**MENISCUS TRIAL STATISTICAL ANALYSIS PLAN**

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| **Protocol Title** | Menstrual health interventions, schooling, and mental health symptoms among Ugandan students (MENISCUS): a school-based cluster-randomised trial |
| **Protocol version** | Version 6.0 August 2023 |
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| 1.0 | 2023-09-24 |
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# 1 Introduction

## 1.1 Background and rationale

Many girls lack basic knowledge, facilities and/or materials for managing menstruation safely and with dignity. Improving menstrual health (MH) can lead to sustained long-term benefits to education, health, and development [1,2]. Many governmental and non-governmental organisations are interested in introducing interventions to improve MH. However, there is a lack of evidence to guide policies and ensure interventions are effective [3,4].

Our formative studies in Uganda contributed to evidence that poor menstrual health is a key factor associated with anxiety among girls and with missing secondary school or class [5]. An effective intervention needs to address lack of knowledge of puberty and menstruation and the social environment (to reduce stigma), as well as practical methods to enable girls to better manage their periods (i.e. pad provision, education about effective pain management, and improvements to school toilet facilities). Our pilot study conducted in Wakiso District in 2017-2018 suggested that an intervention addressing these elements can potentially improve education and mental health outcomes, but a randomised controlled trial is needed for definitive results to drive forward policy changes [6,7].

The MENISCUS intervention consisted of five elements: i) training teachers to improve puberty education, ii) a student-led drama skit about MH, iii) training school members to deliver MH education sessions alongside the distribution of a menstrual kit containing reusable menstrual products, iv) provision of analgesics, and v) improvements to school WASH facilities. In each school, a "Menstrual Health Action Group" consisting of teachers, students, and parents is set up to help coordinate the intervention package.

## 1.2 Primary objective

To evaluate whether the MENISCUS intervention improves i) educational attainment based on the Mathematics, English, and Biology curriculum taught during the intervention delivery, and ii) reduces mental health symptoms among secondary school girls in Uganda.

## 1.3 Secondary objectives

1) To evaluate whether the MENISCUS intervention improves the following secondary outcomes:
    - Knowledge of puberty and menstruation; attitudes towards menstruation (female and male participants, stratified by gender)
    - Menstrual practices at the last menstrual period (LMP)
    - Practice of pain management during LMP
    - Self-efficacy in addressing menstrual needs at LMP
    - Quality of life
    - Prevalence of symptomatic urinary tract infections (UTIs)
    - School and class absence during menses (in a random subsample of female participants)
    - School and class absence overall (in a random subsample of female participants)
    - Self-confidence in mathematics and in science abilities

2) To conduct a process evaluation to assess whether the intervention was implemented with fidelity, and to understand the contextual factors affecting the implementation, the acceptability to participants and the intervention mechanisms
3) To evaluate the costs of setting up and running the intervention package, the unit cost per female student reached and the incremental cost-effectiveness of the intervention per unit increase in selected policy-relevant outcomes, relative to optimised usual care
4) To assess the policy environment around menstrual health in Uganda, focusing on how implementing the intervention contributes to, and aligns with, the attainment of the Government policy objectives on MH management in schools

This Statistical Analysis Plan covers the analysis of the primary and secondary outcomes (Primary Objective and Secondary Objective 1).

### 1.4 Hypotheses

We hypothesised that improved educational attainment, mental health outcomes, and related health- and well-being outcomes will be achieved by improving self-efficacy for MH in Ugandan secondary schools, through improving the MH social and physical environment, and supporting girl's behavioural capability and observational learning.

## 2 Study Design

### 2.1 Trial design

The study was a parallel-arm, cluster-randomised controlled trial with a mixed-methods process evaluation, and economic and policy analyses. Schools (clusters) were randomised 1:1 to immediate delivery of the MENISCUS intervention or optimised usual care (provision of government menstrual management readers and circular). Schools randomised to the optimised usual care arm were offered the intervention after the endline assessment (approximately 1 year after randomisation). In this SAP, the term "intervention" refers to immediate intervention, and "control" to optimised usual care (delayed intervention, delivered after endline).

Female students who joined the S2-S3 class cohort during the intervention delivery period were eligible to be recruited. This "open cohort" design accommodates the dynamic school population, as students may both join and leave the class cohort during the intervention period. In the pilot study, 82% of participants present at baseline were present at the endline survey 9 months later [6]. Primary and secondary outcomes for female students will be assessed among participants present at endline, adjusting for cluster-level mean baseline measures of the relevant outcome where available. Knowledge and attitudes among male students will be assessed through a closed cohort. Further details are described in section 3.4 below.

### 2.2 Changes to the design and analyses

A detailed description of all protocol amendments is included on pages 2-3 of the trial protocol version 6.0. Additional modifications to the measures defined for each secondary outcome are described in section 4.3 and Annex 2.

The secondary outcome on prevalence of bacterial vaginosis (BV), vaginal yeast and urinary tract infections (UTIs) among symptomatic girls was revised to the prevalence of UTIs only among symptomatic girls. This change was approved by the TSC to remove the time burden on schools, participants, and data collection teams.

The study protocol version 5.0 states that data will be analysed using mixed models for repeated measures (MMRM). This has been revised to mixed models adjusting for cluster level mean at baseline as described in section 0, as data were collected at only two time points.

## 2.3 Sample size

The sample size of 60 schools was based on an anticipated harmonic mean of 60 female participants per school at endline. This sample size provides 84% power to detect a standardised mean difference of 0.2 for continuous outcomes, assuming an intra-cluster correlation (ρ) of 0.05 and type 1 error of 0.05. The effect size of 0.2 is that observed for the primary outcome of SDQ score for girls in the pilot [6] and is considered moderate for educational outcomes and hence of policy relevance. The harmonic mean was used to account for variation in school size. We have not adjusted the type 1 error because the two primary outcomes are independent, and an improvement in one without the other will be informative.

The subsample of 1500 girls selected to provide daily diary data on school/class attendance and their menstrual cycle over 40 school days at endline provides >98% power to detect a 20% relative reduction on period-days at endline, based on pilot data [6] and ~89% power to detect this difference by district or other equally sized subgroups. From our pilot, we expect >95% of girls to be menstruating at endline, and this is accounted for in the power calculations where relevant.

Revised power calculations were conducted in March 2022 and reported to the IDMEC in April 2022 (report 1), following indication that due to COVID-19 closures and other reasons the harmonic mean school size may be smaller than 60. This showed that a harmonic mean of 40 female students per school at endline provides 80% power to detect a standardised mean difference of 0.2 assuming an ICC of 0.05.

## 2.4 Randomisation

The 60 trial schools were allocated using 1:1 restricted randomisation. Within each district, the schools were additionally stratified by median UNEB baseline examination score (high/low). Covariate-constrained randomisation was then used to minimise imbalance with respect to key school-level factors (mean baseline examination score, mean past school examination scores, mean baseline SDQ score, government vs. private school, mean score on the Menstrual Practice Needs Scale, menstrual cup uptake, and the number of S2 female participants). Stratification factors (district and high/low baseline examination score) will be included as fixed-effects in all analyses.

A list of 1000 eligible allocations was randomly generated from all allocations meeting the specified balance criteria. One allocation was randomly selected at semi-public randomisation ceremonies held in each district in the presence of representatives from schools, the District Education Officer (DEO), and the Ministry of Education and Sports (MoES), and Ministry of Health (MoH).

## 2.5 Masking

All outcome data will be analysed masked to the trial arm. The assessment of educational attainment will be masked as it is independently administered by UNEB staff, who have no knowledge of arm

allocation. The principal investigator (PI) and the trial statistician will remain masked until data collection and analysis of all primary and secondary outcomes are complete. Participants, school staff, implementers (WoMena Uganda), and the clinical officer will not be masked because it will be clear whether the intervention is being implemented.

### 2.6 Timing of outcome assessments and analysis

The primary and secondary outcomes were assessed in June-August 2023, approximately one year after randomisation and 2-3 months following the completion of intervention delivery from the implementing partner. Diary data for the secondary outcomes on school and class attendance was collected for approximately 12 weeks from April 2023. Final analyses for all outcomes will be performed after the SAP is finalized and the dataset is locked.

## 3 Trial population

### 3.1 Eligibility criteria

#### School-level inclusion criteria:

- Mixed-sex secondary schools with S1–S4 classes
- Day or mixed day/boarding schools.
- At least minimal WASH facilities (including an improved water source and sex-specific sanitation facilities that are functional, usable, and accessible to female students at the time of the rapid assessment eligibility survey)
- Estimated enrolment of 50–125 female S1 students in Wakiso and 40–125 female students in S1 in Kalungu, based on the 2019 report on the Master List of Education Institutions in Uganda [8].

#### School-level exclusion criteria:

- Schools that are currently participating in a menstrual health-related programme
- Boarding schools with no day students
- Single-sex schools
- Schools exclusively for students with disabilities
- Schools where more than approximately ~10% of students or parents of students do not understand Luganda or English.

#### Participant-level inclusion criteria:

- Female students in the class cohort of S2 in 2022 who were enrolled in a trial school at the time of the baseline and/or endline survey
- Male students in the class cohort of S2 in 2022 who were enrolled in a trial school at the time of the baseline survey.
- For the diary sub-study, female trial participants were eligible if they reported having started menstruation at the time of the baseline survey.

## 3.2 School recruitment

Schools were randomly selected from those eligible and willing to participate. They were screened for eligibility in two stages. First, an initial desk review and screening was conducted using the 2019 Master List of Education Institutions for Kalungu and Wakiso districts [8]. Schools that provisionally met the criteria were then stratified into government versus private schools and randomly ordered. Second, a rapid assessment study including phone interviews with head teachers and school observations was undertaken to further determine eligibility according to the criteria outlined above. The rapid assessment was completed according to the randomly ordered list until 60 schools were found to be eligible and willing to participate as demonstrated by signing a memorandum of understanding. School-level consent was sought from the head teacher or director.

## 3.3 Participant recruitment

A CONSORT flowchart (Figure A1-A2) will show recruitment and follow-up of schools and female and male participants.

### Female participant recruitment at baseline

Prior to the baseline survey, schools were asked to provide lists of all students enrolled in S2. Lists were initially collected beginning in November 2021 and later updated once schools reopened following COVID-19-related closures in January 2022. For eligible female students aged below 18 years, informed consent was obtained from a parent or guardian following informational meetings held at the schools. Students who were 18 years or older could provide informed consent themselves. Informed consent/assent was sought from students immediately prior to the baseline survey. Consent/assent to receive a menstrual cup was sought separately from consent/assent for the main trial. The intervention activities started on June 27$^{th}$ 2022 in Kalungu District and on July 26$^{th}$ 2022 in Wakiso District. Students were included in the baseline population if they completed the baseline survey prior to these dates.

### Recruitment of trial participants post-baseline

Female students who joined the S2-S3 cohort up to 31$^{st}$ March 2023 are eligible for the endline assessment. Updated enrolment lists from schools were sought in Term 1 2023 to identify new joiners. Parent/guardian consent and student assent for these new joiners was sought prior to the endline assessments. Any students who had parent/guardian consent at the time of randomisation but had not completed the assent and baseline survey were recruited alongside the new joiners. Socio-demographic data were collected at the time of assent (recruitment).

### Male students

Fifteen male S2 students per school were randomly selected to be recruited into a closed cohort at baseline. The enrolment lists provided by the schools were used as the sampling frame. Students were replaced by the next student on the randomly ordered list if they were found to have left the school, had been absent for the previous 3 school weeks, did not consent, or were unable to be reached on 3 visits to the school. For schools where the total number of boys in S2 was less than 15, all boys were eligible for participation. A waiver was obtained for parent/guardian consent. Male participants were asked for written informed consent. All male participants with baseline data were included in the cohort, even if enrolled after intervention activities started in the District as it is a closed cohort.

## 3.4 Participant follow-up

### Female participants

The endline survey was administered to all recruited female participants present in a trial school at endline (June-August 2023). The study team sought to actively trace female participants no longer enrolled in a trial school at endline (section 4.1), to capture reasons why. We will describe the proportion no longer enrolled at endline by arm and explore factors associated with this. Reasons include dropout from school or transfer to a non-trial school.

Female participants will be categorised as having dropped out of school if we know they are not currently enrolled in any school (including non-trial schools). They will be categorised as "missing" for dropout status if we cannot determine if they are in school.

### Male participants

The endline survey will be administered to all recruited male participants who are attending the same school at endline. Reasons for loss to follow up include dropout from school or transfer to a non-trial school.

### Withdrawal

Participants may withdraw from participation in the individual-level elements of the intervention, from further data collection, or from all aspects of the study including the use of previously collected data. Data from participants who withdraw consent/assent will only be used as indicated on their withdrawal form. The number of withdrawals will be shown in the CONSORT flow chart (Figure 1).

## 3.5 Analysis populations

Primary analysis population: The primary analysis will be conducted according to intention-to-treat (ITT) principles. Schools will be analysed according to the arm they were randomised to regardless of whether they received the intervention. Enrolled female participants with endline survey or UNEB data will form the primary analysis population. Students who switched schools between baseline and endline will be analysed according to the school they are attending at endline.

Female closed cohort: An additional analysis will be carried out within the closed cohort of female participants recruited at baseline who are enrolled at the same school at endline. This replaces a classic per-protocol analysis (which is problematic as there is no clearly-defined appropriate comparison group of those who would have received the intervention if offered, in the control arm). The closed cohort analysis assesses the intervention effect among those who had the chance to be exposed to the intervention for the whole study period in both arms.

Male closed cohort: Outcomes among male students will be assessed in the closed cohort of male participants recruited at baseline who are enrolled at the same school at endline.

# 4 Outcomes

## 4.1 Data sources

Data are collected at two main timepoints, recruitment and endline. Primary and secondary outcome data are collected through:

- A self-completed survey conducted among female and male participants, with urine samples collected from female participants reporting urogenital symptoms in the survey.
- An educational assessment independently administered to female S3 students by the Uganda National Exam Board (UNEB) from July 24-26th 2023. Only scores from trial participants will be used in analyses.
- Daily diaries on menstruation and school/class attendance prospectively completed by a subsample of participants for approximately 12 weeks prior to the completion of the endline survey.

Following the endline survey, phone calls were made to parents of female students who had not participated in the endline UNEB examination nor the endline survey. Data were collected on whether the participant was attending a trial school, attending a non-trial school, or not attending school. The main reason for the latter was obtained. If there was no response to phone calls after 5 attempts, the parent was deemed not reachable.

Further details about data collection and management are given in the trial protocol [7].

## 4.2 Primary outcome definitions

Table 1 below shows the primary outcomes, their measures, variable types, sources of the data, and the analysis population.

**Table 1. Primary outcomes**

| Primary Outcome | Measure | Variable type | Data source | Eligibility |
|---|---|---|---|---|
| Educational attainment | Performance on English, Mathematics, and Biology (weighted equally) taught during the intervention year, using standard normal (z) scores estimated from the trial data. A combined score was generated as a row mean of the z-scores (for the 3 subjects). | Continuous | UNEB examination | All female participants |
| Mental health problems | Mean Total Difficulties Score from the Strengths and Difficulties questionnaire (SDQ-25) [9] | Continuous | Endline survey | All female participants |

## 4.3 Secondary outcome definitions

Table 2 below shows the secondary outcomes, their measures, variable types and sources of the data. The definitions of some measures were amended to ensure comparable denominators and minimise the number of separate measures for each outcome. Details on these changes and the variables used to construct the derived measures are presented in Annex 2.

**Table 2. Secondary outcomes**

| Secondary outcome | Measures | Variable type | Data source | Eligibility |
|---|---|---|---|---|
| 1. Knowledge of puberty and menstruation; myths & attitudes towards menstruation | 1a) Number of knowledge items answered correctly (out of 9).<br>1b) Number of myths & attitudes items with positive responses (out of 3) | Count | Endline survey | All female and male participants (stratified by gender) |
| 2. Menstrual practices at last menstrual period (LMP) | 2a) Use of only adequate menstrual materials that are appropriately cleaned or disposed of at LMP[1]<br>2b) Mean score on Menstrual Practice Needs Scale[2] (MPNS)[10] | Binary<br>Continuous | Endline survey | Female participants who reported having menstruated in the past 6 months[5] |
| 3. Pain management at LMP | Use of an effective pain management method (at least 1 effective method and none of the ineffective methods listed[3]) | Binary | Endline survey | Female participants who reported having menstruated in the past 6 months, and who report pain at LMP[5] |
| 4. Self-efficacy of MH | Mean score on Self-efficacy in Addressing Menstrual Needs Scale (SAMNS)[11] | Continuous | Endline survey | Female participants who reported having menstruated in the past 6 months[5] |
| 5. Quality of life[6] | CHU9D score, calculated as a weighted sum using adolescent Ugandan utility tariffs | Continuous | Endline survey | All female participants |
| 6. Prevalence of urinary tract infection (UTI) | Symptomatic UTI, defined as at least one genital symptom plus leucocyte esterase and/or nitrates with a urine dipstick test | Binary | Endline survey and urine Multistix 8 dipstick result | Female participants who reported having menstruated in the past 6 months[5] |
| 7. School and class absence during menses | 7a) Odds of missing a full school day on period-days relative to non-period days[4]<br>7b) Odds of missing lesson on a school day on period-days relative to non-period days[4] | Binary (per day)<br>Binary (per day) | Daily diary | Random subsample of ~1500 post-menarchal female Participants[7] |

| | | | | |
|---|---|---|---|---|
| 8. School and class attendance overall | 8a) Odds of missing a full school day[4]<br>8b) Odds of missing lessons on a school day[4] | Binary (per day)<br>Binary (per day) | Daily diary | Random subsample of ~1500 post-menarche female participants[7] |
| 9. Self-confidence in Mathematics and science abilities | 9a) Mean score on the Students Confidence in Mathematics scale [12]<br>9b) Mean score on the Students Confidence in Science scale [12] | Continuous<br>Continuous | Endline survey | All female participants |

[1]Defined as using a disposable pad or tampon that is always able to be immediately disposed; a reusable pad, cloth/towel, or homemade pad that is washed with water and soap and dry before use; or a menstrual cup that is boiled during or just before/after LMP; and no inadequate materials reported. Washing and drying of materials was not measured at baseline; this outcome will be adjusted for the baseline measure of use of adequate menstrual materials only.

[2]The MPNS score will be calculated as the weighted average of i) the core items and school-specific items (given 75% weight) and ii) the relevant material-specific items (given 25% weight), since participants answer a different number of items depending on the materials reported.

[3]Pain strategies listed: nothing, *stretching*, *painkillers*, *eating foods with lots of water*, drinking soda, *exercising*, *drinking lots of clean water*, taking antibiotics, *holding a warm water bottle on the stomach*, eating spicy foods, other (italics = considered effective). If the strategy mentioned in "Other" was also effective, this was included, and similarly for non-effective methods. Additional effective strategies mentioned as "Other" were sleep/rest or drinking warm/hot water (the latter was combined with drinking lots of clean water). Additional ineffective strategies included "herbs".

[4]Period defined as days with reported menstrual flow plus one day prior. School days exclude exam days and days when the participants' school was reported as closed (holidays and weekends)

[5] We do not anticipate an intervention effect on the denominator, but if there is imbalance by arm we will adjust for confounders associated with arm and the outcome

[6] The CHU-9D data will be included in the economic evaluation paper, not the main trial outcome paper

[7] The diary data will be weighted by the inverse of the sampling fraction for each school

# 5 Statistical analyses

## 5.1 Baseline characteristics and comparability by arm

Descriptive statistics for school- and individual-level baseline characteristics will be shown by arm and will include the mean and standard deviation (SD) (or median and interquartile range if non-normal) for continuous variables and frequencies and percentages for categorical variables. The following characteristics will be described as in Tables A1-A4:

- **School-level:** number of participants, district, type of school (government vs. private), composition of students (proportion boarding), menstrual cup consent and assent rate, urban vs. rural location, and WASH facility quality (Table A1).
- **Female students:** district, age, schooling category (day vs. boarding), religion, ethnicity, type of primary caregiver, caregiver's education, household size, number of meals eaten the previous day, socioeconomic status score derived from a principal components analysis of household assets and materials variables, and baseline measures of primary and secondary outcomes (where available (Table A2 and A4)).
- **Male students:** district, age, schooling category (day vs. boarding), religion, ethnicity, type of primary caregiver, caregiver's education, household size, number of meals eaten the previous

day, socioeconomic status score, knowledge of puberty and menstruation, and myths and attitudes towards menstruation (Table A3 and A4).

Baseline imbalance by arm was explored prior to finalisation of the SAP and no substantial baseline imbalances were identified in the baseline population. No formal statistical testing was performed to examine differences in baseline characteristics between the trial arms, as any difference would have been due to chance if the randomisation was correctly performed.

## 5.2 Analysis of continuous outcomes

The intervention effect for each primary outcome (educational attainment and SDQ) and continuous secondary outcomes will be presented as the adjusted mean difference in the endline scores between arms with corresponding 95% confidence intervals (CI). The effects will be estimated using linear random-effects (RE) models using a random intercept for school to adjust for within-school clustering. The model will be adjusted for the cluster-level mean of the baseline outcome measure and stratification variables (district and high/low school-level UNEB score). Likelihood ratio tests (LRT) will be used to obtain p-values. The results will be presented as shown in Table A5.

## 5.3 Analysis of count outcomes

For count outcomes (i.e., number of knowledge questions correct among female and male participants), the intervention effects will be presented as incident rate ratios (IRR) with 95%CI estimated using RE Poisson regression models with a random intercept for school to adjust for within-school clustering. The models will include the cluster-level mean baseline outcome measure and stratification variables. The LRT will be used to obtain p-values. If there is evidence of over-dispersion, the RE negative binomial model will be used. If there are issues of non-convergence, the GEE Poisson or negative binomial model will be used. The results will be presented as shown in Table A5.

## 5.4 Analysis of binary outcomes with a single outcome per participant

For the binary outcomes, the intervention effect will be estimated using odds ratios (OR) with 95%CI adjusted for clustering using RE logistic regression to adjust for within-school clustering. The models will include the cluster-level proportion with the baseline outcome measure and stratification variables. The LRT will be used to obtain p-values. The results will be presented as shown in Table A6.

## 5.5 Analysis of outcomes with repeated measures per participant

For secondary outcomes relating to school and class absence during menstruation, period-days are defined from the diary data as the school-days of menstruation (reported menstrual flow) plus the day prior to menstruation. The outcome measures are binary (see Table 2). For these data, there are repeated measures per girl, and analyses will additionally adjust for within-girl clustering (in addition to school-level clustering). This model will be fitted using RE logistic regression with both a random intercept for school and for student respectively. The analysis will include an interaction term between period (yes/no) and intervention arm to estimate the intervention effect on odds of absence of period-days relative to non-period days. To allow for the sampling fraction for diary data of 25 girls per school, the diary data will be weighted by the inverse of the school-level sampling fraction so that the results are representative of the trial population. All models will be adjusted for stratification variables. The LRT will be used to obtain p-values. If there are problems with convergence using the random effects

model, robust standard errors will be used with clustering at school level. The results will be presented as shown in Table A6.

## 5.6 Effect-modification and mediation

Pre-specified potential effect modifiers are given in Table 3. In addition, we will assess baseline SDQ score and baseline UNEB exam score as individual-level effect-modifiers for the two primary outcomes, respectively.

Effect-modification for each of these variables with trial arm will be assessed for primary and selected secondary outcomes by fitting an interaction term with each variable and trial arm in the model. The strength of evidence (p-values) for effect-modification will be assessed using LRT.

We will also explore hypothesised causal pathways through mediation analyses specified in advance as part of the process evaluation.

**Table 3. List of potential effect modifiers**

| Effect modifier | School/individual level | Measure |
|---|---|---|
| 1. District | School level | Binary (Kalungu, Wakiso) |
| 2. School ownership | School level | Binary (government, private) |
| 3. Baseline UNEB exam z-score | School level | Binary (<0, ≥0) |
| 4. S2 size (pre-intervention) | School level | Binary (median as cutoff: <59, ≥59) |
| 5. School type (% boarding students) | School level | Binary (<50% boarding, ≥50% boarding) |
| 6. Age group (at endline) | Individual level | Binary (median as cutoff) |
| 7. Student type (day vs boarding) | Individual level | Binary (day, boarding) |
| 8. Socio-economic status | Individual level | Binary (median as cutoff) |

## 5.7 Sensitivity and additional analyses

The following analyses will be conducted for primary and selected secondary outcomes, and the results will be compared.

**Sensitivity analyses:**

- Analyses using Generalised Estimating Equations with an independence correlation structure and robust standard errors to minimise potential bias due to informative cluster size [13].
- Cluster-level analyses
- Analysis of the intervention effect on "no pain or effective pain management strategy at LMP" as a sensitivity analysis for secondary outcome 3 in case of an intervention effect on any reported pain.

**Additional analyses:**

- Analysis of participants in the closed cohort (described in sub-section 3.5)
- Estimation of the complier average causal effects based on school and individual-level definitions of intervention fidelity and intensity.

## 5.8 Exploratory analyses

We will undertake exploratory analyses of intervention effects on additional outcomes, including:

- School dropout, defined as having left a trial school without known enrolment in another school
- Educational attainment for each subject separately (English, biology, maths)
- SDQ internalising sub-scale
- MPNS sub-scales and school-specific items separately
- Subjective wellbeing (measured by life satisfaction and happiness)
- Experience of teasing
- Perception of school's support for menstrual health
- Knowledge of effective pain management strategies
- Mean score (out of 10) or proportion on social norms items

# 6 Statistical considerations

## 6.1 Missing data

Survey and exam completion rates are expected to be high for girls, so only a small amount of missing data is expected and the primary analyses will be complete case. Sensitivity analyses will however be conducted for the primary outcomes using inverse probability weighting if there was substantial missing data.

## 6.2 Multiple testing adjustment

The two primary outcomes are considered independent due to different causal mechanisms, so an improvement in one without the other will be informative. According to FDA and EMA guidelines, we shall adjust the Type 1 error for multiple testing using the Benjamin-Hochberg (BH) procedure [14]. The procedure states that for the two primary outcomes considering a false discovery rate (FDR) of 0.05: 1) if the larger p-value ≤0.05, then there is evidence for both end points; 2) if the larger p-value >0.05, then the smaller p-value should be ≤0.025 to show evidence for that endpoint, and 3) if the larger p-value >0.05 and the smaller p-value>0.025, then there is no evidence for both endpoints. Despite this procedure, interpretation of the intervention effect will focus on effect sizes and confidence intervals rather than p-values.

For the secondary outcomes, specific inferences will be made for each individual null hypothesis and multiple testing adjustment will not be performed. Given the number of tests performed, the intervention effects will be interpreted with caution [15,16].

## 6.3 Model checks

To check for model fits, quadrature checks will be used for the random effects models. In the case of substantial non-normality, we will consider using bootstrap methods to estimate 95% CI.

### 6.4 Intra-cluster Correlation Coefficient (ICC) and coefficient of variation

The ICC and coefficient of variation will be estimated and reported based on primary and selected secondary outcomes.

## 7 AEs and SAEs reporting

Descriptive statistics including frequencies and percentages will be used to summarise and present AEs reported in the intervention schools, and SAEs by trial arm. Where appropriate, the results will be stratified by district.

## 8 Software

All analyses will be performed using STATA Version 17 and 18 and R version 4.3.2.

# 9 Annexes

## 9.1 Annex 1: tables and figures

**Figure A1. CONSORT chart of school and female participant flow**

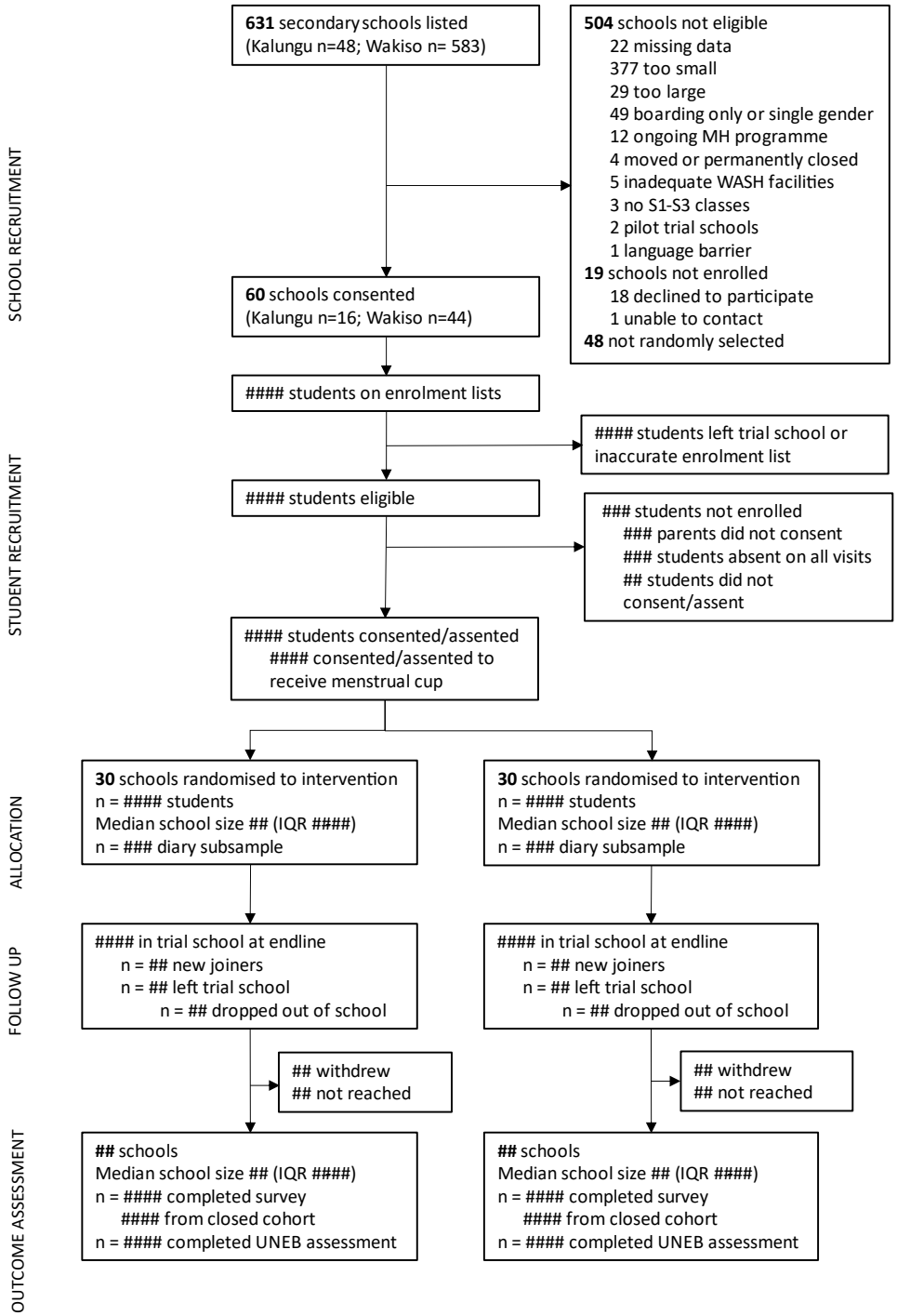

**Figure A2. CONSORT flow chart of male participant flow**

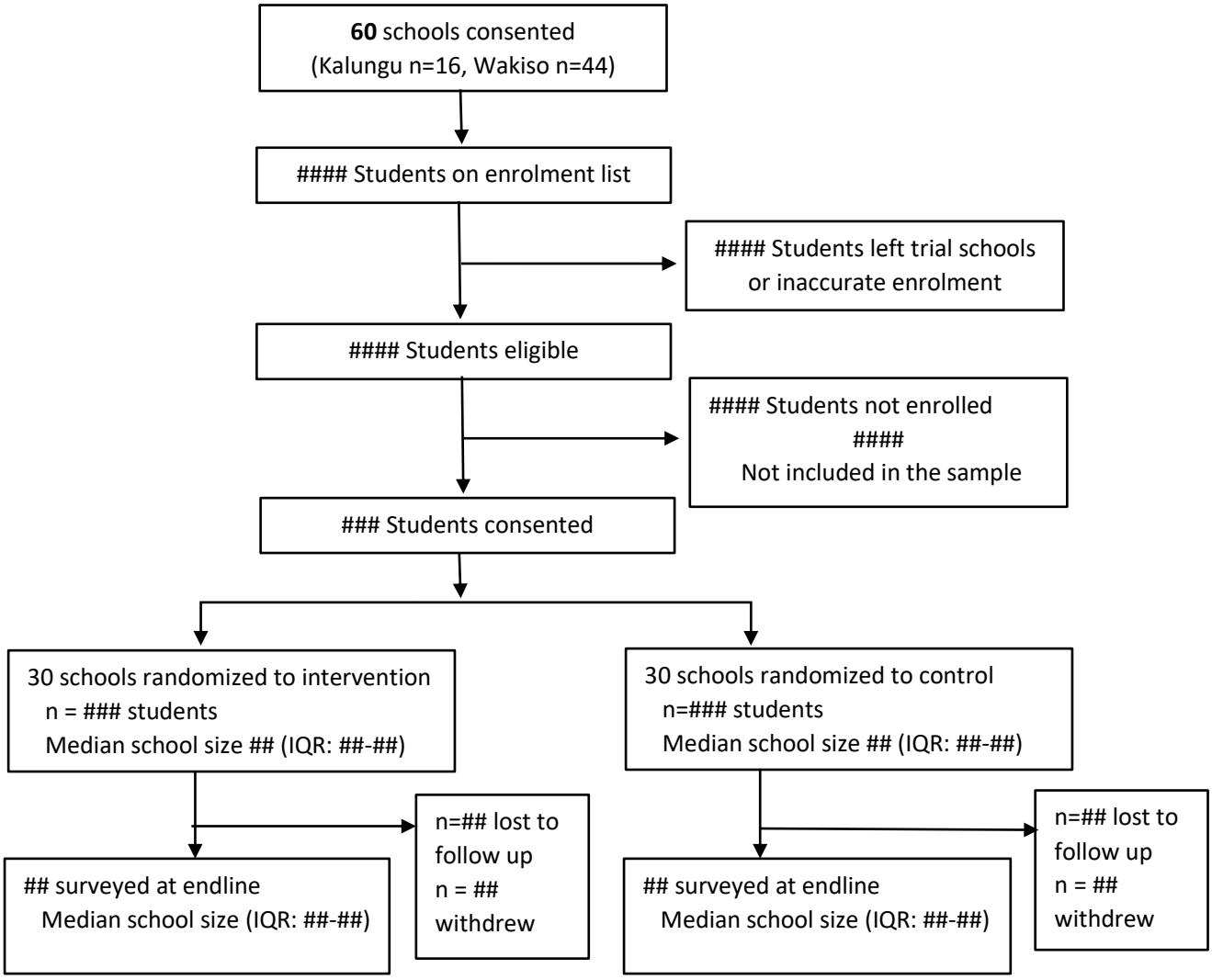

**Table A1. School-level baseline characteristics by trial arm**

| | Total | Arm A | Arm B |
|---|---|---|---|
| **Number of schools** | | | |
| **Mean number of female participants (SD)** | | | |
| **District, n(%)** | | | |
| Wakiso | | | |
| Kalungu | | | |
| Mean school examination score | | | |
| Low (below median) | | | |
| High (above median) | | | |
| **Type of school, n(%)** | | | |
| Government | | | |
| Private | | | |
| **Proportion boarding (%), mean (SD)** | | | |
| **Menstrual cup consent/assent (%), mean (SD)** | | | |
| **WASH facility quality, n (%)** | | | |
| Schools with at least one improved sanitation cubicle that is single-sex (for females) and available, functional, and private at the time of the survey. | | | |
| Schools with at least one cubicle that in addition to the above, has a disposal bin available at the time of the survey. | | | |
| Schools with at least one cubicle that in addition to the above, has a disposal bin and a water source close to the toilet block. | | | |

**Table A2. Female baseline socio-demographic characteristics by trial arm**

| | Total<br>N | Arm A<br>n (%) | Arm B<br>n (%) |
|---|---|---|---|
| **Overall** | | | |
| **District** | | | |
| Wakiso | | | |
| Kalungu | | | |
| **Age in years** | | | |
| Mean (SD) | | | |
| <15 | | | |
| 15 | | | |
| 16 | | | |
| 17 | | | |
| 18+ | | | |
| **Schooling category** | | | |
| Day student | | | |
| Boarding student | | | |
| **Religion** | | | |

| | | | |
|---|---|---|---|
| Roman Catholic | | | |
| Protestant/Anglican/Born again/SDA | | | |
| Muslim | | | |
| Other | | | |
| **Ethnicity** | | | |
| Muganda | | | |
| Non-Muganda | | | |
| **Primary caregiver** | | | |
| Mother | | | |
| Father | | | |
| Self | | | |
| Other | | | |
| **Caregiver's education level** | | | |
| None/less than primary | | | |
| Primary | | | |
| Secondary or more than secondary | | | |
| Don't know | | | |
| **Household size (people)** | | | |
| Mean (SD) | | | |
| 8 or more | | | |
| 6-7 | | | |
| Fewer than 6 | | | |
| **Number of meals eaten yesterday** | | | |
| 3 or more meals | | | |
| 2 meals | | | |
| Fewer than 2 meals | | | |
| **Social Economic Status (SES)[3]** | | | |
| Highest | | | |
| Medium-high | | | |
| Medium | | | |
| Medium-low | | | |
| Lowest | | | |

[3]*This included ownership of assets (like computer, furniture, land etc.), animals and chicken/birds; availability of electricity or solar; source of water; and type of toilet.*

**Table A3. Male student baseline socio-demographic characteristics by trial arm**

| | **Total N** | **Arm A n (%)** | **Arm B n (%)** |
|---|---|---|---|
| **Overall** | | | |
| **District** | | | |
| Wakiso | | | |
| Kalungu | | | |
| Age in years | | | |
| <15 | | | |

| | | | |
|---|---|---|---|
| 15 | | | |
| 16 | | | |
| 17 | | | |
| 18+ | | | |
| **Schooling category** | | | |
| Day student | | | |
| Boarding student | | | |
| **Religion** | | | |
| Roman Catholic | | | |
| Protestant/Anglican/Born again/SDA | | | |
| Muslim | | | |
| Other | | | |
| **Ethnicity** | | | |
| Muganda | | | |
| Non-Muganda | | | |
| **Primary caregiver** | | | |
| Mother | | | |
| Father | | | |
| Self | | | |
| Other | | | |
| **Caregiver's education level** | | | |
| None/less than primary | | | |
| Primary | | | |
| Secondary or more than secondary | | | |
| Don't know | | | |
| **Household size (people)** | | | |
| Mean (SD) | | | |
| 8 or more | | | |
| 6-7 | | | |
| Fewer than 6 | | | |
| **Number of meals eaten yesterday** | | | |
| 3 or more meals | | | |
| 2 meals | | | |
| Fewer than 2 meals | | | |
| **Social Economic Status (SES)[3]** | | | |
| Highest | | | |
| Medium-high | | | |
| Medium | | | |
| Medium-low | | | |
| Lowest | | | |

[3]*This included ownership of assets (like computer, furniture, land etc.), animals and chicken/birds; availability of electricity or solar; source of water; and type of toilet.*

**Table A4. Baseline measures of trial outcome variables by arm**

| | **Total**<br>**N** | **Arm A** | **Arm B** |
|---|---|---|---|

| **Female students, N** | | | |
|---|---|---|---|
| ***Primary outcomes*** | *Mean (SD)* | *Mean (SD)* | *Mean (SD)* |
| Combined maths and biology score (z-scores) | | | |
| SDQ score | | | |
| ***Secondary outcomes (continuous and count)*** | *Mean (SD)* | *Mean (SD)* | *Mean (SD)* |
| Knowledge questions answered correctly[1] | | | |
| Myths and attitudes questions answered positively[2] | | | |
| MPNS score | | | |
| SAMNS score | | | |
| Confidence in maths score | | | |
| Confidence in science score | | | |
| ***Secondary outcomes (binary)*** | *n (%)* | *n (%)* | *n (%)* |
| Used an effective pain management method | | | |
| Reported pain (denominator) | | | |
| **Male students, N** | | | |
| ***Secondary outcomes among male students*** | *Mean (SD)* | *Mean (SD)* | *Mean (SD)* |
| Knowledge questions answered correctly[1] | | | |
| Myths and attitudes questions answered positively[2] | | | |

[1]*Out of 9 questions*

[2]*Out of 3 questions*

**Table A5. Intervention effect for continuous and count outcomes**

| | **Control arm** | | **Intervention arm** | | **Intervention effect** | |
|---|---|---|---|---|---|---|
| | **N** | **Mean (SD)** | **N** | **Mean (SD)** | **Adjusted mean difference (95% CI)[1]** | **p-value** |
| **Primary outcomes (females)** | | | | | | |
| Education attainment | | | | | | |
| SDQ score | | | | | | |
| **Secondary outcomes (females)** | | | | | | |
| Knowledge questions answered correctly[2] | | | | | | |
| Myths and attitudes questions answered positively[3] | | | | | | |
| MPNS score | | | | | | |
| SAMNS score | | | | | | |
| Confidence in Maths score | | | | | | |
| Confidence in Science score | | | | | | |
| **Secondary outcomes (males)** | | | | | | |
| Knowledge questions answered correctly[2] | | | | | | |
| Attitudes questions answered positively[3] | | | | | | |

[1]*Adjusted for baseline outcome measure, district, high/low school-level UNEB score, and school clustering*
[2]*Out of 9 questions*
[3]*Out of 3 questions*

**Table A6. Intervention effect for binary outcomes**

| **Secondary outcome** | **N (%) in control arm** | **N (%) in intervention arm** | **Adjusted OR (95% CI) [1]** | **p-value** |
|---|---|---|---|---|
| **Participant-level measures** | | | | |
| Use of only adequate menstrual materials that are appropriately cleaned or disposed of at LMP | | | | |
| Used an effective pain management method | | | | |
| Prevalence of symptomatic UTI | | | | |
| **Day-level measures** | | | | |
| Full school days missed by girls during their period | | | | |
| School days with classes missed by girls during their period | | | | |
| Full school days missed | | | | |
| School days with lessons missed | | | | |

[1]*Adjusted for baseline outcome measure, district, high/low school-level UNEB score, and school clustering*

**Table A7. Effect-modification for primary outcomes**

| | **Category** | **Mean (SD) in control arm** | **Mean (SD) in intervention arm** | **Adjusted mean difference[1]** | **p-value for effect modification** |
|---|---|---|---|---|---|
| **UNEB score** | | | | | |
| **Effect modifier** | | | | | |
| **District** | Kalungu | | | | |
| | Wakiso | | | | |
| **Ownership** | Government | | | | |
| | Private | | | | |
| **S2 size** | <59 | | | | |
| | >=59 | | | | |
| **Proportion boarding** | <50% | | | | |
| | >=50% | | | | |
| **Median age at baseline** | <15 | | | | |
| | >=15 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| **Type of student** | Day | | | | |
| | Boarding | | | | |
| **SES** | Medium-highest | | | | |
| | Low or low-medium | | | | |
| | | | | | |
| **SDQ score** | | | | | |
| **Effect modifier** | | | | | |
| **District** | Kalungu | | | | |
| | Wakiso | | | | |
| **Ownership** | Government | | | | |
| | Private | | | | |
| **S2 size** | <59 | | | | |
| | >=59 | | | | |
| **Proportion boarding** | <50% | | | | |
| | >=50% | | | | |
| **Median age at baseline** | <15 | | | | |
| | >=15 | | | | |
| **Type of student** | Day | | | | |
| | Boarding | | | | |
| **SES** | Medium-highest | | | | |
| | Low or low-medium | | | | |

[1]*Adjusted for baseline outcome measure, district, high/low school-level UNEB score, and school clustering*

## 9.2 Annex 2: Further details on the secondary outcome measures

### Summary of changes made to secondary outcome measures and rationale

Changes to the measures of the outcomes from what was specified in the protocol paper and protocol v6.0 are as follows (*All measures not listed were unchanged)*:

| Outcome (protocol v4.0) | Measure (protocol v4.0) | Revised measure (protocol v6.0) | Rationale |
|---|---|---|---|
| **1. Knowledge of puberty and menstruation; attitudes towards menstruation** | Proportion answering all knowledge questions correctly. | Number of knowledge items answered correctly (out of 9) | To make full use of the count data and avoid a cut-off |
| | Proportion answering all questions on myths correctly | *Removed and combined with below* | Not measured as separate construct |
| | Proportion with "good responses" on attitudes | Number of myths and attitude items with positive responses (out of 3) | To make full use of the count data and avoid a cut-off |
| **2. Menstrual practices at last menstrual period (LMP)** | Proportion using manufactured methods only at LMP | *Removed* | Use of adequate materials incorporated into below measure |
| | Proportion correctly washing and drying re-usable pads and/or menstrual cups at LMP | *Removed* | Denominator likely to be influenced by the intervention |
| | Proportion with 'adequate MHM at school' at LMP (Self-reported use of clean materials to absorb/collect blood, changed privately, safely, hygienically, and as often as needed) | Proportion using only adequate menstrual materials that are appropriately cleaned or disposed of at their last menstrual period | Restricted to use and disposal of clean materials to limit overlap with MPNS outcome |
| **3. Knowledge and practices of pain management during LMP** | Proportion knowing 4 or more effective pain management methods (Use of painkiller, drinking water, using water bottle, exercise, relaxing, foods with lots of water) | *Removed* | Reduced number of measures to focus on practice of pain management which implies knowledge |
| | Proportion who used an effective pain management method | Proportion who used an effective pain management method (at least 1 effective method and no ineffective methods) | Clarified that no ineffective methods could be reported |
| **5. Quality of life and happiness** | Mean CHU9D score | CHU9D score calculated as a weighted sum using adolescent utility tariffs | Clarified that score would be calculated using validated weights in our population |

| | | | |
|---|---|---|---|
| | Self-reported measure of happiness | *Removed* | Reduced number of measures; moved to exploratory outcome |

## Survey items used to construct derived measures

**Knowledge items:**

*True-False (response options = true, false, don't know)*

1. Changes in the body during puberty happen because of hormones
2. The physical changes related to puberty usually start between 10 and 14 years of age in girls, and between 12 and 16 in boys.
3. Usually, women stop menstruating after about age 40-50
4. Monthly menstruation continues during pregnancy
5. What is menstrual period blood? *(blood from the stomach; blood from the lining of the uterus (womb); I don't know)*
6. What is the entrance to the uterus called? *(Vagina; vulva; cervix; ovary; don't know)*
7. How long does a menstrual period (bleeding) usually last? *(Between 3 to 7 days; exactly 5 days; about 28 days; I don't know)*
8. "How many days are there usually between periods? i.e. the length of the menstrual cycle, from the start of one period to the start of the next" *(Exactly 7 days; exactly 28 days; between 21-45 days; I don't know)*
9. When during the menstrual cycle is a woman most likely to become pregnant? *(Just before her period; during her period; right after her period; after ovulation; I don't know)*

**'Myths & attitudes' items**

*(Response options = disagree a lot, disagree, neither agree nor disagree, agree, agree a lot)*

1. Painkillers cause problems having children (barrenness; obugumba)
2. It is fine for a girl to cook during her period
3. It is fine for a girl to run, dance or cycle during her period

**Effective pain management item**

What did you do to reduce the pain during your last menstrual period? [At least one of underlined options and no ineffective options]

- Nothing
- Stretching
- Painkillers
- Eating foods with lots of water, like watermelon or cucumber
- Drinking soda
- Exercising
- Drinking lots of clean water
- Taking antibiotics
- Holding a warm water bottle on the stomach

- Eating spicy foods
- Other

If the strategy mentioned in “Other” was also effective, this was included, and similarly for non-effective methods. Additional effective strategies mentioned as “Other” were sleep/rest or drinking warm/hot water (the latter was combined with drinking lots of clean water). Additional ineffective strategies included “herbs”.

**School and class absence**

Diary items:
*How many of your lessons did you attend today?*

- Attended all
- Missed some
- Missed all
- Closed/No lessons

*Are you in your period today?*

- No
- Light period
- Moderate period
- Heavy period

Days absent = “missed all”
Days with lessons missed = “missed all” or “missed some”
Days with exams (Did you have an exam today = “yes”) and where the participants’ school is closed are excluded

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