Approximately one in four adolescent schoolgirls and 13% of adolescent schoolboys in Ghana had anemia. Malaria infection, geophagy, and consumption of highly bioavailable iron are associated with hemoglobin concentration among adolescent girls in Ghanaian schools. These modifiable factors may be useful targets for strengthening the Ghanaian anemia reduction strategy for adolescent girls. Malaria infection and consumption of wheat flour products were associated with hemoglobin concentration and anemia among schoolboys. Other determinants of anemia including age, wealth, and body mass and their differential effects by gender may be useful for tailoring anemia reduction efforts to reach both adolescent schoolgirls and schoolboys. In the school setting, anemia reduction strategies might include

improving the availability and accessibility of iron-rich foods and enhancers of iron absorption through school feeding programs and on-campus canteens, introducing policies to mandate the use of fortified grains in schools and decrease the availability of nutrient-poor obesogenic foods, increasing the use of mosquito nets in school housing, and improving health education to promote diverse diets, malaria prevention behaviors, and reduce geophagy.

3.5: Figures and Tables

Table 3.5.1: Characteristics of Adolescent Girls in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions

Characteristic	Overall (n=2,948)	Girls					p-value
		Northern (n=754)	Upper West (n=720)	Volta (n=767)	Western (n=343)	Western North (n=364)	
<i>Demographics</i>							
Mean age, years	16.4 (16.2, 16.6)	16.8 (16.5, 17.1)	16.4 (15.9, 16.9)	16.3 (16.0, 16.6)	15.6 (15.2, 16.0)	16.5 (16.0, 17.1)	<.01
Reached menarche, %	93.8 (91.3, 96.3)	94.4 (91.2, 97.5)	91.3 (85.1, 97.6)	95.1 (91.3, 98.9)	92.4 (86.0, 98.8)	95.8 (91.2, 100.0)	0.64
Wealth tertile, %							<.01
High	43.3 (36.4, 50.2)	33.4 (24.5, 42.3)	29.0 (19.0, 39.0)	50.8 (40.5, 61.0)	71.5 (63.3, 79.8)	49.0 (39.8, 58.1)	
Middle	32.3 (29.1, 35.5)	32.7 (26.3, 39.0)	35.4 (29.3, 41.5)	33.0 (28.6, 37.4)	23.3 (18.0, 28.6)	35.6 (29.2, 42.1)	
Low	24.4 (19.4, 29.4)	33.9 (25.2, 42.6)	35.6 (25.7, 45.5)	16.2 (9.8, 22.7)	5.1 (1.2, 9.1)	15.4 (11.1, 19.8)	
<i>Knowledge and Practices</i>							
Anemia Knowledge							<.01
Heard of anemia and knowledge of causes, prevention, or symptoms, %	63.5 (56.7, 70.4)	46.6 (36.3, 56.8)	69.2 (59.8, 78.6)	84.2 (80.2, 88.3)	65.9 (46.2, 85.7)	59.1 (45, 73.2)	
Heard of anemia, no knowledge of causes, prevention, or symptoms, %	18.7 (15.2, 22.3)	25.7 (20.5, 30.9)	18.3 (11.8, 24.8)	7.6 (4.2, 10.9)	20.3 (9.2, 31.3)	19.4 (11.2, 27.6)	
Never heard of anemia, %	17.7 (13.6, 21.9)	27.7 (19.9, 35.6)	12.5 (8, 16.9)	8.2 (4.8, 11.6)	13.8 (4.6, 23)	21.5 (15.2, 27.8)	
Pre-intervention iron supplementation in last 7 days, %	5.2 (3.5, 6.9)	4.9 (1.0, 8.7)	5.3 (1.9, 8.8)	3.8 (1.7, 5.9)	8.0 (3.4, 12.6)	5.6 (3.3, 7.8)	0.56
Sometimes engage in geophagy, %	23.7 (20.5, 26.8)	24.6 (17.8, 31.4)	23.1 (17.3, 28.9)	30.0 (22.6, 37.4)	18.7 (11.0, 26.3)	15.1 (8.4, 21.8)	0.08
<i>Diet, consumed in previous day</i>							
Rich source of heme iron, % ^a	19.2 (15.6, 22.8)	20.6 (14.1, 27.1)	21.9 (9.1, 34.6)	12.4 (8.7, 16.1)	22.7 (17.7, 27.8)	20.0 (16.6, 23.4)	0.21
Fair source of heme iron, % ^b	68.5 (62.0, 75.1)	56.4 (44.3, 68.5)	34.8 (26.8, 42.8)	93.5 (91.2, 95.7)	91.1 (89.1, 93.1)	87.3 (78.1, 96.5)	<.01
Source of non-heme iron, % ^c	68.3 (63.8, 72.7)	63.6 (55.6, 71.6)	78.4 (71.4, 85.3)	71.5 (66.3, 76.6)	58.1 (48.5, 67.6)	70.7 (60.1, 81.3)	<.01
Iron-fortified cereal and beverages, % ^d	44.1 (37.2, 50.9)	36.0 (23.2, 48.7)	47.7 (39.0, 56.4)	49.9 (38.4, 61.4)	43.8 (22.3, 65.3)	50.9 (42.2, 59.6)	0.32
Wheat flour products, % ^e	59.6 (54.4, 64.8)	52.0 (42.8, 61.2)	53.8 (44.2, 63.5)	74.2 (65.0, 83.4)	55.1 (42.2, 68.0)	69.0 (62.4, 75.6)	<.01
Tea, %	13.7 (10.2, 17.1)	21.4 (12.5, 30.3)	17.5 (12.1, 22.8)	8.6 (0.3, 16.9)	3.4 (0.5, 6.4)	6.5 (1.4, 11.5)	<.01
Citrus fruit, % ^f	23.6 (19.7, 27.5)	19.4 (13.4, 25.5)	12.5 (6.2, 18.8)	30.0 (23.7, 36.2)	21.2 (16.1, 26.2)	47.2 (35.5, 59.0)	<.01
<i>Body Composition</i>							
Thin, % ^g	0.8 (0.3, 1.3)	0.6 (0.0, 1.2)	0.3 (0.0, 0.7)	1.5 (0.4, 2.6)	1.3 (0.0, 3.3)	0.2 (0.0, 0.4)	0.11
Normal weight, % ^h	77.2 (74.8, 79.6)	79.0 (73.7, 84.3)	74.1 (70.5, 77.7)	74.3 (67.9, 80.8)	78.5 (75.6, 81.3)	81.8 (78.6, 85.0)	0.15
Overweight, % ⁱ	18.9 (16.7, 21.0)	18.6 (13.7, 23.4)	22.9 (19.6, 26.1)	19.4 (13.8, 25.0)	15.5 (10.4, 20.6)	15.5 (12.7, 18.4)	0.22
Obesity, % ^j	3.0 (2.1, 4.0)	1.9 (0.6, 3.2)	2.3 (1.0, 3.5)	4.7 (2.9, 6.4)	4.8 (2.0, 7.5)	2.4 (0.5, 4.4)	0.02
<i>Biological Measures</i>							
Malaria, %	24.6 (21.4, 27.9)	29.6 (24.9, 34.4)	27.6 (22.3, 32.9)	20.9 (12.5, 29.2)	15.0 (9.7, 20.4)	24.0 (19.1, 28.9)	<.01
Anemia, % ^k	23.5 (20.0, 27.0)	24.5 (16.0, 33.0)	21.2 (17.7, 24.7)	26.0 (19.5, 32.4)	26.6 (21.1, 32.0)	15.6 (12.0, 19.2)	0.19
Co-occurring anemia and malaria	7.6 (5.8, 9.4)	9.4 (5.7, 13.1)	10.0 (7.3, 12.8)	5.7 (2.6, 8.7)	6.1 (1.0, 11.2)	3.4 (1.2, 5.7)	0.08
Mean hemoglobin concentration, g/dL	12.7 (12.6, 12.8)	12.9 (12.6, 13.2)	12.7 (12.5, 12.8)	12.5 (12.4, 12.7)	12.5 (12.3, 12.7)	12.9 (12.8, 13.0)	<.01

Note: Values are weighted. Complex survey procedures used to account for clustering.

^a Red meats and organ meats.

^b White meats/poultry, eggs, and fish.

^c dark green leafy vegetables, legumes, and seeds.

^d Fortified cereals such as Nestle Cerelac and beverages such as Nido and Milo.

^e Breads, pies, and cakes made with wheat flour;

^f Oranges, lemons, sour sap, etc.

^g Body-mass-index for age (BAZ) <-2SD based on International Obesity Taskforce reference parameters.

^h BAZ between -2SD and +1SD; ⁱ BAZ >+1SD; ^j BAZ>+2SD.

^k Anemia defined using age/sex-specific hemoglobin concentration cut-off values (Children 10-11 years: Hb <11.5 g/dL; Girls ≥ 12 years and boys 12-14 years: Hb <12 g/dL; Boys ≥ 15 years: Hb <13 g/dL). There were 14 cases of severe anemia among girls (Hb <8 g/dL).

Table 3.5.2: Adjusted Model of the Predictors of Hemoglobin Concentration among Adolescent Girls and Boys in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions

Characteristic	Girls (n=2,860)		Boys (n=609) [§]	
	Estimate, g/dL (95% CI) ^a	p-value	Estimate, g/dL (95% CI) ^a	p-value
Geophagy	-0.39 (-0.60, -0.18)	<.01	-0.34 (-1.10, 0.42)	0.37
Malaria	-0.42 (-0.56, -0.27)	<.01	-0.31 (-0.60, -0.02)	0.04
Rich source of heme iron ^b	0.18 (0.00, 0.36)	0.05	0.29 (-0.31, 0.90)	0.34
Fair source of heme iron ^c	-0.11 (-0.25, 0.04)	0.15	-0.01 (-0.30, 0.27)	0.92
Source of non-heme iron ^d	0.00 (-0.17, 0.17)	0.98	-0.08 (-0.40, 0.25)	0.63
Iron-fortified cereal and beverages ^e			-0.12 (-0.39, 0.15)	0.38
Consumed with citrus ^f	0.37 (0.09, 0.65)	0.01	-	
Consumed without citrus ^f	-0.08 (-0.23, 0.07)	0.30	-	
Flour products ^g	-0.04 (-0.17, 0.08)	0.48	-0.17 (-0.46, 0.12)	0.24
Normal weight/thin ^h	ref	-	ref	-
Overweight ⁱ	0.22 (0.03, 0.42)	0.03	-0.05 (-0.51, 0.41)	0.83
Obesity ^j	0.10 (-0.16, 0.36)	0.45		
Pre-intervention iron supplementation in last 7 days	-0.19 (-0.58, 0.21)	0.21	0.80 (-0.06, 1.66)	0.07
Age, years	-0.02 (-0.08, 0.03)	0.40	0.35 (0.27, 0.44)	<.01
Menarche	-0.05 (-0.41, 0.31)	0.77	-	
Wealth				
High	-0.18 (-0.40, 0.04)	0.11	-0.11 (-0.40, 0.17)	0.42
Middle	0.07 (-0.12, 0.27)	0.45	-0.01 (-0.33, 0.31)	0.94
Low	ref	-	ref	-

Note: Values are weighted. Complex survey procedures used to account for clustering.

[§] Boys data only available in Upper West, Western, and Western North regions.

^a Hemoglobin concentration (g/dL).

^b Red meats and organ meats.

^c White meats/poultry, eggs, and fish.

^d Dark green leafy vegetables, legumes, and seeds.

^e Fortified cereals such as Nestle Cerelac and beverages such as Nido and Milo.

^f Oranges, lemons, sour sap, etc. interaction with iron-fortified foods.

^g Breads, pies, and cakes made with wheat flour.

^h Body-mass-index for age (BAZ) <+1SD based on International Obesity Taskforce reference parameters.

ⁱ BAZ >+1SD; ^j BAZ >+2SD. Overweight and obesity were merged for boys due to a very low proportion with obesity (<1%).

Table 3.5.3: Adjusted Model of the Predictors of Anemia among Adolescent Girls and Boys in Ghanaian Schools in Northern, Upper West, Volta, Western, and Western North Regions

Characteristic	Girls (n=2,860)		Boys (n=609) [§]	
	Prevalence Ratio (95% CI) ^a	p-value	Prevalence Ratio (95% CI) ^a	p-value
Geophagy	1.53 (1.26, 1.85)	<.01	1.62 (0.51, 5.18)	0.42
Malaria	1.52 (1.27, 1.82)	<.01	1.39 (0.87, 2.21)	0.17
Rich source of heme iron ^b	0.78 (0.63, 0.97)	0.02	0.66 (0.30, 1.45)	0.30
Fair source of heme iron ^c	1.15 (0.97, 1.36)	0.10	1.00 (0.49, 2.04)	0.99
Source of non-heme iron ^d	1.13 (0.90, 1.42)	0.29	1.18 (0.67, 2.07)	0.57
Iron-fortified cereal and beverages ^e			1.06 (0.59, 1.93)	0.84
Consumed with citrus ^f	0.50 (0.31, 0.81)	<.01	-	
Consumed without citrus ^f	1.13 (0.95, 1.33)	0.17	-	
Flour products ^g	0.9 (0.79, 1.03)	0.11	1.56 (1.00, 2.42)	0.05
Normal weight/thin ^h	ref	-	ref	-
Overweight ⁱ	0.78 (0.62, 0.98)	0.03	2.19 (1.03, 4.66)	0.04
Obesity ^j	1.03 (0.68, 1.55)	0.91		
Pre-intervention iron supplementation in last 7 days	1.13 (0.75, 1.68)	0.56	0.56 (0.06, 4.99)	0.61
Age, years	1.09 (1.01, 1.16)	0.02	0.84 (0.72, 0.99)	0.03
Menarche	0.88 (0.59, 1.32)	0.54	-	
Wealth				
High	1.33 (1.04, 1.70)	0.03	0.87 (0.48, 1.59)	0.66
Middle	0.93 (0.73, 1.19)	0.56	0.83 (0.43, 1.62)	0.59
Low	ref	-	ref	-

Note: Values are weighted. Complex survey procedures used to account for clustering.

[§] Boys data only available in Upper West, Western, and Western North regions.

^a Hemoglobin concentration (g/dL).

^b Red meats and organ meats.

^c White meats/poultry, eggs, and fish.

^d Dark green leafy vegetables, legumes, and seeds.

^e Fortified cereals such as Nestle Cerelac and beverages such as Nido and Milo.

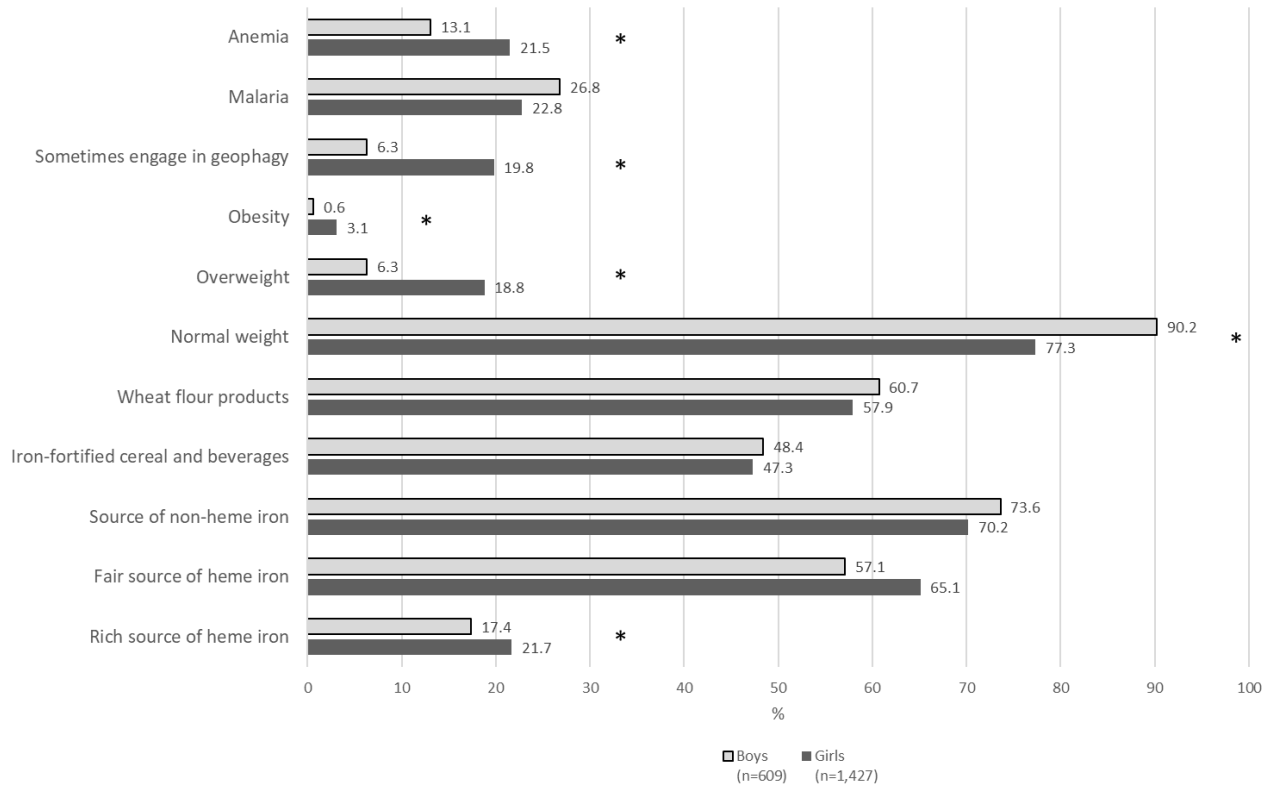
^f Oranges, lemons, sour sap, etc. interaction with iron-fortified foods.

^g Breads, pies, and cakes made with wheat flour.

^h Body-mass-index for age (BAZ) <+1SD based on International Obesity Taskforce reference parameters.

ⁱ BAZ >+1SD; ^j BAZ >+2SD. Overweight and obesity were merged for boys due to a very low proportion with obesity (<1%).

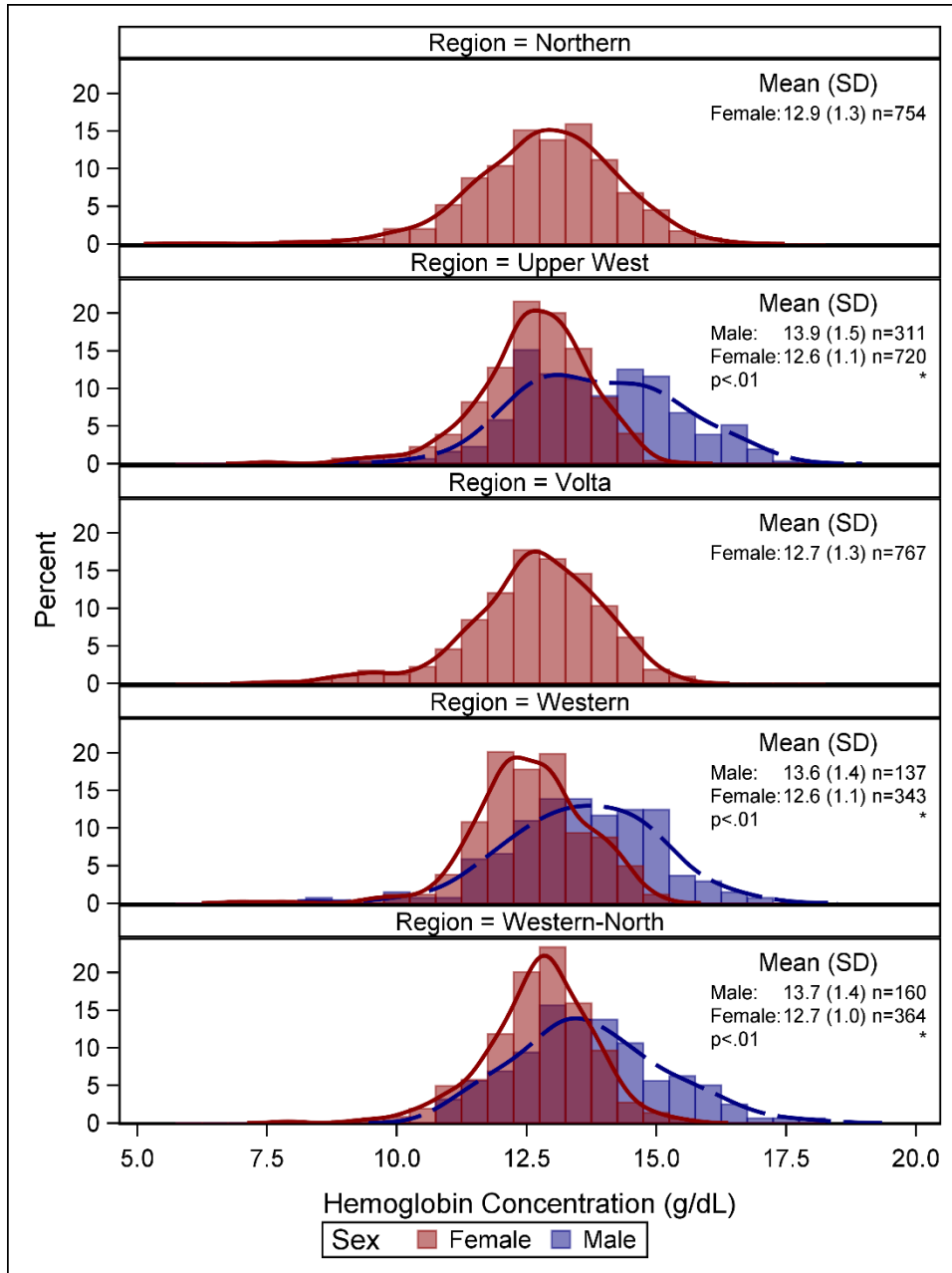
Figure 3.5.1: Characteristics of Adolescent Girls and Boys in Ghanaian Schools in Upper West, Western, and Western North Regions



Note: *p<.05. Values are weighted. Complex survey procedures used to account for clustering. Data for boys only available for Upper West, Western, and Western-North regions.

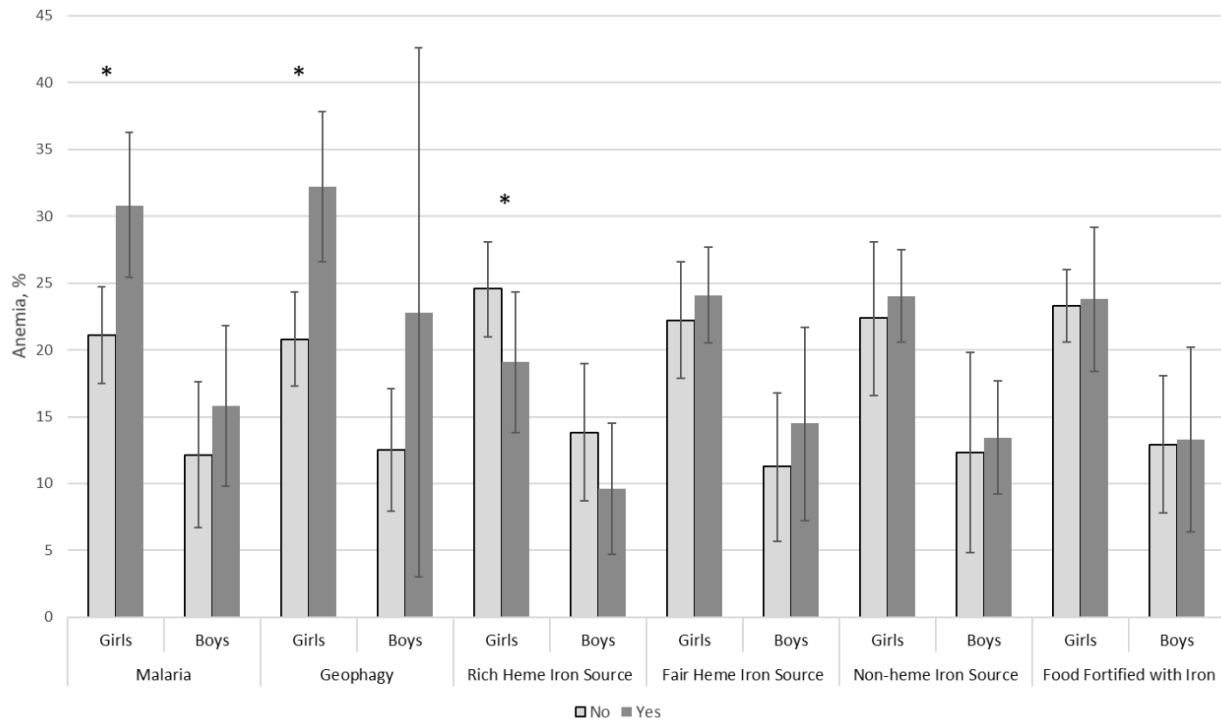
Rich sources of heme iron included red meats and organ meats; Fair sources of heme iron included white meats/poultry, eggs, and fish; Sources of non-heme iron included dark green leafy vegetables, legumes, and seeds; Fortified foods included cereals such as Nestle Cerelac and beverages such as Nido and Milo; Anemia was defined using age/sex-specific hemoglobin concentration cut-off values (Children 10-11 years: Hb <11.5 g/dL; Girls ≥ 12 years and boys 12-14 years: Hb <12 g/dL; Boys ≥ 15 years: Hb <13 g/dL).

Figure 3.5.2: Distribution of Hemoglobin Concentration among Adolescent Girls and Boys in Ghanaian Schools by Region (n=2,948)



Note: Unweighted descriptive statistics and histograms. * $p < .01$. Complex survey procedures and weights used to account for clustering in testing the differences in mean hemoglobin concentration between girls and boys.

Figure 3.5.3: Unadjusted Prevalence of Anemia among Adolescent Girls and Boys in Ghanaian Schools by Malaria, Geophagy, and Selected Dietary Variables, Northern, Upper West, Volta, Western, and Western North Regions (n=2,948)



Note: *p<.05. Values are weighted. Complex survey procedures used to account for clustering. Data for boys only available for Upper West, Western, and Western-North regions.

Rich sources of heme iron included red meats and organ meats; Fair sources of heme iron included white meats/poultry, eggs, and fish; Sources of non-heme iron included dark green leafy vegetables, legumes, and seeds; Fortified foods included cereals such as Nestle Cerelac and beverages such as Nido and Milo; Anemia was defined using age/sex-specific hemoglobin concentration cut-off values (Children 10-11 years: Hb <11.5 g/dL; Girls ≥ 12 years and boys 12-14 years: Hb <12 g/dL; Boys ≥ 15 years: Hb <13 g/dL).

References (Chapter 3)

1. Patton GC, Sawyer SM, Santelli JS, Ross DA, Afifi R, Allen NB, Arora M, Azzopardi P, Baldwin W, Bonell C, et al. Our future: a Lancet commission on adolescent health and wellbeing. *Lancet*. 2016;387(10036):2423-78.
2. Das JK, Salam RA, Thornburg KL, Prentice AM, Campisi S, Lassi ZS, Koletzko B, Bhutta ZA. Nutrition in adolescents: physiology, metabolism, and nutritional needs. *Ann N Y Acad Sci*. 2017;1393(1):21-33.
3. Bhutta ZA, Lassi ZS, Bergeron G, Koletzko B, Salam R, Diaz A, McLean M, Black RE, De-Regil LM, Christian P, et al. Delivering an action agenda for nutrition interventions addressing adolescent girls and young women: priorities for implementation and research. *Ann N Y Acad Sci*. 2017;1393(1):61-71.
4. Schneider BC, Dumith Sde C, Lopes C, Severo M, Assuncao MC. How Do Tracking and Changes in Dietary Pattern during Adolescence Relate to the Amount of Body Fat in Early Adulthood? *PLoS One*. 2016;11(2):e0149299.
5. Movassagh EZ, Baxter-Jones ADG, Kontulainen S, Whiting SJ, Vatanparast H. Tracking Dietary Patterns over 20 Years from Childhood through Adolescence into Young Adulthood: The Saskatchewan Pediatric Bone Mineral Accrual Study. *Nutrients*. 2017;9(9).
6. University of Ghana, GroundWork, University of Wisconsin-Madison, KEMRI-Wellcome Trust, UNICEF. Ghana micronutrient survey 2017. Accra, Ghana; 2017.
7. 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):2607-17.
8. Balarajan Y, Ramakrishnan U, Ozaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. *Lancet*. 2011;378(9809):2123-35.
9. Mohandas N, An X. Malaria and human red blood cells. *Medical microbiology and immunology*. 2012;201(4):593-8.
10. Mensah FO, Twumasi P, Amenawonyo XK, Larbie C, Jnr AKB. Pica practice among pregnant women in the Kumasi metropolis of Ghana. *International Health*. 2010;2(4):282-6.
11. Abu BAZ, van den Berg VL, Raubenheimer JE, Louw VJ. Pica Practices among Apparently Healthy Women and Their Young Children in Ghana. *Physiol Behav*. 2017;177:297-304.
12. Miao D, Young SL, Golden CD. A meta-analysis of pica and micronutrient status. *American Journal of Human Biology*. 2014;27(1):84-93.
13. Borgna-Pignatti C, Zanella S. Pica as a manifestation of iron deficiency. *Expert Rev Hematol*. 2016;9(11):1075-80.
14. Canete A, Cano E, Munoz-Chapuli R, Carmona R. Role of Vitamin A/Retinoic Acid in Regulation of Embryonic and Adult Hematopoiesis. *Nutrients*. 2017;9(2).
15. Nguyen PH, Gonzalez-Casanova I, Nguyen H, Pham H, Truong TV, Nguyen S, Martorell R, Ramakrishnan U. Multicausal etiology of anemia among women of reproductive age in Vietnam. *European journal of clinical nutrition*. 2015;69(1):107-13.
16. Petry N, Olofin I, Hurrell RF, Boy E, Wirth JP, Moursi M, Donahue Angel M, Rohner F. The Proportion of Anemia Associated with Iron Deficiency in Low, Medium, and High Human Development Index Countries: A Systematic Analysis of National Surveys. *Nutrients*. 2016;8(11).
17. Ghana Health Service, Ghana Education Service, UNICEF-Ghana, Emory University Global Health Institute, Centers for Disease Control and Prevention (CDC). Impact evaluation of a school-based integrated adolescent nutrition and health Programme with Iron and Folic-Acid supplementation intervention among adolescent girls in Ghana. Cantonments, Accra Ghana: UNICEF-Ghana; 2019.
18. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Abridged ed. Champaign, Ill.: Human Kinetics Books; 1991. vi, 90 p. p.

19. World Health Organization (WHO). Iron deficiency anaemia assessment, prevention, and control: A guide for programme managers. Geneva: WHO, UNICEF, UNU; 2001.
20. Mamudu HM, Veeranki SP, John RM. Tobacco use among school-going adolescents (11-17 years) in Ghana. *Nicotine Tob Res.* 2013;15(8):1355-64.
21. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ.* 2000;320(7244):1240-3.
22. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ (Clinical research ed).* 2007;335(7612):194-.
23. Vyas S, Kumaranayake L. Constructing socio-economic status indices: How to use principal components analysis. *Health Policy Plan.* 2006;21(6):459-68.
24. Stadlmayr B, Charrondiere UR, Enujiugha VN, Bayili RG, Fagbohoun EG, Samb B, Addy P, Barikmo I, Ouattara F, Oshaug A, et al. West African Food Composition Table. Rome: Food and Agriculture Organization of the United Nations (FAO); 2012.
25. Nyumuah RO, Hoang TC, Amoafu EF, Agble R, Meyer M, Wirth JP, Locatelli-Rossi L, Panagides D. Implementing large-scale food fortification in Ghana: lessons learned. *Food Nutr Bull.* 2012;33(4 Suppl):S293-300.
26. Wirth JP, Woodruff BA, Engle-Stone R, Namaste SM, Temple VJ, Petry N, Macdonald B, Suchdev PS, Rohner F, Aaron GJ. Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr.* 2017;106(Suppl 1):416S-27S.
27. Carpenter CE, Mahoney AW. Contributions of heme and nonheme iron to human nutrition. *Critical Reviews in Food Science and Nutrition.* 1992;31(4):333-67.
28. Zijp IM, Korver O, Tijburg LBM. Effect of Tea and Other Dietary Factors on Iron Absorption. *Critical Reviews in Food Science and Nutrition.* 2000;40(5):371-98.
29. SPRING, Ghana Health Service. Ghana: Landscape Analysis of Anemia and Anemia Programming. Arlington, VA: Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING) project; 2016.
30. World Health Organization (WHO). Guideline: Intermittent iron and folic acid supplementation in menstruating women. Geneva: WHO; 2011. Report No.: 9789241502023.
31. Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. *Int J Vitam Nutr Res.* 2004;74(6):403-19.
32. Shahani S, Braga-Basaria M, Maggio M, Basaria S. Androgens and erythropoiesis: past and present. *J Endocrinol Invest.* 2009;32(8):704-16.
33. U.S. Agency for International Development. Malaria Operational Plan FY 2018. Washington, D.C.: USAID; 2018.
34. Abdul-Kahad A, Moorthy D, Murphy H. Reducing Anemia in Ghana: The SPRING approach and lessons learned. Washington, D.C.: U.S. Agency for International Development (USAID); 2017.
35. Christian P, Smith ER. Adolescent Undernutrition: Global Burden, Physiology, and Nutritional Risks. *Annals of Nutrition and Metabolism.* 2018;72(4):316-28.
36. Gibson RS. Principles of nutritional assessment. 2nd ed. New York: Oxford University Press; 2005.

Chapter 4: A School-Based Weekly Iron and Folic Acid Supplementation Program is Effective at Reducing Anemia in a Prospective Cohort of Ghanaian Adolescent Girls

Lucas Gosdin, MPH^{1,2}, Andrea J Sharma, PhD^{2,3}, Katie Tripp, MSc², Esi Foriwa Amoafu, MSc⁴, Abraham B Mahama, MPH⁵, Lilian Selenje, MSc⁵, Maria Elena Jefferds, PhD², Reynaldo Martorell, PhD^{1,6}, Usha Ramakrishnan, PhD^{1,6}, and O. Yaw Addo, PhD^{1,2,7}

¹Nutrition and Health Sciences, Laney Graduate School, Emory University, 1518 Clifton Rd. Atlanta, GA, USA; ²Nutrition Branch, Centers for Disease Control and Prevention, 4770 Buford Hwy, Atlanta, GA, USA;

³U.S. Public Health Service Commissioned Corps, Atlanta, GA; ⁴Ghana Health Service of Ministry of Health, PO Box M44, Ministries, Accra, Ghana; ⁵UNICEF-Ghana, 4-8th Rangoon Close, Cantonments, Accra, Ghana; ⁶Hubert Department of Global Health, Rollins School of Public Health, Emory University;

⁷Emory Global Health Institute, Atlanta, GA USA;

Abstract

Background: School-based iron and folic acid (IFA) supplementation is recommended for adolescent girls in countries with high burdens of anemia; however, there is insufficient evidence of its context-specific effectiveness.

Methods: Using data from a pre-post, longitudinal design, we evaluated the effectiveness of school-based weekly IFA supplementation in reducing the burden of anemia and increasing hemoglobin concentration (Hb) in two regions of Ghana. Generalized linear mixed effects models (GLMM) with schools (clusters) as random effects were used to quantify the change in anemia prevalence difference and mean Hb difference associated with cumulative IFA tablet consumption over one school year, controlling for participant-level potential confounders. A cut-point for minimum effective cumulative IFA consumption that is reflective of adequate Hb was derived following receiver operating characteristic curve analysis. This cut-point was verified by a restricted cubic spline model of IFA consumption and Hb.

Findings: The analytical sample included 60 schools and 1,387 girls ages 10-19 years. The prevalence of anemia declined during one school year of the intervention from 25.1% to 19.6%. Students consumed a mean of 16.4 IFA tablets (range: 0-36). IFA consumption was positively associated with Hb and negatively associated with anemia. On average, each additional IFA tablet consumed over the school year was associated with a 5% reduction in the adjusted odds of anemia at follow-on, though the relationship is non-linear. The cut-point for minimum effective consumption was 26.3 tablets.

Interpretation: School-based weekly IFA supplementation is effective in improving Hb and reducing anemia prevalence among schoolgirls in Ghana, though most participants consumed fewer than the minimum effective number of IFA tablets. Increasing intake adherence may further improve anemia outcomes in this population.

Funding: This evaluation was funded by a cooperative agreement between UNICEF and the U.S. Centers for Disease Control and Prevention.

4.1: Background

Globally, iron deficiency anemia is a leading cause of morbidity and mortality among adolescent girls 10-19 years of age.⁽¹⁾ Anemia is defined by a low circulating hemoglobin concentration, a protein critical to the transport of oxygen.⁽²⁾ Anemia has negative consequences in the short term such as reduced immune function,⁽³⁾ aerobic capacity,⁽⁴⁾ and metabolism,⁽⁵⁾ which can lead to increased illnesses, lethargy, fatigue, and lack of concentration.⁽⁶⁾ Total body hemoglobin in the low-normal range but without anemia is associated with decreased maximal oxygen uptake (VO₂Max).⁽⁷⁾ In the intermediate and long term, iron deficiency anemia is associated with reduced work capacity⁽⁸⁾ and cognition,⁽⁹⁾ which can lead to reduced human capital⁽⁶⁾ and lost academic potential.⁽¹⁰⁾ Anemia during pregnancy can lead to poor outcomes such as hemorrhage, preterm birth, low birth weight, perinatal mortality, and neonatal mortality.⁽¹¹⁾

Anemia has a complex and context-specific etiology.⁽¹²⁾ Blood disorders, micronutrient deficiencies, parasitic infections including helminths and malaria, overweight/obesity, and blood loss all contribute to the burden of anemia throughout the world.^(6,13) In Ghana, adolescents carry a high burden of micronutrient deficiencies related to anemia. For example in the national micronutrient survey conducted in 2017, 26% of girls 15-19 years old suffered from anemia, 15% had iron deficiency anemia, and 57% had folate deficiency.⁽¹⁴⁾ Our 2019 survey of in-school adolescents in three regions found that the prevalence of anemia among girls 10-19 years of age was 22%, significantly higher than the prevalence among boys of the same age (13%).

Schools have been identified as important delivery platforms for nutrition interventions among adolescents.⁽¹⁵⁾ A recent meta-analysis showed that supplementation with iron and folic acid (IFA) tablets through schools is effective in reducing the prevalence of anemia among adolescent girls, using data from 15 studies and from 7 different countries.⁽¹⁶⁾ The World Health Organization (WHO)

recommends intermittent IFA supplementation to all women during pregnancy and to women of reproductive age (15-49 years of age), including adolescents and to school aged children (5-12 years of age), where the prevalence of anemia exceeds 20%.^(17,18) However, few countries with high rates of anemia have a program in place for adolescents, and the African continent has very limited experience with this type of program.⁽¹⁹⁾ Schools may be an effective delivery platform in Ghana since secondary school attendance has been increasing. In 2018, nearly half of girls 12-14 years (49%) were enrolled in junior high school, and 30% of girls 15-17 years were enrolled in senior high schools, up from 25% in 2016. With free public senior high school introduced in 2017, enrollment is expected to further increase.

Intervention

The Girls' Iron-Folic Acid Tablet Supplementation (GIFTS) Program is an integrated health and nutrition education program with IFA supplementation for the control of anemia among adolescent girls in Ghana. The program was rolled out in three phases. At the beginning of the school year in September/October 2017, Phase I of the program began in four of Ghana's ten regions:^b Brong-Ahafo, Northern, Upper East, and Volta.

The main delivery platform for the intervention is junior high, senior high, and technical/vocational schools. Though the program follows the WHO recommendations, benchmarks for program adherence have not been evaluated. There is a dose-response relationship between IFA supplementation and hemoglobin concentration; however, because of the down-regulation of iron absorption in iron repletion,⁽²⁰⁾ there may be a point at which this relationship plateaus and could be interpreted as a minimum effective number of weekly IFA tablets needed for adequate Hb as defined by anemia cut-offs in this population. This could be used as a program metric for determining effective adherence.

^b In December 2018, Ghana's ten regions were divided into 16. Northern became Savannah, Northern, and North East. Volta became Volta and Oti.

We hypothesize that routine weekly supplementation with IFA in schools improves hemoglobin concentration and reduces anemia among adolescent schoolgirls in Ghana. This study aims to measure the effectiveness of weekly school-based IFA supplementation on anemia status and Hb and determine a minimum effective number of weekly IFA tablets over one school year associated with a reduction in anemia prevalence in a prospective cohort of Ghanaian adolescent schoolgirls.

4.2: Methods

Study Design and Setting

An evaluation was designed as a pre-post, longitudinal study with a cohort of girls and schools from two of the Phase I regions, nested within the implementation of the GIFTS Program over one school year. In schools, all students received regular health and nutrition education sessions. This included key messages about anemia risk factors, the consequences of anemia, prevention of anemia, prevention of malaria, water, sanitation, and consumption of an iron-rich and diverse diet. Educators also provided counseling and key messages on the use and benefits of IFA tablets. Additionally, adolescent girls received weekly supplementation with an IFA tablet containing 182.4mg ferrous fumarate (60mg of elemental iron) and 0.40mg folic acid through directly observed therapy. IFA tablets were given on a single day of the week, but schools were instructed to provide a makeup opportunity to girls who were absent on distribution day. Weekly IFA consumption data were recorded for each adolescent girl into a classroom register over the school year (30-36 school weeks).

For the nested evaluation, Volta and Northern regions were purposively selected. Within each region, 15 junior high schools (JHS) and 15 senior high schools (SHS) or technical/vocational schools were selected using probability proportional to size sampling from a list of all schools (public and private) and their previous year's enrollment of girls. The total primary sampling units (schools) were 837 JHS and 68 SHS in Northern region and 1,225 JHS and 104 SHS in Volta region. Sixty (60) total schools were selected. To

detect a 10% minimum reduction based on an estimated background prevalence rate of 40% anemia at a fixed power of 80%, a 2-sided 95% significance level a sample of 1,552 was required. At the beginning of the 2017-2018 school year, 29 girls in each school were selected using simple random sampling. After approximately 9 months, at the end of the school year, participating girls were followed up.

Questionnaires were recorded and administered by trained enumerators using tablet-based electronic data collection. Questionnaires consisted of demographic characteristics, a food frequency questionnaire, and knowledge, attitudes, and practices related to anemia and IFA. Food frequency was assessed over the previous 24 hours using a modified food frequency questionnaire emphasizing sources of dietary iron.⁽²¹⁾ Height and weight were collected following standard anthropometric methods.⁽²²⁾ Capillary blood was used to measure hemoglobin concentration using a HemoCue® 301 (Ängelholm, Sweden) and malaria antibodies using the CareStart™ Rapid Diagnostic Test (AccessBio, New Jersey, USA). Girls testing positive for malaria or with moderate-severe anemia were referred for treatment at local health centers. During the follow-on survey, the total number of IFA tablets consumed by each selected girl was abstracted for each term from class IFA registers and additional data on program experiences were collected from students and teachers.

Study Variables

Household wealth was calculated following principal components analysis of household assets and divided into tertiles. The school was classified as rural, peri-urban, or urban using national census data. Food frequency data were categorized based on iron content or relevant interactions.⁽²³⁾ Rich sources of heme iron included red meats and organ meats. Fair sources of heme iron included white meats such as poultry and pork, fish, and eggs. Rich sources of non-heme iron included dark green leafy vegetables and legumes. Foods and beverages fortified with iron included locally available cereals and beverages marketed as fortified with an iron fortificant on the label. Wheat flour fortification in Ghana is poor; only

13% of samples in a 2011 survey were fortified to the required standard.⁽²⁴⁾ Accordingly, we did not group wheat flour products with fortified foods and beverages. Benchmarks set by stakeholders were used to describe coverage and intensity of the intervention: 1) taking at least one IFA tablet and 2) taking at least 10 IFA tablets over the school year. The cumulative number of IFA tablets consumed was categorized within each term and over the school year.

BMI-for-age z-scores (BMIZ) were calculated following International Obesity Taskforce age-specific parameters, and cut-offs for thinness (BMIZ < -2), overweight (+1 < BMIZ ≤ +2), and obesity (BMIZ > +2) were applied.⁽²⁵⁾ The small proportion with thinness (<1%) was grouped with normal weight for further analyses. Malaria results were dichotomized as positive or negative. Participants with hemoglobin concentrations (Hb) <10 g/dL or a positive malaria result were referred for treatment at their local health facility. Anemia was defined using age-specific Hb cut-off values (10-11 years: Hb <11.5 g/dL; ≥ 12 years: Hb <12 g/dL).⁽²⁾ No adjustment for altitude or smoking was performed since all populations lived at elevations below 1000 meters⁽²⁾ and smoking is extremely rare among adolescent girls in Ghana.⁽²⁶⁾

Statistical Analysis

Confidence intervals and p-values for comparisons of continuous data were calculated using complex survey procedures with Taylor series variance, where appropriate. Rao-Scott chi-square tests were used to test for differences in proportions. Mean and prevalence differences were calculated between baseline and follow-on for health and dietary characteristics of study participants. To understand the factors that influenced the change in hemoglobin concentration and anemia, adjusted differences in the change in anemia prevalence and hemoglobin concentration were calculated from population margins of generalized linear mixed effects models (GLMM) using maximum likelihood estimation and accounted for clustering at the school-level as random effects. Adjusted models included the cumulative number of IFA tablets consumed over one school year and potential confounders including demographics (age and

wealth tertile), school characteristics (level and rurality), health (malaria, BMI category, and geophagy), and diet (sources of iron and citrus) as fixed effects. Repeated measures (both baseline and follow-on) were used for health and dietary variables. Categories of cumulative IFA consumption were based on program targets of a minimum of 10 weeks of supplementation for the school year; therefore, groups of 10 IFA were used to capture gradations of consumption. The 1-10 group was the reference group for multivariable analysis because of a more robust sample size in comparison to the zero-dose group. Collinearity was assessed by variance inflation factor after which menarche was excluded as a covariate for collinearity with age. We examined effect modification between cumulative IFA tablets consumed and the change in anemia prevalence difference by other model covariates.

To separate the potential treatment and prevention effects of IFA supplementation from a usual temporal changes in Hb concentration over an 8-month window for adolescents, we conducted a sensitivity analysis categorizing the change in anemia status in four groups: 1) prevention, 2) treatment, 3) sustained anemia, 4) developed anemia. Prevention was defined as having no anemia at baseline and follow-on. Treatment was defined as having anemia at baseline and not at follow-on. Sustained anemia was defined as having anemia at both baseline and follow-on. Developed anemia was defined as having a normal Hb at baseline but had anemia at follow-on. We compared the mean number of tablets consumed across each group using adjusted ANCOVA model with Taylor series variance.

Having examined the association between IFA tablets consumed and Hb or anemia, an exploratory data analysis was conducted to examine the dose-response relationship between them and to identify a minimum effective number of weekly IFA tablets. In order to determine the minimum effective number of cumulative weekly IFA tablets over one school year, receiver operating characteristic (ROC) curve analysis was used. A binary logistic regression was used modeling the probability of no anemia and the cumulative number of weekly IFA tablets consumed over one school year, controlling for potential confounding variables including demographics (age and wealth tertile), school characteristics (level and

rurality), health (malaria, BMI category, and geophagy), and diet (sources of iron and citrus). The fitted logistic function was solved for the minimum effective number of cumulative IFA tablets for identifying the predicted probability of no anemia at the point of minimum misclassification. Precision around the minimum effective cut point was derived from percentile bootstrap (1000 replicates) estimation. A restricted cubic spline model was built to examine both linearity and curvilinear trends in the relationship between cumulative IFA consumption and the change in Hb, and the number of knots was automatically chosen based on model fit and empirical distribution. The adjusted associations between anemia or hemoglobin concentration at follow-on and the minimum effective and current program targets for the cumulative number of IFA tablets consumed were then examined following multivariable regression. This was done to evaluate the potential utility of each target associated with reduced population prevalence of anemia. Sampling weights were applied where appropriate. A priori alpha was set at 0.05. All analyses were conducted in SAS 9.4 unless otherwise noted.

Role of the funding source

The authors were employed by the organizations that either provided funding or technical support for this evaluation.

4.3: Results

A total of 1,551 selected girls (94.8%) agreed to participate and completed the baseline survey; at follow-on, 1,412 participated again (91.0%) (Figure 4.6.1). Thirty students who were older than 19 years at baseline were excluded for a final analytical sample of 1,521 at baseline and 1,387 at follow-on. At baseline, participants were, on average, 15.7 years old (range: 10-19 years) and most had reached menarche (84.7%). Students primarily attended government schools (93.3%) located in rural settings (53.5%) (Table 4.6.1).

There were significant differences between the baseline and follow-on in the health and dietary characteristics of participants. The proportion of girls with anemia or malaria significantly declined over time (-5.4 percentage points and -17.7 percentage points, respectively) with a corresponding increase in mean hemoglobin concentration (+0.2 g/dL). Over the two time points, there were also significant increases in the proportion that reported consuming sources of iron and citrus fruits. There were no significant changes in body composition or the proportion engaging in geophagy (Table 4.6.2).

A total of 28,005 IFA tablets were consumed by the study participants over the study period during the 2017/18 academic year, an average of 16.4 tablets per girl (range: 0-36) (Table 4.6.3). In terms of program coverage and adherence, most students (89.5%) had consumed at least one tablet during the school year, and nearly 75% had taken more than 10 tablets (Table 4.6.3). The cumulative number of IFA tablets consumed varied by term with more students consuming six or more tablets during term 1 than in the remaining two terms ($p < .0001$) (Figure 4.6.2). At follow-on, 10% of girls had never consumed an IFA tablet, of which 15.7% had anemia. Among the remaining 1,239 girls with dosage information at follow-on, 14.8% consumed 1-10 tablets, of which 25.7% had anemia. Another 38.0% consumed 11-20 tablets with 22.4% anemia, 29.5% consumed 21-30 tablets with 16.1% anemia, and 7.2% consumed more than 30 tablets with 10.3% anemia (Table 4.6.3).

The restricted cubic spline model had four knots at the fifth (0 tablets), thirty-fifth (20 tablets), sixty-fifth (27 tablets), and ninety-fifth (33 tablets) percentiles and shows that there is a positive non-linear relationship between IFA dosage and change in Hb ($p < .0001$) (Figure 4.6.3). For IFA consumption between 0-20 tablets, each additional tablet consumed was associated with a near zero increase in Hb (0.003 g/dL); whereas, for consumption between 27-33 tablets, each additional tablet was associated with a 0.17 g/dL increase in Hb.

In adjusted repeated measures analysis, the group of girls who had never taken an IFA tablet had an adjusted decrease in anemia prevalence (21.7 to 18.4%). This group had among the highest baseline Hb and a larger proportion in JHS; however, this group did not differ in household wealth, pre-intervention iron supplementation, diet, or BMI category (data not shown). The adjusted prevalence of anemia increased among the group who had consumed between 1 and 10 tablets (22.0 to 29.2%), and their Hb decreased (12.7 to 12.6 g/dL). Changes observed in the 1-10 tablets group were not significantly different from those who had never consumed a tablet (Supplemental Table 4.6.1). The adjusted anemia prevalence decreased and Hb increased for the remaining groups. The adjusted population prevalence of anemia (as least square marginals from GLMMs) decreased substantially in the group who had consumed 11-20 tablets (31.0 to 24.1%), and their Hb increased (12.7 to 12.8 g/dL). There were also declines in the prevalence of anemia for the groups that had consumed 21-30 and >30 tablets (20.6 to 17.8% and 23.2 to 17.0%, respectively). Their Hb also increased (12.9 to 13.1 g/dL and 12.7 to 13.0 g/dL, respectively) (Figures 4.6.4 and 4.6.5). Except for the consumers of only 1-10 tablets, with each category of increasing number of IFA tablets consumed, there was a corresponding increase in Hb ($p=0.029$) and decrease in anemia ($p=0.024$). There was evidence of possible effect modification by wealth and rurality in the relationship between the number of tablets consumed and the change in anemia prevalence; however, the estimates were small, unstable, and not practically meaningful (results not shown). There was no evidence of effect modification by malaria status.

In the sensitivity analysis of potential treatment and prevention effects (table not shown), the girls who experienced a treatment effect from the IFA tablets ($n=173$) consumed an average of 2.7 more tablets than those who remained anemic ($n=137$) (20.6 vs. 17.9; $p=0.03$) adjusted for age, wealth, school level, rurality, malaria, and diet. Those who did not develop anemia (897) consumed a similar adjusted average number of tablets as those who had experienced treatment effect (20.3 vs. 20.6 tablets; $p>0.05$). Girls who had a normal Hb at baseline but had anemia at follow-on ($n=100$) consumed one less

tablet on average than those who experienced a treatment effect (19.6 vs. 20.6) but this difference was not statistically significant. The repeated measures model suggests a dose-response relationship between the cumulative number of IFA tablets taken over one school year and Hb at follow-on. We formally tested for linear and non-linear trends in the association between Hb change and IFA using restricted cubic spline (RCS) models and found statistically significant non-linear trends ($p < 0.001$, Figure 4.6.3). This non-linearity demonstrated by the RCS model indicates there may be plateauing of potential impact on Hb change at certain IFA doses that may be useful for setting program benchmarks. Investigating this relationship further, a model of anemia at follow-on and the cumulative number of IFA tablets consumed (adjusted for baseline Hb, a squared term of cumulative IFA tablets to account for non-linearity, age, household wealth, BMI category, geophagy, malaria, and diet) has good predictive power with 82.1% AUC. The derived cut-point for the population minimum effective number of cumulative IFA tablets consumed over one school year is 26.3 tablets (95%CI: 25.5, 27.8).

4.4: Discussion

This longitudinal, pre-post study provides evidence for the effectiveness of school-based IFA supplementation in reducing the burden of anemia in a programmatic setting in Ghana. The prevalence of anemia decreased by 5.4 percentage points (22%), and the mean hemoglobin concentration increased by 0.15 g/dL. Similar declines in anemia prevalence were observed in India's adolescent IFA supplementation program (30% in pilot regions and 5-24% during national scale-up).^(27,28) Except for the small group of girls who had never consumed an IFA tablet, consumers of more tablets had a greater adjusted decrease in prevalence of anemia and a greater adjusted increase in Hb over the study period. We observed a statistically significant departure from linear dose-response relationship between IFA consumption and Hb with plateau ranges beyond which there was sharp increase in the change in hemoglobin levels at about 26 IFA tablets (Figure 4.6.3). Similarly, there was an overall significant trend between categories of IFA consumption separately with anemia and hemoglobin from GLMMs (type-3

test). Although the overall trend persisted, pairwise comparisons of associations across IFA consumption categories (0, 1-10, 11-20, 20-30, >30) yielded inconsistent results potentially due to unbalanced and/or smaller sample sizes. For example, the group of never-consumers had the smallest sample size (n=68), in comparison to the other categories, resulting in unstable estimates of changes in anemia and Hb with wider confidence intervals after accounting for additional predictors. Further, because the biologic IFA-Hb relationship is curvilinear, it might not translate into linear change in anemia across IFA consumption categories.

We found 26 weekly tablets over the school year may be the minimum effective number of IFA tablets over one school year in this population. This cut point is consistent with the non-linear dose-response relationship identified by the RCS model. The World Health Organization recommendation for intermittent IFA supplementation (three months on, three months off) amounts to approximately 26 tablets per year, nearly identical to the cut-point derived in our analysis. This cut-point is more than double the current program benchmark of a minimum of 10 tablets over the school year. This benchmark was set because it is approximately one-third of the weeks of the school year, though the length of the school year varies between approximately 30-36 weeks. Program benchmarks may need to be raised, given that there are additive increases in Hb levels with consumption greater than 26 tablets. While the large proportion of girls (76%) who had consumed at least 10 tablets over the school year shows that adherence to the current program benchmark is feasible, only 24% had consumed at least 26 tablets. This suggests that three-quarters of students are missing the full benefit of the program. Intake adherence is lower in this program than in similar IFA programs,^(29,30) implying program bottlenecks.

This study is representative of two regions of Ghana during the first year of the intervention. The study is limited by the absence of a control group. Individual-level and district-level randomization were not feasible for such a program carried out through existing health and education frameworks. Instead, a pre-post design was used, nested within the implementation of a large program. Causal inference is

limited in such a design because changes observed may not be due to the intervention but rather some other factors that also changed over time. In this study, three key factors – diet, malaria, and age– changed between baseline and follow-on. However, we have presented adjusted models that account for these changes. Adding to evidence of the intervention’s effect is the dose-response relationship observed between cumulative IFA consumption, recorded during directly observed therapy, and change in Hb. Still, the models are not exhaustive as they lack other potential contextual and individual predictors of hemoglobin concentration such as blood disorders, micronutrient deficiencies, and other illnesses. The minimum effective cut-point for cumulative weekly IFA tablets provides a data-driven target for the maximum population benefit, and the bootstrapped approach corrects for potential overfitting and optimism bias. However, the cut-point is based on an adjusted model that, while having good predictive qualities, cannot perfectly predict anemia. There is growing interest in IFA supplementation of adolescents through school-based delivery. To our knowledge, Ghana is the first sub-Saharan country to implement IFA supplementation among adolescent girls and has the only active national program in Africa. While iron absorption is mediated by its bioavailability, gut integrity, iron stores, and infection, these results represent a promising avenue for anemia control in this population.

4.5: Conclusion

Supplementation with weekly iron and folic acid tablets in schools may have improved hemoglobin concentration and reduced anemia among adolescent girls in Ghana independent of other contributors to the burden of anemia in this population. These effects observed after a relatively short time make IFA supplementation in schools a promising intervention for addressing the burden of anemia in Ghana. The calculated minimum effective number of IFA tablets suggests that improved intake adherence would improve population benefit from the program. Program targets should be higher than the current target of 10 tablets over one school year. Further research is needed to understand the

drivers of adherence to IFA supplementation for improving the program and its impact on anemia control and prevention.

4.6: Figures and Tables

Figure 4.6.1: Participant Flow Chart for Baseline and Follow-on Surveys of Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

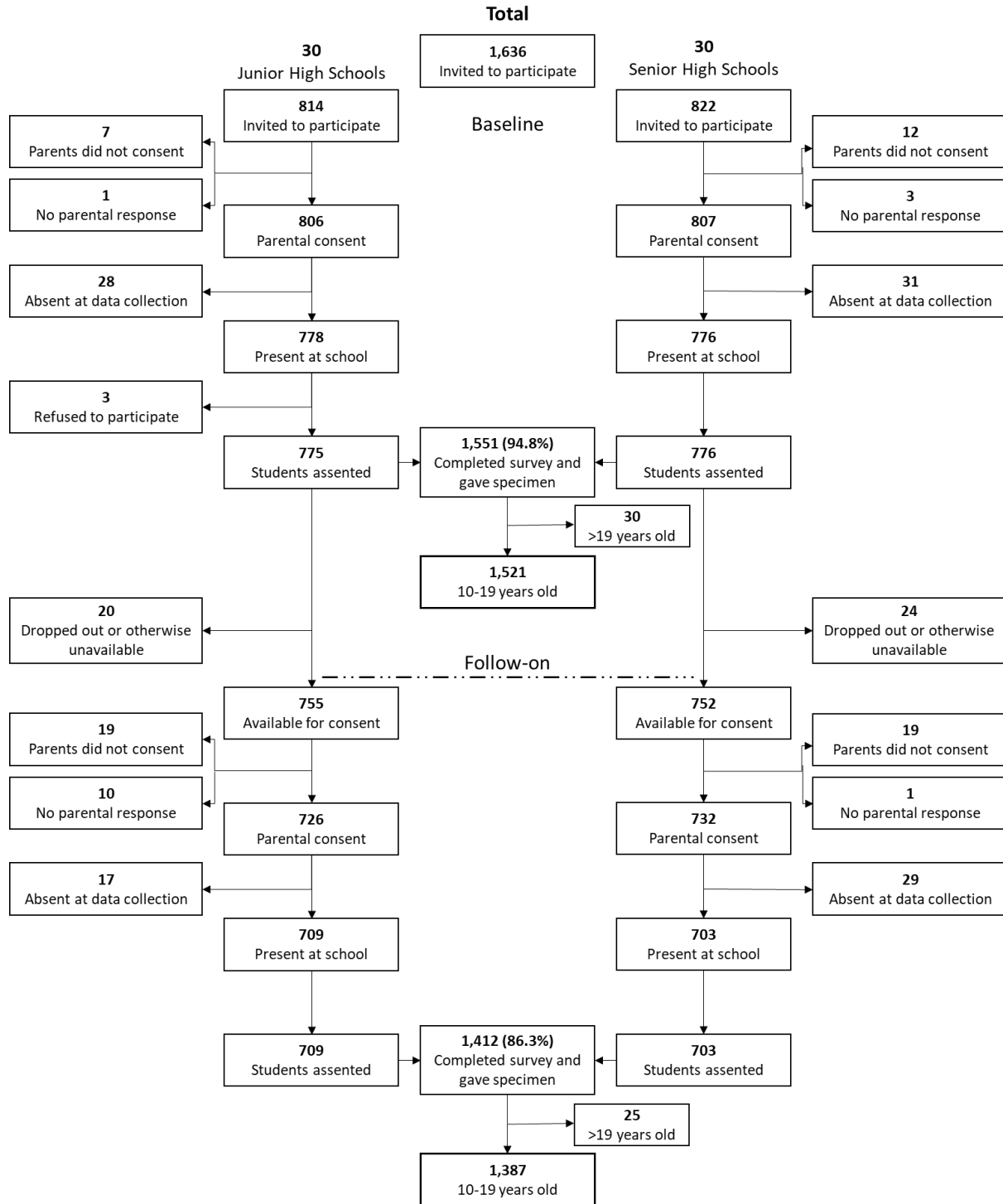


Table 4.6.1: Demographic Characteristics of Participants in the Baseline Survey of Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Characteristic	Baseline	
	n	Mean or % (95% CI)
<i>Demographics</i>		
Age, years	1,521	15.7 (15.3, 16.1)
Reached menarche, %	1,289	84.7 (80.1, 89.4)
<i>School</i>		
Level		
Junior high school, %	773	50.8 (37.6, 64.1)
Senior high school, %	700	46.0 (32.8, 59.2)
Vocational school, %	48	3.2 (0.0, 7.7)
Type		
Private, %	102	6.7 (0.6, 12.8)
Government, %	1,419	93.3 (87.2, 99.4)
Location		
Rural, %	813	53.5 (40.2, 66.7)
Peri-urban, %	438	28.1 (16.1, 40.1)
Urban, %	287	18.4 (8.2, 28.6)

Note: Unweighted. 95% CI are based on Taylor series variance estimates to account for the complex sampling design.

Table 4.6.2: Health and Dietary Characteristics at Baseline and Follow-on and the Population Average Changes over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Characteristic	Baseline		Follow-on		Difference ^a	
	n	Mean or % (95% CI)	n	Mean or % (95% CI)	Value (95% CI)	p-value
<i>Health</i>						
Anemia, %	363	25.1 (21.8, 28.4)	255	19.6 (16.5, 22.8)	-5.4 (-8.8, -2.1)	0.001
Hemoglobin concentration (g/dL)	1,521	12.7 (12.6, 12.8)	1,387	12.9 (12.8, 13.0)	0.2 (0.1, 0.3)	0.001
Positive malaria rapid diagnostic test, %	504	26.1 (22.9, 29.3)	210	8.4 (6.6, 10.3)	-17.7 (-21.0, -14.4)	<.001
Thinness (BMIZ <-2SD), %	23	1.0 (0.3, 1.6)	20	0.8 (0.3, 1.3)	-0.2 (-0.7, 0.3)	0.484
Overweight (+1SD < BMIZ ≤ +2SD), %	221	18.9 (15.8, 22.0)	211	20.0 (16.7, 23.3)	1.1 (-1.5, 3.7)	0.405
Obesity (BMIZ >+2SD), %	32	3.0 (1.7, 4.3)	35	3.4 (1.9, 4.8)	0.3 (-0.4, 1.1)	0.377
Practice geophagy (eating soil or clay), %	450	26.8 (23.5, 30.0)	301	23.3 (19.8, 26.7)	-3.5 (-7.6, 0.6)	0.095
<i>Diet (consumption in previous 24 hours)</i>						
Rich source of heme iron, % ^b	264	17.3 (14.4, 20.1)	370	24.0 (20.7, 27.2)	6.7 (2.6, 10.8)	0.001
Fair source of heme iron, % ^c	1,137	71.3 (67.7, 74.9)	1,142	78.6 (75.1, 82.0)	7.2 (2.7, 11.8)	0.002
Rich source of non-heme iron, % ^d	1,033	66.8 (63.2, 70.4)	1,115	71.9 (68.2, 75.7)	5.2 (0.2, 10.1)	0.042
Foods and beverages fortified with iron, % ^e	449	41.6 (37.8, 45.3)	605	54.1 (50.2, 58.1)	12.6 (8.0, 17.1)	<.001
Citrus fruits, % ^f	483	23.7 (20.6, 26.8)	579	34.5 (30.8, 38.2)	10.8 (6.1, 15.6)	<.001

Note: Proportions and means are weighted to be representative of all eligible girls in the school. BMIZ=body mass index (kg/m²) for age z-score by the International Obesity Task Force reference population. IFA=iron-folic acid.

^a Differences are mean difference or prevalence difference. 95% confidence intervals and p-values are based on Taylor series variance estimates to account for the complex sampling design.

^b Red meats such as beef, lamb, goat, or wild game and organ meats;

^c Other animal source foods including eggs, poultry, and fish;

^d Dark green leafy vegetables, legumes, nuts, and seeds;

^e Cereal and beverages fortified with iron Milo, Ovaltine, Cerelac, Yumvita, or Nido;

^f Citrus fruits including oranges, lemons, pineapple, mango, etc.

Table 4.6.3: Iron-folic Acid (IFA) Tablets Consumed among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana over One School Year and Anemia Prevalence at Follow-on

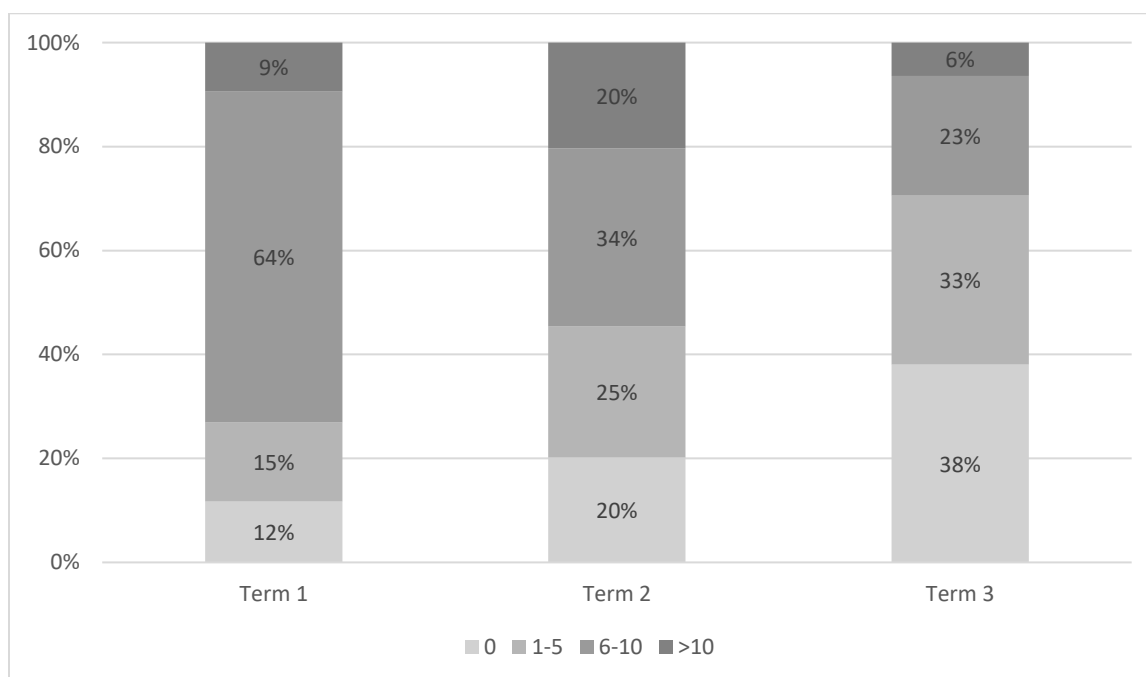
Cumulative IFA Tablets Consumed	Proportion of Students at Follow-on		Proportion with Anemia at Follow-on	
	n	% (95% CI) ^a	n	% (95% CI) ^b
0	68	10.5 (1.4, 19.6)	10	15.7 (7.2, 25.8)
1 – 10	134	14.8 (4.7, 24.9)	35	25.7 (16.7, 35.4)
11 – 20	267	38.0 (19.6, 56.5)	59	22.4 (16.4, 28.9)
21 – 30	649	29.5 (16.0, 42.9)	96	16.1 (12.3, 20.6)
>30	189	7.2 (0.8, 13.6)	28	10.3 (5.4, 16.7)
Grand total of IFA tablets consumed			28,005	
Mean (minimum, maximum) number of IFA tablets consumed			16.4 (0, 36)	

Note: Proportions and means are weighted to be representative of all eligible girls in the school.

^a 95% CI are based on Taylor series variance estimates to account for the complex sampling design.

^b Estimates and 95% CI were obtained from bootstrapped replication and are unadjusted.

Figure 4.6.2: Iron-folic Acid (IFA) Tablets Consumed among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana over One School Year by Term



Note: Proportions are weighted to be representative of all eligible girls in the school.

Supplemental Table 4.6.1: Adjusted Change in Anemia Prevalence Difference and Hemoglobin Concentration Mean Difference from Baseline to Follow-on among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana by Participant Characteristics

Variable	Change in Anemia (p.p.) ^b	Change in Hemoglobin concentration (g/dL) ^c
	Adjusted Diff. (95% CI) ^d	Adjusted Diff. (95% CI) ^d
<i>Demographic Characteristics</i>		
Age, years	0.7 (-1.1, 2.5)	-0.07 (-0.12, -0.02)**
Wealth index (tertile)		
Middle vs. lowest	-6.5 (-12.6, -0.4)*	0.00 (-0.17, 0.16)
Highest vs. lowest	-13.9 (-20.2, -7.5)***	0.15 (-0.03, 0.32)
<i>School</i>		
Junior vs senior/vocational high school	-3.0 (-10.8, 4.8)	-0.20 (-0.41, 0.02)
Rural vs urban	-5.9 (-13.3, 1.6)	0.34 (0.13, 0.55)**
Peri-urban vs urban	-12.2 (-19.6, -4.8)**	0.43 (0.22, 0.64)***
<i>Health</i>		
Positive vs negative malaria test ^a	-0.9 (-8.7, 6.8)	0.16 (-0.05, 0.37)
Overweight vs normal weight ^a	-0.1 (-6.9, 6.6)	-0.04 (-0.23, 0.15)
Obesity vs normal weight ^a	-5.8 (-20.4, 8.7)	0.09 (-0.32, 0.50)
Practice geophagy vs non-practicing ^a	-6.1 (-12.5, 0.4)	0.47 (0.29, 0.65)***
<i>Diet (consumption in previous 24 hours)</i>		
Rich source of heme iron vs not consumed ^a	3.6 (-3.2, 10.4)	-0.10 (-0.29, 0.09)
Fair source of heme iron vs not consumed ^a	-2.9 (-10.2, 4.4)	0.27 (0.07, 0.48)**
Rich source of non-heme iron vs not consumed ^a	0.2 (-6.5, 6.9)	-0.15 (-0.34, 0.03)
Foods and beverages fortified with iron vs not consumed ^a	-4.2 (-10.2, 1.9)	0.03 (-0.14, 0.21)
Citrus fruits vs not consumed ^a	5.2 (-1.0, 11.5)	-0.15 (-0.32, 0.03)
<i>Cumulative number of IFA tablets consumed^e</i>		
0	-10.4 (-22.0, 1.1)	0.20 (-0.13, 0.53)
1 – 10	ref	ref
11 – 20	-14.1 (-22.6, -5.5)**	0.24 (-0.01, 0.48)
21 – 30	-9.9 (-18.1, -1.7)*	0.33 (0.10, 0.56)**
>30	-13.3 (-23.8, -2.8)*	0.46 (0.17, 0.76)**

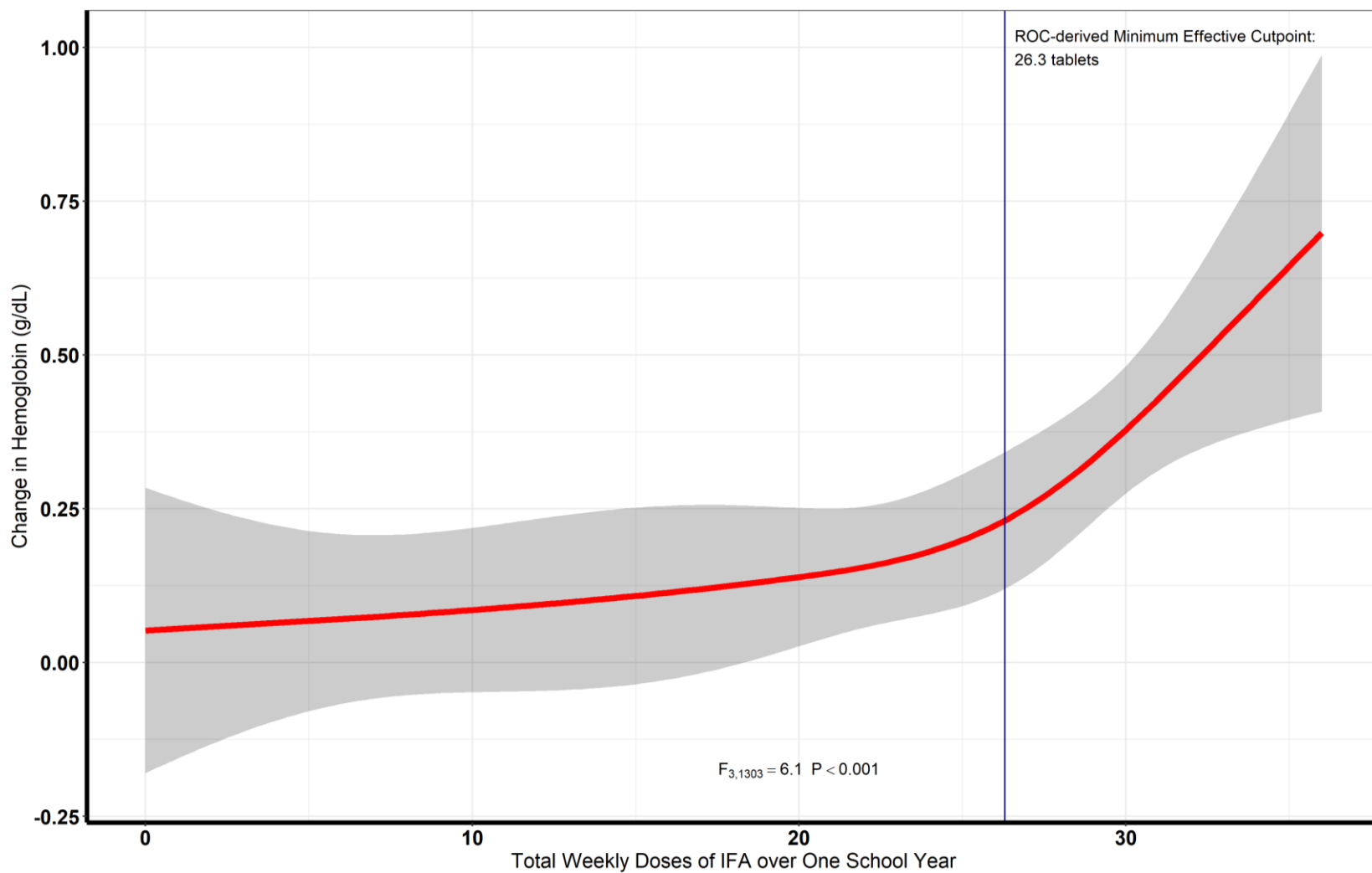
Note: Estimates are weighted to be representative of all eligible girls in the school. Estimates, 95% confidence intervals, and p-values are calculated from generalized mixed models using maximum likelihood estimation and account for clustering in school and intra-individual covariance.

*p<0.05; **p<0.01; ***p<0.001;

^a Repeated measures used. ^b Percentage point (p.p.) difference in the change in the population prevalence of anemia from baseline to follow-on.

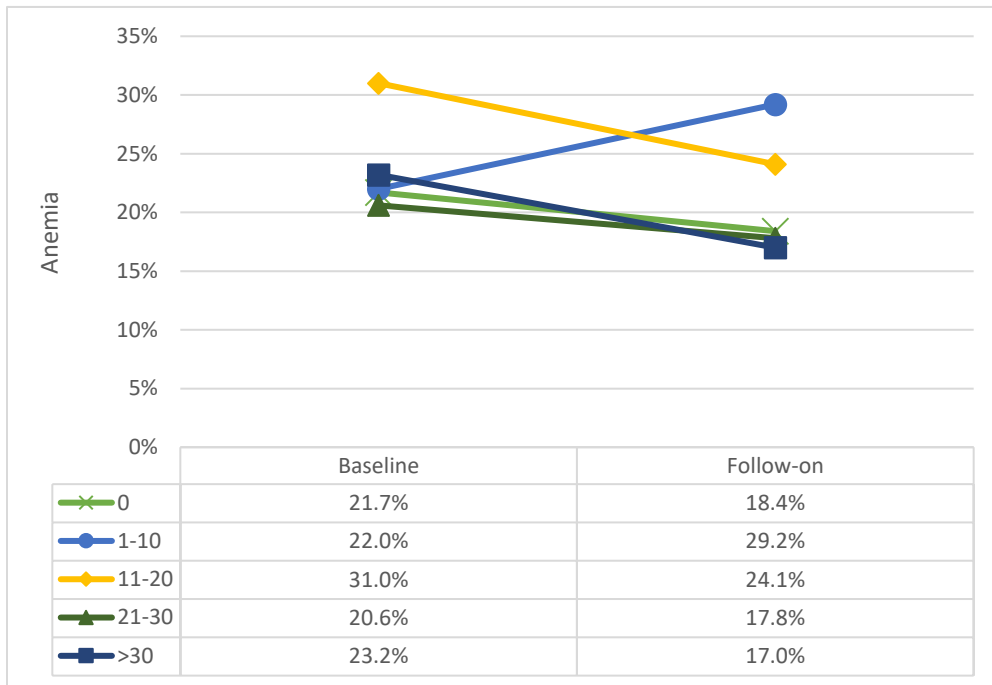
^c Difference (g/dL) in the change in the population average hemoglobin concentration from baseline to follow-on. ^d Adjusted for other variables in the table including demographics, school, health, diet, and IFA tablets consumed. ^e Anemia model p-value for trend: 0.024; Hb model p-value for trend: 0.029; Increasing categories of consumption may not correspond directly to decreases in anemia due to the curvilinear relationship; The reference category was 1-10 tablets because of the robust sample size compared to the zero-dose category.

Figure 4.6.3: The Relationship between the Cumulative Iron-folic Acid (IFA) Tablets Consumed and the Change in Hemoglobin Concentration over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana



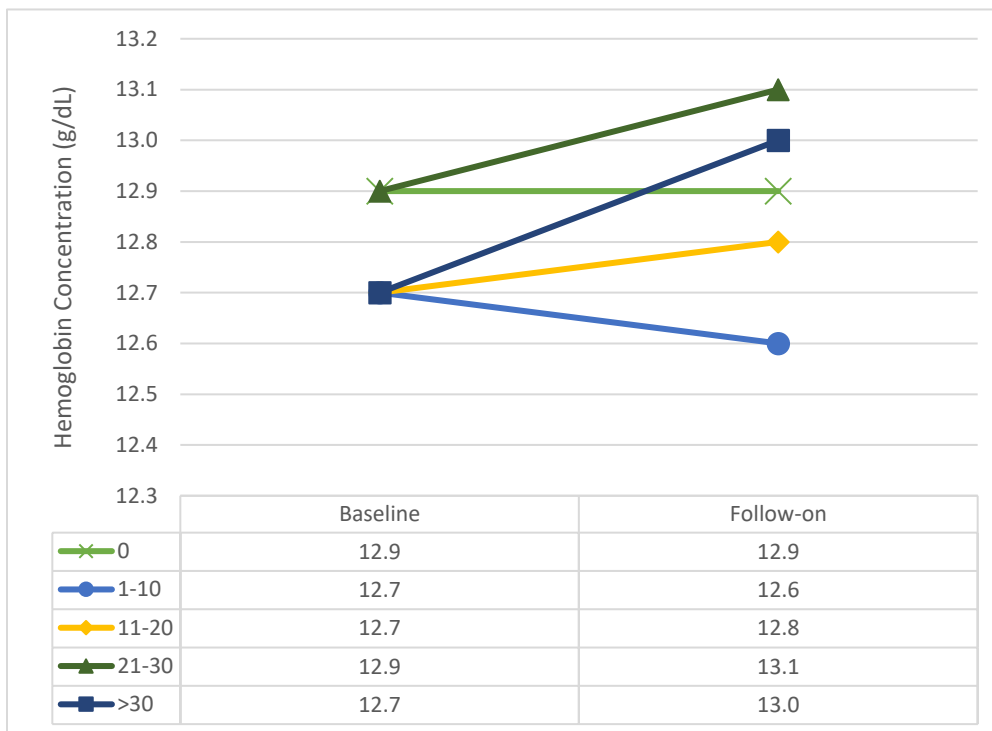
Note: Knots at 0, 20, 27, and 33 tablets.

Figure 4.6.4: Adjusted Change in Anemia Prevalence Difference by Cumulative IFA Tablets Consumed over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana



Note: Estimates are weighted to be representative of all eligible girls in the school. Estimates and p-values are calculated from generalized mixed models using maximum likelihood estimation and accounted for clustering in school and intra-individual covariance. Adjusted for demographics, school level and geography, body mass index, malaria, pica, and diet. p-value for trend = 0.024

Figure 4.6.5: Adjusted Change in Mean Hemoglobin Difference by Cumulative IFA Tablets Consumed over One School Year among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana



Note: Estimates are weighted to be representative of all eligible girls in the school. Estimates and p-values are calculated from generalized mixed models using maximum likelihood estimation and accounted for clustering in school and intra-individual covariance. Adjusted for demographics, school level and geography, body mass index, malaria, pica, and diet. p-value for trend = 0.029

Table 4.6.4: Adjusted Model of Anemia at Follow-on among Adolescent Schoolgirls in the Northern and Volta Regions of Ghana

Variable	Adjusted Odds Ratio (%95 CI)
Cumulative number of IFA tablets consumed	0.95 (0.90, 0.99)*
Cumulative number of IFA tablets consumed, squared ^a	1.00 (1.00, 1.00)*
Baseline hemoglobin concentration, g/dL	0.33 (0.25, 0.44)***
Age, years	1.17 (1.02, 1.35)*
Wealth tertile	
Middle vs. lowest	0.60 (0.34, 1.05)
Highest vs. lowest	0.34 (0.17, 0.67)**
Overweight vs normal weight	1.21 (0.63, 2.31)
Obesity vs normal weight	0.78 (0.19, 3.23)
Practice geophagy vs non-practicing	1.32 (0.77, 2.27)
Positive vs negative malaria test	1.40 (0.59, 3.31)
Rich source of heme iron vs not consumed ^b	1.23 (0.72, 2.09)
Fair source of heme iron vs not consumed ^c	1.07 (0.55, 2.09)
Rich source of non-heme iron vs not consumed ^d	1.54 (0.87, 2.73)
Foods and beverages fortified with iron vs not consumed ^e	1.50 (0.93, 2.40)
Citrus fruits vs not consumed ^f	0.89 (0.50, 1.59)

Note: Estimates are weighted to be representative of all eligible girls in the school. Estimates, 95% confidence intervals, and p-values are calculated using Taylor series variance and account for clustering in school and intra-individual covariance. *p<0.05; **p<0.01; ***p<0.001;

^a Model also accounted for cumulative IFA consumption squared to address nonlinearity of the association.

^b Red meats such as beef, lamb, goat, or wild game and organ meats; ^c Other animal source foods including eggs, poultry, and fish; ^d Dark green leafy vegetables, legumes, nuts, and seeds; ^e Cereal and beverages fortified with iron Milo, Ovaltine, Cerelac, Yumvita, or Nido; ^f Citrus fruits including oranges, lemons, pineapple, mango, etc. Dietary variable measured over previous 24 hours.

References (Chapter 4)

1. WHO. Global Accelerated Action for the Health of Adolescents (AA-HA!), Geneva: World Health Organization, 2017.
2. WHO. Iron deficiency anaemia assessment, prevention, and control: A guide for programme managers. Geneva: World Health Organization, UNICEF, UNU; 2001.
3. Hassan TH, Badr MA, Karam NA, et al. Impact of iron deficiency anemia on the function of the immune system in children. *Medicine (Baltimore)* 2016; **95**(47): e5395.
4. Dawson H, Piñero DJ, Beard JL. Iron metabolism: A comprehensive review. *Nutr Rev* 1996; **54**(10): 295-317.
5. Beard JL. Iron requirements in adolescent females. *J Nutr* 2000; **130**(2): 440S-2S.
6. Balarajan Y, Ramakrishnan U, Ozaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. *Lancet* 2011; **378**(9809): 2123-35.
7. Otto JM, Montgomery HE, Richards T. Haemoglobin concentration and mass as determinants of exercise performance and of surgical outcome. *Extrem Physiol Med* 2013; **2**(1): 33-.
8. Haas JD, Brownlie Tt. Iron deficiency and reduced work capacity: A critical review of the research to determine a causal relationship. *J Nutr* 2001; **131**(2S-2): 676S-88S; discussion 88S-90S.
9. Sive A, Berg A, Perez EM, et al. Maternal iron deficiency anemia affects postpartum emotions and cognition. *J Nutr* 2005; **135**(2): 267-72.
10. Halterman JS, Kaczorowski JM, Aligne CA, Auinger P, Szilagyi PG. Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics* 2001; **107**(6): 1381-6.
11. Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr* 2016; **103**(2): 495-504.
12. Wirth JP, Woodruff BA, Engle-Stone R, et al. Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr* 2017; **106**(Suppl 1): 416S-27S.
13. Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. *Blood* 2014; **123**(5): 615-24.
14. University of Ghana, GroundWork, University of Wisconsin-Madison, KEMRI-Wellcome Trust, UNICEF. Ghana Micronutrient Survey 2017. Accra, Ghana, 2017.
15. Bhutta ZA, Lassi ZS, Bergeron G, et al. Delivering an action agenda for nutrition interventions addressing adolescent girls and young women: priorities for implementation and research. *Ann N Y Acad Sci* 2017; **1393**(1): 61-71.
16. Salam RA, Hooda M, Das JK, et al. Interventions to Improve Adolescent Nutrition: A Systematic Review and Meta-Analysis. *Journal of Adolescent Health* 2016; **59**(4, Supplement): S29-S39.
17. WHO. Guideline: Intermittent iron supplementation in preschool and school-age children. Geneva: World Health Organization; 2011.
18. WHO. Guideline: Intermittent iron and folic acid supplementation in menstruating women. Geneva: World Health Organization (WHO), 2011.
19. Global Database on the Implementation of Nutrition Action. Geneva, Switzerland: World Health Organization; (accessed November 20, 2019).
20. Stipanuk MH, Caudill MA, editors. Biochemical, physiological, and molecular aspects of human nutrition. 3rd ed. St. Louis, Missouri: Saunders, an imprint of Elsevier Inc.; 2013.
21. Beck KL, Kruger R, Conlon CA, et al. The relative validity and reproducibility of an iron food frequency questionnaire for identifying iron-related dietary patterns in young women. *J Acad Nutr Diet* 2012; **112**(8): 1177-87.

22. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books; 1988.
23. Stadlmayr B, Charrondiere UR, Enujiugha VN, et al. West African Food Composition Table. Rome: Food and Agriculture Organization of the United Nations (FAO), 2012.
24. Nyumuah RO, Hoang TC, Amoafu EF, et al. Implementing large-scale food fortification in Ghana: lessons learned. *Food Nutr Bull* 2012; **33**(4 Suppl): S293-300.
25. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; **320**(7244): 1240-3.
26. Mamudu HM, Veeranki SP, John RM. Tobacco use among school-going adolescents (11-17 years) in Ghana. *Nicotine Tob Res* 2013; **15**(8): 1355-64.
27. Aguayo VM, Paintal K, Singh G. The Adolescent Girls' Anaemia Control Programme: a decade of programming experience to break the inter-generational cycle of malnutrition in India. *Public Health Nutr* 2013; **16**(9): 1667-76.
28. Malhotra S, Yadav K, Kusuma Y, Sinha S, Yadav V, Pandav CS. Challenges in scaling up successful public health interventions: Lessons learnt from resistance to a nationwide roll-out of the weekly iron-folic acid supplementation programme for adolescents in India. *Natl Med J India* 2015; **28**(2): 81-5.
29. Vir SC, Singh N, Nigam AK, Jain R. Weekly iron and folic acid supplementation with counseling reduces anemia in adolescent girls: a large-scale effectiveness study in Uttar Pradesh, India. *Food Nutr Bull* 2008; **29**(3): 186-94.
30. Risonar M, Tengco L, Rayco-Solon P, Solon F. The effect of a school-based weekly iron supplementation delivery system among anemic schoolchildren in the Philippines. *Eur J Clin Nutr* 2008; **62**(8): 991.

Chapter 5: Barriers and Facilitators of Iron and Folic Acid Supplementation within a School-based Integrated Nutrition and Health Promotion Program among Ghanaian Adolescent Girls

Lucas Gosdin^{1,2}, Andrea J Sharma^{2,3}, Katie Tripp², Esi Foriwa Amoafu⁴, Abraham B Mahama⁵, Lilian Selenje⁵, Maria Elena Jefferds², Usha Ramakrishnan^{1,6}, Reynaldo Martorell^{1,6}, and O. Yaw Addo^{1, 2, 7}

¹Nutrition and Health Sciences, Laney Graduate School, Emory University, 1518 Clifton Rd. Atlanta, GA, USA; ²Nutrition Branch, Centers for Disease Control and Prevention, 4770 Buford Hwy, Atlanta, GA, USA;

³U.S. Public Health Service Commissioned Corps, Atlanta, GA; ⁴Ghana Health Service of Ministry of Health, PO Box M44, Ministries, Accra, Ghana; ⁵UNICEF-Ghana, 4-8th Rangoon Close, Cantonments, Accra, Ghana; ⁶Hubert Department of Global Health, Rollins School of Public Health, Emory University;

⁷Emory Global Health Institute, Atlanta, GA USA;

Abstract

Background: We sought to evaluate the barriers and facilitators of program fidelity to a school-based anemia reduction program with weekly iron-folic acid (IFA) supplementation.

Methods: We analyzed directly observed weekly IFA consumption data collected longitudinally and serial cross-sectional data from a representative survey of 60 secondary schools and 1,387 adolescent girls in the Northern and Volta regions after one school year of the intervention (30-36 weeks). We carried out a bottleneck analysis to characterize the levels of IFA coverage and used adjusted generalized linear mixed effects models (GLMMs) to quantify the school and student drivers of IFA intake adherence.

Results: 90% of girls had ever consumed the tablet, while 56% had consumed ≥ 15 tablets (mean 16.4, range: 0-36). Among consumers, 88% of girls liked the tablet, and 27% reported undesirable changes. School-level factors represented 75% of the variance in IFA consumption over the school year. Total IFA tablets consumed was associated with the ability to make up missed IFA distributions (+1.4 tablets [95% CI: +0.8, +2.0]), junior vs. senior secondary school (+5.8 [+0.1, +11.5]), educators' participating in a program-related training (+7.6 [+2.9, 12.2]), and educator perceptions that implementation was difficult (-6.9 [-12.1, -1.7]) and was an excessive time burden (-4.4 [-8.4, -0.4]).

Conclusions: Most girls consumed the weekly IFA tablet and found IFA tablets acceptable, but adherence to supplementation throughout the school year was lower. While the IFA supplementation program reached Ghanaian schoolgirls in these regions, school-level factors were barriers to adherence. Program modifications such as expanded training, formalized make-up IFA distributions, sensitization activities, and additional support to senior high schools may improve adherence. Other modifications such as spreading the responsibility for IFA distribution and streamlining monitoring may reduce the burden at the school level. Strengthening the health education component and improving knowledge of IFA among students may also be beneficial.

5.1: Background

The World Health Organization recommends weekly intermittent supplementation with iron and folic acid (IFA) for the control of anemia among adolescent girls ages 15-19 years and school-aged children 5-12 years in areas where the prevalence of anemia is 20% or higher ^(1,2). With a national anemia prevalence of 26.4% among non-pregnant girls ages 15-19 years, anemia is a problem of moderate public health significance in Ghana ^(3,4). To address this problem, the Girls' Iron-Folic acid Tablet Supplementation (GIFTS) Program, an integrated health and nutrition education program with intermittent weekly IFA supplementation was designed to reach adolescent girls ages 10-19 years through two delivery platforms: schools and local health centers. The first phase of the program began in the Brong-Ahafo, Northern, Upper East, and Volta regions of Ghana beginning in October 2017^c.

School-based IFA supplementation has substantial benefit in reducing the prevalence of anemia under experimental conditions such as randomized trials ^(5,6); however, there is limited information on how these interventions perform in in real-world settings. Contextual factors drive program performance and are likely responsible for the differences observed between efficacy and effectiveness studies. Guided by the Social-Ecological Model, factors affecting the success of school health programs can be identified at various levels: community, school, family, and individual factors ⁽⁷⁾. Barriers and facilitators have been described in terms of resources, capacity, enabling environment, knowledge, attitudes, and perceptions ^(8,9) and factors span from national policies to individual perceptions. Cross-sector collaborations have been identified by school-based programs as a key driver of program success because of the synergizing of resources and networks, but they may also create dysfunction ^(9,10,11). At the community level, caregivers and other community members influence programs through their support, resistance, or indifference, which may be influenced by cultural norms, media, and sensitization activities ⁽¹⁰⁾. Several

^c In December 2018, Ghana's ten regions were divided into 16. Brong-Ahafo became Bono, Bono East, and Ahafo. Northern became Savannah, Northern, and North East. Upper East maintained the same boundaries. Volta was divided into Volta and Oti.

factors at the school level should also be considered such as procurement and stock outs, the system for administration of tablets, absenteeism, time commitment, and motivation of implementers ^(8,9,12).

Training can improve the knowledge, attitudes, and skills of teachers, which influence program fidelity ⁽⁹⁾. Teacher participation may also be affected by their workload and perceptions of anemia risk and IFA benefit ⁽¹³⁾. Knowledge, attitudes, and perceptions toward anemia risk and IFA may influence a student's willingness to participate, and once she has participated, any physical or cognitive changes she attributes to the tablets may also affect adherence ⁽¹⁴⁾. In addition, a student's physical maturity may influence her ability to swallow tablets and her household socio-economic and food security status may dictate her access to food and water for safe and appropriate consumption of IFA tablets (Figure 5.5.1).

The school is a useful platform for intermittent IFA supplementation among adolescents as it has several advantages. One such advantage is regular access to a portion of the target population. In Ghana in 2018, nearly half of girls 12-14 years (49%) were enrolled in junior high school, and 30% of girls 15-17 years were enrolled in senior high schools, up from 25% in 2016 ⁽¹⁵⁾. With free public senior high school introduced in 2017, enrollment is expected to further increase. Schools also offer an existing infrastructure for administration of the program and an educational environment where sensitization of students can be easily integrated. With these advantages, addressing the barriers to school-based IFA supplementation and leveraging facilitators of adherence could lead to high coverage of the intervention.

The GIFTS program was rolled out in three phases: it began in four regions during the 2017-2018 school year and became a nationwide program in the 2019-2020 school year. An evaluation of two of the Phase I regions estimated a 26% reduction in the prevalence of anemia over one school year, but adherence, defined as the number of tablets consumed each week of the school year following program launch (30-36 weeks), was sub-optimal (approximately half consumed 15 or fewer tablets) ⁽¹⁶⁾. Improving program implementation fidelity and intake adherence could achieve a greater improvement in hemoglobin

concentration and anemia control in the population. However, due to very limited experience in adolescent IFA supplementation on the continent of Africa and none in Ghana, there is little evidence available for improving adherence to the intervention. Our aim was to identify bottlenecks in the coverage of IFA and to describe the key barriers and facilitators that may cause or mitigate against such bottlenecks in Ghana's school-based adolescent IFA supplementation program.

5.2: Methods

Description of the Intervention

Training of staff from the education and health sector was conducted just prior to the rollout of the GIFTS program in each region. This was carried out in cascading trainings from the regional level to the schools and health centers. For the school-based portion of the intervention, the objective of the training was to deliver information regarding the program to the school focal person who would train other school staff. The training covered anemia causes, consequences, and prevention; benefits and potential side effects of IFA; program logistics; administration of IFA tablets; and monitoring.

IFA tablets were distributed through the existing government health system to the district level where they were provided in some cases to district education offices who distributed them to individual schools and in other cases to local health centers who distributed them to schools. The intervention provided IFA tablets to all girls aged older than 10 years in junior high, senior high, and technical/vocational schools, both public and private, on a set day of the week following a meal and with water. No tablets were given during holidays and breaks. Health and nutrition education were also addressed in the training; however, this component was carried out through the existing school health education and promotion program. The intervention is fully described elsewhere ⁽¹⁶⁾.

Sampling and Data Collection

In September 2017, a baseline nutrition survey was conducted in junior high schools (JHS), senior high schools (SHS), and vocational/technical schools in Northern and Volta regions of Ghana. Vocational schools were treated as SHS. These regions were purposively selected from the four Phase I regions for the GIFTS program. A stratified two-stage sampling frame was used. First, probability proportional to size sampling was used to select 60 schools, 15 JHS and 15 SHS from each region, followed by simple random sampling of girls within each school. The sampling frame included all the public and private schools, treated as clusters, with school type (dichotomized as JHS or SHS) as strata. In Northern region, there was a denominator of 837 candidate schools (clusters) in the JHS-stratum and 68 in the SHS-stratum, and in Volta region, there were 1,225 JHS and 104 SHS. Within each school, 29 girls were randomly selected by simple random sampling. The derived sample size was powered to detect a 10% minimum change in the prevalence of anemia based on a background prevalence of 40% with 80% power and 95% significance level with 10% oversampling to account for non-participation and correcting for an intra-class correlation coefficient as high as 10% for repeated measures ⁽¹⁷⁾.

A focal person (teacher) for the GIFTS program was surveyed at each school – for a total of 60 school-level interviews and the baseline survey collected data from 1,521 in-school adolescent girls ages 10-19 years. At the end of the school year, after approximately 8 months of the intervention, the participant schools and girls were followed-up for another round of data collection. At follow-up, the school questionnaire (administered to a teacher) included information about school facilities, school health and nutrition activities, and specific questions related to the GIFTS program including perceptions of IFA and experiences with the distribution of IFA tablets. The student questionnaire asked girls about their knowledge of anemia and IFA, experiences with the program, and basic demographic information. The number of IFA tablets consumed by each survey participant in each school term was abstracted from classroom-level registers that collected individual IFA tablet consumption data for all girls in real time throughout the school year.

Statistical Analysis

Post stratification sampling weights were applied in all analyses. Sampling weights were applied where appropriate, and complex survey procedures in SAS 9.4 were used in all analyses to account for sampling strata and clusters. Statistical significance was defined by an alpha level of 0.05.

Wealth ranking was calculated following principal components analysis of household assets and divided into tertiles ⁽¹⁸⁾. We used census data to categorize schools as rural, peri-urban, or urban ⁽¹⁹⁾. Knowledge of anemia and IFA were calculated using a composite score of correct responses to three multiple-response questions about the causes, symptoms, and prevention of anemia and two multiple-response questions on awareness and benefits of IFA, respectively, and divided into tertiles.

Indicators of IFA supplementation coverage were categorized based on Tanahashi's levels of healthcare coverage, which consist of availability, accessibility, acceptability, contact, and effectiveness ⁽²⁰⁾. A bottleneck is a barrier to 100% healthcare coverage, and usually quantified as 100 - % coverage ⁽²⁰⁾.

The total number of IFA tablets consumed, abstracted from registers, was categorized and compared over basic characteristics. Self-reported consumption of an IFA tablet during the school year (yes/no) was also compared by characteristics of individual students and schools. Rao-Scott chi-squared tests were used for differences in proportions, and design-based t-tests were used for continuous variables.

To examine the associations between potential barriers and facilitators at the student and school levels and adherence to IFA supplementation, adjusted models of the continuous total number of IFA tablets consumed over the school year, abstracted from registers, were built using generalized linear mixed models (GLMM). Two adjusted GLMMs of the school- and student-level predictors of the total number of IFA tablets were constructed based on a conceptual model (Figure 5.5.1). The first model was restricted to students who had consumed at least one tablet to understand drivers of intake adherence (effectiveness coverage) among those who had ever consumed IFA tablets. The second model included

all survey participants to understand the relationship between these factors and intake adherence within the entire population of schoolgirls. Model diagnostics included multicollinearity and influential point checks (2 influential observations were excluded from the final mixed models). A mixed model with clusters (schools) as random intercept was used to estimate intra class correlation. This enabled variance decomposition of the total number of IFA tablets consumed over the school year for quantifying the proportion of variance explained by student- or school-level factors.

5.3: Results

The final analytical sample included 1,387 girls ages 10-19 years from 60 schools. Classroom-level GIFTS program registers were missing for at least one term in three schools, reducing the sample with complete IFA consumption data to 1,307 girls. Figure 5.5.2 shows the levels of coverage and bottlenecks. Ninety percent (90%) of schoolgirls consumed at least one IFA tablet over the school year, implying a bottleneck of 10% in base-level effectiveness coverage. The mean intake was 16.4 tablets (range 0-36) over the year. However, only 56% consumed at least 15 tablets: approximately half of the tablets they were eligible to receive during the follow-up period (one school year). In terms of recent exposure, 66% of the girls reported having consumed the tablet during the previous 2 weeks, and 90% of schools had distributed IFA tablets in the week prior to the follow-up survey. Among those who had ever consumed an IFA tablets (n=1,314), nearly a quarter (23%) of schoolgirls reported that they did not have another opportunity to make up a missed IFA distribution, 21% reported ever refusing to receive an IFA tablet, and 13% had received a tablet that they later threw away. From the school survey (n=60), half of schools (48%) reported difficulties implementing the IFA program, but only 13% had difficulties with the program from community members at some point during the school year. Four schools (7%) had experienced a stock-out of IFA tablets, of which only two schools had ever missed a distribution due to a stock-out.

Figure 5.5.3 shows total IFA consumption by age, school level, wealth, and geographic location. Higher proportions of younger girls (10-14 years) were in higher categories of IFA consumption compared to girls

15-19 years ($p<0.05$). Girls in 10-14 years of age had consumed 6.7 (95% CI: 2.2, 11.3) more tablets, on average, than the girls aged 15-19 years (22.6 vs. 15.9 tablets, $p<0.01$; data not shown). The largest proportion of junior high schoolgirls (69%) had consumed 21-30 tablets over the school year, but among senior high and vocational schoolgirls 42% had consumed 11-20 tablets and only 23% of them had consumed 21-30 tablets ($p<0.01$). IFA consumption differed significantly by wealth: more girls from the low wealth tertile had consumed ≥ 11 tablets than their peers from higher wealth tertiles ($p<0.01$). No significant difference in IFA consumption by geographic location was observed ($p=0.24$).

Results of the bivariate analysis of student characteristics by self-reported consumption of IFA tablets are presented in Table 5.5.1. In crude comparisons, self-reported ever consuming an IFA tablet over the school year differed significantly by knowledge of IFA tablets and receiving health education sessions on malaria, deworming and clean water/hand hygiene (each $p<0.05$). There were no statistically significant differences in self-reported consumption of IFA tablets by age, menarche, wealth, knowledge of anemia, health education, IFA counseling, or receiving health education sessions on anemia, menstruation, eating iron-rich foods, or geophagy. Among consumers, 88% of girls liked the IFA tablets, and 11% did not. Approximately 38% of IFA consumers experienced desirable changes such as improved health (22%), increased appetite (22%), increased strength (13%), increased activeness (8%), decreased sleepiness (5%), and improved concentration (3%) (data not shown). One quarter of consumers (27%) noticed undesirable changes such as dizziness (4%), excessive hunger (3%), nausea, stomach pain, headaches, constipation, and dark/smelly stool (all $\leq 1\%$) (data not shown). About one-third of those who noticed any changes reported heavier or longer menses, while an equal proportion said it made their menses more regular. Twenty-seven percent reported they had ever consumed an IFA tablet on an empty stomach.

Results of the bivariate analysis of school-level characteristics by self-reported consumption of IFA tablets are presented in Table 5.5.2. Among girls who had ever consumed an IFA tablet, 96% attended a school who kept a written record of their supply of IFA tablets, while only 70% of girls who reported never taking

an IFA tablet attended a school who recorded their IFA supply ($p < 0.01$). Educator training on the GIFTS program was associated with consuming at least one IFA tablet (67% vs 22%, $p = 0.002$). Most (98.5%) of the never consumers were in senior high school ($p < 0.01$). Schools size was also a factor in the proportion of girls who never consumed an IFA tablet. For example, the largest schools (>500 girls) had 84% of the never consumers and only 61% of the consumers ($p < 0.05$). Nearly 70% of consumers attended schools where the educator respondent reported issues with girls refusing IFA tablets, while over 99% of never consumers attended schools reporting the same ($p < 0.05$). Fifty-five percent of consumers attended schools where the educator respondent thought the program was too time-consuming, while only two percent of never consumers attended a school where this perception was reported ($p < 0.01$). Fewer than half (48.3%) of girls who never consumed an IFA tablet attended a school whose educator respondent thought the IFA program was important for the health of girls, while 82% of consumers attended a school who thought it was important ($p < 0.01$).

Table 5.5.3 shows the results of the adjusted linear mixed model among consumers of IFA tablets adjusted for student- and school-level factors. The ability to make up a missed IFA distribution was the only statistically significant student-level predictor. JHS vs. SHS, educator training on the GIFTS program, and educator experiences and perceptions of the program were significant school-level predictors. Girls who reported the ability to make up missed IFA distributions consumed an average of 1.44 ($p < 0.01$) more tablets over one school year than those who did not have that ability. Girls from schools with an educator who received GIFTS program implementation training consumed an adjusted average of 7.57 ($p < 0.01$) more tablets. Girls in JHS who consumed an adjusted average of 5.76 ($p < 0.05$) more tablets relative to girls in SHS. In schools reporting issues with refusals to consume IFA tablets, girls consumed an adjusted average of 4.02 ($p < 0.05$) fewer tablets. In schools where the school educator respondent thought the program was difficult to implement and too time-consuming, girls consumed an adjusted average of 6.92 ($p < 0.01$) and 4.41 ($p < 0.05$) fewer tablets over one school year respectively.

Table 5.5.4 shows the results of the adjusted linear mixed model among all participants, adjusting for student- and school-level factors. Only school-level factors including training, program experiences, and perceptions of the program predicted the total IFA tablets consumed over one school year, even after accounting for student level factors as fixed effects. Girls from schools with a teacher who received GIFTS program implementation training had an adjusted average of 7.72 ($p < 0.001$) more IFA tablets. Girls from schools reporting issues with refusals consumed an adjusted average of 4.24 ($p < 0.05$) fewer tablets. Girls attending a school in which the educator respondent viewed the IFA program as difficult to implement and time consuming consumed an adjusted average of 6.50 and 4.33 fewer tablets, respectively (each $p < 0.05$). Over 75% of the variance around the total number of IFA tablets consumed over one school year was explained at the school level, with approximately 25% coming from factors at the student level.

5.4: Discussion

In this study, we found that 90% of adolescent girls attending schools in two regions of Ghana had ever consumed an IFA tablet during the school year, and 56% consumed 15 or more weekly tablets during the year. The school was largely responsible for the variability in the total number of IFA tablets consumed, indicating that addressing school-level factors would be effective in improving adherence to the intervention. Other evaluations of similar interventions have highlighted contextual factors as predictors of adherence, but also pointed to student-level predictors such as sensitization, perceptions, and side effects^(12,21,22). Importantly, previous studies have not quantified the relative contribution of factors to consumption of IFA tablets. Key strengths of our study are the representative nature of the study sample, longitudinally collected data for IFA consumption, multiple sources of data including program registers, students, and educators, and use of variance decomposition methods. The study is representative of 2,234 schools and approximately 400,000 schoolgirls in two regions of Ghana. The longitudinal collection of the number of IFA tablets consumed through direct observation may reduce recall bias in the outcome, and the multi-level model accounts for student- and school-level factors in the hierarchical structure in which they exist and enables interpretation of cluster effects.

This analysis has several limitations. We were unable to examine ecological variables such as political and economic factors; perceptions, experiences, and motivations of other educators; and community attitudes and beliefs. There may also be social desirability and recall bias in the self-reported predictors at the student and school levels. There is excellent agreement between the self-reported and monitoring consumption data, suggesting that consumption may be accurately captured. However, 13% reported receiving an IFA tablet and throwing it away at some point during the school year, a source of misclassification in the abstracted consumption data. This analysis also has no data on absenteeism which may have been a key individual-level predictor of consumption and would explain the magnitude of the benefit of make-up distributions. The educator respondent for the school questionnaire, while in

most cases the focal person for the program, did vary in some cases. Finally, there may be residual confounding for which the models are unable to account.

School-level factors were prominent in the GLMM analysis, while student-level factors had little relationship with IFA consumption. In adjusted models, the ability to make up a missed IFA distribution, educator training, and the educators' experiences and perceptions were associated with the number of IFA tablets consumed. Having another opportunity to make up a missed IFA distribution may mitigate the effects of absenteeism on program adherence. Making up a missed distribution reflect both student-level agency in seeking a missed IFA tablet and school-level structures that tracked students and allowed for make-up distributions. Educator training on the program remains a key predictor of the number of IFA tablets consumed, even in adjusted models. The educator's experiences and perceptions of the program may influence their motivation and ultimately the performance of the program in their school. This is supported by research showing that knowledge of risks and benefits improves adherence to micronutrient interventions ^(23,24). However, educator training was not associated with perceptions of the program on the school survey (data not shown). Negative perceptions of the difficulty and time burden suggest the need for other modifications at the school level that may also improve adherence such as spreading the responsibility for distribution and streamlining monitoring.

Adherence to IFA consumption is somewhat lower in the GIFTS program than weekly IFA programs in India where complete adherence (one tablet every week throughout the school year) was above 80% in most regions, but ranged from 53% to 99% ^(8,22). Bottlenecks at the levels of acceptability, accessibility, and contact may be responsible for sub-optimal adherence to the program (Figure 5.5.2). This study investigated the student- and school-level facilitators and barriers that may be responsible for creating or eliminating these bottlenecks. In bivariate analyses, the number of IFA tablets consumed differed by girls' age, household wealth, and level of school (JHS vs. SHS). Adolescents experience barriers to swallowing tablets that are often overcome with age and practice ⁽²⁵⁾. However, the inverse relationship

observed between age and IFA tablet adherence may be related to increased decision-making power with age that is increasingly influenced by factors outside of parents and teachers⁽²⁶⁾, or it may be a proxy for level of school or absenteeism. Students at JHS consumed more tablets than students at SHS. These differences may be related to the smaller size of JHS and other structural differences, which allow for better management of distribution and sensitization activities. Fear that the IFA tablet is contraception or a fertility drug was pervasive and, though not a predictor of consumption in this analysis, it may have been an underlying factor more heavily affecting the consumption behaviors of older girls in SHS. Household wealth was expected to have a positive association with IFA consumption as it may be a proxy for school attendance, increasing opportunities to consume tablets^(27,28). However, the inverse was observed in crude analyses and significance was attenuated with no clear direction of the association in adjusted models. Girls from higher income households may have a greater sense of agency to reject IFA tablets. School-level factors may also be responsible for the observed crude associations as girls from the high wealth tertile were more represented in SHS (46.2%) than JHS (32.1%). The evaluation took place during the first year of free SHS, which increased enrollment in SHS and may have changed the wealth profiles therein. Addressing structural barriers in this evolving context may present additional challenges.

In crude analyses, a girl's level of knowledge about IFA tablets and receipt of certain health education sessions were associated with whether she ever consumed an IFA tablet. It is unclear why health sessions related to malaria, deworming, and clean water/hand hygiene are related to whether a student consumes IFA tablets. Health teachers may highlight the linkage of these topics with anemia, increasing awareness of the condition; however, sessions specifically covering anemia and IFA tablets were not associated with whether students consumed an IFA tablet. These relationships are no longer present in adjusted models suggesting the presence of confounding.

Level of school, enrollment, educator training, appropriate accounting for IFA tablets, and the educators' experiences and perceptions were also associated with whether girls ever consumed an IFA tablet. As previously discussed, level and enrollment may both be elements of the school's capacity for effective programming. Educator training emerged as a strong predictor of IFA consumption. It is notable that training only occurred one time in these regions, highlighting the impact of a single training. Annual training of school focal persons and expanding the list of trainees to include other key stakeholders such as head teachers may improve program fidelity and educator perceptions of the program and their motivation. This would also ensure the continuity of the program during staff turnover. Appropriate accounting for the IFA tablets in the school may improve the availability of IFA tablets, as the school is better able to maintain knowledge of the location, quantity, and condition of its stock. Challenges such as improper storage of IFA tablets can be addressed through adequate training at all levels ^(10,29,30), frequent interaction between health staff and teachers, and thorough monitoring ⁽¹²⁾.

Our findings suggest that school-level factors are responsible for the coverage and adherence to IFA supplementation. Additional support to large and senior high schools may improve coverage where the program is a greater burden because of the number of students and organizational structure of the school. Differences in these schools such as boarding, complex academic calendars, and rotation of students through classrooms present challenges for distribution of tablets, tracking adherence, and organizing education sessions. However, these challenges also present opportunities for the intervention to increase the number of contacts and integrate the intervention into existing activities. Ensuring annual training of school staff, including school leadership, may also be beneficial. Training for school staff and students should include guidance on making up missed distributions. Strategies to sensitize and motivate school staff may also benefit the program, as attitudes about the program predicted coverage and adherence to it.

School-level factors associate with IFA consumption included training of school leadership, perceptions of the IFA program, experiences with refusals, and the ability to make up missed IFA distributions. These factors arising from the first-year evaluation may be useful areas of focus for improving the GIFTS program as it matures into a national program. Understanding the perceptions and attitudes of key program stakeholders including school leadership and teachers who are responsible for carrying out the program may provide additional useful information for strengthening the program and supporting its long-term sustainability. Strengthening the health education component and improving knowledge of IFA among students may also produce benefit after school-level factors are addressed. The school is the foundation for the program and may be the most appropriate place to begin for improving coverage and adherence to IFA consumption.

5.5: Figures and Tables

Figure 5.5.1: Conceptual Framework of the Barriers and Facilitators of School-based Iron and Folic Acid (IFA) Supplementation

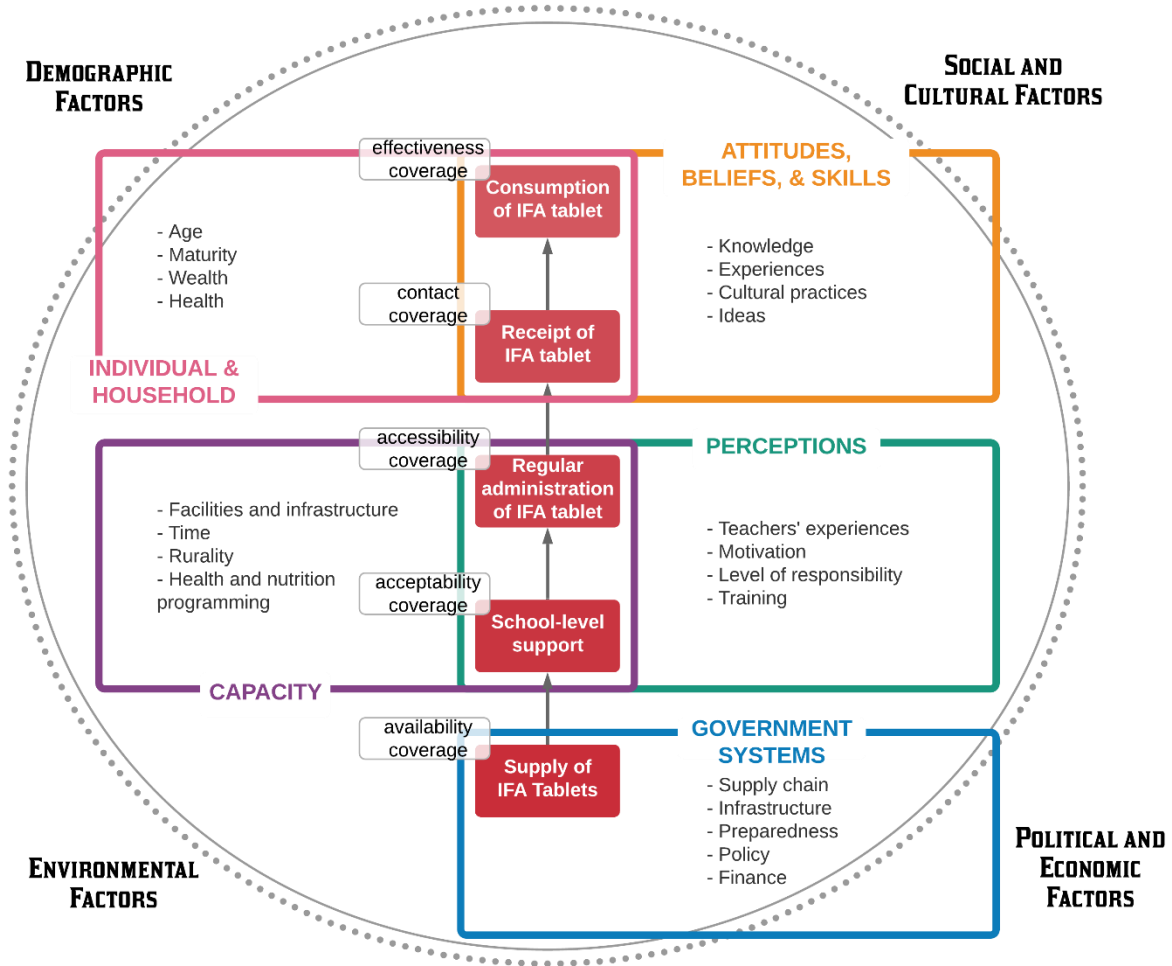
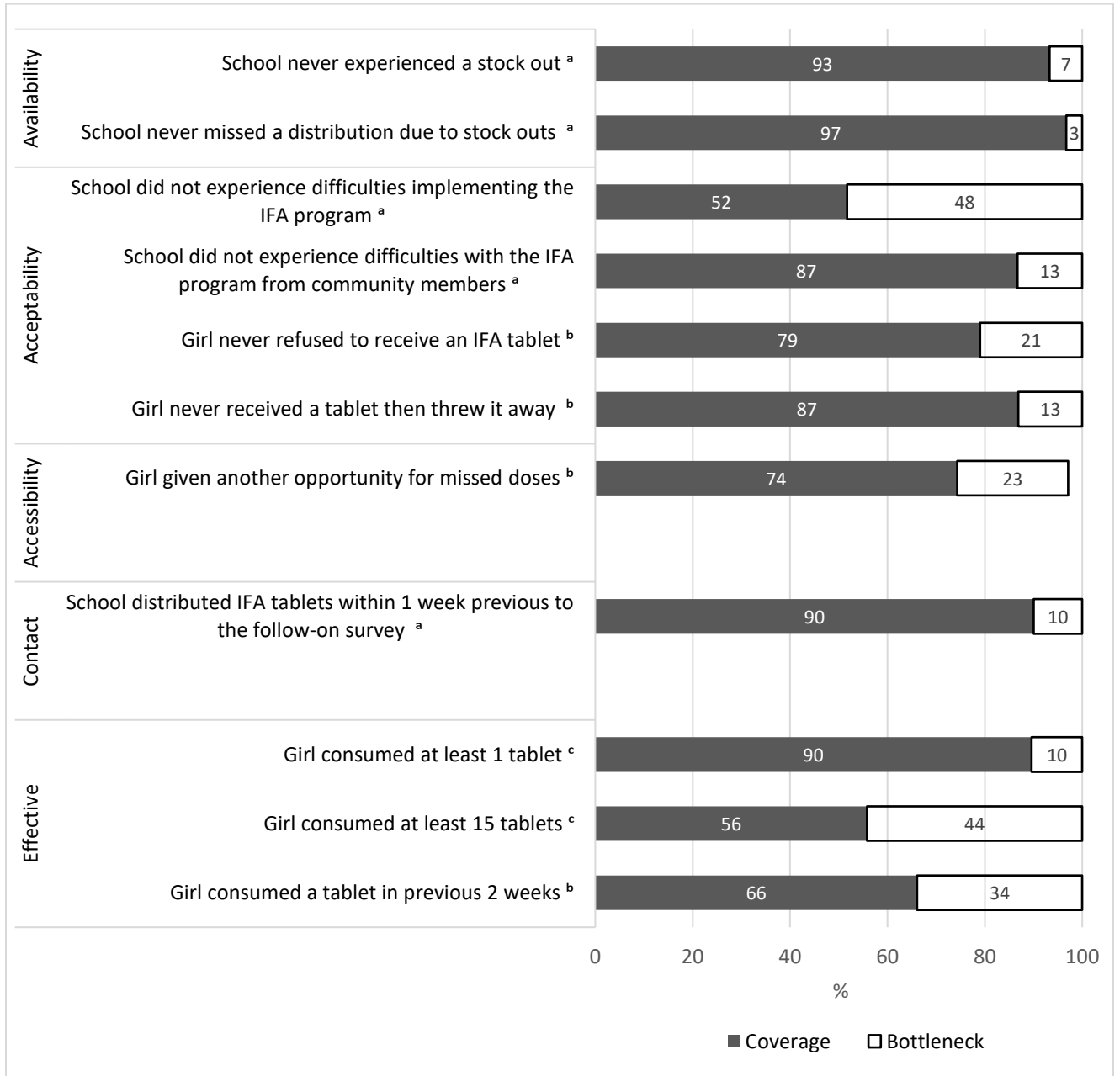


Figure 5.5.2: Levels of Iron and Folic Acid (IFA) Supplementation Coverage and Bottlenecks among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions



Note: Proportions are weighted at the student level to be representative of eligible girls in the school.

^a n=60 schools. Data from cross sectional follow-up survey.

^b n=1,314 girls, only among those who had ever consumed a tablet. Data from cross sectional follow-up survey.

^c n=1,307 girls, sample size reduced due to missing IFA distribution registers. Data from iron and folic acid distribution registers.

Figure 5.5.3: Total Iron and Folic Acid Tablets Consumed Over One School Year by Basic Participant and School Characteristics among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,307)

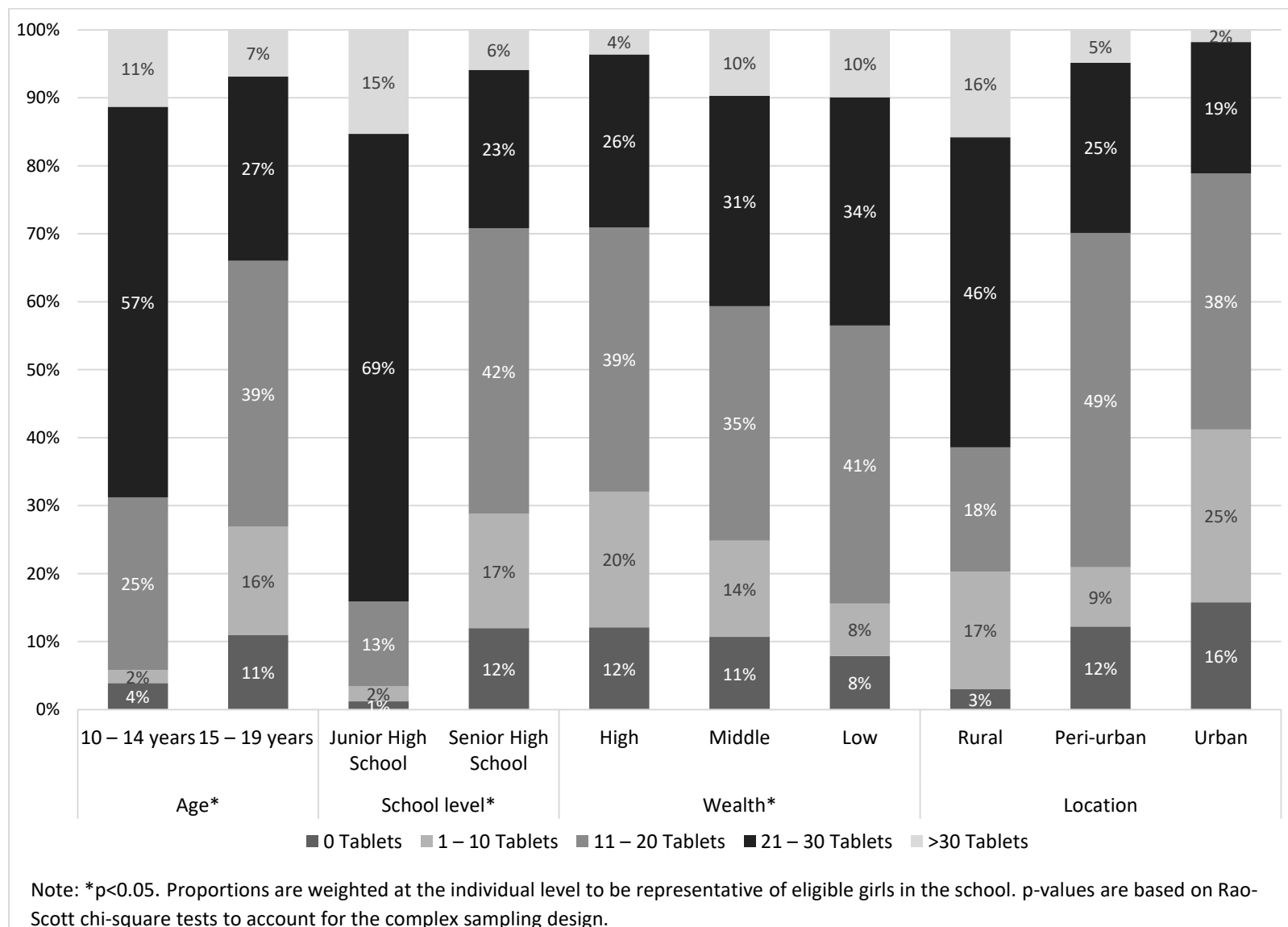


Table 5.5.1: Student Characteristics by Self-reported Consumption of Iron-folic Acid (IFA) Tablets Over One School Year among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions

Characteristic	Never Consumed IFA (n=73)		Consumed At Least 1 IFA (n=1,314)		p-value ^a	Overall (n=1,387)	
	n	% (95% CI)	n	% (95% CI)		n	% (95% CI)
Student							
<i>Demographics</i>							
Age					0.079		
10 – 14 years	8	2.7 (0.0, 6.6)	303	8.4 (4.1, 12.7)		311	7.6 (3.8, 11.5)
15 – 19 years	65	97.3 (93.4, 100)	1011	91.6 (87.3, 95.9)		1076	92.2 (88.2, 96.1)
Reached menarche	67	98.0 (95.5, 100)	1175	96.1 (94.3, 98.0)	0.272	1242	96.3 (94.6, 98.0)
Wealth tertile					0.229		
High	31	48.5 (36.6, 60.4)	438	40.3 (32.2, 48.4)		469	41.2 (33.3, 49.0)
Middle	24	31.4 (26.8, 36.0)	439	31.9 (27.5, 36.3)		463	31.9 (28.1, 35.7)
Low	18	20.1 (8.1, 32.1)	437	27.7 (20.9, 34.6)		455	26.9 (20.1, 33.7)
<i>Knowledge, Attitudes, and Practices (KAP)</i>							
Knowledge of anemia ^b					0.981		
High	18	31.1 (5.8, 56.3)	369	32.1 (25.5, 38.7)		387	32.0 (25.0, 39.0)
Middle	25	33.6 (24.5, 42.6)	436	34.3 (29.5, 39.1)		461	34.2 (29.8, 38.7)
Low	30	35.4 (17.6, 53.1)	509	33.6 (28.3, 38.8)		539	33.7 (28.4, 39.1)
Knowledge of IFA ^b					0.036		
High	12	23.2 (11.3, 35.2)	452	37.7 (32.0, 43.4)		464	36.6 (30.8, 42.3)
Middle	14	23.7 (12.3, 35.0)	324	23.5 (20.3, 26.8)		338	23.5 (20.2, 26.9)
Low	29	53.1 (39.3, 66.9)	528	38.8 (32.0, 45.5)		557	39.9 (33.2, 46.6)
<i>IFA Program Experiences</i>							
Took an IFA tablet on an empty stomach	-	-	361	26.9 (20.5, 33.4)	-	-	-
Likes IFA tablets	-	-	1258	87.9 (83.7, 92.1)	-	-	-
Does not like IFA tablets	-	-	82	11.2 (6.8, 15.6)	-	-	-
Desirable changes upon taking IFA tablets ^c	-	-	594	37.9 (29.2, 46.7)	-	-	-
Undesirable changes upon taking IFA tablets ^d	-	-	322	26.9 (21.2, 32.6)	-	-	-
Shared IFA tablet experiences with friends/family	-	-	714	52.5 (45.4, 59.6)	-	-	-
Able to make up a missed IFA distribution	-	-	1111	76.9 (69.9, 83.8)	-	-	-
Received IFA counseling	7	11.7 (2.2, 21.3)	298	18.4 (13.8, 23.0)	0.260	305	17.7 (13.4, 22.0)
Received health education	29	42.1 (25.4, 58.7)	702	46.4 (40.4, 52.4)	0.631	731	46.0 (40.4, 51.6)
Topics of health education sessions received in previous year							

Anemia	27	34.1 (23.2, 45.0)	679	43.0 (37.3, 48.6)	0.187	706	42.1 (37.1, 47.0)
Malaria	31	36.7 (20.0, 53.4)	791	54.1 (49.0, 59.1)	0.035	822	52.3 (46.9, 57.7)
Deworming	14	15.2 (10.1, 20.3)	398	24.8 (19.8, 29.8)	0.009	412	23.8 (19.2, 28.3)
Clean water and/or hand washing	50	67.0 (56.6, 77.4)	1111	79.7 (74.6, 84.9)	0.022	1161	78.4 (73.7, 83.1)
Menstruation	52	69.6 (56.8, 82.4)	1055	74.8 (71.0, 78.5)	0.426	1107	74.2 (70.6, 77.8)
Eating iron rich foods	31	39.7 (32.1, 47.3)	729	48.6 (42.2, 55.0)	0.132	760	47.7 (42.2, 57.8)
Avoiding eating soil or clay	21	19.1 (4.4, 33.8)	527	32.1 (26.0, 38.1)	0.130	548	30.7 (24.7, 36.7)

Note: Estimates are weighted at the student level to be representative of eligible girls in the school. ^a Rao-Scott chi-square testing the difference between never consumed and consumed at least one IFA tablet. 95% confidence intervals and p-values for student characteristics are based on Taylor series variance estimates to account for the complex sampling design. ^b Knowledge of anemia and IFA were respectively calculated using a composite score of correct responses to questions about anemia (awareness, signs, causes, and effects) and IFA (awareness and effects) and divided into tertiles. ^c Desirable changes included improved health, increased appetite, increased strength, decreased sleepiness, improved concentration, and more regular menstruation. ^d Undesirable changes included dizziness, nausea, stomach pain, headaches, constipation, dark/smelly stool, excessive hunger, and heavier/longer menstruation.

Table 5.5.2: School-level Characteristics by Self-reported Consumption of Iron-folic Acid (IFA) Tablets Over One School Year among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions

Characteristic ^a	Never Consumed IFA (n=73)		Consumed At Least 1 IFA (n=1,314)		p-value	Overall (n=1,387)	
	n	% (95% CI)	n	% (95% CI)		n	% (95% CI)
School							
<i>Government Systems and Supply of Tablets</i>							
Experienced stock outs of IFA tablets	0	-	89	1.8 (0.0, 4.1)	-	89	1.6 (0.0, 3.6)
Missed a distribution due to stock out	0	-	34	0.4 (0.0, 1.1)	-	34	0.4 (0.0, 1.0)
<i>Storage of IFA tablets</i>							
At the school	73	100	1207	83.2 (64.1, 100)		1280	84.9 (67.4, 100)
At someone's home	0	-	107	16.8 (0.0, 35.9)	-	107	15.1 (0.0, 32.6)
Records IFA tablet supply appropriately	45	70.3 (24.7, 100)	1189	96.1 (92.3, 99.9)	0.011	1234	93.4 (86.5, 100)
Educator respondent received training	22	21.9 (0.0, 51.8)	954	67.0 (48.3, 85.6)	0.002	976	62.3 (42.8, 81.7)
<i>School Characteristics</i>							
<i>School level</i>							
Junior high	8	1.5 (0.0, 3.6)	700	15.1 (6.9, 23.3)	<0.001	708	13.7 (6.3, 21.1)
Senior high/vocational	65	98.5 (96.4, 100)	614	84.9 (76.7, 93.1)		679	86.3 (78.9, 93.7)
<i>Enrollment</i>							
<100 girls	6	0.8 (0.0, 2.2)	498	7.3 (3.0, 11.5)	0.030	504	6.6 (2.7, 10.4)
100-299 girls	2	0.7 (0.0, 2.0)	443	20.6 (9.1, 32.0)		445	18.5 (8.1, 28.9)
300-500 girls	18	15.0 (0.0, 39.1)	111	11.6 (1.0, 22.2)		129	11.9 (1.3, 22.5)
>500 girls	47	83.5 (58.9, 100)	262	60.6 (43.1, 78.1)		309	63.0 (46.5, 79.5)
<i>Location</i>							
Rural	14	8.5 (0.0, 20.6)	732	30.8 (14.2, 47.4)	0.346	746	28.5 (12.9, 44.1)
Peri-urban	42	55.0 (8.5, 100)	352	45.7 (25.0, 66.4)		394	46.7 (26.5, 66.8)
Urban	17	36.6 (0.0, 83.8)	230	23.5 (6.7, 40.4)		247	24.9 (6.9, 42.8)
<i>Resources and Capacity</i>							
Functioning toilets/latrines	66	86.4 (59.7, 100)	1088	90.3 (81.7, 98.8)	0.668	1154	89.8 (80.1, 99.6)
Functioning handwashing stations	29	42.7 (0.0, 89.2)	937	69.0 (49.7, 88.3)	0.247	966	66.2 (47.2, 85.3)
Active health clubs	25	42.3 (0.0, 89.0)	613	56.7 (37.4, 76.0)	0.530	638	55.2 (36.0, 74.4)
<i>Previous year activities (school perspective)</i>							
Nutrition counseling	49	48.4 (2.0, 94.7)	599	39.2 (19.0, 59.4)	0.692	648	40.1 (20.5, 59.8)
Deworming	29	39.0 (0.0, 84.5)	372	45.9 (25.0, 66.5)	0.770	401	45.0 (24.8, 65.3)
Anemia screening	33	52.8 (6.5, 99.1)	568	29.9 (12.6, 47.3)	0.224	601	32.3 (13.8, 50.9)
Malaria control counseling	51	77.6 (49.0, 100)	706	55.4 (35.6, 75.2)	0.176	757	57.7 (38.6, 76.9)

Counseling on anemia	61	67.4 (19.6, 100)	684	42.0 (22.5, 61.5)	0.311	745	44.7 (25.2, 64.1)
Counseling on IFA tablets	61	67.4 (19.6, 100)	890	50.4 (30.1, 70.7)	0.495	951	52.2 (32.0, 72.3)
Frequency of health sessions					-		
More than once per month	7	1.1 (0.0, 2.9)	215	5.0 (0.7, 9.3)		222	4.6 (0.7, 8.5)
Once per month	15	35.8 (0.0, 83.2)	445	23.0 (8.1, 37.8)		460	24.3 (7.7, 40.9)
Once or twice per term	51	63.1 (15.9, 100)	602	70.0 (53.7, 85.9)		653	69.1 (51.9, 86.3)
Once or twice per year	0	-	52	2.3 (0.0, 5.9)		52	2.0 (0.0, 5.3)
Average time spent giving health education sessions					0.045		
<30 minutes	1	0.4 (0.0, 1.2)	319	30.6 (10.0, 51.2)		320	27.5 (8.1, 46.8)
30 – 60 minutes	60	67.0 (19.4, 100)	863	52.5 (32.0, 73.0)		923	54.0 (33.7, 74.3)
> 1 hour	12	32.6 (0.0, 80.4)	132	16.9 (1.6, 32.1)		144	18.5 (1.5, 35.5)
<i>Perceptions and Experiences</i>							
Experienced difficulties implementing IFA program	29	34.3 (0.0, 72.5)	637	65.7 (46.4, 85.0)	0.080	637	65.7 (46.4, 85.0)
Experienced difficulties with IFA program from community members	15	10.1 (0.0, 24.3)	180	11.1 (0.0, 22.5)	0.858	195	11.0 (0.0, 22.2)
Girls had concerns about taking IFA	51	71.6 (25.7, 100)	905	68.3 (47.6, 89.0)	0.894	956	68.6 (49.0, 88.2)
Girls refused to consume IFA	72	99.1 (97.0, 100)	880	69.7 (49.0, 90.4)	0.024	952	72.7 (53.3, 92.2)
Thoughts on IFA program							
Difficult to implement	15	33.6 (0.0, 81.2)	200	36.5 (14.8, 58.2)	0.903	215	36.2 (14.9, 57.5)
Too time consuming	2	2.1 (0.0, 6.1)	546	54.9 (35.3, 74.5)	0.004	548	49.4 (29.4, 69.4)
Important for the health of girls	40	48.3 (1.9, 94.7)	1048	82.3 (69.2, 95.4)	0.010	1088	78.8 (62.6, 95.0)
Educator knowledge of anemia ^b					0.641		
High	19	46.3 (0.0, 93.2)	445	31.1 (12.4, 49.8)		464	32.7 (13.3, 52.0)
Middle	14	11.7 (0.0, 34.4)	392	24.9 (9.6, 40.2)		406	23.5 (9.1, 38.0)
Low	40	42.0 (0.0, 87.6)	477	44.0 (23.4, 64.6)		517	43.8 (23.8, 63.8)

Note: Estimates are weighted at the student level to be representative of eligible girls in the school. ^a Rao-Scott chi-square testing the difference between never consumed and consumed at least one IFA tablet. ^b Educator knowledge of anemia was calculated using a composite score of correct responses to questions about anemia (awareness, signs, causes, and effects) and divided into tertiles.

Table 5.5.3: Predictors of the Total Number of Iron and Folic Acid (IFA) Tablets Consumed Over One School Year, Among Consumers of IFA among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,231)

Variable	Adjusted Estimate (95% CI)
<i>Student</i>	
<i>Demographics</i>	
Age, standardized	0.00 (-0.40, 0.39)
Wealth tertile	
High	-0.40 (-1.10, 0.30)
Middle	0.51 (-0.17, 1.18)
Low	ref
<i>Knowledge, Attitudes, and Practices</i>	
Knowledge of anemia, standardized ^a	-0.19 (-0.48, 0.09)
Knowledge of IFA tablets, standardized ^a	0.03 (-0.26, 0.32)
Has ever consumed an IFA tablet on an empty stomach	-0.11 (-0.69, 0.47)
Likes IFA	0.50 (-0.35, 1.34)
Changes noticed upon taking IFA	
No changes	ref
Desirable changes ^b	0.44 (-0.13, 1.01)
Undesirable changes ^c	-0.36 (-0.94, 0.23)
Shared IFA tablet experiences with friends/family	0.04 (-0.50, 0.57)
Received health education	0.32 (-0.29, 0.94)
Received IFA counseling	-0.14 (-0.95, 0.66)
Able to make up a missed IFA distribution	1.44 (0.83, 2.01)***
<i>School</i>	
<i>Government Systems</i>	
Missed a distribution due to stock out	-0.30 (-11.37, 10.77)
Storage of IFA tablets	
At the school	2.06 (-6.19, 10.31)
At someone's home	ref
Records IFA tablet supply appropriately	1.51 (-4.13, 7.14)
Educator Respondent received training on the IFA program	7.57 (2.89, 12.24)**
<i>Resources and Capacity</i>	
School level	
Junior high	5.76 (0.07, 11.45)*
Senior high/vocational	ref
Enrollment, standardized	-1.16 (-4.24, 1.92)
Location	
Rural	1.85 (-3.13, 6.83)
Peri-urban	1.35 (-3.33, 6.03)
Urban	ref
Active health clubs	0.73 (-3.95, 5.41)
Previous year activities	
Nutrition counseling	-0.08 (-3.73, 3.57)
Deworming	1.17 (-3.56, 5.90)
Anemia screening	-0.84 (-5.76, 4.08)
Malaria control counseling	1.73 (-2.32, 5.78)
Counseling on anemia	-6.26 (-14.33, 1.81)
Counseling on IFA tablets	0.16 (-5.87, 6.19)

Frequency of health sessions	
More than once per month	3.24 (-3.87, 10.34)
Once per month	ref
Once or twice per term	1.53 (-2.61, 5.68)
Once or twice per year	-2.09 (-10.96, 6.77)
Average time spent giving health sessions	
<30 minutes	ref
30 – 60 minutes	-1.47 (-5.72, 2.78)
> 1 hour	4.95 (-0.94, 10.85)
<i>Perceptions and Experiences</i>	
Experienced difficulties implementing IFA program	1.38 (-2.76, 5.52)
Experienced difficulties with IFA program from community members	-0.99 (-5.94, 3.96)
Girls had concerns about taking IFA tablets	-0.55 (-5.53, 4.43)
Girls refused to consume IFA tablets	-4.02 (-8.04, -0.01)*
Thoughts on IFA program	
Difficult to implement	-6.92 (-12.14, -1.70)**
Too time consuming	-4.41 (-8.44, -0.37)*
Important for the health of girls	3.34 (-1.31, 7.98)
Educator knowledge of anemia, standardized ^d	-0.31 (-3.21, 2.59)

Note: Estimates are weighted at the student level to be representative of eligible girls in the school. *p<0.05; **p<0.01; ***p<0.001 ^a Knowledge of anemia and IFA were respectively calculated using a composite score of correct responses to questions about anemia and IFA. ^b Desirable changes included improved health, increased appetite, increased strength, decreased sleepiness, improved concentration, and more regular menstruation. ^c Undesirable changes included dizziness, nausea, stomach pain, headaches, constipation, dark/smelly stool, excessive hunger, and heavier/longer menstruation. ^d Educator knowledge of anemia was calculated using a composite score of correct responses to questions about anemia.

Table 5.5.4: Predictors of the Total Number of Iron and Folic Acid (IFA) Tablets Consumed Over One School Year, Among all participants among Adolescent Girls in Ghanaian Schools in Northern and Volta Regions (n=1,298)

Variable	Adjusted Estimate (95% CI)
<i>Student</i>	
<i>Demographics</i>	
Age, standardized	-0.13 (-0.54, 0.29)
Wealth tertile	
High	-0.33 (-1.05, 0.39)
Middle	0.47 (-0.24, 1.17)
Low	ref
<i>Knowledge, Attitudes, and Practices</i>	
Knowledge of anemia, standardized ^a	-0.12 (-0.38, 0.15)
Received health education	0.01 (-0.63, 0.64)
Received IFA counseling	0.08 (-0.75, 0.92)
<i>School</i>	
<i>Government Systems</i>	
Storage of IFA tablets	
At the school	1.53 (-5.75, 8.82)
At someone's home	ref
Records IFA tablet supply appropriately	2.32 (-3.19, 7.82)
Educator Respondent received training	7.72 (3.82, 11.62)***
<i>Resources and Capacity</i>	
School level	
Junior high	5.40 (-0.20, 11.01)
Senior high/vocational	ref
Enrollment, standardized	-1.70 (-4.75, 1.36)
Location	
Rural	1.70 (-3.05, 6.44)
Peri-urban	1.33 (-3.29, 5.94)
Urban	ref
Active health clubs	0.16 (-4.38, 4.69)
Previous year activities	
Nutrition counseling	0.01 (-3.44, 3.46)
Deworming	1.99 (-2.61, 6.60)
Anemia screening	-1.24 (-6.01, 3.61)
Malaria control counseling	1.77 (-2.22, 5.76)
Counseling on anemia	-5.89 (-12.91, 1.14)
Counseling on IFA tablets	0.11 (-5.45, 5.67)
Frequency of health sessions	
More than once per month	3.13 (-3.91, 10.16)
Once per month	ref
Once or twice per term	1.34 (-2.39, 5.07)
Once or twice per year	-1.91 (-10.68, 6.85)
Average time spent giving health sessions	
<30 minutes	ref
30 – 60 minutes	-1.68 (-5.88, 2.51)
> 1 hour	5.23 (-0.56, 11.01)

Perceptions and Experiences

Experienced difficulties implementing IFA program	1.57 (-2.44, 5.57)
Experienced difficulties with IFA program from community members	-1.65 (-6.54, 3.24)
Girls had concerns about taking IFA tablets	-0.38 (-5.30, 4.53)
Girls refused to consume IFA tablets	-4.24 (-8.22, -0.27)*
Thoughts on IFA program	
Difficult to implement	-6.50 (-11.64, -1.37)*
Too time consuming	-4.33 (-8.27, -0.38)*
Important for the health of girls	3.30 (-1.20, 7.80)
Educator Knowledge of anemia, standardized ^b	-0.23 (-3.10, 2.63)

<i>Variance Decomposition</i>	<i>Proportion of Variance</i>
School	75.3
Student	24.7

Note: Estimates are weighted at the student level to be representative of eligible girls in the school. *p<0.05; **p<0.01; ***p<0.001; ^a Knowledge of anemia was calculated using a composite score of correct responses to questions about anemia. ^b Educator knowledge of anemia was calculated using a composite score of correct responses to questions about anemia.

References (Chapter 5)

1. WHO. Guideline: Intermittent iron and folic acid supplementation in menstruating women. Geneva: World Health Organization (WHO); 2011. Report No.: 9789241502023.
2. WHO. Guideline: Intermittent iron supplementation in preschool and school-age children. Geneva: World Health Organization; 2011.
3. University of Ghana, GroundWork, University of Wisconsin-Madison, KEMRI-Wellcome Trust, UNICEF. Ghana micronutrient survey 2017. Accra, Ghana; 2017.
4. WHO. Iron deficiency anaemia assessment, prevention, and control: A guide for programme managers. Geneva: World Health Organization, UNICEF, UNU; 2001.
5. Salam RA, Hooda M, Das JK, Arshad A, Lassi ZS, Middleton P, Bhutta ZA. Interventions to improve adolescent nutrition: A systematic review and meta-analysis. *J Adolesc Health*. 2016;59(4, Supplement):S29-S39.
6. Joshi M, Gumashta R. Weekly iron folate supplementation in adolescent girls—an effective nutritional measure for the management of iron deficiency anaemia. *Glob J Health Sci*. 2013;5(3):188.
7. Lohrmann DK. A complementary ecological model of the coordinated school health program. *Public Health Rep*. 2008;123(6):695-703.
8. Aguayo VM, Paintal K, Singh G. The Adolescent Girls' Anaemia Control Programme: A decade of programming experience to break the inter-generational cycle of malnutrition in India. *Public Health Nutr*. 2013;16(9):1667-76.
9. Roche ML, Bury L, Yusadiredja IN, Asri EK, Purwanti TS, Kusyuniati S, Bhardwaj A, Izwardy D. Adolescent girls' nutrition and prevention of anaemia: a school based multisectoral collaboration in Indonesia. *BMJ*. 2018;363:k4541.
10. Malhotra S, Yadav K, Kusuma Y, Sinha S, Yadav V, Pandav CS. Challenges in scaling up successful public health interventions: Lessons learnt from resistance to a nationwide roll-out of the weekly iron-folic acid supplementation programme for adolescents in India. *Natl Med J India*. 2015;28(2):81-5.
11. Cavalli-Sforza T, Berger J, Smitasiri S, Viteri F. Weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans, and contributions toward achievement of the millennium development goals. *Nutr Rev*. 2005;63(12 Pt 2):S152-8.
12. Risonar M, Tengco L, Rayco-Solon P, Solon F. The effect of a school-based weekly iron supplementation delivery system among anemic schoolchildren in the Philippines. *Eur J Clin Nutr*. 2008;62(8):991.
13. D'Agostino A, Ssebiry F, Murphy H, Cristello A, Nakiwala R, Otim K, Sarkar D, Ngalombi S, Schott W, Katuntu D, et al. Facility- and community-based delivery of micronutrient powders in Uganda: Opening the black box of implementation using mixed methods. *Matern Child Nutr*. 2019;15(S5):e12798.
14. Priya S, Datta S, Bahurupi Y, Narayan K, Nishanthini N, Ramya M. Factors influencing weekly iron folic acid supplementation programme among school children: Where to focus our attention? *Saudi J Health Sci*. 2016;5(1):28-33.
15. Enrolment ratios [Internet]. United Nations Education Scientific and Cultural Organization. 2019 [cited 04 February 2020]. Available from: <http://data.uis.unesco.org>.
16. Ghana Health Service, Ghana Education Service, UNICEF-Ghana, Emory University Global Health Institute, Centers for Disease Control and Prevention (CDC). Impact evaluation of a school-based integrated adolescent nutrition and health Programme with Iron and Folic-Acid supplementation intervention among adolescent girls in Ghana. Cantonments, Accra Ghana: UNICEF-Ghana; 2019.
17. Murray DM. Design and analysis of group-randomized trials. New York: Oxford University Press; 1998. xi, 467 p. p.

18. Vyas S, Kumaranayake L. Constructing socio-economic status indices: How to use principal components analysis. *Health Policy Plan*. 2006;21(6):459-68.
19. Ghana Statistical Service. Population and Housing Census. Accra, Ghana: Ghana Statistical Service; 2010.
20. Tanahashi T. Health service coverage and its evaluation. *Bull World Health Organ*. 1978;56(2):295-303.
21. Kheirouri S, Alizadeh M. Process evaluation of a national school-based iron supplementation program for adolescent girls in Iran. *BMC Public Health*. 2014;14(1):959.
22. Vir SC, Singh N, Nigam AK, Jain R. Weekly iron and folic acid supplementation with counseling reduces anemia in adolescent girls: a large-scale effectiveness study in Uttar Pradesh, India. *Food Nutr Bull*. 2008;29(3):186-94.
23. Tumilowicz A, Habicht J-P, Mbuya MNN, Beal T, Ntozini R, Rohner F, Pelto GH, Fisseha T, Haidar J, Assefa N, et al. Bottlenecks and predictors of coverage and adherence outcomes for a micronutrient powder program in Ethiopia. *Matern Child Nutr*. 2019;15(S5):e12807.
24. Ford ND, Ruth LJ, Ngalombi S, Lubowa A, Halati S, Ahimbisibwe M, Mapango C, Whitehead Jr RD, Jefferds ME. Predictors of micronutrient powder sachet coverage and recent intake among children 12–23 months in Eastern Uganda. *Matern Child Nutr*. 2019;15(S5):e12792.
25. Hansen DL, Tulinius D, Hansen EH. Adolescents' struggles with swallowing tablets: barriers, strategies and learning. *Pharm World Sci*. 2007;30(1):65.
26. Patton GC, Sawyer SM, Santelli JS, Ross DA, Afifi R, Allen NB, Arora M, Azzopardi P, Baldwin W, Bonell C, et al. Our future: a Lancet commission on adolescent health and wellbeing. *Lancet*. 2016;387(10036):2423-78.
27. Saasa SK. Education among Zambian children: linking head of household characteristics to school attendance. *Vulnerable Child Youth Stud*. 2018;13(3):239-46.
28. Shehu HK. Factors influencing primary school non-attendance among children in north west Nigeria. *Lit Inf Comput Educ J*. 2018;9(2).
29. Jefferds MED, Mirkovic KR, Subedi GR, Mebrahtu S, Dahal P, Perrine CG. Predictors of micronutrient powder sachet coverage in Nepal. *Matern Child Nutr*. 2015;11(S4):77-89.
30. Reerink I, Namaste SM, Poonawala A, Nyhus Dhillon C, Aburto N, Chaudhery D, Kroeun H, Griffiths M, Haque MR, Bonvecchio A, et al. Experiences and lessons learned for delivery of micronutrient powders interventions. *Matern Child Nutr*. 2017;13(S1):e12495.

Chapter 6: A Qualitative Analysis of Program Fidelity, Innovation, and Perspectives of Educators and Parents after Two Years of the Girls' Iron-Folic acid Tablet Supplementation (GIFTS) Program

Lucas Gosdin^{1,2}, Esi Foriwa Amoafu³, O. Yaw Addo^{1,2,4}, Andrea J Sharma^{2,5}, Xoeshe Ashigbi³, Braima Mumuni³, Ruth Situma⁶, Usha Ramakrishnan^{1,7}, Reynaldo Martorell^{1,7}, and Maria Elena Jefferds²

¹Nutrition and Health Sciences, Laney Graduate School, Emory University, 1518 Clifton Rd. Atlanta, GA, USA; ²Nutrition Branch, Centers for Disease Control and Prevention, 4770 Buford Hwy, Atlanta, GA, USA;

³Ghana Health Service of Ministry of Health, PO Box M44, Ministries, Accra, Ghana; ⁴Emory Global Health Institute, Atlanta, GA USA; ⁵U.S. Public Health Service Commissioned Corps, Atlanta, GA;

⁶UNICEF-Ghana, 4-8th Rangoon Close, Cantonments, Accra, Ghana; ⁷Hubert Department of Global Health, Rollins School of Public Health, Emory University;

Abstract

To address the burden of anemia among adolescent girls in Ghana, government agencies and non-governmental organizations established the Girls' Iron-Folic acid Tablet Supplementation (GIFTS) program in 2017. An evaluation of the first year of the program found that while iron and folic acid (IFA) supplementation reached nearly all adolescent girls in schools during the first year of the program, adherence was below the population minimum effective number of tablets over the school year for most girls. We sought to further investigate the drivers of program uptake and adherence and understand how these factors might be modified to improve the program and promote its sustainability. After stratifying by level, size, geographic location, and intake adherence during year one, 16 schools were purposively selected from 5 regions of Ghana. For each school, we conducted semi-structured key informant interviews with 1 educator at the district level, 3 educators at the school level, and one parent leader. Each interview was recorded, transcribed, and coded based on deductive and inductive themes. Themes included distribution of IFA tablets (supply chain, method, responsibility, time burden, and consumers); perceptions, attitudes, and awareness (educators, parents, and students); sensitization; health and nutrition education; training and resources; and motivation (intrinsic and extrinsic). Relevant themes were divided by educators, parents, and students. The results indicated that, after two years of implementation, schools had adapted the program, and widespread changes in attitudes and beliefs about the IFA tablets had improved their acceptability. However, limitations remained including supply chain, program ownership, communication between health and education sectors, training, motivation, and other resources. These results may be used to improve intake adherence and program fidelity in Ghana's IFA program and have applications for similar programs in low- and middle-income countries.

6.1: Introduction

Anemia remains a problem of public health significance in Ghana. In 2017, the prevalence of anemia among adolescent girls 15-19 years of age was 26%.⁽¹⁾ To address this problem, the Ghana Health Service (GHS) and Ghana Education Service (GES) – in collaboration with UNICEF, the Centers for Disease Control and Prevention (CDC), and other international agencies – implemented the Girls’ Iron-Folic acid Tablet Supplementation (GIFTS) program. The GIFTS program was integrated into the existing School Health Education Program of the Ghana Education Service and the existing community outreach activities of the Ghana Health Service. The program targets all adolescents ages 10-19 years with health and nutrition education, promoting behavior change to control and prevent anemia. In addition, girls ages 10-19 years are given weekly iron and folic acid (IFA) tablets, following recommendations by the World Health Organization.^(2,3) In schools, this is done through directly observed therapy each week while school is in session.

The evaluation of the GIFTS program focused on the school-based platform because of resource constraints, the novelty of school as the delivery platform for micronutrients, and in light of rising school attendance rates due to the introduction of free public secondary school.⁽⁴⁾ Schools have the advantages of regular access to the target age group, an environment of learning, and highly educated staff. Still, quantitative evaluations showed that while the program had reached 90% of the students during the first year, intake adherence was below the minimum effective number of IFA tablets (26 tablets) for 76% of students.⁽⁵⁾ Only about half of students received 15 tablets: approximately half of the tablets for which they would have been eligible over the school year.⁽⁶⁾ Similar programs, like India’s Adolescent Girls’ Anemia Control Program, have had high adherence to IFA supplementation with girls consuming between 88% and 99% of tablets on average over one year in five evaluated states⁽⁷⁾. However, in Andhra Pradesh girls consumed an average of 53% of tablets, which was attributed to supply stock-outs.⁽⁷⁾ Additional analyses of Year 1 of the GIFTS program showed that school-level factors were

primarily responsible for the variation in the total number of IFA tablets consumed by students during the first school year. Lessons learned from India's program suggest intake adherence can be improved by using existing delivery platforms, clearly defining roles and responsibilities, involving stakeholders at all levels, using communication strategies that focus on the benefits of the program to adolescent health and school performance, maintaining a robust supply chain, using fixed-day distribution, utilizing simple monitoring tools, and prioritizing a limited number of evidence-based interventions to deliver as a package.⁽⁷⁾ While the GIFTS program design follows these lessons learned, there is a need to understand program fidelity and other elements that are not design-based such as cross-sectoral communication, perceptions and attitudes, institutional commitment, and program ownership by educators.⁽⁸⁾

There is limited evidence on the perceptions, attitudes, and beliefs of students and educators towards the GIFTS program,⁽⁶⁾ and there is no information on the perceptions of parents. Misconceptions about the effects of IFA tablets may have caused some girls to refuse IFA supplementation. While educators reported giving health talks, most students had not received regular health and nutrition education during the first year of the program, and students' associated knowledge was only marginally improved.⁽⁶⁾

A qualitative study design was chosen because it enables a deeper and more nuanced assessment of explanations for phenomena. Qualitative methods are also useful when measurement is a challenge such as when assessing perceptions, attitudes, and motivations.⁽⁹⁾ This work was guided by a conceptual framework built on Bronfenbrenner's Social-Ecological Model⁽¹⁰⁾ and Tanahashi's levels of health service coverage⁽¹¹⁾ with elements from the Innocenti Framework on Food Systems for Children and Adolescents⁽¹²⁾ (Figure 6.5.1). This framework first guided the quantitative analysis of the barriers and facilitators of IFA consumption in the GIFTS program; however, while the quantitative analysis identified relationships between the studied factors and IFA consumption, it was unable to provide explanations

for why the relationships might exist. The quantitative analysis also only provided the perspective of one educator role at each school.

We sought to describe potential drivers of intake adherence, explain how these factors influence the success of the program, and understand how they might be modified to improve it. We also sought to describe health and nutrition education from the perspectives of multiple stakeholders and understand potential explanations for its deficits.

6.2: Methods

Sites

As part of a pre-post, longitudinal evaluation of Phase I of the GIFTS program in 2017-2018, 60 schools were randomly selected from two of the four Phase I regions: Northern (now Northern, Savannah, and North East) and Volta (now Volta and Oti). From these schools, four junior high schools (JHS) and four senior high schools (SHS) or vocational schools in each of the two regions were purposively selected using stratification by average total number of IFA tablets consumed during Year 1 (high vs. low), geographical location (rural vs. urban), and school size (large vs. small) by enrollment of girls. This resulted in a balance of schools within strata. There were 16 schools selected as locations for key informant interviews (Figure 6.5.2).

Participant Selection

Key informants were chosen at multiple levels: 1) district SHEP coordinator, 2) head teacher, 3) GIFTS focal person, 4) non-health teacher, and 5) Parent-Teacher Association (PTA) or School Management Committee (SMC) chairperson. Preference was given to the selection of the district SHEP coordinator, but the Girl Child Officer, the district-level official charged with activities that promote gender equity, was selected in the absence of a district SHEP. The head teacher is the executive of the school, referred to as the principal in the North American system. In six schools, the head teacher was unwilling or unable to be interviewed and the assistant head teacher or house master/mistress was interviewed in

their stead. The selection of the non-health teacher was delegated to the head teacher in each school. Criteria for the selection of the non-health teacher were as follows: 1) they must not be directly responsible for the GIFTS program, 2) they must teach a subject outside of health science, nutrition, or physical activity, and 3) preference was given to teachers who had been in the school since October 2017 (the start of the GIFTS program). The PTA or SMC chairperson was identified by the head teacher or program focal person in each school.

Data Collection

Six qualitative interviewers, two females and four males, were chosen from GHS staff with language and interviewing skills appropriate for the context. All interviewers had prior interviewing experience and training. Teams were trained on qualitative interviewing techniques, goals of the study, ethics protocols, use of interview guides, use of recording devices, and summarizing interviews. During the training, interview guides were reviewed for clarity and revised as needed. Interviewers practiced in pairs including effective probing and writing interview summaries. A pilot and pre-test of interview guides was conducted in three schools during the training week prior to the start of data collection. Following the pilot, interview guides were further refined and interviewer practiced with the final interview guides. Teams of three traveled to each region. Data collection occurred over nine days at the start of the 2019-2020 school year.

Semi-structured key informant interviews were used to collect information from respondents. Interview guides were developed based on deductive themes around the distribution of IFA tablets, sensitization and beliefs, health and nutrition education, and acceptability of purchasing. Four separate interview guides were created for each respondent category (Appendix I). Interviewers used the same guide with head teachers and GIFTS focal persons. Interview guides were designed to assist interviewers in using open-ended questions, covering the topics of deductive themes, and using effective probing questions when necessary. Interviews were designed to be conducted in English, the *lingua franca* of Ghana. Since

formal education is done in English, we anticipated that educator interviews would be completed in English but that some PTA/SMC chairperson interviews may be conducted in local languages.

Individually, interviewers conducted interviews in a private location and recorded then using stereo digital recording devices. Educator interviews lasted an average of approximately 45-60 minutes, and PTA/SMC interviews lasted approximately 10-15 minutes. After each, interviewers completed a summary consisting of at least three paragraphs covering their overall impressions of the interview, interesting findings, and outstanding questions that were unanswered in the interview. These summaries were included with each interview.

Ethical considerations

Ethical approval for this project was also obtained from the Ghana Ministry of Health Ethics Committee. The GIFTS project was exempted from review by the Emory University Institutional Review Board. The US Centers for Disease Control and Prevention determined this project was public health practice. Written informed consent was obtained from all participants. Recordings were kept secure throughout data collection and de-identified recordings and transcripts were transferred to the CDC team where they were stored on password-protected computers.

Data Analysis

English language interviews were transcribed verbatim and the seven interviews conducted in local languages were translated to English during transcription. Translation and transcription were conducted by a professional third-party service in Accra, Ghana. A sub-sample of transcripts (~10%) were compared to the recordings to verify accuracy of transcription by a member of the study team. No errors were found during this review, and transcriptionists carefully insert pauses, laughter, background interruptions, and other vocalizations.

A thematic analysis method was used.⁽¹³⁾ All transcripts were thoroughly read, and a coding system was developed based on deductive themes. The primary analyst began by coding one interview from each

respondent category and modified the coding system based on these transcripts. Only minor modifications were necessary. In order to assess inter-rater reliability, one interview from each respondent category was independently segmented and coded by a second analyst. Percent agreement was 89% for code occurrence within each document and 53% for code intersection at the segment level at a minimum 50% overlap. Kappa score for code intersection was 0.50, calculated as percent agreement minus percent agreement due to chance divided by one minus percent agreement due to chance. These values were determined to be acceptable for the purposes of this research and because a single analyst fully coded the transcripts.⁽¹⁴⁾

Though saturation of themes and perspectives was reached at around the halfway point, all transcripts were segmented and coded to make use of all data and uncover any potential differences by school strata. Coded segments were then examined to identify patterns as well as the breadth of responses within each code. Themes emerged from codes and relationships between codes. Themes were compared across the strata of respondent category, school level, school size, and IFA intake adherence. Interviewers' summaries helped confirm relevant themes. Coding and analyses were conducted in MAXQDA 2018.

Data were presented under themes and select quotations were used to reinforce the findings. Finally, a draft of the analysis was reviewed and edited by the leading interviewers from each region to ensure that it aligned with their understanding.

6.3: Results

In total, 77 key informant interviews were conducted with 16 respondents of each category except for PTA/SMC chairperson, as three were not located during data collection. Six PTA/SMC chairperson interviews and one GIFTS focal person interview were conducted in a local language, while the remaining 70 were conducted in English. A total of 2,741 minutes of interviews were recorded. Males

accounted for 49 of 77 respondents. Most head teachers, teachers, and PTA/SMC chairpersons were male, while most GIFTS focal persons and district SHEP coordinators were female. Table 6.5.1 provides a summary of key findings, implications, and potential solutions.

Distribution of IFA Tablets

There are three terms in the school year. Ten schools had already distributed IFA tablets in the current term, and five had distributed during the previous term. One school had not distributed tablets since the second term of the previous school year.

Supply Chain

Models of IFA supply chain varied according to district SHEP coordinators. All reported that the district nutrition officer (DNO) received the supply from regional medical stores. Commonly, these were distributed to schools by health personnel including the DNO or community health nurses (CHN). In some cases, district SHEP coordinators were included in the distribution of tablets to schools. One reported that they notified head teachers through a WhatsApp™ platform to collect them from the district SHEP office, while more remote schools had their tablet delivered to the local health center or Community-based Health and Planning Service (CHPS) zone. Some district SHEP coordinators felt they had been left out of the supply chain altogether, and one preferred that Ghana Education Service (GES) take control of supply chain. Principal issues were differing terminology and priorities between health and education staff and confusion caused by distribution through CHPS zones because they do not align with the GES “circuit” system.

“We [educators] all understand the same language... A lot of [educators] don’t feel comfortable working with nurses. [Educators] think [nurses] are always interrupting lessons, but school officers, they always welcome us in the schools. So, I recommend that [tablets] should be sent directly to the municipal and district officers.” – District SHEP Coordinator

“Ghana Health Service they deal with zones or sub-districts, and GES we deal with circuits. So the nurses [have] their [...] sub zones or sub-districts with schools located

in their sub zone. The nurse in-charge will go to region and take the tablet and then after the allocation has been done and at their outfit, the nurse in-charge in that particular school sends the tablet to the schools at the beginning of every term.” – District SHEP Coordinator

The supply of IFA tablets was consistent for most schools; however, five schools reported that they had issues with shortages and/or expiring tablets. The resulting stock-outs lasted between one week and two entire terms. While most stock-outs occurred during the previous year, two schools were experiencing shortages at the time of interview. One issue identified was receiving the tablets late in the school year. No patterns were observed in the characteristics of schools with supply chain issues.

“I remember one of the teachers coming to complain that the drugs were not enough and that it couldn’t reach. They, [national program], need to get enough drugs to run the program. Also sometimes the time the drugs come is late so we are not able to administer it before they come.” – Head Teacher

The method of resolving shortages of IFA was varied. While some district SHEP coordinators and focal persons stated that shortages should be reported to the district level directly, others stated it is reported to the local health center or on the WhatsApp™ platform for head teachers.

“We have community nurses all over the place. Either report to them or report directly to the Municipal SHEP Coordinator.” – District SHEP Coordinator

Methods of Distribution of IFA Tablets within Schools

A majority of schools followed a similar method of distribution with only minor differences. Method of distribution did not follow any pattern of school size, level, or location. All schools reported they distribute tablets on Wednesdays, and most focal persons volunteered that students were given make-up doses up to the following Wednesday.

"Actually we distribute it every Wednesday and if a student is absent, when she comes the next day we try and give her, we'll be giving it until the next Wednesday, if that student couldn't come we give the person absent or zero." -Focal Person

Tablets were most commonly distributed by the GIFTS program focal person (Figure 6.5.3). Focal persons were commonly assisted by other teachers, head teachers, and students, though in five of the schools, the focal person distributed them alone. Two schools gave responsibility for distribution to class or health prefects, which are student leaders. One school gave the tablets to class teachers to distribute themselves. These alternatives were reported to increase the efficiency of distribution. Students were typically called class-by-class to a central location or the focal person went class-to-class; however, some focal persons called students individually to their offices. Commonly, tablets were given after breaks, lunch, or assembly, though some gave during worship, after school, or in the dormitories.

"After second break, after they finish eating, we will call the girls in one class, mention their name, they will come with their water, give them the folic acid, [and] they will take it in front of me." - Focal Person

Most focal persons expressed the need for clean water, and one-quarter of them provided the water themselves. Some highlighted the need for girls to eat before taking the tablet. One focal person created a system of reminding girls on Tuesdays to eat before consuming the tablet.

"Tuesday ... when we assemble for closing I tell [students] that tomorrow is another week so those who have not been eating before coming to school for tomorrow they should try and get something to eat before they come or they bring money. When it is break they go and buy food and after break I call them class by class ... and give it out." –Focal Person

Perceived Time Burden

There was a wide range in the estimated time burden of the GIFTS program on a typical distribution day, ranging from 2 minutes to 7 hours. Time burden did not follow any pattern of school size, level, or

location. However, time burden was greatest among district SHEP coordinators as their duties involved traveling to schools where they spent most of the day supervising. This responsibility was most time consuming in rural districts where travel conditions prevented visiting multiple schools in one day. Many focal persons spent more than 30 minutes on the program, while most teachers and head teachers spent less than 30 minutes (Figure 6.5.4). Perceptions of the time burden were not necessarily linked to the estimates of the time devoted to the program. Attitudes were split between those who felt that it was not very time consuming and those who felt that it took too much of their time, especially instructional time.

“It takes a lot of time and especially on such days; I become very exhausted because I have three separate lessons on that day: three classes plus the activity itself.” – Focal Person

“Even though it takes my time but not too much of time.” – District SHEP Coordinator

Challenges in Weekly Distribution of IFA Tablets in Schools

Challenges in distribution included shortages, expiring tablets, religious fasting, students not eating prior to distribution, lack of water, student and focal person absences, negative perceptions about IFA by students and parents, side-effects, sporting or cultural events, intrusion into instructional time, examination periods, and insufficient GIFTS program registers. By the start of the third year of the GIFTS program, most schools had overcome some of these challenges. Religious fasting was considered by affected schools to be a time to pause distribution. Some schools adjusted the time of distribution so students would be more likely to eat and have water prior to distribution. Some schools provided water themselves, often at the focal person’s expense. Absent students were allowed to make up their missed tablet before the next distribution, and other educators filled in for absent focal persons. When sporting events disrupted the time meant for distribution of tablets, make-up distributions were held. Some

schools adjusted the time of distribution to avoid instructional time. Still, not all schools had implemented these strategies and the aforementioned challenges remained for some schools.

"It's very, very tedious. Moving from one class to the other, carrying water around because you have to beg [girls]. If you ask [students] to buy water, they'll tell you they don't have a pesewa to buy water." - Focal Person

"The distribution is not easy. Moving from class to class, talking, at times you have to pat some of [the students] before they take it. [...] You'll say, 'Oh sweetie, take it. This one is good'. 'It can't do anything to you'." - Focal Person

Consumers of IFA Tablets Outside of the Target Population

Respondents were aware of the target population of the GIFTS program in schools. However, innovations put into place nationally and at the school level resulted in consumption of the tablet by people outside the target of adolescent girls attending schools. Nationally, female teachers were encouraged to consume the tablets to serve as role models for the students and because the anemia burden is high for women of reproductive age. Most schools reported that female teachers were consuming the IFA tablet with students; however, a minority of schools' leadership believed the tablets were solely for girls and did not allow teachers to consume it. Schools with teachers consuming it reported that students more easily accepted the IFA tablet.

"Because when you see a teacher also taking the same drug, then it means it is not a poison, it is something that will help your system, so I think it has increased the enrolment, as compared to the previous one." – Focal Person

A few schools had male teachers who also consumed the IFA tablet. Some believed the tablet was tailored to women and men should not consume it. A small number of schools had male teachers interested in consuming the tablet, but they were not permitted. Most focal persons, head teachers, and district SHEP coordinators reported that they, other staff, and/or male students wanted IFA tablets

to be given to male students. Some schools had boys consume IFA tablets: some during the first week to show girls that it was unrelated to contraception or fertility and others during the final weeks before the surplus of IFA tablets expired.

“[GHS staff from Accra] advised us that we should bring the boys on board, so that [girls] will feel comfortable taking it, so we brought the boys on board.” – Teacher

Less common consumers of IFA from schools were family members of educators including children and wives, girls who were no longer enrolled in school, and boys who appeared malnourished or anemic. One such boy was reported as having sickle cell disease. Distribution to students with sickle cell was a point of confusion. Some correctly recounted their training to exclude girls with sickle cell disease from distribution, while others reported that the IFA tablet was improving the health of students with the condition. Another point of confusion surrounds consumption of IFA during menstruation. While most correctly discussed IFA tablets as helpful in replacing blood lost during menstruation, some stated that they advise girls not to consume the tablet while menstruating.

“We were informed by the health people ... that [students with sickle cell disease] will not be part of it because they take the folic acid already.” – Head Teacher

“There is one girl who is sickle cell ... and when they started taking it when she took it she had pains throughout the night and she couldn’t sleep that’s why she said she wouldn’t take again. So I encouraged her to take and when she took it, the next week she was okay, the system was used to it so she was taking and nothing was happening to her again.” – Focal Person

Two sisters reported that their seizures had stopped upon consuming the IFA tablet, and their family was given an entire bottle of IFA tablets by the focal person to include their 8-year-old sister with the same condition. Another focal person reported treating a girl with one IFA tablet every day for several weeks after she experienced a heavy loss of blood.

Perceptions, Attitudes, and Awareness

Educators and PTA/SMC chairpersons reported on the perceptions, attitudes, and awareness of educators, parents, and students.

Educators

Most educators reported positive feelings about the program's intended physical and cognitive health benefits. Most could explain the purpose of IFA as a way to prevent anemia and/or improve a person's blood, and many identified blood lost during menstruation as the reason for targeting girls. IFA tablets were commonly referred to as a "drug." Most identified folic acid as a component of the tablet, but fewer named iron.

"I know that folic acid is very, very good for every human being, especially the girls, the student girls. You know at times when you are in your menses, you know some of the problems that you face, because you are losing blood and the hemoglobin is down, you cannot pay attention in class. So as for the supplement or the GIFTS program it was a very good program to help the student girls, but because the education didn't go down well from the beginning, that was what made the students afraid of, or lose interest in the supplement." – Teacher

A large portion of educators advocated for the boys to be included in the distribution of IFA tablets.

"I think we have been advocating that it should also be extended to the boys since they also lose blood." – Teacher

Many educators linked the program to positive changes they had observed among the girls including reduced sleepiness and absences, better attention and academic performance, and improved physical appearance. Educators who consumed the tablets themselves reported improvements in their own health. Some educators feared the program would end and pleaded that it continues.

"So ever since the beginning of the program in the school, initially I observe that particularly from one... about three girls, four girls, will not be in school... Some of them when they come to school, ... you realize they always sleep in the class, but after taking the supplement, you realize that most of the girls are doing... The average girl attendance in the school is far better than the boys weekly. So, I realize that the program is very effective. So for me, I'll not relent on my effort... If it can continue to

eternity in the schools, I'll be very grateful.” – Head Teacher

“Actually, when you get to the schools and you see the girls they look fresh and through interactions with teachers the girls no longer dormant during mathematics and other subjects actually they are actively participating in class. That is, those who have taken it with their faith.” – District SHEP Coordinator

A small number of educators reported that their colleagues did not participate because of their view that the tablet was contraception or harmful in some way. One district SHEP coordinator reported that the focal person at a religious school would not distribute the IFA tablets because of the person's perception that the tablet was associated with blood. This focal person was replaced with a willing educator.

“Interviewer: So how do other teachers feel about the tablets?

Head Teacher: ... Normally at gatherings, we make these announcements, some of them understand the concept, but some too, just as I mentioned earlier, their mind is that it is a way of family planning... I do not know the reason for which they are trying to scare them that don't take it because it is a way of family planning ..., so I really cannot speak for those teachers...”

Educators were also concerned about how the distribution of IFA tablets infringes on instructional time. Some focal persons reported that it cost them time as an instructor, and other educators discussed how it took the girls' time away from classes.

“I think what I see is that it is a good program, it is a good thing which needs to be encouraged. Anything you start has difficulties, so in our school we started not quite too long, so I think with the education now the children are aware, they are fully aware of its advantages. So all that I'll say is that as I mentioned earlier on, the time they normally do the distribution must be looked at, so that it will not have anything to do with or to affect classes.” – Head Teacher

Many educators expressed a need for more support or compensation as they felt the program was outside their normal duties. Some district SHEP coordinators highlighted circuit supervisors as underutilized sources of support for the program.

“The only problems we have had so far is about complaints from the teachers that it’s an additional responsibility being given them not by the GES, but there is nothing to motivate them, so that is in a way making them feel a bit reluctant.” – District SHEP Coordinator

“...the Circuit Supervisors were not part of the training and since ... they have their respective circuits they also do close monitoring in the schools. So, I think if the circuit supervisors were also trained, even though after the training we brief them, but if they are also trained so that they will have in-depth knowledge about the program, so that when they also go to their monitoring they will monitor the implementation of the program.” – District SHEP Coordinator

Parents

Most educators reported that at the start of the GIFTS program, parents cautioned girls against consuming the IFA tablet because they believed it was contraception or otherwise related to reproductive health. After two years of the program, educators reported few persistent issues from parents after the initial wave of misconceptions about the effects of the tablet subsided.

“People were saying that it is a form of family planning so the children should not take it because they won’t give birth after the school. Some too are saying that when they are taking it, their menses will overflow so they won’t take it, some also say that when they are taking it, their menses stopped, a whole lot of things so we managed to talk to them, we go there, we go to the school to sensitize them on the folic acid. [...] We went there to talk to them so I think things are normalizing now.” – District SHEP Coordinator

PTA/SMC chairpersons also reported initial misgivings about the program. They placed the blame for these beliefs on a lack of proper sensitization and stated that their attitudes changed following sensitization.

“Initially we heard it was a ploy, it’s for family planning. Then later we got explanation that it is not family planning. It was the education that was not properly done that is why this misconception came.” – PTA Chairperson

Many parents were aware and supportive of the program. The PTA/SMC chairpersons for schools that held sensitization meetings or lived in communities that held sensitization activities had more knowledge and awareness of the program than others who did not attend such sensitization meetings.

“This program I attended a seminar at [village] chief’s compound with this my sheik. So they educated us more about it, before they started, they sensitized the schools and girls about the importance of this drug: that it boosts their immune system so that ... every month, [when] they lose blood ...this drug [will] sustain [them]. [...] It is very good for the blood, for the girls.” – PTA Chairperson

Many of the PTA/SMC chairpersons that were aware of the program associated changes that they observed in their girls with the IFA tablet. Their observations included better academic performance, positive changes to menstruation, and better physical appearance.

“Since [girls] started taking the tablets, it is two years now for me what I’ve realized is that mostly, previously the boys were doing good but I don’t know I was still even contemplating in my mind, what makes my school girls sudden change. I now realize that even end of just third term exams it was girls who dominated the whole of the whole school, and even last year BECE is now girls, girls even the best student in my school so I was contemplating, is it this drug having something to do with learning or something like that. Yes, for overall best it was a girl. It is the first time, since the two years they just started... Previously it was just boys.” – PTA Chairperson

Awareness and acceptance by the PTA/SMC chairperson coincided with reported success in the distribution of IFA by educators. One PTA/SMC chairperson at the best-performing school during Year 1 reported that he supervised distribution every week to ensure that every girl consumed the IFA tablet. However, four PTA/CMS chairpersons (two from each region) were unaware the program was in place. Those who were not previously aware of the program were accepting of it upon learning about its existence in the interview.

“It is today am hearing of [the GIFTS program]. But that notwithstanding, there are times that your woman goes to the hospital and they are told they have anemia and you have to buy eggs and many other things. All this come about because we don’t have what it takes to prevent it at the early stages. So, if we start early, giving them

*these drugs, by the time they become of age, this anemia issue will no longer exist.” –
PTA Chairperson*

Students

Educators and PTA/SMC chairpersons reported that most girls participated without issue following additional sensitization on the IFA tablet. Educators stated that students had misconceptions when the program was first introduced. Nearly every respondent reported that beliefs associating the tablet with contraception, fertility, abnormal menstruation, and side effects had subsided over time. At the beginning, some students had avoided swallowing the tablet by spitting it out later, but these issues were resolved through closer monitoring and more sensitization. However, some schools still struggled with refusals because of these misconceptions.

“First [girls] were told it was something that will prevent them from having sex. They were having the fear that when they take the drug they may fall sick due to some drug they some took some time ago something like the elephantiasis drug that was distributed they took some and all of them were feeling sick and they lie down. So due to that experience they were afraid to take this one initially. So those who claim they were taking, they took it and went out and spit it out. Yea that was the initial stage, later on when I realized this was what they were doing I re-explained to them to really get the concept what it is for and they understood and they are now taking it.” – Head Teacher

Educators overwhelmingly expressed a desire that male students be included, and they reported that boys both teased the girls for consuming the tablet and wished to take part in the program.

“For the boys, they also have their misconception they say why we are discriminating, why are they all in class, and when it comes to certain drugs we don’t give them? And, especially when they were all educated and given reasons why the drug is given, they said they also need to build their immune system, they also need, they feel they should also be part of it.” – Head Teacher

Sensitization

Some schools had formal sessions with students and parents to explain the benefits of IFA, and some educators spoke to students informally during distribution. Sensitization was viewed as the cause of positive changes in the attitudes and beliefs surrounding IFA tablets. Educators and PTA/SMC chairpersons expressed regret that the sensitization had not happened sufficiently before the roll out of the program. Educators identified the need for more sensitization but felt this was the responsibility of the health sector or someone outside the community.

“The major concern is education. I think that there is the need for whichever body it is that is in charge of this to once in a while come and talk to us. Come and talk to the students; because the last time we had a program, sometime last year, ... the discussion was just done at the District Assembly there at a workshop. And when they came they tried to put together some twenty or so sampled students to discuss it with them, expecting that they will also go and share the information with their colleagues. I think that it is not enough and that is why perhaps, the, some of the students feel adamant about it or some of the students are not still convinced that for whatsoever reason they should go in for the tabs. So if there is a more, more education and faces keep coming around to monitor, they’ll see the importance of it and also join.” – Focal Person

District SHEP Coordinators also identified a need for more sensitization of parents and suggested the PTA and SMC leadership as starting points.

“To me for the program to be sustained we need the support of the parents. I think to improve the program if orientation or sensitization exercise will be organized for at least the executives of PTA and SMC.” – District SHEP Coordinators

Formal sensitization activities took place at the community level through radio and community meetings. One school held “dramas” in the school and at a PTA meeting as an innovative way to sensitize students, educators, and parents on anemia and IFA. Several schools held meetings with their PTA/SMC, and a small number of PTA/SMC chairpersons reported sensitizing parents themselves.

“Initially [parents] were afraid it would prevent their children from bearing children in the near future but after we explained to them, they accepted it.” – PTA Chairperson

The information given during the sensitization efforts ranged from comprehensive lessons to counseling during distribution. While educators had a general sense of the benefits of IFA and the reasons for the program, most lacked a comprehensive knowledge of anemia, the components and benefits of IFA tablets, who should consume IFA tablets, how one should take IFA tablets, and potential side effects of IFA tablets. These aspects were missing from sensitization efforts of most educators.

Health and Nutrition Education

Health and nutrition education is not consistent across schools. The GIFTS program did not develop a curriculum or knowledge standards for schools, though it did provide printed resources for sensitization on IFA and health and nutrition education. Schools were about evenly split between those that had a plan for conducting such sessions and those that did not.

*“Interviewer: How do you decide that we’ll talk about this or we’ll talk about that?
Focal Person: Well, sometimes you just sit down and think about it, you consult, I don’t work alone, I have my assistant. I say “Ah, don’t you think that we can discuss this with the students and then we pick it up from there, if we look among us the stuff, if there’s any teacher who has more knowledge on that aspect then involve the person and the person shares his experience or her experience with the children.”*

“You know, it is the nurse that has been coming to do [health and nutrition education]. We have designed our action plan though. Aha so anytime we have such program, we invite her to come. Last time she came to talk to them about personal hygiene and also talk to them about drug abuse.” – Focal Person

Some educators lacked the knowledge and resources needed to conduct effective health and nutrition education. Apart from sensitization efforts, few schools or district SHEP coordinators reported creating new health and nutrition education sessions or resources due to the GIFTS program. Some educators led health and nutrition education sessions, while others relied on visits from health workers. Health and nutrition education topics included anemia, diet, bullying, truancy, pregnancy, water and sanitation, hygiene, malaria, sexual and reproductive health, hepatitis, and HIV. Topics were not covered systematically and some schools did not include nutrition in their sessions.

Training and Resources

Levels of educator training fell into three broad categories: 1) those who received formal training at the start of the program, 2) those who had received a brief orientation from a colleague who was trained, and 3) those who received no training at all. Many focal persons were trained at the start of the program in 2017, but four of the interviewed focal persons had not received formal program training. All four of the untrained focal person belonged to schools in the lower half of intake adherence during the Year 1 quantitative evaluation. Most head teachers had been given an orientation to the program by trained focal persons. Most non-health teachers were untrained. However, in one case, the school received ongoing training through the academic year from the district nutrition officer.

Nearly all educators reported the need for additional training both to refresh focal persons and to train other stakeholders such as head teachers. Teacher turnover was another common reason for requesting additional training. Some focal persons highlighted the need for more materials for sensitization and health and nutrition education.

“To help me do my work effectively, I think they should train more teachers. Yes, maybe a SHEP coordinator and the female teachers we are (laughs), we are bound to go on leaves and other things, so if I’m not the only person who has been trained, and other teachers too have been trained, I think it can help.” – Focal Person

“I will say because of forgetfulness, we the teachers, we are here doing other things not only the, this thing, so the teacher might forget about some of the things they’ve learnt at the workshop. So, if they can give us a resource pack—a book which um, all the good things about this will be written in it for the teacher to easily be referring to anytime she wants to do a program. Yes so that is they should give us some guide or a resource book that we can easily refer to.” – Focal Person

Educators described subsequent interactions with health workers and their trained peers as “orientations.” These were used for informing untrained educators and refresh trained educators periodically; however, educators did not view these as equivalent to training. District SHEP coordinators stressed the need for continual training or orientation. Some included themselves as trainers of focal

persons or school SHEP coordinators, while others viewed this as the responsibility of the health sector.

District SHEP coordinators also required fuel for visiting schools to monitor, supervise, and in some cases deliver IFA tablets to schools.

“I think for the program to be improved you have to give them orientation, that’s the school based SHEP coordinators. Also, so that they will ... have in-depth knowledge about the program meaning those that we came back to train some of them have left the district, so those new ones we have to give them orientation so that they will take over the program because we want the program to be sustained.” – District SHEP Coordinator

“Like fuel, for instances last week I pleaded with [the health] office that you should support me to reach all the schools and when I received something small I was able to roam round all the villages even though I had to supplement to be able to complete. That is my work but you really need to do something so that while we do the work our pockets also don’t dry up.” – District SHEP Coordinator

Motivation

Within the key informant interviews, we attempted to classify motivation for participating in the program into intrinsic motivation – “doing something because it is inherently interesting or enjoyable” – and extrinsic motivation – “doing something because it leads to a separable outcome.”⁽¹⁵⁾

Intrinsic

Respondents had a variety of roles in the GIFTS program including monitoring, supervision, sensitization, health and nutrition education, distribution of IFA tablets, calling the names of students to receive tablets, maintaining order during distribution, and taking the tablet in front of students. All educators’ felt their role in the program was important, regardless of what the role was.

“[My role] is critical in the sense that the girls are our students and we go into the various classes to teach them. Our main focus is for them is to understand what we are teaching them so if they usually lose blood through the natural menstruation that they go through, they will be unable to understand what we teach them because it is painful. As a teacher I need to teach them well and they also need to understand. So once they go through this natural process, I took it upon myself to give out the

drugs.” – Focal Person

“I serve as a role model, because before you give it out, you take, when you take it they are also motivated, because some of the stories behind the issue is that maybe they were giving it out, they were giving them the supplements to maybe prevent them from giving birth in the future. We know the myths in our country when they are taking or doing a program. They’ll say these white men are just trying to give us some HIV or whatever, so when we take it, we give it to them, they know that this tablet is authentic or valid that our teacher involved, the leader, or the teacher.” –

Teacher

Many cited their views on the importance of girls’ health and the positive results they had seen as motivation for their participation. Many also reported their connection to the girls as parents, role models, and caretakers. Connection with the school and community was also identified as a source of motivation. For example, the PTA chairperson who supervised every IFA tablet distribution was also the son of the school’s founder and namesake. Another focal person talked about how the students were like her children. Others reported that teachers who did not participate often were not native to the school’s location and frequently left for their home communities.

“Anything that has to do with health I think I am interested in it, I think aside being a teacher and know that it is not only the classroom work, in the school you are more or less like a mother, if you are male, a father to the children. It is not only the academics as much as we’re trying to impart values and other things to them. We also want to make sure that they are in good health. So me, though we are not given anything for doing this, but I like it, I like doing it because at the end of the day, it is going to help these girls and that motivates me.” – Focal Person

Extrinsic

Many focal persons stated they were motivated to participate in the program because they had been assigned this role. Some educators had support and supervision from head teachers, and many had supervision from district SHEP coordinators. However, many educators reported the need for more monitoring of the program. A small number of schools had direct support and supervision from the PTA/SMC.

“PTA Chairperson: The help we give is that when the children are about to take the drug, some of them are afraid, some put it in their mouths and pretend to swallow it but later go and spit it out, so when they are about to take the drug, we coax and encourage them to take the drug

Interviewer: So what work has the PTA done with the teachers to ensure the drug intake goes up?

PTA Chairperson: The work that we do as I said is that, we encourage the girls and make sure everyone takes the drug before we leave

Interviewer: So that means that every day when they are about to take the drug, you come to the school?

PTA Chairperson: Yes, I always come”

Many focal persons and teachers felt they should receive additional compensation for their work on the GIFTS program as cash, commendations, or other rewards. Head teachers noted the extra workload of focal persons and advocated for additional compensation for them.

“The concern I have is about the teachers in charge, he takes his time I think this an extra curricula activity which he needs some kind of motivation. He should have been motivated but since the inception of the program we have not seen any motivation yet.” – Head Teacher

Some educators highlighted the need for more recognition of their work on the GIFTS program.

“I think we are doing a very good job that we need to be motivated. Even though we know that ... it will help the children and because of that, we will want to do it, I think if they motivate us it will also let us feel like at least what we are doing they are also appreciating it. [...] Like any incentives or anything that they think they can use to motivate us, once a while...” – Focal Person

Acceptability for Purchasing

Some educators believed parents would pay a low cost (about 10GH, or <2USD) per year for the IFA tablets but only if proper sensitization was done. There was a widespread belief that most parents would not pay without increased awareness of the benefits of IFA supplementation. Many cited the poverty of their communities or general resistance of parents to pay fees. Some educators feared a levy

would violate the newly instituted free education policies, and others feared it would further disadvantage children from poor households or drive misconceptions about the program.

“Actually you know when they get to know this is a program for the education service and from the Ghana Health Service they are thinking it’s free. So, when you tell them 10 cedis it will be a problem because this is a village and mostly they don’t have some social amenities and I think only water and electricity is not there. So they don’t have enough information from television and the radio. Even when they launched this program in [District] they didn’t not know. I went on YouTube and took it to them then they realize this is a program, and they realized chiefs and other people were there. The dignified people were there, and if they think it is a bad program, they wouldn’t come and support it. So, that is how they were convinced that this is a true program. I think they have on their mind that this is a government program, so when you have to charge them 10 cedis I think you have to convince them and don’t know how.” – Focal Person

“Once money is involved, they’ll use that to say no. Regardless of the misconception they have of it, they’ll use this as a stand point to tarnish it. Yes, they’ll use the cost element to downplay the importance it has to play here.” – Head Teacher

However, about two-thirds of PTA/SMC chairpersons would be willing to pay and would convince other parents to pay. A few PTA/SMC chairpersons stated that due to the unstable local economy and poverty, most parents would be unable to pay at their schools.

“Yes that is if they understand what they are paying for that this is something good for my child, my girl. This is good for her. This will help her in this way or that way. If the person is able to understand, have that understanding. Eh, I want to believe that there are people, a lot of them who will be willing to pay for it.” – PTA Chairperson

6.4: Discussion

The results indicate that after two years of implementation schools had adapted to the GIFTS program, and widespread changes in attitudes and beliefs about the IFA tablets had improved their acceptability.

Many educators, PTA/SMC chairpersons, and students identified positive changes within those who took IFA tablets and encouraged the program to remain in place. GIFTS program focal persons in some schools exceeded expectations by taking on additional responsibilities such as provision of water and cups to students, sole responsibility for distribution and monitoring, and transportation of tablets from the district level. Head teachers recognized the contributions of focal persons and advocated for compensation for their additional responsibilities. Educators and parents were motivated to support and participate in the program by their own desires to improve the health of students and by external factors such as supervision and support from others.

Still, some challenges remained. Timely provision of tablets and maintenance of the supply chain were weaknesses that should be addressed at the national, regional, and district levels. Implementing a consistent channel of communication regarding the supply chain and improving the timeliness of monitoring may help to reduce shortages and expired tablets. This aligns with evidence from similar programs in India where state-level disruptions in supply chain led to shortages ⁽⁷⁾ and Indonesia where data sharing between education offices and district health offices was used to strengthen the supply chain ⁽⁸⁾.

Some educators felt their work goes unrecognized and unrewarded. Educators offered suggestions for motivating focal persons such as T-shirts, caps, books, commendations, lunches, a borehole for water, money for water, and additional salary. District SHEP coordinators specifically identified the need for money for fuel to travel to schools for monitoring and supervision. Evidence from Indonesia found similar motivators for educators including understanding the program's potential effect on health and

school performance; however, they used acknowledgement by school and district leadership as an extrinsic motivator⁽⁸⁾, something the GIFTS program is lacking.

Some negative perceptions persisted in a minority of students and parents, though most respondents had engaged students in sensitization and many had spoken with parents about IFA tablets. However, some schools' parent leadership remained unaware of and unengaged by the program. Empowering educators to sensitize other educators and parents may improve acceptance of IFA tablets; however, they must have the training and resources to complete such sensitization activities.

Schools in the top and bottom of average IFA intake adherence during the first school year were no longer distinguishable in their adherence to the program, as reported by focal persons. Educators who gave their schools lower marks in the distribution of IFA tablets reported more misconceptions by students, parents, and other educators and had more troubles with IFA supply chain and procurement of water. No clear patterns emerged with regard to geographic location, level, or size of the school. This is in contrast to the quantitative analysis and may be due to the method of selection with few schools with each strata or other aspects of the school's experience that were not discussed in the interviews. Additionally, there was a variety of experiences represented in these data, which may have obscured patterns by these strata.

Training was a pervasive theme with most district SHEP coordinators and school focal persons having formal training. Few others had a formal training, though most had an orientation by health workers or the focal persons in their schools. Schools where focal persons had little or no training had more troubles with adherence to the GIFTS program, aligning with the results of the first year quantitative analysis.

The health and nutrition education component would benefit from a systematic approach to ensure that relevant topics are covered with sufficient frequency. That boys felt left out of the program furthers

highlights the deficit in program fidelity. The GIFTS program was designed to be an anemia program that includes health and nutrition education for all adolescents, not only girls. Reinforcing the inclusion of boys in GIFTS program-related health and nutrition education would improve program fidelity, decrease the perception that boys are left out, and potentially improve the health of adolescent boys. Many teachers requested more training and support from health workers because they lacked the knowledge and skills to educate students on health and nutrition topics. Further strengthening of inter-sectoral partnerships is needed to facilitate this type of collaboration.

While some district SHEP coordinators worked closely with district nutrition officers, other districts had challenges with inter-agency partnerships. Increasing a sense of ownership of the program among district SHEP coordinators and including other education sector staff such as circuit supervisors may improve collaboration, supervision, and support at multiple levels.

As with all qualitative studies, there is subjectivity in the interpretation of findings; however, the research team has taken a systematic approach and interviewers and national coordinators were included in finalizing the analysis. Another limitation of this study is that reports of student perceptions relied on adults because no students were interviewed. Educator and parent report of student perceptions is incomplete and may be inaccurate. However, because of resources constraints and the fact that focus groups with students were routinely held as part of monitoring activities, we focused on educators and school-level factors to build on previous work showing their importance. This analysis also captures a single point in time and relies on recall in reflecting on occurrences and perceptions over the previous two years. While this study did not aim to represent all educators and parents in the studied regions, it does provide a breadth of information from a diverse groups of schools and a large group of key informants at multiple levels and with varied roles. Further work may be needed to develop sustainable options for training and motivating educators and to determine the specific resources needed to improve health and nutrition education. This study fills gaps in

understanding local supply chain, program fidelity, perceptions, attitudes, motivation, and willingness to pay that may be used to improve the functioning of the GIFTS program and may have applications for similar planned programs in the region.

6.5: Figures and Tables

Table 6.5.1: Summary Findings from Interviews with 77 Educators and PTA/SMC Chairpersons in 16 Ghanaian Schools

Themes	Findings	Implications	Potential Solutions or Improvements
Distribution of IFA Tablets - Supply Chain	Lack of ownership by education sector and differences in organizational structure between education and health sectors	Education sector not an equal partner and disruptions in supply chain occur	Include education sector at all levels and align supply chain with education organizational structure
	Communication about supply chain is inconsistent	Extended supply shortages and lack of timely reporting	Leverage existing reporting mechanisms and promote the use of technology in a standardized manner
	Few schools had shortages of IFA tablets and expired tablets	Students missed doses	Provide tablets earlier in the school year and improve communication and monitoring of IFA tablet supply
Distribution of IFA Tablets - Methods within Schools	Standard weekly distribution day (Wednesday)	Uniform expectations at all program levels	Maintain current practice
	The GIFTS program focal person is responsible for distribution at most schools	Failure to fulfill this responsibility by one individual may have resulted in no tablets being distributed	Ensure that focal persons have assistants for regular support and that can fill in when needed
	Tablets are typically given outside of instructional time and after food has been eaten	Ensured that girls do not fall behind in class and that they did not take it on an empty stomach	Assist schools who do not currently follow these methods with arranging the distribution schedule to occur outside of instructional time and after food has been eaten
	Lack of clean water	Tablets taken with unsafe water or water had to be purchased by students or educators	Incorporate clean water activities into the GIFTS program such as distribution of clean water and testing water sources at schools
Distribution of IFA Tablets - Perceived Time Burden	Attitudes about the time burden were split with district SHEP coordinators and program focal persons spending the most time	May have taken time away from the other responsibilities of educators and led to burn out	Spread responsibilities within schools and streamline the tools and supervisory responsibilities of district SHEP coordinators

Distribution of IFA Tablets - Challenges within Schools	Festivals, observances, examinations, and school events caused missed distributions	Students missed doses despite being otherwise present or available for school	Consider culturally appropriate ways to modify the distribution method such as sending tablets home to be consumed or modify the schedule to account for holidays and examinations
	Insufficient program registers caused missed distributions	Students missed doses and monitoring is incomplete	Ready additional program registers and train educators on stop-gap methods of recording tablets in the event of insufficient registers
Distribution of IFA Tablets- Consumers Outside the Target Population	Not all female teachers consumed IFA tablets	Incomplete coverage of female teachers and students lacked a role model for consumption	Expand sensitization to include female teachers
	Male teachers consumed IFA tablets in some schools	Increased modeling of IFA consumption, but may have left fewer tablets available for students	Evaluate the need for male teachers to consume the tablets and train educators
	Male students consumed a limited number of tablets in some schools	May have reduced the perception that the tablets were for altering girls' reproductive health and left fewer tablets for the targeted girls	Evaluate the need and safety for male students to consume the tablet and develop a protocol for distribution, if distribution is deemed useful
	Confusion over special uses of IFA tablets such as for students with sickle cell disease or while menstruating	Students may have received inappropriate, dangerous, or inadequate doses of IFA tablets	Retrain educators on appropriate distribution and special cases for excluding or including students
Perceptions, Attitudes, and Awareness - Educators	Most reported positive feelings about IFA tablets and had basic knowledge of IFA	Educators had basic information to sensitize students to IFA tablets	Expand training to ensure that all educators have a basic understanding of anemia and IFA tablets
	Many lacked depth of knowledge of IFA tablets and anemia	Few educators were able to deal with complex questions or situations	Expand training of focal persons and head teachers to ensure they can deal with complex questions and situations
	Linked positive changes observed in girls to consumption of IFA tablets	Educators may have been more motivated in their work	Reinforce key messages about the benefits of IFA tablets so that positive outcomes continue to be noticed
	Advocated for boys to be included	Educators believed that the program would benefit boys	Evaluate the need and safety for male students to consume the tablet

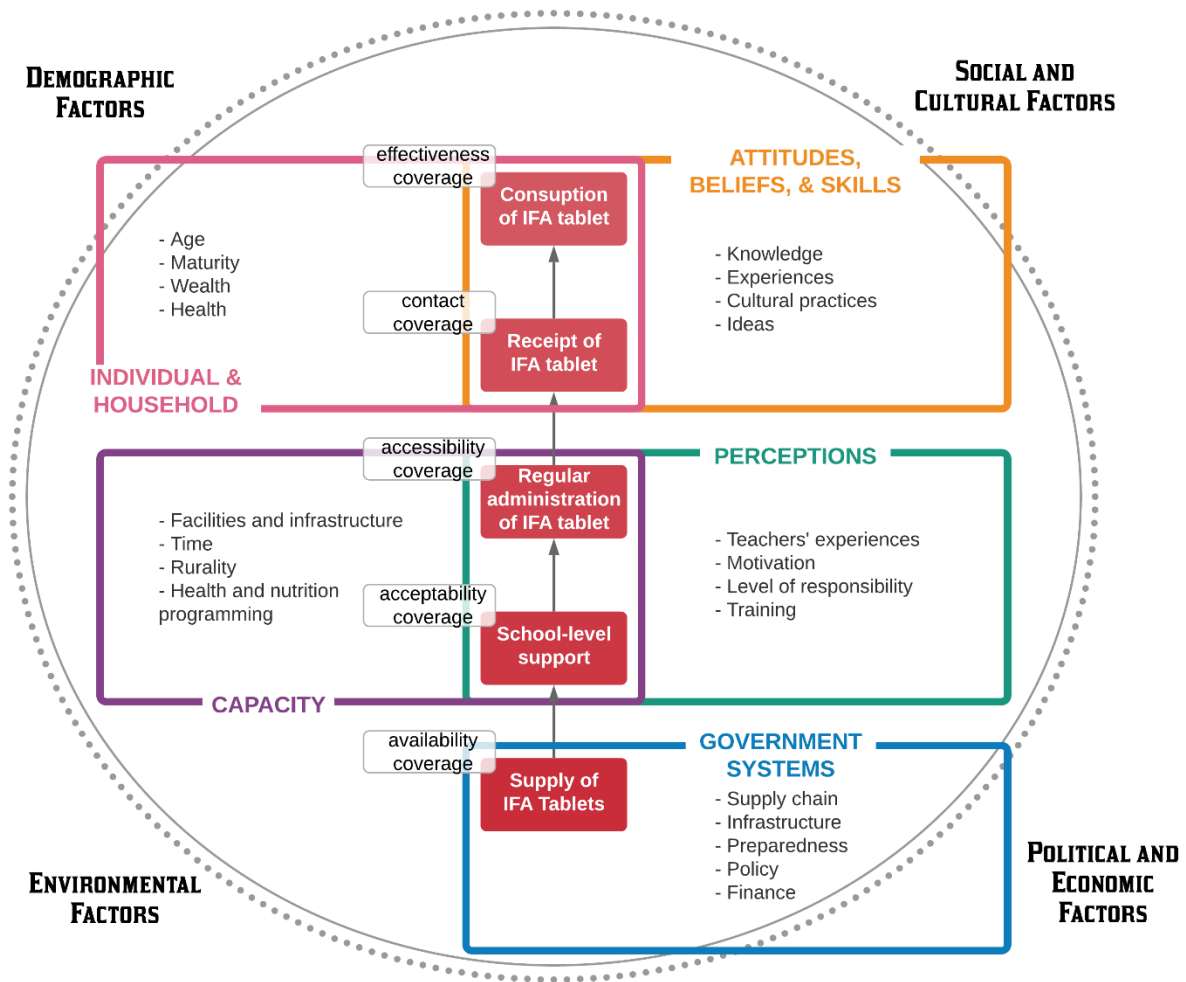
	Few educators had negative views of IFA tablets	Negative views may spread to other educators, students, and community members	Provide resources to district SHEP coordinators and program focal persons for addressing misconceptions among teachers
Perceptions, Attitudes, and Awareness - Parents	Initial suspicions that the IFA tablet was contraception	Led to refusals to consume IFA tablets	Sensitization was reported to reduce misconceptions over time
	Few parents remained unaware of the IFA program	Violation of parents' rights to make informed decisions about the health of their children and may lead to negative feelings when they become aware of the program	Improve early academic year sensitization of parents through media and parent meetings
	Attributed positive changes in girls to consumption of IFA tablets	More willingness for girls to participate	Increased sensitization activities among parents that highlight the benefits of IFA tablets
	Few PTA/SMC chairpersons supervised distribution	Where occurring, more motivation for educators and increased ownership and decision-making power of parents	Increase engagement of PTA/SMC and invite participation in the program where possible
Perceptions, Attitudes, and Awareness - Students	Early misconceptions about IFA tablets	Led to refusals to consume IFA tablets	Sensitization was reported to reduce misconceptions over time
	Undesirable changes / side-effects	Led to refusals to consume IFA tablets	Increased sensitization activities and counseling on IFA to identify and address true side-effects and correct misconceptions
	Receiving but refusing to swallow the tablet	Reduced consumption and over reporting	This problem subsided over time through improved perceptions of IFA tablets and increased monitoring of consumption within schools
	Male students wished to participate in the program	Male students supported the program but the health and nutrition education component was not communicated as a program benefit or not received by male students	Train educators to ensure that health and nutrition education is given to all students and communicated as being part of the program

Sensitization	Both formal and informal sensitization activities were held	Students received multiple forms of communication on IFA tablets	Provide more resources for sensitization
	Sensitization viewed as the cause of positive changes in attitudes and beliefs surrounding IFA tablets	Refusals declined	Provide more resources for sensitization
	Sensitization was insufficient and late	Misconceptions were formed early and led to refusals at the beginning	Provide more resources for sensitization and create a timeline for delivering key messages
	Educators felt that sensitization was the responsibility of the health sector	Educators may have relied on sensitization of the health sector, while the health sector relied on educators	Clearly define roles of each sector related to sensitization
Health and Nutrition Education	The program provided educational resources but no curriculum, and about half of schools had a plan for health and nutrition education	Program fidelity was inconsistent across schools	Provide more resources and a curriculum for health and nutrition education
	Educators lacked knowledge and resources for effective health and nutrition education, and some relied on support from health workers	Quality of health and nutrition education may have been poor within some schools	Provide more training and resources for health and nutrition education; improve cross-sectoral collaboration
	Topics were varied, not covered systematically, and some never included nutrition	Quality and focus of health and nutrition education may have been poor within some schools	Provide more training and resources for health and nutrition education; improve cross-sectoral collaboration
Training and Resources	Training was inadequate to refresh the knowledge of focal persons, account for teacher turnover, and reach head teachers and other educators	Educators lacked the knowledge, skills and motivation needed for program fidelity	Increase the frequency of training and the number of stakeholders trained
Motivation - Intrinsic	All educators' felt their role in the program was important, regardless of what the role was	Educators were motivated to fulfill their roles	Maintain this perception through recognition of their work
	Positive changes attributed to tablets motivated educator participation	Educators felt the program was worthwhile	Maintain this perception through continued sensitization

	Connection to students and the community was also cited as motivation	Educators completed their work for the good of their students and community	Craft messages that promote this sense of connection between the program and their community
Motivation - Extrinsic	Support and supervision motivated educator participation	Educators completed what was encouraged and required by their supervisors	Increase the buy-in of head teachers to promote more active support and supervision at the school level
	Educators desired compensation or other rewards for their work on the program that was viewed as outside their normal responsibilities	Educators may have experienced burnout because of a lack of reward for extra work	Consider appropriate and sustainable incentives for educators actively involved in the program
	Educators need more recognition for their work on the program	Educators may have experienced burnout because of a lack of recognition for extra work	Implement ways to recognize the work of educators on the GIFTS program
Acceptability for Purchasing	Widespread view of educators that parents would not pay even a small fee for IFA tablets	A fee for the IFA tablet may not be accepted by parents	Consider alternative ways to fund the program
	Some educators thought parents may be willing to pay with proper sensitization	Educators did not feel that parents are well-informed about the benefits of IFA tablets	Improved sensitization of parents
	Some educators feared a levy would violate the newly instituted free education policies, and others feared it would further disadvantage children from poor households or drive misconceptions about the program	A fee for IFA tablets may result in backlash and inequitable distribution	Design any fee on a sliding scale or other such scheme to promote equity and combine with sensitization activities
	Many PTA/SMC chairpersons found payment for IFA tablets acceptable and felt they could convince other parents to pay	Leaders of parents felt differently about the acceptability of purchasing tablets than educators	PTA/SMC chairpersons are more privileged than other parents but they may be helpful for promoting a fee or incorporating a fee into the PTA dues

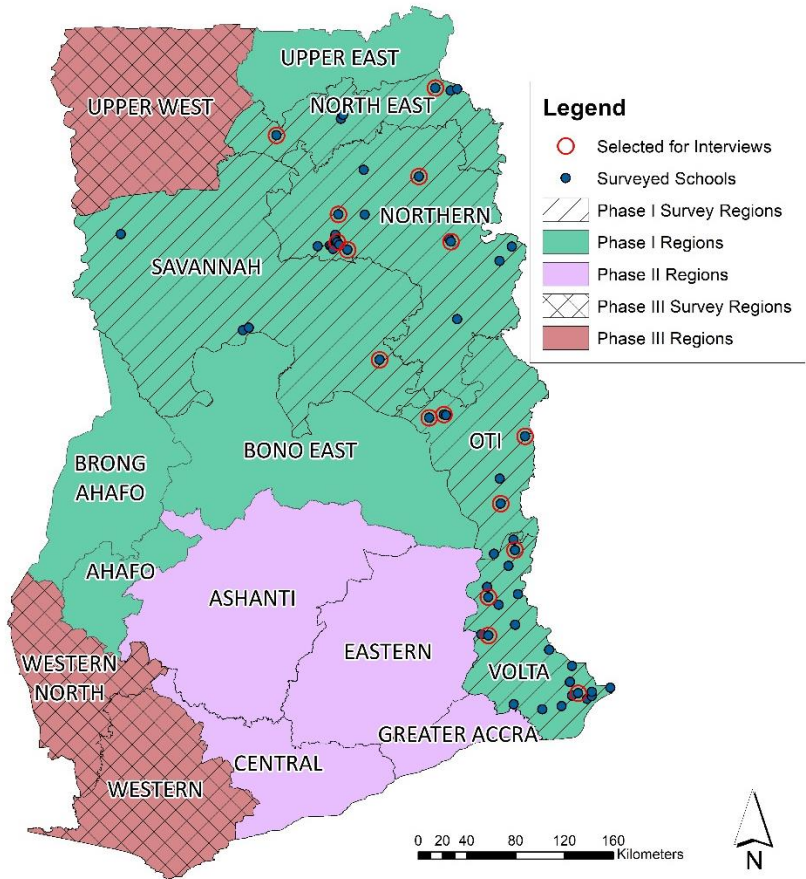
Note: GIFTS=Girl's Iron-Folic acid Tablet Supplementation; IFA=Iron-Folic acid; PTA=Parent-Teacher Association; SHEP=School Health Education and Promotion; SMC=School Management Committee

Figure 6.5.1: Conceptual Framework of the Barriers and Facilitators of a School-based Adolescent Anemia Control Program with Iron-Folic acid Supplementation



Note: This framework is rooted in the Social-Ecological Model (Bronfenbrenner, 1979) and incorporates elements from Tanahashi's levels of health service coverage (1978) and the Innocenti Framework on Food Systems for Children and Adolescents (UNICEF, 2018)

Figure 6.5.2: Regional Map of Ghana, GIFTS Program Phases, and Study Sites



Note: A random displacement of up to 10 kilometers has been added to the position of the surveyed schools.

Figure 6.5.3: Primary Distributor of IFA Tablets in 16 Schools in Ghana

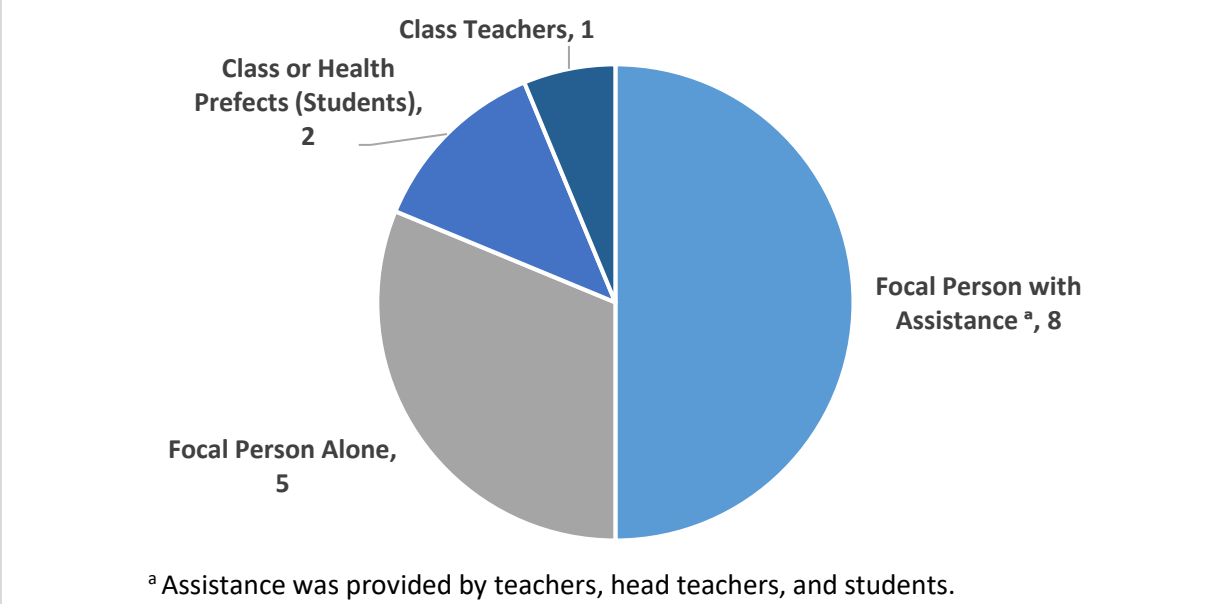
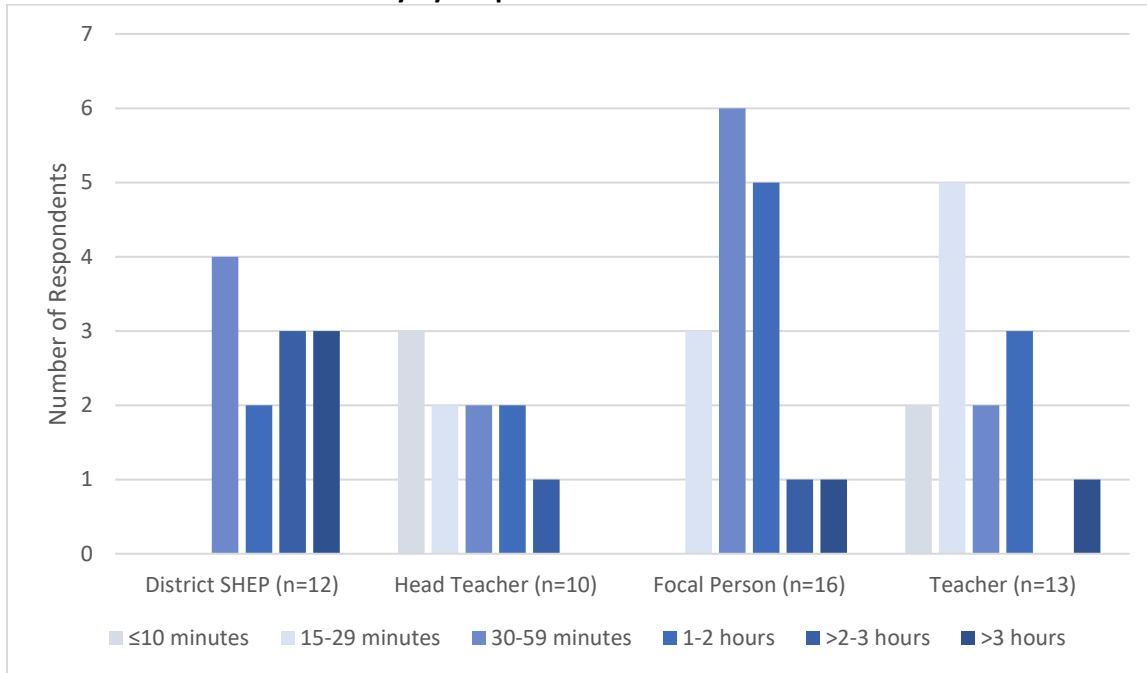


Figure 6.5.4: Reported Time Devoted to Girls Iron-Folic acid Tablet Supplementation (GIFTS) Program in 16 Schools on Distribution Day by Respondent Role



References (Chapter 6)

1. University of Ghana, GroundWork, University of Wisconsin-Madison *et al.* (2017) *Ghana micronutrient survey 2017*. Accra, Ghana.
2. WHO (2011) *Guideline: Intermittent iron and folic acid supplementation in menstruating women*. no. 9789241502023. Geneva: World Health Organization (WHO).
3. WHO (2011) *Guideline: Intermittent iron supplementation in preschool and school-age children*. Geneva: World Health Organization.
4. UNESCO Institute for Statistics (2019) *Enrolment ratios: United Nations Education Scientific and Cultural Organization*.
5. Gosdin L, Sharma AJ, Tripp K *et al.* (2020) A school-based weekly iron and folic acid supplementation program is effective at reducing anemia in a prospective cohort of Ghanaian adolescent girls. *In Progress*.
6. Ghana Health Service, Ghana Education Service, UNICEF-Ghana *et al.* (2019) *Impact evaluation of a school-based integrated adolescent nutrition and health Programme with Iron and Folic-Acid supplementation intervention among adolescent girls in Ghana*. Cantonments, Accra Ghana: UNICEF-Ghana.
7. Aguayo VM, Paintal K, Singh G (2013) The Adolescent Girls' Anaemia Control Programme: A decade of programming experience to break the inter-generational cycle of malnutrition in India. *Public Health Nutr* **16**, 1667-1676.
8. Roche ML, Bury L, Yusadiredja IN *et al.* (2018) Adolescent girls' nutrition and prevention of anaemia: a school based multisectoral collaboration in Indonesia. *BMJ* **363**, k4541.
9. Hennink M, Hutter I, Bailey A (2010) *Qualitative Research Methods*: SAGE Publications.
10. Bronfenbrenner U (1979) *The ecology of human development*: Harvard university press.
11. Tanahashi T (1978) Health service coverage and its evaluation. *Bull World Health Organ* **56**, 295-303.
12. UNICEF (2018) *Food Systems for Children and Adolescents: Working together to secure nutritious diets*. Florence Italy: Office of Research, Innocenti.
13. Kuckartz U, McWhertor A (2014) *Qualitative text analysis : a guide to methods, practice & using software*. Los Angeles: SAGE.
14. Campbell JL, Quincy C, Osserman J *et al.* (2013) Coding in-depth semistructured interviews: Problems of unitization and intercoder reliability and agreement. *Sociological Methods & Research* **42**, 294-320.
15. Ryan RM, Deci EL (2000) Intrinsic and Extrinsic Motivations: Classic Definitions and New Directions. *Contemporary Educational Psychology* **25**, 54-67.

Chapter 7: Expanded Discussion

7.1: Summary of Findings

For Aim 1, we found that the prevalence of anemia among adolescent girls was nearly double the prevalence among boys. Predictors of anemia and hemoglobin concentration (Hb) were not identical between girls and boys. Predictors among girls included age, geophagy, malaria, diet, and body mass index (BMI). Predictors of anemia among boys included age, malaria, diet, and BMI. Age and BMI each had opposite associations with anemia among boys and girls with age increasing anemia and overweight decreasing anemia among girls. Dietary sources of iron predicted anemia prevalence among both boys and girls. Rich sources of heme iron were negatively associated with anemia among girls, and wheat flour products (predominantly not fortified with iron) were positively associated with anemia among boys.

In the Aim 2 analyses, we found that the prevalence of anemia declined from 25.1% to 19.6% after 8 months of exposure to weekly IFA supplementation. Cumulative weekly IFA tablets consumed was positively associated with Hb and negatively associated with anemia. IFA supplementation had a curvilinear dose-response relationship with Hb. We also found that the minimum effective number of IFA tablets for achieving adequacy of Hb over one school year in this population was 26 (i.e., 1 IFA tablet per week during at least 26 weeks over the school year).

For Aim 3, we estimated that 90% of schoolgirls received at least one IFA tablet over the first year; however, 76% had not received the minimum effective number of tablets. Bottlenecks were identified at the levels of acceptability, accessibility, and effectiveness coverage. School-level factors explained 75% of the variance associated with increased IFA dosage. The ability to make up missed doses, school level (junior vs. senior secondary), and educators' program-related training were positively associated with the total number of weekly IFA tablets consumed, and educator perceptions on the difficulty of

implementation and excessive time burden of the program were negatively associated with the total number of IFA tablets consumed.

The qualitative findings of the Aim 4 analysis indicated that, after two years of implementation, schools adapted the program, and widespread changes in attitudes and beliefs about the IFA tablets improved their acceptability. Educators and parents observed positive changes in consumers of IFA tablets and were motivated to continue the program. School GIFTS program focal persons took on many of the responsibilities for the program and their efforts were highlighted by their supervisors and colleagues. Most educators viewed the acceptance and integration of the program as improving over time. However, limitations remained including disrupted supply chain, lack of program ownership, mediocre cross-sectoral and vertical communication, inadequate educator training, lack of extrinsic motivators, unsystematic health and nutrition education, and insufficient program resources.

7.2: Comparison of Findings to Similar Studies

There is extensive literature on the predictors of anemia in various contexts, which was used to build models of the predictors in our analyses. Large studies among women of reproductive age have found the predictors of anemia to include iron deficiency, inflammation, vitamin A insufficiency, wealth, minority ethnicity/caste, age, and hookworm infection.^(1,2) Studies of preschool children have found similar predictors and also included malaria and poor sanitation.⁽³⁾ However, these predictors were not consistent across all countries studies, differing by contextual factors such as inflammation and infection. This underscores the need for context-specific examinations of anemia. There are fewer studies of adolescent girls, but one small agriculture-focused study in Ghana identified age, wealth, household dietary diversity, and agro-ecological zone to be predictors of anemia among adolescents.⁽⁴⁾ Data on predictors of anemia among men and adolescent boys is much sparser relative to women of reproductive age, but some included level of education, age, wealth, BMI, HIV/AIDS, and malaria.⁽⁵⁾

In our study, boys and girls had several similar factors associated with anemia and Hb including malaria, geophagy, and wealth. There is a large body of evidence that malaria is associated with anemia as plasmodium parasites promote destruction of erythrocytes and inhibit erythropoiesis.⁽⁶⁾ Though rarely studied in adolescents, the practice of pica, an umbrella term including geophagy, has been associated with anemia among women, though competing hypotheses of physiological mechanisms persist.⁽⁷⁾ The positive relationship between wealth and anemia is unexpected and counter to most studies of anemia.⁽¹⁾ However, we hypothesized that this is related to the ongoing societal nutrition transition that supports the consumption of energy-dense and nutrient-poor foods, the effects of which may differ by cultural or societal norms.⁽⁸⁾ Lower wealth households may depend on traditional foods in this context, while higher wealth households have an increased ability to acquire packaged or prepared foods. Alternatively, the wealth index is based on household assets, which for adolescent girls may not adequately represent her socio-economic status, especially for girls living in boarding schools.

Age, BMI, and components of the diet had differing associations with anemia and Hb by sex. Girls had increased prevalence of anemia with age, while boys had decreased prevalence of anemia with age.

Diverging effects of age by gender on anemia have been observed in other studies, including in Ghana, perhaps because of the onset and establishment of menstruation during adolescence in girls.^(4,5)

Hemoglobin plays a role in muscle density and strength, while at this age boys are gaining more muscle mass with age at a rate higher than among girls perhaps contributing to the declining anemia prevalence with age observed in boys.⁽⁹⁾ Boys with overweight/obese BMI had an increased prevalence of anemia, while girls with overweight BMI had lower prevalence of anemia. The inverse association between overweight/obesity and anemia has been observed among women in several other countries,^(10,11) owed perhaps to the increase in food intake and thus increased opportunity for consumption of key micronutrients such as iron, vitamin B12, and folic acid. There is also a biologically plausible pathway for a positive relationship between overweight/obesity and anemia observed in boys. Overweight/obesity is

associated with chronic inflammation because of increased adiposity. The release of pro-inflammatory cytokines promotes hepcidin secretion, which in turn downregulates iron absorption, suppresses the release of iron from cells, and can lead to anemia of chronic disease.⁽¹²⁾ An alternative explanation is that overweight/obesity among boys is a proxy for an energy-dense diet that may lack key micronutrients such as iron. This is consistent with the positive association between consumption of wheat flour products (inadequately fortified in Ghana ⁽¹³²⁾) and anemia among boys.

The 22% reduction in the prevalence of anemia over the study period found in Chapter 4 is consistent with the 33% reduction in risk reported by a meta-analysis of IFA intervention trials in schools.⁽¹⁴⁾ The difference is expected because real-world conditions often present more challenges than the controlled conditions of efficacy trials but suggests there may be room for improving the program's impact. Many included trials were focused on a single intervention; whereas, the GIFTS program was an integrated package of health and nutrition education and IFA supplementation, which has the potential to improve its impact but also complicates its delivery. A reduction of 5.5 percentage points (p.p.) in the population prevalence of anemia is a decrease of approximately 22,000 cases of anemia among adolescent girls in schools within the surveyed regions over only 8 months. This effect extended to all 3 million adolescent girls in Ghanaian schools might avert 165,000 cases of anemia. Further, a reduction of 5.5 p.p. is also much larger than the approximate 0.025 p.p. annual decrease in anemia prevalence among non-pregnant women 15-49 years in the Central and West Africa region between 1995 and 2011.⁽¹⁵⁾ While regional trends may differ from individual countries, this comparison highlights the dramatic decrease associated with this integrated IFA intervention.

In a Cochrane review among studies of menstruating women and adolescents, IFA supplementation had a dose-response relationship with Hb but not with anemia.⁽¹⁶⁾ In our study, we observed a dose-response relationship with Hb and with anemia. This is potentially due to the distribution of Hb values in our data with most baseline values being near the cut-offs for anemia. An increasing dose of IFA would

push a greater number across this threshold and prevent others from falling below the anemia cut-off. The curvilinear relationship between IFA tablets and Hb is consistent with the commonly observed biological response to iron replacement therapy.⁽¹⁷⁾ Other studies have not derived a population cut-point for the minimum effective quantity of IFA tablets for achieving adequacy of Hb; however, our cut-point is consistent with the WHO recommendations for intermittent IFA supplementation (3 months of supplementation followed by a 3 month break).⁽¹⁸⁾

Similar studies of community-based IFA supplementation found that individual-level factors were associated with adherence and that supply chain was the only associated health center-level factor.⁽¹⁹⁾ Studies of school-based IFA supplementation of adolescent girls in India and Indonesia also identified supply of IFA as a critical factor for adherence.^(20,21) We found school-level structural factors and educator perspectives and training were primary barriers and facilitators to intake adherence rather than individual-level knowledge, attitudes, or beliefs. The target population and delivery platform are likely explanations for our findings in Ghana. Adolescents in schools are accustomed to following the expectations of their educators, but this age also marks an increase in peer influence.⁽²²⁾ Applied to the GIFTS program, peer influence may have left little variation in individual-level knowledge, attitudes, and beliefs within schools. Other demographic factors were not associated with intake adherence suggesting that inequities in distribution may be limited. These findings should not de-emphasize the importance of addressing potential individual-level program barriers. These findings suggest that addressing barriers and improving facilitators at the school level may be a starting point for promoting intake adherence.

Many of our qualitative findings are consistent with those from India including the need for cross-sectoral collaboration, involvement of multiple school stakeholders, utilizing student leaders, sensitization of students and stakeholders, and integration into existing systems and infrastructure.⁽²³⁾ Cross-sector collaborations have been identified by other school-based supplementation programs as a key driver of program uptake and adherence.^(21,24) Several similar programs have highlighted the need

for effective communication to the target population and their communities.^(23,24,25,26) Several of our findings related to educators are unique because of the design of the program: operating through educators rather than health workers. These include time burden, responsibilities, and knowledge of educators. Consistent with retrospective evaluations of the scale-up of India's program,⁽²³⁾ potential solutions for many of the issues highlighted in the qualitative study center on improved communication and collaboration between the health and education sectors, strengthening the supply chain, spreading the responsibility for distribution within schools, improving sensitization activities, improving the engagement of parents, and increasing the frequency of and stakeholders involved in trainings.

7.3: Study Strengths and Limitations

This dissertation has several limitations. We were unable to perform a complete analysis of the etiology of anemia among Ghanaian adolescents, and we lack other potential proximal predictors of anemia such as micronutrient status, inflammation, HIV, hookworm or other infections, blood disorders, and a more complete examination of diet. The food frequency methods we utilized were based on validated methods for women of reproductive age but had not been validated after modifications or within adolescents. The short recall period and single data collection at baseline and follow-on means that usual intake of individuals was not collected, rather we assume to have an approximation of usual intake of the population, which is also subject to seasonal food availability.

Our study is limited by the absence of a contemporaneous counterfactual. While it is reasonable to assume that changes observed over time are real because they happen within the same individuals, we cannot be certain that changes would not have happened in the absence of the intervention.

Seasonality could have played a key role in the changes because of two main reasons: malaria and diet.

The interaction of endemic malaria and micronutrient deficiencies in Ghana makes malaria-induced anemia a perennial problem.^(27,28) The density of the malaria parasite and severity of malaria infection are positively associated with hepcidin secretion leading to the sequestration of iron in malaria-infected

individuals.⁽²⁹⁾ This suggests that ingested iron is poorly utilized by individuals with malaria infection and supplemental iron may not be as effective for anemia control in populations where malaria is not adequately addressed. This adaptive mechanism, which may lead to low serum ferritin, can also create difficulties in the classification of iron deficiency in malaria-infected individuals. Patterns of diet also change with the availability of agricultural products. However, although there were significant changes over the school year in malaria burden (follow-on was conducted during a higher transmission season) and diet, there was no evidence of interaction by malaria in the association between IFA tablets and anemia or hemoglobin concentration. All adjusted models control for these factors, which could minimize the confounding effects of seasonality in our estimates; however, residual confounding by unknown or unmeasured variables is still possible. Finally, our method of classifying malaria did not measure parasitic load or stage of infection which would have enabled a more sensitive examination of the relationships between malaria and anemia because of the parasite's effects on red blood cells.

We were also able to show a clear dose-response relationship between Hb and the number of IFA tablets consumed, which gives more suggestion of a causal relationship. This relationship is observed despite some evidence that IFA consumption was slightly over-reported due to 13% of students spitting out a tablet after pretending to swallow it at some point during the school year. This issue was reported as a problem only during the start of the program and was resolved through sensitization and closer supervision during distribution. We hypothesized that this misclassification would bias our estimates towards the null. The reduction in anemia prevalence might have been greater had the issue of spitting out tablets not occurred. Nonetheless, these issues were minimal as there was excellent (100%) agreement between the student report of ever consuming the tablet and the abstracted consumption data.

The qualitative study was not completed within a representative sample of schools; however, the large number of schools with diverse characteristics provides an approximation of the breadth of experiences

in Phase I schools. The absence of student respondents limits interpretation of their perspectives, which may be key individual-level drivers of program participation. Key informant interviews may suffer from social desirability bias; however, interviewers encouraged candor and stressed confidentiality to minimize the risk of these biases. The single time-point of the interviews also limits the capture of changing information, experiences, or motivations over time. The interviews were primarily conducted in English, but cross-cultural differences between the respondents and the analyst could have led to misinterpretations of responses. However, local co-investigators participated in the analysis and interpretation, which likely reduced this issue.

This dissertation is strengthened by the use of rigorous quantitative and qualitative methods to evaluate adolescent anemia and school-based anemia control programming in Ghana. The overall effectiveness study used a longitudinal cohort design to measure individual-level changes. Each analysis used an adequate sample size and had a high participation rate (>90%). Multi-level models had a sufficient number of clusters ⁽³⁰⁾ and individuals to achieve the desired statistical power. Qualitative interviews reached saturation for all themes and had respondents for each a priori stratum. Validated and standardized methods were used in the measurement of height, weight, Hb, and malaria. Longitudinal measurement of the IFA number of tablets consumed eliminates recall bias, though other control variables such as diet and geophagy were based on participant recall. However, there were missing registers from three schools that reduced the analytic samples size. The use of objective variables and multiple sources of data including schools, students, and registers allows for some evaluation of data quality and sensitivity analyses. The cut-point for the minimum effective number of weekly IFA tablets provides a data-driven target for achieving adequacy of Hb in the population, and the use of a statistical bootstrapped approach corrects for potential overfitting and optimism bias around estimates. ⁽³¹⁾ The multi-level model of IFA consumption controls for cross-level confounding while examining the predictors of consumption in the hierarchical structure in which they exist.

7.4: Remaining Research Gaps and Next Steps

To our knowledge, this work is the first to evaluate an anemia control program with IFA supplementation in schools in sub-Saharan Africa. However, there are still several research gaps. Understanding the burden of blood disorders would increase precision by enabling exclusion of individuals with these conditions from the program and analyses. An assessment of iron and folic acid deficiency and inflammation would improve our understanding of which adolescents stand to benefit most from IFA supplementation and how it affects micronutrient status. An ongoing evaluation in Phase III includes biomarkers of iron and inflammation and includes boys in the evaluation. However, it does not include an assessment of folic acid status. Further study of adolescent diets in Ghana is needed to estimate the contribution of iron and folic acid in the diet and to understand the nutrient gap that the IFA tablet aims to fill. These studies may also evaluate the need for multiple micronutrient supplementation.

Government officials intend to move towards local production of the iron-folic acid supplement using public-private partnerships. Currently supplied supplements do not contain the WHO-recommended quantity of folic acid, only 400 µg rather than the recommended 2800 µg. Local production may provide an opportunity to meet the recommendation and study the effects of an increase dose. Thorough formative research is needed to tailor the tablet for adolescent girls. Such research may uncover the need for a chewable tablet to eliminate the barriers caused by water scarcity or a different color tablet.

Specific strategies for addressing barriers to intake adherence will need to be evaluated. Some problematic areas of the program identified by the qualitative study will require further investigation such as strategies for improving the behavior change component for students within schools. Further, strategies for improving the communication and collaboration between the health and education sectors and promoting the joint ownership of the program will need to be tested.

The health center delivery platform of the intervention designed to reach out-of-school girls through local health centers remains unevaluated. A complete analysis of its effectiveness and the barriers to intake adherence is needed to ensure equity of the program for out-of-school girls. While the enrollment of younger adolescents is high (>80%), approximately 40% of older adolescents are not enrolled in secondary schools. ⁽³²⁾ This means that equitable distribution may not occur if the focus is solely on the school platform, and additional efforts are required to ensure that the health center platform reaches girls missed by the school platform. In addition, a formal evaluation of sensitization activities within communities is needed to understand the reach of such activities and their effectiveness in improving awareness and understanding of the GIFTS program and to identify a minimum package of effective strategies for sustainable replication. A study of other potential downstream impacts of the program is also needed. It is unclear how the introduction of the integrated anemia control program among adolescent girls might have affected school attendance and performance, awareness and uptake of IFA for antenatal care, micronutrient supplementation of children, or other anemia prevention behaviors within the families of participating adolescents. Finally, the cost-effectiveness and cost-benefit have yet to be evaluated. As a national program, a significant investment is being made in the GIFTS program by the ministries of health and education and international partners. Determining the cost-effectiveness and cost-benefit of the program will be useful data points for decision-makers in Ghana and in other countries seeking to address anemia among their adolescent population.

7.5: Conclusions

The burden of anemia among adolescent girls in Ghana is moderately high. Though several factors are associated with anemia in this population, school-based IFA supplementation is effective at reducing the burden of anemia among adolescent schoolgirls. Barriers and facilitators to intake of IFA supplements stem primarily from the school level and program infrastructure rather than student-level behaviors

during the first year of implementation. However, there is interaction between these levels as training and sensitization activities can foster a cooperative spirit among educators, parents, and students. Further strengthening of training, communication, motivation, and supply chain may improve program fidelity and intake adherence with downstream effects on Hb and anemia. Further research is needed to understand the potential application of these findings to the health center platform for reaching adolescent who do not attend schools.

References (Chapter 7)

1. Wirth JP, Woodruff BA, Engle-Stone R *et al.* (2017) Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr* **106**, 416S-427S.
2. Nguyen PH, Gonzalez-Casanova I, Nguyen H *et al.* (2015) Multicausal etiology of anemia among women of reproductive age in Vietnam. *Eur J Clin Nutr* **69**, 107-113.
3. Engle-Stone R, Aaron GJ, Huang J *et al.* (2017) Predictors of anemia in preschool children: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *Am J Clin Nutr* **106**, 402s-415s.
4. Azupogo F, Aurino E, Gelli A *et al.* (2019) Agro-ecological zone and farm diversity are factors associated with haemoglobin and anaemia among rural school-aged children and adolescents in Ghana. *Maternal & child nutrition* **15**, e12643.
5. Ejigu BA, Wencheko E, Berhane K (2018) Spatial pattern and determinants of anaemia in Ethiopia. *PLoS One* **13**, e0197171.
6. Mohandas N, An X (2012) Malaria and human red blood cells. *Medical microbiology and immunology* **201**, 593-598.
7. Miao D, Young SL, Golden CD (2014) A meta-analysis of pica and micronutrient status. *American Journal of Human Biology* **27**, 84-93.
8. Popkin BM, Adair LS, Ng SW (2012) Global nutrition transition and the pandemic of obesity in developing countries. *Nutrition Reviews* **70**, 3-21.
9. Cesari M, Penninx BW, Lauretani F *et al.* (2004) Hemoglobin levels and skeletal muscle: results from the InCHIANTI study. *J Gerontol A Biol Sci Med Sci* **59**, 249-254.
10. Qin Y, Melse-Boonstra A, Pan X *et al.* (2013) Anemia in relation to body mass index and waist circumference among chinese women. *Nutrition Journal* **12**, 10.
11. Eckhardt CL, Torheim LE, Monterrubio E *et al.* (2008) The overlap of overweight and anaemia among women in three countries undergoing the nutrition transition. *European Journal of Clinical Nutrition* **62**, 238-246.
12. Cheng P-p, Jiao X-y, Wang X-h *et al.* (2011) Hcpidin expression in anemia of chronic disease and concomitant iron-deficiency anemia. *Clinical and Experimental Medicine* **11**, 33-42.
13. Nyumuah RO, Hoang TC, Amoafu EF *et al.* (2012) Implementing large-scale food fortification in Ghana: lessons learned. *Food Nutr Bull* **33**, S293-300.
14. Salam RA, Hooda M, Das JK *et al.* (2016) Interventions to improve adolescent nutrition: A systematic review and meta-analysis. *J Adolesc Health* **59**, S29-S39.
15. Stevens GA, Finucane MM, De-Regil LM *et al.* (2013) 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* **1**, e16-25.
16. Fernández-Gaxiola AC, De-Regil LM (2019) Intermittent iron supplementation for reducing anaemia and its associated impairments in adolescent and adult menstruating women. *Cochrane Database of Systematic Reviews*.
17. Girelli D, Ugolini S, Busti F *et al.* (2018) Modern iron replacement therapy: clinical and pathophysiological insights. *International Journal of Hematology* **107**, 16-30.
18. WHO (2011) *Guideline: Intermittent iron and folic acid supplementation in menstruating women*. no. 9789241502023. Geneva: World Health Organization (WHO).
19. Wendt A, Stephenson R, Young M *et al.* (2015) Individual and facility-level determinants of iron and folic acid receipt and adequate consumption among pregnant women in rural Bihar, India. *PLoS one* **10**, e0120404-e0120404.

20. Aguayo VM, Paintal K, Singh G (2013) The Adolescent Girls' Anaemia Control Programme: A decade of programming experience to break the inter-generational cycle of malnutrition in India. *Public Health Nutr* **16**, 1667-1676.
21. Roche ML, Bury L, Yusadiredja IN *et al.* (2018) Adolescent girls' nutrition and prevention of anaemia: a school based multisectoral collaboration in Indonesia. *BMJ* **363**, k4541.
22. UNICEF Office of Research - Innocenti (2017) *The adolescent brain: A second window of opportunity*. Florence: UNICEF Office of Research - Innocenti.
23. Malhotra S, Yadav K, Kusuma Y *et al.* (2015) Challenges in scaling up successful public health interventions: Lessons learnt from resistance to a nationwide roll-out of the weekly iron-folic acid supplementation programme for adolescents in India. *Natl Med J India* **28**, 81-85.
24. Cavalli-Sforza T, Berger J, Smitasiri S *et al.* (2005) Weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans, and contributions toward achievement of the millennium development goals. *Nutr Rev* **63**, S152-158.
25. Reerink I, Namaste SM, Poonawala A *et al.* (2017) Experiences and lessons learned for delivery of micronutrient powders interventions. *Matern Child Nutr* **13**, e12495.
26. Suchdev PS, Ruth L, Obure A *et al.* (2010) Monitoring the Marketing, Distribution, and Use of Sprinkles Micronutrient Powders in Rural Western Kenya. *Food and Nutrition Bulletin* **31**, S168-S178.
27. U.S. Agency for International Development (2018) *Malaria Operational Plan FY 2018. President's Malaria Initiative*. Washington, D.C.: USAID.
28. Abdulkareem BO, Adam AO, Ahmed AO *et al.* (2017) Malaria-induced anaemia and serum micronutrients in asymptomatic Plasmodium falciparum infected patients. *Journal of parasitic diseases : official organ of the Indian Society for Parasitology* **41**, 1093-1097.
29. Casals-Pascual C, Huang H, Lakhai-Littleton S *et al.* (2012) Hcpidin demonstrates a biphasic association with anemia in acute Plasmodium falciparum malaria. *Haematologica* **97**, 1695-1698.
30. Maas CJM, Hox JJ (2005) Sufficient Sample Sizes for Multilevel Modeling. *Methodology: European Journal of Research Methods for the Behavioral and Social Sciences* **1**, 86-92.
31. Efron B (1979) Bootstrap Methods: Another Look at the Jackknife. *Ann Statist* **7**, 1-26.
32. UNESCO Institute for Statistics (2019) Enrolment ratios: United Nations Education Scientific and Cultural Organization.

Appendices

Appendix 1: Key Informant Interview Guides

Interview Guide

District SHEP Coordinator

Establish Rapport

1. Greeting
2. Introduce yourself: *My name is _____, I am here with the Ghana Health Service and UNICEF to interview teachers and SHEP coordinators about their experiences with the GIFTS Programme.*
[Ask easy questions to build rapport.]
3. *Thank you for welcoming us to your district*

Introduction to the Study

1. Overview of the study: *After the roll-out of the GIFTS programme to reduce anemia among schoolgirls in the first 4 regions, we are returning to understand how the program has gone during year 2 and ways in which it can be improved. Today we are interviewing stakeholders to understand how the GIFTS Programme has been received and implemented in your district.*
2. Reason for selection: *You have been selected because your school is a beneficiary of the GIFTS Programme. At each school we are interviewing stakeholders in the program. May I have your full name? (Write down.)*

Consent

1. Voluntary: *I will explain to you the purpose and scope of the interview before asking whether you would like to participate. It is your choice whether to participate and refusing at any point will not affect your standing at this school. If you feel uncomfortable answering any question, you may ask me to skip to the next subject.*
2. Time commitment: *The interview should take us about 45 minutes – 1 hour.*
3. Recording: *It will also be recorded on this device. It is necessary to record your answers because I cannot write fast enough to take down everything you say during this interview. Your name will be removed from the recording, and our team will listen to it again to understand fully your responses.*
4. Risk: *There are no physical risks to participating. Your information, responses, and the recording of your voice will be kept confidential.*
5. Benefits: *You will not receive any additional compensation for participating; however, your insights will benefit the improvement of the GIFTS Programme in schools throughout the country.*
6. *Do you have any questions?*
7. **Give time to read consent form and sign.**

BEGIN RECORDING: Be sure that the counter begins.

A. DISTRIBUTION

State the name of the school, district, and respondent clearly for the recording.

1. **Main Question:** (Knowledge) Tell me what you know about the IFA programme (GIFTS).
2. **Main Question:** (Supply chain) *Thinking about the last academic year (term/semester), describe for me the process of distributing IFA to schools.*

(Wait for answers. If not discussed, use probes to understand important elements.)

- a. **Probe:** *How does the IFA get to the district and schools?*
- b. **Probe:** *Who is responsible for distribution to the schools and receiving the IFA at schools?*
- c. **Probe:** *How would you describe the supply of IFA tablets in your district? How regular? Any shortages?*
- d. **Probe:** *What happens if a school runs out of IFA tablets?*

CHECK THAT RECORDER IS WORKING

3. **Main Question:** (Differences) *Have there been any changes in the way you give out IFA to the girls? Please describe any changes. Please explain why things changed or did not.*

- a. **Probe:** *What things did your district have to change or improve since the start of the GIFTS Programme?*

4. **Main Question:** (Role) *What is your role in the IFA Programme (GIFTS)?*

- a. **Probe:** *How much of your time does that take (hours and minutes)?*
- b. **Probe:** *How critical is your role in the distribution of IFA tablets?*
- c. **Probe:** *What motivates you to participate?*

5. **Main Question:** (Barriers) *Tell me about any weeks of school that no IFA tablets are given. What reasons are there for not giving IFA tablets?*

6. **Main Question:** (Strengths and Perceptions) *How do you think the IFA distribution is going?*

- a. **Probe:** *What do you think goes well with IFA tablets distribution?*
- b. **Probe:** *How do you feel about IFA tablets?*
- c. **Probe:** *How do education staff (colleagues and school teachers) feel about the IFA tablets?*
 - i. *How do you know?*
- d. **Probe:** *How do you think students (girls and boys) feel about the IFA tablets?*
 - i. *How do you know?*

7. **Main Question:** (Limitations) *What do you think could be improved with IFA distribution?*

- a. **Probe:** *What resources would be helpful to improve IFA tablet distribution?*

B. SENSITIZATION

1. **Main Question:** (Events) *What kinds of sensitization activities have been done with parents or community members related to the GIFTS Programme, since the inception of the program? Please tell me about those events.*
 - a. **Probe:** *Who attended? Where were they held?*
 - b. **Probe:** *What kind of information was given?*
 - c. **Probe:** *How helpful has this been?*
2. **Main Question:** *Do you talk to school health teachers (SHEP coordinators) and teachers about IFA? Tell me about any information you give them.*
3. **Main Question:** (Perceptions) *How do parents and community members feel about the GIFTS Programme? How do you know?*

C. HEALTH EDUCATION

1. **Main Question:** (Sessions) *Tell me about any forms of support you provide to school health teachers related to health and nutrition education.*
 - a. **Probe:** *Have you developed any new education resources because of the GIFTS Programme? Could you tell me about those?*
 - b. **Probe:** *What could be done to improve the health and nutrition talks given to students?*

D. TRAINING

1. **Main Question:** (Training) *Describe any training you received about the IFA/GIFTS programme?*
 - a. **Probe:** *Who provided the training?*
 - b. **Probe:** *When were you last trained?*
 - c. **Probe:** *How influential has this training been?*
2. **Main Question:** (Training needs) *What types of training support could the program provide you or your district?*
 - a. **Probe:** *Any additional training? Why is this necessary or not?*
 - b. **Probe:** *Any resources?*

E. Willingness to Pay

1. **Main Question:** *In your opinion, do you think parents would be willing to pay about 10 cedis per year for the IFA tablets? What is your reason?*

F. FINAL THOUGHTS

1. **Main Question:** *Before I end the recording, do you have anything else to say about the GIFTS Programme?*

Thanks: *Thank you for your time. Your perspective is very important, and we are grateful for your commitment to the education and well-being of students. I will now end the recording.*

Interview Guide

School GIFTS Focal Person and Head Teacher

A. DISTRIBUTION

1. **Main Question:** (Knowledge) Tell me what you know about the IFA programme (GIFTS).
2. **Main Question:** (Time of last distribution) I'd like to begin by asking you some questions about the last time the school gave out IFA tablets. *Please tell me about when the school last gave out IFA.* (Wait for answer. If not sure, use probes to help understand approximate time since last distribution.)
 - a. **Probe:** *Was IFA given out since the current term began?*
 - b. **Probe:** *Was IFA given out last July (or another month last term)?*
 - c. **Probe:** *Has it been over a year since IFA was given out?*
3. **Main Question:** (Last distribution) *How does your school distribute the IFA tablets? Describe the process.* (Wait for answers. If not discussed, use probes to understand important elements.)
 - a. **Probe:** *How are students organized to receive IFA tablets?*
 - b. **Probe:** *Who distributes the tablets and records who took them?*
4. **Main Question:** (Differences) *Have there been any changes in the way your school gives out IFA to the girls? Please describe any changes. Please explain why things changed or did not.*
 - a. **Probe:** *What things did your school have to change or improve since the start of the GIFTS Programme?*
5. **Main Question:** (Role) *What is your role during the distribution? Tell me what you do during this time.*
 - a. **Probe:** *How much of your time does that take (hours and minutes)?*
 - b. **Probe:** *How important is your role in the distribution of IFA tablets?*
 - c. **Probe:** *What motivates you to participate?*
6. **Main Question:** (Barriers) *Tell me about any weeks of the school term that no IFA tablets are given. What reasons are there for not giving IFA tablets?*
 - a. **Probe:** *What reasons might there be for a student not to receive an IFA tablet?*
7. **Main Question:** (Strengths and Perceptions) *How do you think the IFA distribution is going?*
 - a. **Probe:** *What do you think goes well with IFA tablets distribution?*
 - b. **Probe:** *How do your personal views about IFA tablets?*
 - c. **Probe:** *How do other teachers, the head teacher, or health teachers feel about the IFA tablets?*
 - i. *How do you know?*
 - d. **Probe:** *How do you think students (girls and boys) feel about the IFA tablets?*
 - i. *How do you know?*

8. **Main Question:** (Limitations) What concerns do you have about the IFA program?
 - a. **Probe:** *What do you think could be improved with IFA distribution?*
9. **Main Question:** (Use of IFA) Do teachers take the tablet in this school? *Which teachers? Do you also take it?*
 - a. **Probe:** Why or why not?

B. SENSITIZATION

1. **Main Question:** (Events) *What kinds of sensitization activities have been done with parents or community members related to the GIFTS Programme, since the inception of the program? Please tell me about those events.*
 - a. **Probe:** *Who attended?*
 - b. **Probe:** *What kind of information was given?*
2. **Main Question:** *Do you talk to students about IFA? Tell me about any information you give students. How often does this happen?*
3. **Main Question:** (Perceptions) *How do parents and community members feel about the GIFTS Programme? How do you know?*

C. HEALTH EDUCATION

1. **Main Question:** (Sessions) *Do you give health and nutrition talks to students. If no, what are the reasons? If yes, please describe the health talks.*
 - a. **Probe:** *What do you talk about? How do you decide what topics to talk about? What resources would you require?*
 - b. **Probe:** *What do you tell students about what IFA does for them (positive and negative)?*
 - c. **Probe:** *Have you created any new health talks because of the IFA programme? Could you tell me about those?*
 - d. **Probe:** *What could be done to improve the health talks you give to students?*
 - e. **Probe:** What nutrition topics have you talked about?

D. TRAINING

1. **Main Question:** (Training) *Describe any training you received about the IFA/GIFTS programme?*
 - a. **Probe:** *Who provided the training?*
 - b. **Probe:** *How long ago was the training?*
2. **Main Question:** (Training needs) *What other training support could the program provide you?*

E. Willingness to Pay

1. **Main Question:** In your opinion, do you think parents would be willing to pay about 10 cedis per year for the IFA tablets? What is your reason?

F. FINAL THOUGHTS

1. **Main Question:** *Before I end the recording, do you have anything else to say about the GIFTS Programme?*

Thanks: *Thank you for your time. Your perspective is very important, and we are grateful for your commitment to the education and well-being of students. I will now end the recording.*

Interview Guide

Teacher

A. DISTRIBUTION

State the name of the school and respondent clearly for the recording.

1. **Main Question:** (Knowledge) Tell me what you know about the IFA programme (GIFTS).
2. **Main Question:** (Time of last distribution) I'd like to begin by asking you some questions about the last time the school gave out IFA tablets. *Please tell me about when the school last gave out IFA.*
(Wait for answer. If not sure, use probes to help understand approximate time since last distribution.)
 - b. **Probe:** *Was IFA given out since the current term began?*
 - c. **Probe:** *Was IFA given out last July (or another month last term)?*
 - d. **Probe:** *Has it been over a year since IFA was given out?*

3. **Main Question:** (Last distribution) *How does your school distribute the IFA tablets? Describe the process.*

(Wait for answers. If not discussed, use probes to understand important elements.)

- e. **Probe:** *How are students organized to receive IFA tablets?*
- f. **Probe:** *Who distributes the tablets and records who took them?*

CHECK THAT RECORDER IS WORKING

4. **Main Question:** (Differences) *Have there been any changes in the way your school gives out IFA to the girls? Please describe any changes. Please explain why things changed or did not.*

- g. **Probe:** *What things did your school have to change or improve since the start of the GIFTS Programme?*

5. **Main Question:** (Role) *What is your role during the distribution? Tell me what you do during this time.*

- h. **Probe:** *How much of your time does that take (hours and minutes)?*
- i. **Probe:** *How important is your role in the distribution of IFA tablets?*
- j. **Probe:** *What motivates you to participate?*

6. **Main Question:** (Strengths and Perceptions) *How do you think the IFA distribution is going?*

- k. **Probe:** *What do you think goes well with IFA tablet distribution?*
- l. **Probe:** *How do your personal views about IFA tablets?*
- m. **Probe:** *Are other teachers, the head teacher, or health teachers supportive of the IFA tablets?*
 - i. *How do you know?*
- n. **Probe:** *What do you tell students about what IFA does for them (positive and negative)?*
- o. **Probe:** *How do you think students (girls and boys) feel about the IFA tablets?*
 - i. *How do you know?*

p. **Probe:** *What reasons might there be for a student not to receive an IFA tablet?*

7. **Main Question:** (Limitations) *What do you think could be improved with IFA distribution?*

Probe: *What resources would be helpful to improve IFA tablet distribution?*

8. **Main Question:** (Use of IFA) *Do teachers take the IFA tablet in this school? Which teachers? Do you also take it?*

q. **Probe:** *Why or why not?*

B. SENSITIZATION

1. **Main Question:** (IFA counseling) *Do you talk to students about IFA? Tell me about any information you give students. How often does this happen?*

2. **Main Question:** (Perceptions) *How do parents and community members feel about the IFA/GIFTS Programme? How do you know?*

C. HEALTH EDUCATION

1. **Main Question:** (Sessions) *Do you give health and nutrition talks to students. If no, what are the reasons? If yes, please describe the health talks.*

a. **Probe:** *What health and nutrition topics have you talked about? How do you decide what topics to talk about? What resources would you require?*

b. **Probe:** *What could be done to improve the health and nutrition talks you give to students?*

D. TRAINING

1. **Main Question:** (Training) *Describe any training you received about the IFA/GIFTS programme?*

a. **Probe:** *Who provided the training?*

b. **Probe:** *How long ago was the training?*

2. **Main Question:** (Training needs) *What types of training support could the program provide you?*

E. Willingness to Pay

1. **Main Question:** *In your opinion, do you think parents would be willing to pay about 10 cedis per year for the IFA tablets? What is your reason?*

E. FINAL THOUGHTS

1. **Main Question:** *Before I end the recording, do you have anything else to say about the GIFTS Programme?*

Thanks: *Thank you for your time. Your perspective is very important, and we are grateful for your commitment to the education and well-being of students. I will now end the recording.*

Interview Guide

Chairperson of PTA or School Management Committee

1. **Main Question:** (Awareness) *What do you know about the GIFTS Programme/IFA?*
 - a. **Probe:** *What have you heard?*
 - b. **Probe:** *What does the IFA tablet do for the person who takes it?*
 - c. **Probe:** *What problem does it solve?*
 - d. **Probe:** *Where did this information come from?*
2. **Main Question:** (Perceptions) *What do you think about the GIFTS Programme/IFA?*
3. **Main Question:** (Perceptions) *How do other parents feel about the IFA tablets?*
 - r. *How do you know?*
 - s. *Do other parents ask you about the IFA programme? Why or why not?*
4. **Main Question:** (Perceptions) *Which community leaders are aware of the IFA programme? What is their opinion about IFA? How do other community members feel about the IFA tablets?*
 - t. *How do you know?*
5. **Main Question:** (Sensitization) *Has the school ever met the PTA about the GIFTS Programme? What did they tell you?*
6. **Main Question:** (Observations) *Do you know any children that take IFA tablets? Which children receive IFA tablets (girls/boys, older/younger)? Tell me about any changes you have noticed since they started taking IFA.*
 - u. **Probe:** *Tell me about any children you know that do not take IFA tablets.*
7. **Main Question:** (Support) *What support do you give the GIFTS Programme?*
8. **Main Question:** (Sensitization) *What kinds of sensitization activities do you do with parents or community members?*
9. **Main Question:** *In your opinion, do you think parents would be willing to pay about 10 cedis per year for the IFA tablets? What is your reason?*
10. **Main Question:** *Before I end the recording, do you have anything else to say about the GIFTS Programme?*

Thanks: *Thank you for your time. Your perspective is very important, and we are grateful for your commitment to the education and well-being of students. I will now end the recording.*

END RECORDING

Write summary of the interview.

Appendix 2: Distribution of Hemoglobin Concentration at the Baseline and Follow-on Surveys of the Phase I Evaluation of the GIFTS Program

