Post-intervention Epidemiology of STH in Bangladesh: data to sustain the gains

Short title: Evaluation of the impact of 12 years of PCT: STH epidemiology in Bangladesh

Sanjaya Dhakal[1¶], Mohammad Jahirul Karim[2¶], Abdullah Al Kawsar[2&], Jasmine Irish[1&], Mujibur Rahman[2], Cara Tupps[1], Ashraful Kabir[1&], Rubina Imtiaz[1*¶]

1 Children Without Worms, The Task Force for Global Health, Atlanta, GA, USA

2 Communicable Disease Control, Ministry of Health & Family Welfare, Dhaka, Bangladesh

Corresponding author

E-mail: rimtiaz@taskforce.org

¶ SD, MJK and RI contributed equally to this work.

& JI, AAK and AK contributed equally to this work.

Abstract

Introduction

In 2008, Bangladesh initiated Preventive Chemotherapy (PCT) for school-age children (SAC) through bi-annual school-based mass drug administration (MDA) to control Soil-Transmitted Helminth (STH) infections. In 2016, the Ministry of Health and Family Welfare's Program on Lymphatic Filariasis Elimination and STH (ELFSTH) initiated district-level community impact assessments with Children Without Worms (CWW) using standardized, population-based sampling to measure the post-intervention STH burden across all ages (≥ 1 yr) for the three STH species.

Methods & Principal Findings

The Integrated Community-based Survey for Program Monitoring (ICSPM) was developed by CWW and was used to survey 12 districts in Bangladesh from 2017 – 2020. We combined the individual demographic and parasite-specific characteristics from 10 districts and linked them with the laboratory data for collective analysis. Our analysis identified district-specific epidemiologic findings, important for program decisions.

Of the 17,874 enrolled individuals, 10,824 (61%) provided stool samples. Overall, the prevalence of any STH species was substantially reduced to 14% from 79.8% in 2005. The impact was similar across all ages. STH prevalence was below 10% in 10 districts collectively, but remained high in 4 districts, despite their high reported PCT coverage in previous years.

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Among all, Bhola district was unique because it was the only district with high Trichuris prevalence.

Conclusion

Bangladesh successfully lowered STH prevalence across all ages despite targeting SAC only. Data from the survey indicate significant number of adults and pre-school age children (PSAC) were self-deworming with purchased pills. This may account for the flat impact curve across all ages. Overall prevalence varied across surveyed districts, with persistent high transmission in the northeastern districts and a district in the central flood zone, indicating possible service and ecological factors. Discrepancies in the impact between districts highlight the need for district-level data to evaluate program implementation after consistent high PCT coverage.

Authors Summary:

Bangladesh government conducted school-based mass drug administration (MDA) for over 10 years to control soil-transmitted helminth (STH) infections. School-based evaluations of MDA indicate a reduction in STH burden among school-aged children (SAC). To further assess the impact on the community, Children Without Worms and the Ministry of Health and Family Welfare's Program on Lymphatic Filariasis Elimination and STH (ELFSTH) initiated district-level community impact surveys in 12 districts. We share the results from the latter 10 districts here.

Our analysis of 10,824 interviews and stool samples from 10 districts showed an estimated 14% of community members infected with at least one species of STH. This finding is substantially lower than the baseline STH prevalence (79.8%) estimated in 2005. Bangladesh's successful impact was achieved across all ages despite only treating SAC. Deworming source data showed significant numbers of adults and pre-school age children (PSAC) self-dewormed with locally purchased pills. Prevalence varied across the surveyed districts, with persistent high transmission in the northeastern districts and a district in the central flood zone, indicating possible ecological and service factors contributing to persistent infections. Discrepancies in the impact across districts highlights the need for sub-national level data to evaluate program performance fllowing consistent high intervention.

1 Introduction

2   In 2001, the World Health Organization (WHO) recommended that member states

3 control Soil-Transmitted Helminthiasis (STH) morbidity through preventive chemotherapy (PCT)

4 in endemic regions. The recommended guidance utilizes a school-based platform to target one

5 high-risk group, school-age children (SAC) through mass drug administration (MDA) to achieve

6 at least 75% coverage consistently for five years. Once this is achieved, an impact assessment

7 survey is recommended (1). Like many developing countries, Bangladesh bears a high burden of

8 STH. An estimated STH prevalence of 79.8% (44% of which was moderate-to-high intensity,

9 MHI, of Ascaris) among school-aged Bangladeshi children was reported in 2005 (2). By January

10 2020, Bangladesh had completed 23 rounds of school-based bi-annual MDA with Mebendazole.

11 Bangladesh receives the largest Mebendazole donation of all endemic countries (approximately

12 20% of the global donation) and has an excellent supply chain record over the past 5 years (SCF-

13 NTD data: CWW pulled June 2020).

14   Annual coverage data from Bangladesh indicates consistent coverage of greater than

15 75% for more than five years before ICSPM surveys began in 2017 (3). Previously, PCT coverage

16 data was used as a proxy to indirectly evaluate the impact of deworming on the STH burden (3,

17 4). A major limitation of this approach was the inability to assess the true burden of disease in

18 the community at risk because; 1.) MDA targets only SAC (a small proportion of the at-risk

19 population, 2.) the quality of coverage data is not tested, and 3.) targeted parasites have

20 variable sensitivity to the single drug used for MDAs (5, 6). Additionally, PCT coverage data does

21 not include children outside schools and adults. Available evidence indicates that these

22 additional risk populations such as pre-school-age children (PSAC) and adults, particularaly

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23   women of reproductive age (WRA) are also at risk of STH infection and share a substantial

24   disease burden (7-9).

25   Therefore, to better understand the community-level program impact, the ELFSTH

26   Program, the Bangladesh Ministry of Health & Family Welfare (MOHFW) collaborated with

27   Children Without Worms (CWW) to conduct community-level impact assessment surveys called

28   Integrated Community-based Survey for Program Monitoring (ICSPM) from 2017 to 2020. The

29   main objectives of the surveys were:

30   i.   To estimate the statistically valid prevalence of STH infection and prevalence of

31   moderate to high-intensity infection (MHII) in PSAC, SAC and adults (greater

32   than 14 years old), powered to the district level, and

33   ii.   To evaluate potential correlates of STH infection rates including sanitation &

34   hygiene behaviors (household level) and history and source of deworming

35   (individual level).

36   In this paper, we present the results of concatenated survey data from 10 districts

37   conducted between 2017 and 2020, focusing on parasite- and age-specific prevalence and

38   infection intensity as well as the geographic variation of STH prevalence. This paper also

39   presents how these results are applicable for use by the ELFSTH program towards future

40   program actions, and how this approach can assist other similarly advanced NTD programs

41   around the world.

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43   **Methods:**

44   **Study design**

45   ICSPM surveys were conducted in 12 districts, representing 7 out of 8 divisions across

46   Bangladesh, to evaluate the impact of MDA at the community level for each parasite and each

47   risk group; to validate deworming pill intake and pill source within six months before the

48   survey, and to assess the effect of select WASH variables at the household level. Based on age,

49   we defined three risk groups as follows:

50   • 1 – 4 pre-school age children (PSAC)

51   • 5 – 14 school-age children (SAC)

52   • greater than 14 years old (adults)

53   The districts were selected by the Bangladesh ELFSTH as a good evaluation unit (EU) as

54   the district is the most common administrative unit for implementation decisions where these

55   results could be utilized. Figure 1 shows the years of each survey for the 10 districts.

56   The ICSPM survey is a community-based, cross-sectional survey based on probability

57   proportional to size sampling (PPSS). The details of the ICSPM survey methodology is available

58   on the CWW website (http://www.childrenwithoutworms.org/). Briefly, the survey design entails a

59   cross-sectional, mixed cluster & random systematic sample methodology and has been

60   previously detailed (10). The ICSPM methodology primarily relies on WHO's "Assessing the

61   epidemiology of STH during a transmission assessment survey (11). We targeted a sample size

62   of 332 for each risk group, which gave us one-sided 95% confidence for determining if the <10%

63   prevalence, action threshold was achieved. Since the average non-response rate in the first

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64   two pilot districts was around 40%, we enrolled 465 individuals in each risk group in subsequent

65   districts to account for this. The sampling interval was based on the proportion of each risk

66   group within the population. The survey team used the Survey Sample Builder (SSB) tool, which

67   was adapted to the ICSPM methodology, an excel program developed by Neglected Tropical

68   Diseases Support Center, The Task Force for Global Health (TFGH) to select clusters and risk

69   groups within the households.

70   We used the Kato-Katz method to identify and count the eggs of STH parasites following

71   standard WHO methodology using 2-slides per stool specimen. Ten percent of slides were

72   tested blindly by another laboratory scientist for quality control. Three data sets (Household,

73   Individual, and Laboratory) were downloaded from the secure cloud-based data-hosting

74   platform and saved in local computers at CWW, Atlanta. After basic data cleaning, household

75   data were first merged with individual data and later with laboratory data making one linked

76   data file for each district. We recoded and reformatted variables as necessary to align across

77   the districts before combining the individual data files from surveyed districts. Finally, we

78   prepared one analytical data file for this report by stacking 10 individual data files from each of

79   the surveyed districts. According to the 2011 national population census, this analysis

80   represents about 15.5% of the Bangladesh population.

81   We used SAS version 9.4 (SAS Inc., Cary NC, USA) to manage and analyze the data. We

82   accounted for the cluster sample survey design in all analyses using appropriate SAS

83   procedures. Chi-square (χ^2) test was used to assess differences in prevalence between risk

84   groups and p-values ≤ 0.05 were considered significant. Since the survey was powered to detect

85   the prevalence of STH and MHII down to a threshold of <10% at the district level, only upper

86   sided, 95% confidence limits are reported. We also ran some explorative analyses at the sub-

87   district level, which lacked statistical power but provide useful insights for further program

88   actions.

89   Participation in the survey was voluntary and participants provided verbal consent

90   before the main survey. Bangladesh Medical Research Council approved the survey protocol.

91

92   **Results:**

93   <u>**Basic characteristics**</u>

94   Of 17,874 enrollees, 11,022 (62.0%) provided stool samples for laboratory examination.

95   In total, 198 (1.6%) records were excluded during the data cleaning process due to;

96   a.) IDs present in only one dataset

97   b.) duplicate IDs with mismatching data across other variables, and

98   c.) data entry errors.

99   The final dataset had 10,824 records which were used for the analysis presented here (figure 2).

100   <u>**Prevalence and Intensity of STH Infections:**</u>

101   The overall prevalence of any STH infection in 10 districts was 14.0% (figure 3). There

102   was no statistical difference in the prevalence of STH infection across the risk groups. We did

103   not observe statistically different prevalence between females (14.4%) and males (13.4%). Of

104   the three tested parasites, *Ascaris* was the most common (10.5%) followed by *trichuris* (4.4%).

105   The prevalence of hookworm was less than 1% in all risk groups, so the results for hookworm

106   prevalence are not shown. Three districts with the highest STH prevalence were Sunamganj

107   (40.4%), Bhola (36.5%), and Sirajganj (26.9%). In contrast, Satkhira (2.0%), Jhenaidah (2.4%),

108   and Manikganj (3.1%) had the lowest STH prevalence (figure 3).

109   Overall, the intensity of STH MHII for 10 districts was 3.3%. Bhola (10.6%), Sunamganj

110   (10.4%), Sirajganj (7.1%), and Moulvibazar (3.6%) were four districts with MHII above the WHO-

111   recommended threshold of <1%, while the remaining 6 districts had achieved this goal with

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112   MHII ranging from 0.0% to 0.2% (table 1). This is a significant achievement for the national

113   program and signifies the achievement of the WHO goal of eliminating STH morbidity in

114   majority districts.

115   We further explored three high prevalence (>20%) districts- Sunamganj, Bhola, and

116   Sirajganj- to understand if there were any geographic concentrations of STH infection at the

117   sub-district level. Figure 4 illustrates the STH prevalence by sub-districts in these three high-

118   prevalence districts. The prevalence of STH was higher than 50% in two sub-districts (Dowara

119   Bazar and Dakshin Sunamganj) of Sunamganj and one sub-district (Belkuchi) of Sirajganj district.

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121   **History of deworming**

122   The proportion of self-reported deworming was highest among SAC (75.6%) followed by

123   adults (69.1%) and PSAC (51.9%) for the 9,386 (86.7%) individuals who provided the history of

124   deworming in the previous 6 months (table 2).

125   Among responders (n= 7,469) to the query of the location of deworming, 88.6% of SAC

126   reported getting dewormed through school-based MDA, while 85.1% adults and 76.2% of PSAC

127   were dewormed through locally purchased deworming medicines (figure 5).

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129   **Discussion:**

130   To our knowledge, this is the first time an impact evaluation of MDA directed at one

131   specific risk group, SAC, has shown a significant reduction in STH prevalence across all age

132   groups in a given community. Our analysis of pooled data from community-based surveys in 10

133   districts in Bangladesh found a substantial reduction in overall STH prevalence from 79.8%

134   (2005) to 14.0% (2017-2020) across all risk groups after more than 10 years of school-based

135   systematic biannual PCT for SAC. Despite SAC being the only targeted risk group for MDA, the

136   data shows no statistically significant differences in STH prevalence among PSAC, SAC, and

137   adults. Although we did not specifically explore potential impact variables on the community

138   prevalence, we speculate that the following factors might have contributed to this observation:

139   1. Change in health-seeking behavior in adults, namely purchasing deworming

140   medication for themselves and family members outside of school (correlates with data on

141   the source of deworming for PSAC and adults). This could be attributed to the positive

142   results of school-based MDA encouraging out-of-school villagers to seek deworming, and

143   2.   Improved WASH factors have increased access to improved sanitation at the

144   household level.

145   In a recent national school survey of 5 to 12-year-old schoolchildren from 106 schools

146   across the country (data not published yet), Bangladesh ELFSTH reported a lower STH

147   prevalence than the prevalence derived from ICSPM surveys for the same age range (8.1% vs.

148   13%). Similarly, the MHII among this age group was 1.7% in the school-based survey and 2.6%

149   with the ICSPM. The school-based survey had some limitations, including:

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150   a. A small proportion of only school-going children were sampled as the targeted

151   population rather than the entire endemic community.

152   b. The survey was not statistically powered to the program implementation level, nor the

153   national school-attending population.

154   The observed difference in STH prevalence by school versus community-based surveys

155 indicates that the school-based surveys may not be the right tool to estimate the true

156 prevalence and intensity of STH for sub-national level program planning. This is especially true

157 for advanced programs where prevalence is generally reduced and remaining aggregated areas

158 of continuing transmission need to be reliably identified to redistribute precious resources for

159 most efficient actions.

160   According to the latest WHO guidance(12), the 2030 goal for STH morbidity elimination is

161 achieved when a country/region reaches <2% MHII. The school survey indicates that

162 Bangladesh has achieved this goal and can halt MDA for 2 years per WHO guidance (13).

163 However, the population-based ICSPM data for the same risk groups in the same geographic

164 areas shows the true prevalence of intensity to be still > 2. The more granular ICSPM data

165 provides more meaningful guidance to the program, i.e. reducing MDAs in low prevalence areas

166 but increasing interventions in clusters of high transmission that persist. Our findings are similar

167 to those from a school based survey in Sri Lanka (14).

168   Therefore, for countries with mature programs who have reach the WHO goal of

169 consistent coverage above 75% for 5 years, we recommend a statistically valid, population-

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170   based sampling approach to assess the sub-national level impact on prevalence and intensity of

171   STH for use in data-driven program decision-making or policy adjustments.

172   Additionally, our analysis revealed that the impact of STH control measures is not uniform

173   across the country: it was significantly reduced in six districts, while the other four still carry a

174   burden of higher prevalence and intensity. Potential factors influencing the impact of MDA on

175   STH prevalence and intensity may be related to the local population and individual

176   characteristics, as well as service processes related to intervention quality such as:

177   1. Varied baseline STH prevalence and intensity. (data not available)

178   2. Population movement across district borders, bringing the infection from other areas.

179   3. The complicated relationship between drug distributors and targeted risk groups.

180   4. Variable environmental or ecological characteristics among districts that support longer

181   survival of STH eggs in the soil.

182   5. False rumors or distrust of government programs about the 'real' purpose of the

183   treatment, and

184   6. Responses to local socio-cultural control measures.

185   Among high STH prevalent districts, STH prevalence ranged from 5.1% (Kazipur sub-

186   district, Sirajganj) to 71% (Dowara Bazar sub-district, Sunamganj). All corresponding sub-

187   districts (Sunamganj and Bhola), seven of nine sub-districts (Sirajganj), and one of seven sub-

188   districts (Moulvibazar) had a prevalence of more than 20%.

189   The Bangladesh national NTD program's STH control office plans to use these findings to

190   design a focused intervention program in select sub-districts to lower unexpected high

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191   prevalence. Additionally, the national program may use these findings to make decisions for

192   altering the frequency of MDA programs in low prevalence districts.

193   To further explore the consistent impact across all age groups, we reviewed the pill intake

194   and their source data by age group and by district as well as collectively for all 10 districts. This

195   revealed that a large proportion of PSAC and adults reported the purchase of locally available

196   drugs as the primary source of deworming in the past 6 months. This finding has potential

197   implications for the national program as it may indicate communal behavioral change towards

198   self-investment in preventive health. This could be a spillover effect of the sustained impact of

199   school deworming in these districts, signaling that school-based MDA and accompanying

200   community messaging raises awareness of the positive health outcomes of deworming,

201   triggering treatment-seeking behavior in community members who do not have access to

202   school MDAs but do have local access to affordable, high quality deworming medicines

203   (Bangladesh generic manufacturers and formulations of benzimidazoles: CWW web-survey,

204   2019). These initial findings need further exploration and, if confirmed, will be an important

205   factor influencing a national policy of sustainable domestic financing guided by quality disease,

206   socio-behavioral and pharmacological data. Similar behavioral changes should be explored by

207   other national programs that have quality generics available locally for deworming.

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208   **Conclusion:**

209   After 23 rounds of school-based MDA to lower the burden of STH infection since 2008, a

210   review of survey data from 10 districts in Bangladesh shows that it is close to eliminating the

211   infection as a public health problem from most of the country. To sustain current progress and

212   move forward, Bangladesh needs to identify and treat all community members at risk in the

213   persistent high-prevalence pockets of geographic areas, such as Sunamganj, Bhola, and

214   Sirajganj. Community-based surveys may serve as better tools for a true assessment of PCT in

215   endemic communities compared to more common school-based surveys and additional

216   information on deworming sources is a valuable resource for national programs with high,

217   multi-year coverage.

218   **Limitations:**

219   The ICSPM surveys had some limitations including a higher than expected stool

220   nonresponse rate, possible recall bias (particularly the responses to the history and location of

221   deworming questions), and gender inequity among adult respondents. Additionally, the timing

222   between the stool sample deposit by the survey respondents and testing in the laboratory may

223   have been longer than "ideal" due to geographical challenges so may have underestimated the

224   hookworm prevalence slightly but there is only one published study that documents the "ideal"

225   specimen testing interval for hookworms (15) and additional studies have shown little or no

226   hookworm in south Asia.

227   It is of note that Bangladesh's ELFSTH treated 19 LF-endemic districts with Albendazole

228   (also active against STH worms) to control Lymphatic Filariasis (LF) through community-based

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229   MDAs from 2001 to 2014. While these LF-focused MDAs also impacted the STH prevalence in

230   those 19 districts, these treatments did not affect ICSPM results as the LF program ceased in

231   2014 and ICSPM started data collection in 2017.

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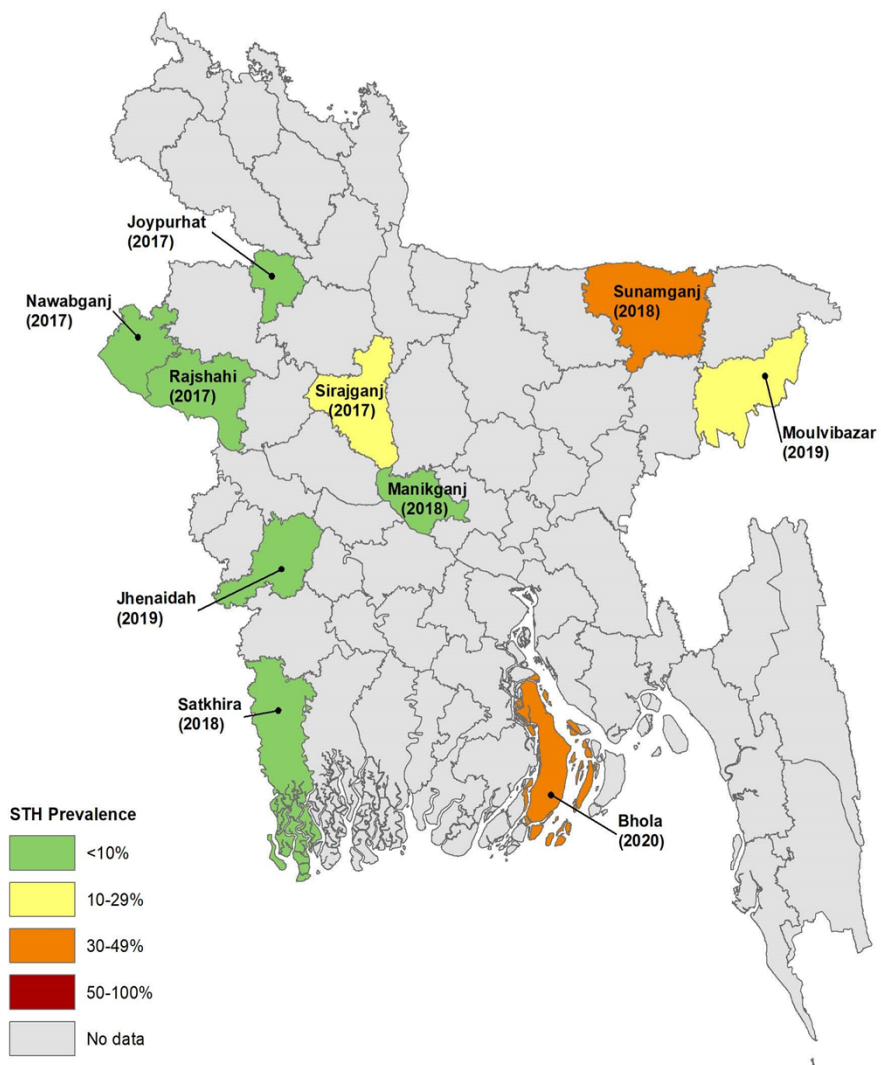
Figure 1: Geographical distribution of ICSPM surveys, year of survey and STH prevalence range
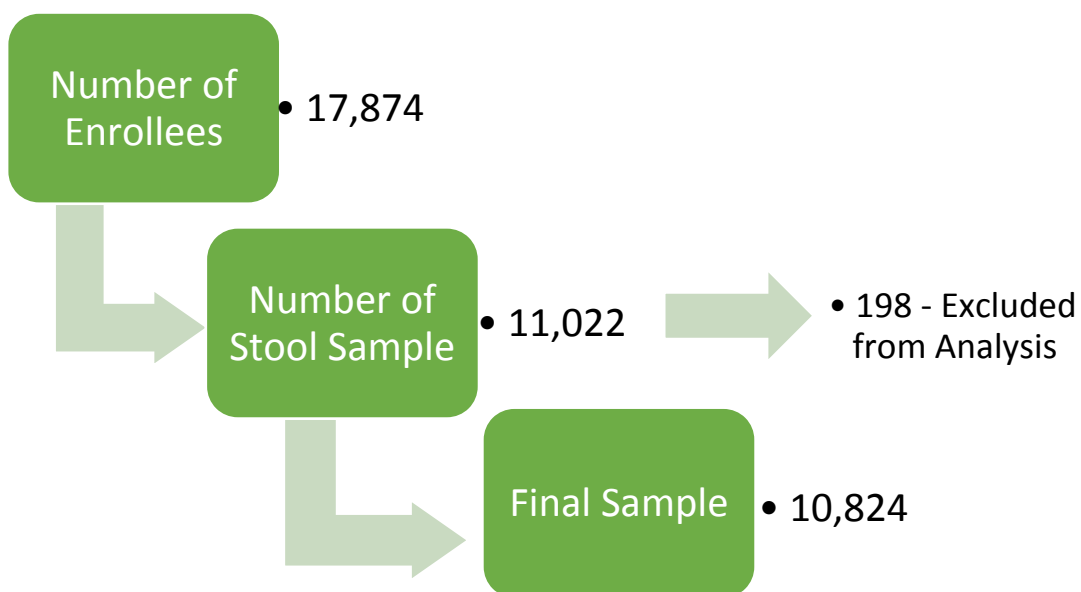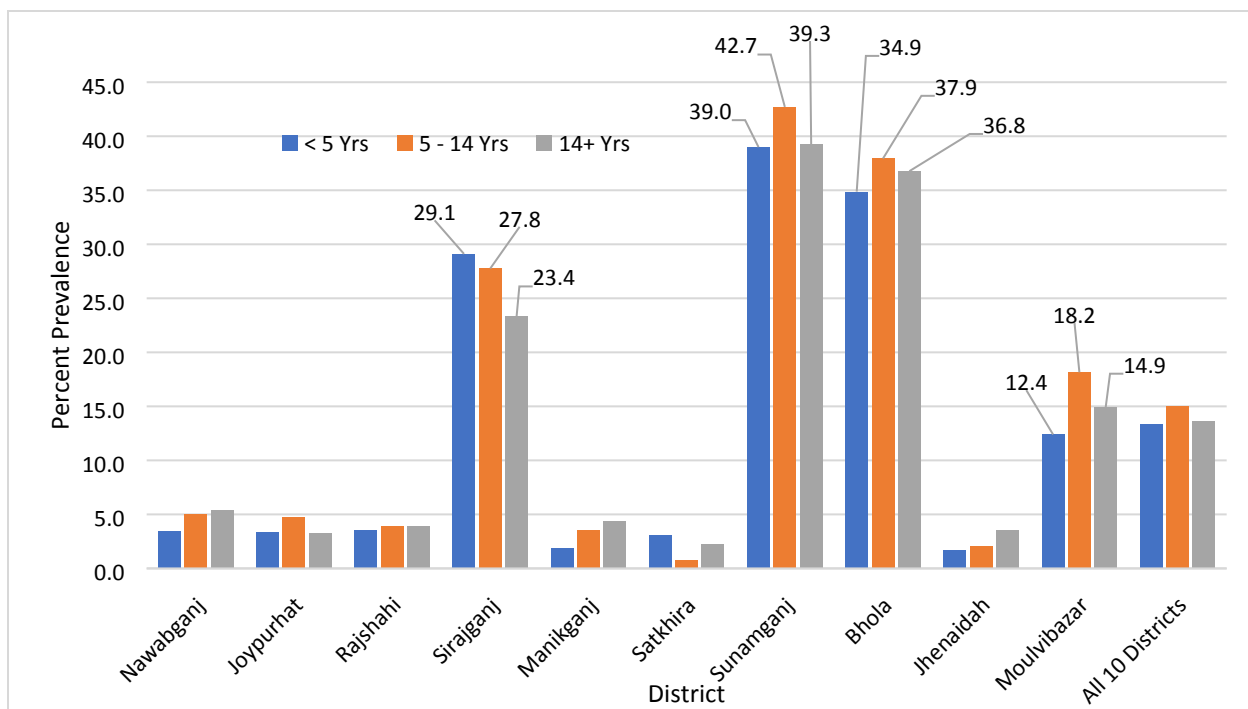
Figure 2: Flow chart of sample selection

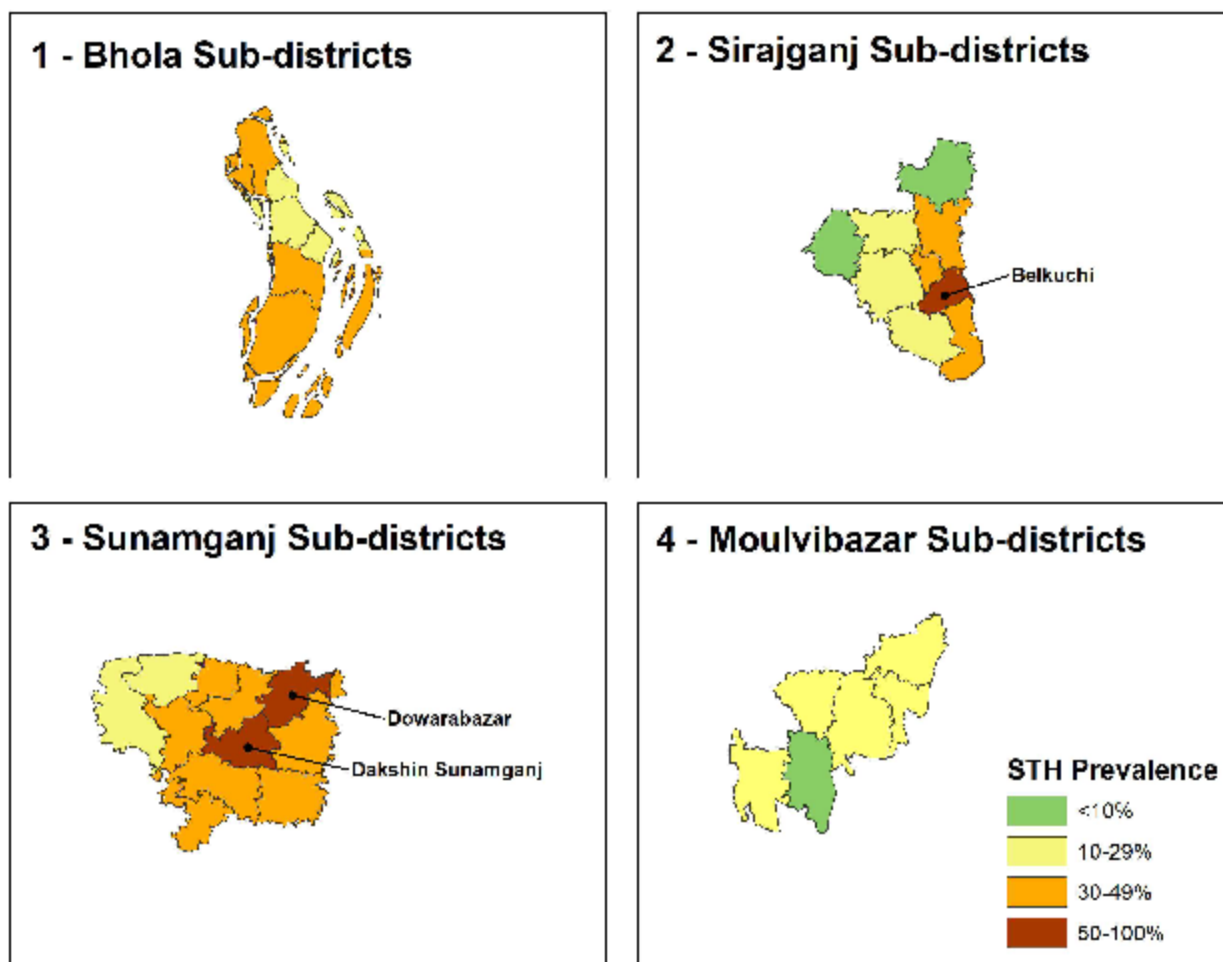**Figure 3: Prevalence of any STH infection by district and age group**

Figure 4: STH prevalence by sub-districts in the highest prevalent ICSPM districts
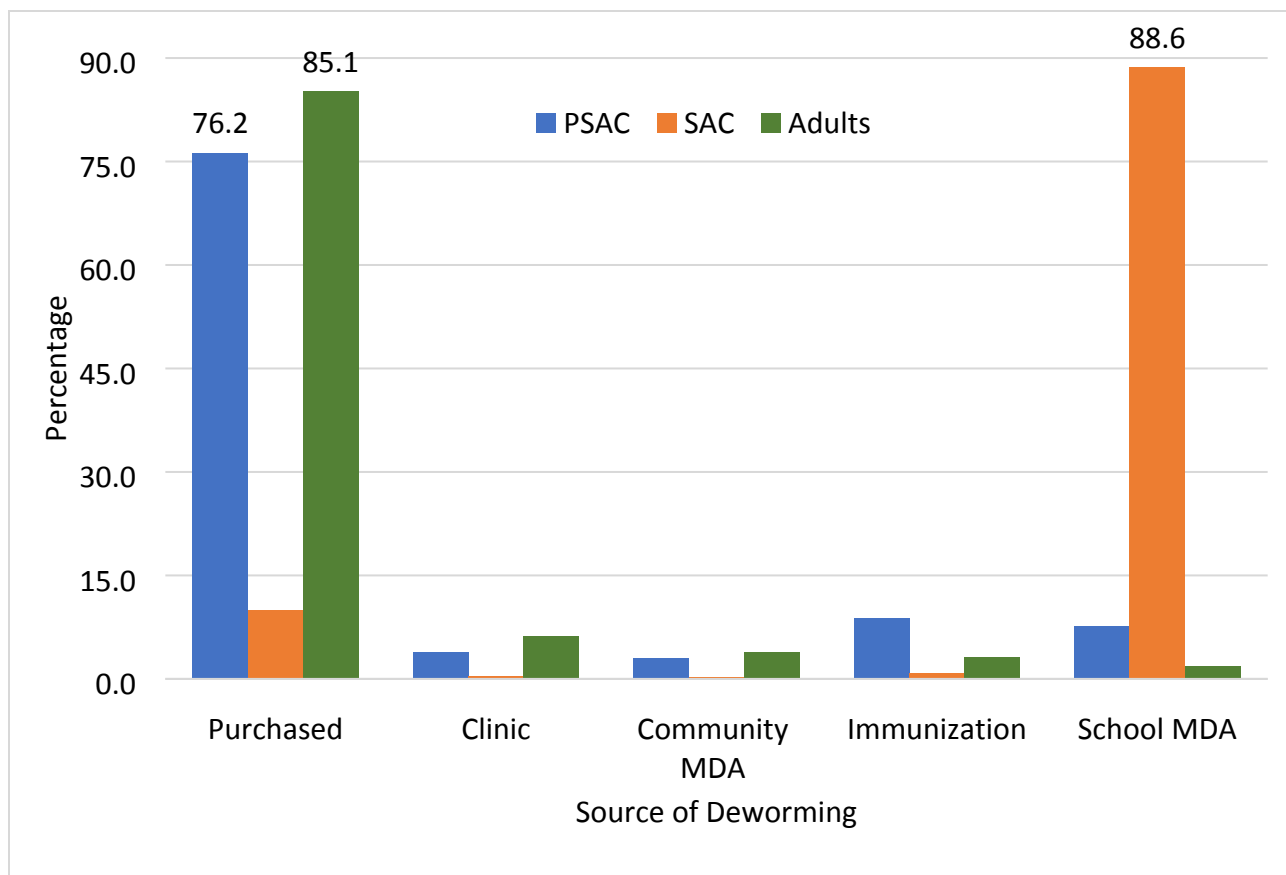
Figure 5: Source of deworming among those who reported deworming in the previous year

Table 1: Intensity of STH morbidity by district

District	Intensity of STH Morbidity among All (Prevalence %)			All Ages (%)
	PSAC	**SAC**	**Adults**	
Sirajganj	7.0	6.6	7.8	7.1
Sunamganj	12.2	8.6	10.2	10.4
Bhola	12.0	11.1	8.5	10.6
Moulvibazar	3.6	4.8	2.4	3.6
All 10-districts	**3.6**	**3.4**	**2.7**	**3.3**

Table 2: History of deworming within the past 6 months

History of deworming	Risk group N (%)			All Ages (%)
	PSAC	**SAC**	**Adults**	
Yes	1053 (37.3)	2733 (75.6)	755 (25.6)	4541 (48.4)
No	1769 (62.7)	884 (24.4)	2192 (74.4)	4845 (51.6)
All 10-districts	2822 (100)	3617 (100)	2947 (100)	9386 (100)