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Effects of household concrete floors on maternal and child health: the CRADLE trial – a randomised controlled trial protocol

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ABSTRACT

Introduction Early life soil-transmitted helminth (STH) infection and diarrhoea are associated with growth faltering, anaemia, impaired child development and mortality. Exposure to faecally contaminated soil inside the home may be a key contributor to enteric infections, and a large fraction of rural homes in low-income countries have soil floors. The objective of this study is to measure the effect of installing concrete floors in homes with soil floors on child STH infection and other maternal and child health outcomes in rural Bangladesh.

Methods and analysis The Cement-based flooRs AnD chiLd hEalth trial is an individually randomised trial in Sirajganj and Tangail districts, Bangladesh. Households with a pregnant woman, a soil floor, walls that are not made of mud and no plan to relocate for 3 years will be eligible. We will randomise 800 households to intervention or control (1:1) within geographical blocks of 10 households to account for strong geographical clustering of enteric infection. Laboratory staff and data analysts will be blinded; participants will be unblinded. We will instal concrete floors when the birth cohort is in utero and measure outcomes at child ages 3, 6, 12, 18 and 24 months. The primary outcome is prevalence of any STH infection (*Ascaris lumbricoides*, *Necator americanus* or *Trichuris trichiura*) detected by quantitative PCR at 6, 12, 18 or 24 months follow-up in the birth cohort. Secondary outcomes include household floor and child hand contamination with *Escherichia coli*, extended-spectrum beta-lactamase producing *E. coli* and STH DNA; child diarrhoea, growth and cognitive development; and maternal stress and depression.

Ethics and dissemination Study protocols have been approved by institutional review boards at Stanford University and the International Centre for Diarrheal Disease Research, Bangladesh. We will report findings on ClinicalTrials.gov, in peer-reviewed publications and in stakeholder workshops in Bangladesh.

Trial registration number NCT05372068.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Using a randomised design in a large sample will allow us to minimise potential confounding by household wealth, which may have influenced prior observational studies' findings on concrete floors and health.
⇒ Measurement of a diverse set of health outcomes within different domains (infections, antimicrobial resistance, child growth, cognitive development, mental health, quality of life) will capture broad potential benefits of the intervention.
⇒ Longitudinal measurements will capture any variation in intervention impact as children learn to sit, crawl, walk and spend more time outdoors and their exposures change.
⇒ Rich data on intermediate variables on household contamination and maternal bandwidth, time use, and mental health will allow us to investigate whether concrete floors influence child health and development primarily through environmental or maternal pathways.
⇒ It is possible that child exposures outside the home will attenuate the effect of concrete floors on child health outcomes.

INTRODUCTION

The United Nations has enshrined basic housing as a human right, and housing improvements are associated with improved health.[1 2] Yet, 58.8% of homes in low-income countries are unimproved, with soil floors and walls[3] made of palm or thatch, and few studies have investigated health benefits of housing upgrades in low- or middle-income countries (LMICs). In low-income homes, inadequate sanitation infrastructure can result in contamination of household soil and surfaces with human and animal faeces. In particular, soil floors are a reservoir for enteric pathogens such as soil-transmitted helminths (STH), *Shigella* and pathogenic *Escherichia coli*.[4–6] Multiple studies have found that the amount of *E. coli* and STH is similar

or higher on soil floors inside the home than on latrine floors.[5 7 8] *Ascaris lumbricoides* eggs are extremely hardy and can survive for years in soil; other STH species can survive for weeks or months.[9 10] Soil is also a reservoir of antimicrobial resistant pathogens because microorganisms in soil can exchange genes with those in faeces deposited on soil.[11] Children frequently play, eat and drink on floors that are contaminated with human or animal faeces, and young children frequently ingest soil, increasing their risk of infection with STH, other enteric pathogens and antimicrobial resistant pathogens.[12–19]

Collectively, enteric infections, including STH and diarrhoea, are a major contributor to the global burden of disease. They were the third leading cause of death for children<5 years in 2019.[20] Chronic STH infection is associated with an increased risk of child wasting, anaemia, dysentery, intestinal obstruction, impaired child development and mortality.[21 22] Hookworm infection alone is responsible for up to US$139 billion in annual productivity losses globally.[23] In addition to increased risk of mortality, early life diarrhoea is associated with growth faltering, anaemia and impaired child development.[24–30]

Existing interventions to reduce enteric infections, such as water, sanitation and hygiene (WASH), do not address soil exposure, and a recent meta-analysis found that low-cost household WASH interventions did not reduce enteric pathogen prevalence in household soil samples.[31] Further, WASH interventions require sustained behaviour-change promotion, which limits scalability.[32] In addition, recent WASH trials had only modest effects on diarrhoea and mixed effects on STH infections.[32 33] Alternative interventions that reduce environmental pathogen reservoirs and do not require sustained behaviour change are urgently needed to improve child health in LMICs.

Installing finished floors, such as concrete, in homes with soil floors is a promising potential intervention to reduce child enteric infection. Concrete floors are easier to keep clean than soil floors, which may contribute to lower levels of faecal pathogens on surfaces, and subsequently on hands and fomites. Concrete may also interrupt the life cycle of STH, which require soil to reach their infective stage.[9] A recent meta-analysis of observational studies estimated that the odds of any enteric or parasitic infection were 0.75 times lower and the odds of helminth infections were 0.68 times lower in homes with improved floors (eg, concrete, wood) versus unimproved floors (eg, soil).[34] In addition, studies have found protective associations between improved floors and diarrhoea.[35 36]

By making homes more comfortable and easier to keep clean, floor upgrades can also improve quality of life and reduce stress. A study in Mexico found that installing concrete floors was associated with 10.6% lower stress, 12.5% lower depression and 18.7% higher satisfaction with quality of life among mothers.[36] Slum upgrades, including concrete or wood floor installation, have been found to improve sleep, quality of life and happiness.[37 38] Though findings from these studies are promising, all prior research has been observational, and associations may be confounded by household wealth.

Concrete floors could also influence child development through either an environmental pathway or maternal pathway (figure 1). In the environmental pathway, installing concrete floors removes the majority of soil from the home's interior and makes the home easier to clean, reducing child exposure to enteric pathogens, likely also reducing enteric infections, which are associated with impaired child development.[39–41] In the maternal pathway, if concrete floors make the living environment more comfortable and easier to clean, this may result in increased maternal bandwidth[42]—the ability to problem solve, recall information, reason logically, plan and allocate attention and initiate and control actions.[43] Higher levels of maternal working and short-term memory are independently associated with maternal scaffolding behaviours when interacting with young children.[44 45] These scaffolding behaviours are associated with child cognitive skills at age 4 years.[45] Further, by reducing

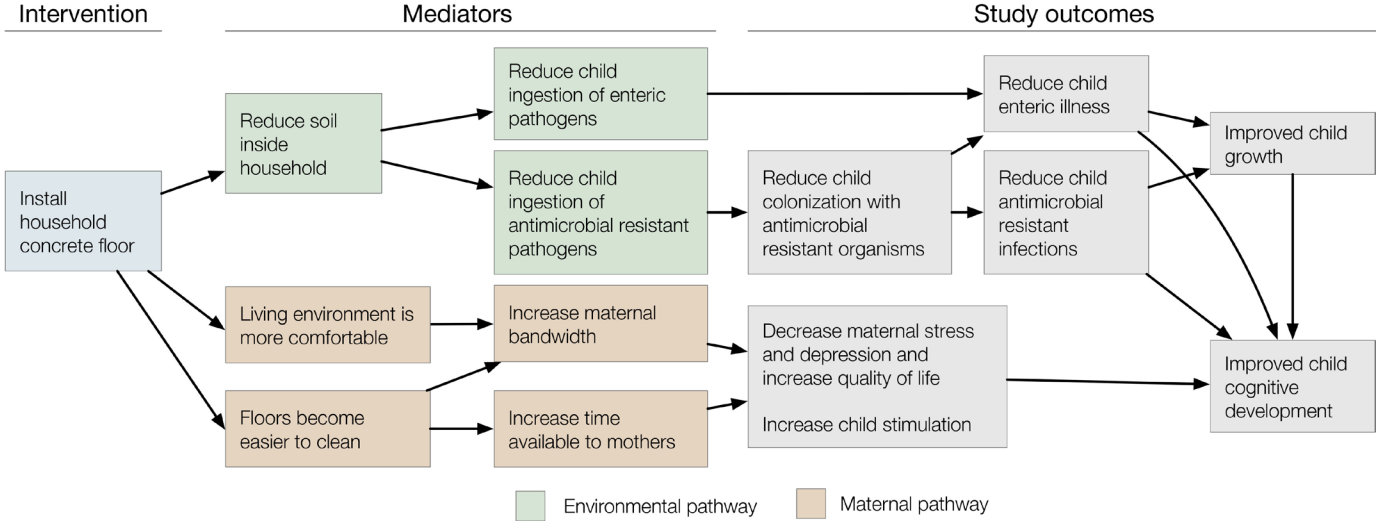

Figure 1 Hypothesised mechanisms of intervention effects.

the time required to clean floors, concrete floors may increase mothers' discretionary time. This may increase their ability to seek medical care and/or devote time to preventive health behaviours for themselves or their children and engage in scaffolding behaviours that promote child development.[46]

Objectives

Here, we describe the protocol for the Cement-based flooRs AnD chiLd hEalth (CRADLE) trial, a randomised trial in Sirajganj district, Bangladesh, to determine whether concrete floors reduce child STH infection and diarrhoea. Using a randomised design will minimise confounding that may have influenced prior observational studies. We will investigate the mechanism through which concrete floors influence health using rich environmental assessments, video observations of child activities and biopsychosocial measurements of mothers. Our longitudinal design will allow us to investigate sustainability over 2 years and capture any variation in intervention impact as children learn to sit, crawl, walk and spend more time outdoors and their exposures change. Cost-effectiveness analyses incorporating maternal and child outcomes will inform decisions about whether to scale up concrete floor installation. This study will generate rigorous evidence to inform policies about whether concrete floors should be delivered as a health intervention in rural, low-income settings.

METHODS AND ANALYSIS

Study design

The CRADLE trial is an individually randomised trial in Sirajganj and Tangail districts, Bangladesh. The trial will enrol households with soil floors and a pregnant woman in her second or third trimester. For each block of 10 geographically contiguous households, we will randomise households 1:1 to intervention or control. We will instal concrete floors when the birth cohort is in utero so that children in the intervention arm receive the intervention from birth. We will measure outcomes longitudinally when children are aged 0, 3, 6, 12, 18 and 24 months (figure 2). While STH prevalence is generally higher among primary school-aged children, we chose to focus on the first 2 years of life, when children's exposure to household floors is greatest. Between 6 and 24 months, children frequently sit, play, crawl and eat on household floors and generally spend more time inside versus outside the home. After this age, children's outdoor exposures increase; while household concrete floors may still benefit older children, we expect that potential effects would be smaller. Additionally, the first 1000 days of life are considered critical for child development and therefore present an important window for health interventions.[47]

Study site

Our study site is located in Chauhali and Belkuchi upazilas (subdistricts) in Sirajganj district and Nagarpur upazila in Tangail district, Bangladesh (figure 3). Chauhali upazila is approximately 210 km^2 and includes 34 449 households, Belkuchi upazila is approximately 164 km^2 and includes 96 110 households, and Nagarpur upazila is approximately 267 km^2 and includes approximately 83 885 households.[48 49] Research staff from the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) will enrol households in all unions of Chauhali and Belkuchi and unions adjacent to Chauhali in Nagapur. Approximately 66% of households in our study area have mud floors, and the region is vulnerable to flooding and erosion.[50 51] According to the Chauhali Upazila Health and Family Planning Office, there is a high percentage of open defecation in this region, and clinical diagnoses of STH infections are common. The primary STH control strategy in Bangladesh consists of a biannual school-based deworming campaign whereby a single dose of mebendazole is administered to school-aged children.[52 53]

Inclusion and exclusion criteria

We will enrol households that meet the following criteria: (1) residence in Chauhali upazila or adjacent upazilas in Sirajganj or Tangail districts in Bangladesh; (2) household floors made entirely of soil or earth; (3) households with a pregnant woman at 13–30 weeks of gestation at the time of enrolment; (4) households with no plans to relocate in the next 2–3 years. Pregnancy status will be self-reported. Primary outcomes will be measured in the child (or children, in the case of multiples) born to enrolled women (ie, 'index children'). We will exclude households that are not strictly residential (eg, those that include a business) and households with floor size greater than 500 square feet. Household walls in the study site are typically made of tin, but some household walls are constructed with mud, cement or straw, sticks or jute. We will exclude households with mud walls as installing concrete floors may reduce structural stability; for all other wall types, wall structures can remain in place during floor construction.

Outcomes

Our primary outcome is the prevalence of any of the following STH infections, *Ascaris lumbricoides, Necator americanus or Trichuris trichiura,* detected using quantitative PCR (qPCR) in child stool at 6, 12, 18 or 24 months after the birth of the index child. Secondary outcomes include the prevalence of each STH species by qPCR at child ages 6, 12, 18 or 24 months and caregiver-reported diarrhoea in the past 7 days and diarrhoea confirmed using stool consistency[54] at each follow-up. Additional secondary outcomes are listed in table 1, and details are listed in online supplemental appendix table 1.

Sample size calculation

The overall trial sample size was determined based on the primary outcome of prevalence of any STH at any follow-up (ages 6, 12, 18 or 24 months). We estimated the required sample size using the standard formula

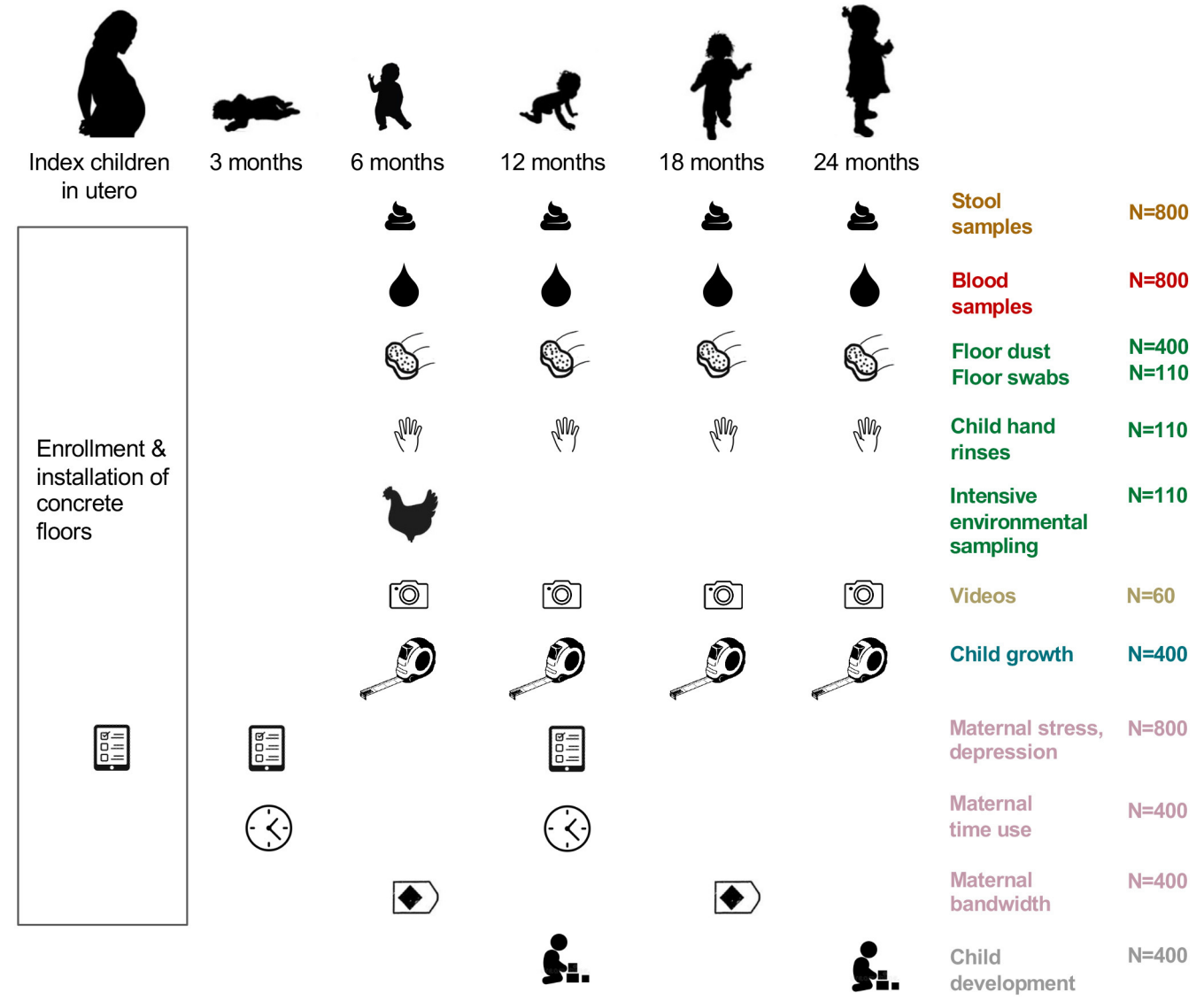

Figure 2 Planned measurements in the CRADLE trial Intensive environmental samples collected at the 6-month follow-up include courtyard soil, floor soil, food, drinking water, chicken faeces, cow faeces. CRADLE, Cement-based flooRs AnD chiLd hEalth.

for comparisons of two groups with repeated measures of a binary outcome.[55] From 2017 to 2020 in Sirajganj District, the prevalence of *Ascaris lumbricoides* was 25.1%, and the prevalence of *Trichuris trichiura* was<10%.[53] To be conservative, we assumed the prevalence of any STH in the control group over four follow-up rounds would be 20%. In our prior analyses of the association between concrete floors and any STH, the unadjusted prevalence ratio was 0.40 (95% CI 0.28, 0.56),[56] and the adjusted prevalence ratio was 0.73 (95% CI 0.52, 1.01).[57] We set the null hypothesis at a prevalence ratio of 1 (no difference between groups at any follow-up (ages 6, 12, 18 or 24 months)) and assumed a minimum detectable prevalence ratio of 0.70. We assumed intraclass correlation=0.066 for repeated measurements of STH prevalence among children<2 years.[58] Assuming a Type I error=0.05 and Type II error=0.20, for a two-sided hypothesis test, the required number of households per arm is 336. Inflating this to account for 15% loss to follow-up and 10 households per randomisation block, the total required sample size across both arms is 800. 15% loss to follow-up was assumed based on the findings from the prior trial carried out by our team in rural Bangladesh,[59] in which 6.5% of pregnant women miscarried or had stillbirths, 3.5% of children died by 12-month follow-up and<1% died between 12 and 24 months follow-up.

Patient and public involvement

To support the translation of the trial's findings into programmes and policies, we will conduct stakeholder engagement workshops in Bangladesh during the trial preparation phase and results dissemination. We will engage different stakeholders from health, housing and construction sectors (Government of Bangladesh, engineering institutes, non-governmental organisations (NGOs) in housing and shelters, commercial companies

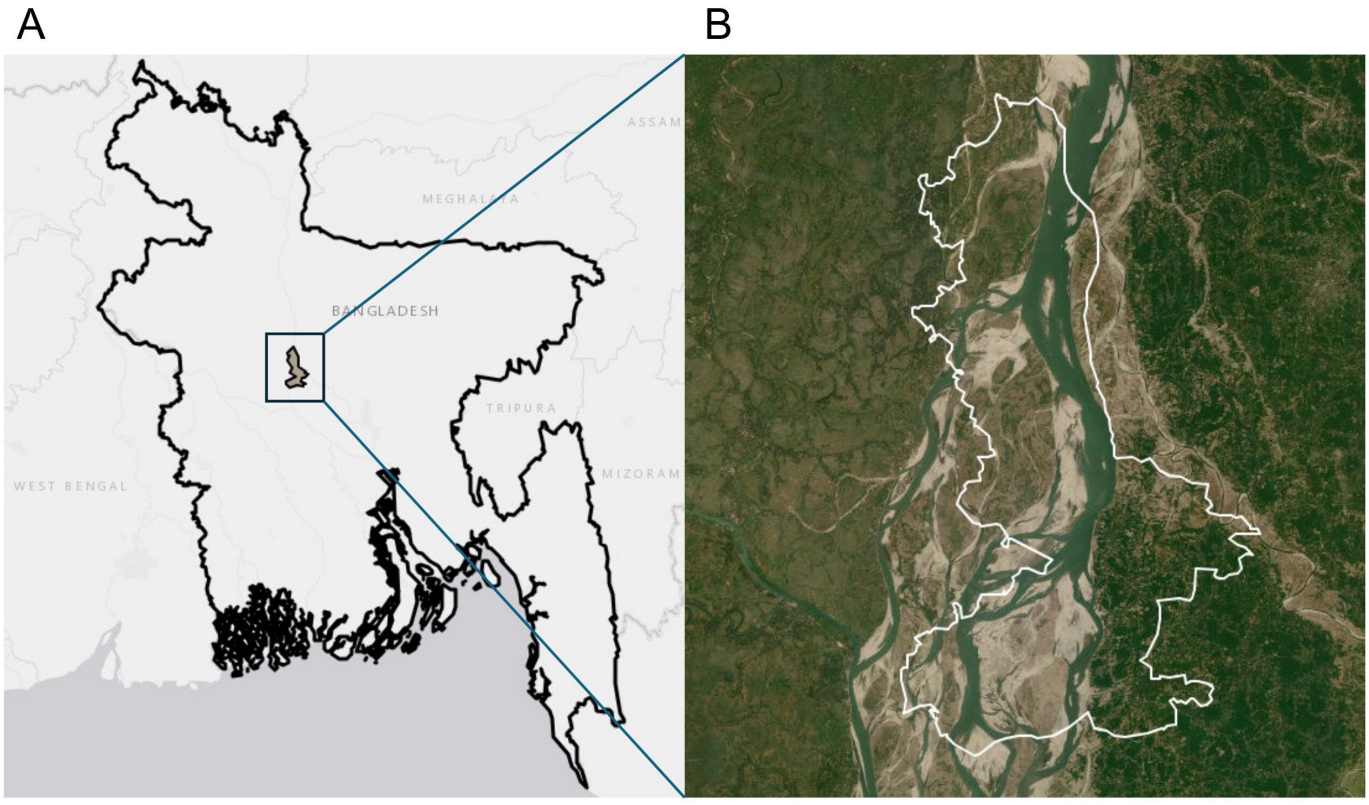

Figure 3 CRADLE study site map. (A) Map of study site location within Sirajganj and Tangail districts, Bangladesh. Base map source: Esri, TomTom, Garmin, FAO, NOAA, USGS, OpenStreetMap contributors and the GIS User Community. (B) Exterior boundary of unions included in the study site in Chauhali, Belkuchi and Nagarpur unions of Sirajganj and Tangail districts. Base map source: Esri, HERE, Garmin, OpenStreetMap contributors and the GIS User Community. CRADLE, Cement-based flooRs AnD chiLd hEalth; FAO, Food and Agriculture Organization of the United Nations; GIS, Geographic Information Systems; NOAA, National Oceanic and Atmospheric Administration; USGS, United States Geological Survey.

on sustainable construction materials) and stakeholders working in climate change adaptation strategies for housing, shelters and water and sanitation. During the first workshop, we will gain input on proposed concrete floor design, health outcome measurement and planned research outputs from stakeholders. We

Table 1 Outcome measures

Child outcomes	Maternal outcomes	Environmental outcomes
► Prevalence of any soil-transmitted helminth infection (primary outcome) ► Prevalence of individual soil-transmitted helminth infections ► Diarrhoea prevalence ► Child gut microbial communities ► Child antimicrobial resistance genes ► Length-for-age Z-score ► Weight-for-length Z-score ► Weight-for-age Z-score ► Frequency of child soil contact ► Frequency of child soil ingestion ► Mean ASQi Z-score at 12 and 24 months ► Mean overall Family Care Indicator score at 12 and 24 months	► Maternal stress ► Maternal depression ► Maternal satisfaction with quality of life ► Memory span ► Non-verbal reasoning score ► Maternal cognitive inhibition ► Maternal cognitive flexibility and attention shifting ► Maternal daily discretionary time	► Any soil-transmitted helminth prevalence in household floor samples ► Prevalence of individual soil-transmitted helminth infections in household floor samples ► Larvated *Ascaris lumbricoides* prevalence in household floor samples ► Larvated *Trichuris trichiura* prevalence in household floor samples ► Culturable *E. coli* abundance in household floor samples ► Culturable cefotaxime-resistant *E. coli* prevalence in household floor samples ► Culturable *E. coli* abundance in child hand rinse samples ► Culturable extended spectrum beta-lactamase (ESBL) producing *E. coli* prevalence in household samples ► ESBL-coding genes in household samples ► Mass of floor dust (g per m^2) ► Microbial communities in environmental samples ► Antimicrobial resistance genes in environmental samples

ASQi, Ages and Stages Questionnaire Inventory.

will also identify the gaps and areas for improvement in current policies, programmes and resources related to housing in rural Bangladesh. In both workshops, we will discuss bottlenecks and potential barriers to scaling up a potential improved flooring intervention and challenges related to sourcing sustainable materials for household floors.

The study team will convene community engagement meetings in each union and upazila in the study site. Attendees will include administrative officials, elected members, religious leaders and local non-elected leaders. To build trust with the community, the study team will introduce study objectives, discuss potential community benefits, explain the randomisation process and intervention implementation plan and address any concerns. If community leaders agree, then the team will proceed with recruitment. icddr,b will meet with leaders every 6 months to provide updates on study activities and learn about any other ongoing interventions in the study area.

Enrolment

Enrolment is planned from November 2023 to August 2024. Field staff will select a random location in each union using spatial software. If a union spans both sides of the Jamuna river or one of its distributaries, a new random location will be used on each side of the river. The eligible household nearest to the random location will be selected as the first household. Field staff will discuss the trial with adults in the eligible household, including pregnant mothers, and obtain written informed consent from pregnant women and either their husband or the head of each household (online supplemental appendix 1). Field staff will then spin a bottle and move towards the next eligible household in the direction indicated by the top of the bottle. To prevent contamination, in which the intervention influences the control arm through reduced disease transmission between households in the intervention and control arms, we will ensure a minimum 100 m buffer between study households.

Baseline survey

The study team will administer a baseline survey to record household construction materials, household census, assets, income, animal ownership, WASH infrastructure and practices, demographics, maternal depression and the illness and activities of a non-index child aged<3 years (index children will be in utero) (table 2; online supplemental appendix 2). Surveys will include questions about satisfaction with housing and floor quality. Field staff will visually assess floors for cracks, damage, cleanliness and the presence of animal faeces, food scraps or trash. Field staff will record participant names and cell phone numbers to assist with tracking should participants relocate during the follow-up period. Field staff will receive standardised training on survey administration and sample collection.

Randomisation

The trial will use household-level randomisation stratified by geographical block. This design will ensure that intervention and control groups are evenly distributed across the study area and support baseline balance of participant characteristics between arms. Using a block randomised design is also expected to increase study efficiency by accounting for strong geographical clustering of enteric infection.[60] As households are enrolled, they will be formed into geographical blocks of 10 spatially contiguous households. There will be no spatial overlap in geographical blocks. Using R statistical software, a Stanford investigator not involved in the data collection will randomly assign households within each block to control and intervention arms in a 1:1 ratio. A random subsample of 50 intervention households stratified by block will be assigned to receive a green concrete floor. Due to the nature of the intervention, it will not be possible to blind participants to a randomised study arm. Laboratory staff and data analysts will be blinded during primary and secondary outcome analyses of intervention effects.

Intervention

A local NGO that is not involved in the research will instal concrete floors in 400 intervention households before the birth cohort is born. The control group will receive no interventions. The construction team will remove the top layer of the floor and then create a compacted soil foundation. To increase durability during floods and heavy rainfall, the minimum floor height will be 18 inches. They will retain or change the soil foundation of the home according to the household's preference. The soil foundation will then be covered with a sand layer followed by a layer of bricks and then a cement-based mortar, followed by sealant. The installation process takes approximately 5 days, and then the floor must cure for approximately 7 days. The entire process takes approximately 14 days, and during this time household members will temporarily relocate, and they will return when curing is complete. If it has rained recently, the field team will wait at least 2 days after it stops raining before installing the concrete floor.

In a subsample of the treatment arm (n=50), we will use an alternative cement mix with fly ash that is a waste product and therefore offsets (ie, lowers) the greenhouse gas emissions of the portion of cement that it replaces. 20% of ordinary Portland cement will be replaced with fly ash, and commercially produced 'green' blocks will be used instead of traditional bricks as supply availability permits. Green blocks will be made of a mixture of cement, fly ash, water and recycled aggregates.

Participant retention

To minimise attrition in the control arm, we will compensate mothers from control households with 500 Bangladeshi Taka (US$4.27) after completion of each follow-up survey at 3, 6, 12, 18 and 24 months.

Table 2 Summary of variables measured in surveys

		Baseline	Birth	3 months	6 months	12 months	18 months	24 months
Household characteristics	Household construction materials	X			X	X	X	X
	Household census	X			X	X	X	X
	Household assets	X			X	X	X	X
	Parental education and employment	X			X			X
	WASH infrastructure and practices	X			X	X	X	X
	Animal ownership and husbandry	X			X	X	X	X
	Animal presence in the home	X			X	X	X	X
	Human and animal faeces in the home	X			X	X	X	X
Perinatal outcomes	Prenatal and birth outcomes		X					
Anthropometry	Length, weight, head circumference	X	X	X	X	X	X	X
Illness symptoms	Child illness symptoms (eg, diarrhoea)	X			X	X	X	X
Flooring	Floor durability assessment	X			X	X	X	X
	Floor hygiene and maintenance	X			X	X	X	X
Child activities	Child motor skills				X	X	X	X
	Child cognitive development					X		X
	Child feeding practices				X	X	X	X
	Child play locations				X	X	X	X
Maternal outcomes	Quality of life	X		X		X		X
	Satisfaction with housing	X			X	X	X	X
	Perceived Stress Scale	X		X		X		
	Edinburgh Postnatal Depression Scale	X		X		X		
	Maternal bandwidth				X		X	
	Maternal time use			X		X		
Flooding status	Household flooding status	X			X	X	X	X
Water, sanitation, handwashing	Water storage, latrine access, child faeces management, handwashing	X			X	X	X	X
Vaccination	Vaccination status of index child			X	X	X	X	X
Deworming and antimicrobials	Deworming status of household members	X			X	X	X	X
	Antimicrobial use of mother and index child	X			X	X	X	X
	Antimicrobial use in domestic animals	X			X	X	X	X
Food consumption	Animal milk consumption practices				X	X	X	
Environmental sampling	Environmental sample collection				X	X	X	X

WASH, water, sanitation and hygiene.

Follow-up measurements

Follow-up measurements are expected to occur from February 2024 to January 2027. Field staff will conduct follow-up surveys in all intervention and control households at 3, 6, 12, 18 and 24 months (table 2). They will conduct household surveys, blood spot and stool collection in the full study sample (n=800). The following potential mediators and outcomes will be measured in subsamples: maternal bandwidth, time use and child cognitive development (n=400), environmental samples (n=400 for STH by qPCR, n=110 for STH larvation detected using microscopy, n=110 for *E. coli*, n=110 for extended-spectrum beta-lactamase producing *E. coli* (ESBL-E), video observations (n=60) (figure 2). When selecting subsamples of households for additional measurements, households will be randomly selected stratified by geographical block and study arm. Additional subsamples will be nested within the largest group. The same subsamples will be used across follow-up rounds for those with repeated measures. If any of the households included in the subsamples are lost to follow-up at a particular measurement, they will be replaced with another block-stratified randomly sampled household from the same study arm.

Birth survey

Field staff will ask study participants to call them once a mother begins labour and when the index child is born. A survey will be conducted as early as possible after birth (up to 4 weeks from birth) to record obstetrical and birth outcomes. If the mother is temporarily residing away from the study household, field staff will travel to the mother's location if it is within a study upazila. The birth survey includes questions about antenatal care utilisation, delivery location, delivery mode, obstetrical complications, gestational age and neonatal mortality. Field staff will measure weight, length and head circumference.

Household surveys

At each follow-up, the field team will administer a survey to mothers of the birth cohort to assess any changes to housing materials, household membership and household assets (table 2). Follow-up surveys will collect the same measurements as baseline as well as maternal bandwidth, maternal time use, child motor and cognitive development, child anthropometry and child vaccination status. Additionally, mothers will be asked to report index child illness symptoms and daily activities for the index child.

Verbal and social autopsy

For all index child deaths during the study period, including stillbirths, we will perform verbal autopsies to ascertain the potential cause of death. We will perform a structured verbal autopsy using the 2022 WHO Verbal Autopsy Instrument. Interviews will be conducted as soon as feasibly possible up to 1 year following child death. Verbal autopsy questionnaires will be administered by staff with a minimum of 12 years of formal education. Two independent physicians will review survey responses and assign the cause of death. If physicians assign different causes of death, a third physician will independently review the survey responses, and the final cause of death will be determined through a consensus meeting. Physicians will classify the cause of death using International Classification of Diseases 10th revision codes.

In addition to verbal autopsy, we will conduct a social autopsy through in-depth interviews with parents and family members of the index child to understand social and contextual factors contributing to each child death. The social autopsy will use an instrument adapted from the INDEPTH Network (International Network for the Demographic Evaluation of Populations and their Health) Social Autopsy Tool (http://www.indepth-network.org/resources/tools) (online supplemental appendix 3). It will begin with an open-ended question asking respondents to summarise events and factors that led up to the child's death. Then staff will ask questions related to household decision making, caregiver recognition of illness, care-seeking behaviours, quality of care received, housing-related factors and recent social and economic changes in the household. The data collected from social autopsies will be analysed qualitatively to identify common themes contributing to child deaths in the study population.

Stool collection

At 6, 12, 18 and 24-month follow-ups, field staff will provide caregivers with a sterile container to collect stool from the index child. They will return to pick up the collected stool the following morning and will characterise stool consistency using the modified Bristol Stool Form Scale for children.[54] Field staff will aliquot 0.5 g of stool with 1 mL of Zymo DNA/RNA Shield (Zymo Research, Irvine, California, USA) at the household for stool specimens that will be used for metagenomic sequencing. The samples will be transported on ice to the icddr,b laboratory in Dhaka while maintaining a temperature from 4–10°C. For qPCR analyses, 0.5 g stool will be aliquoted with 1 mL 100% ethanol and stored at −80°C prior to qPCR analysis. For antimicrobial resistance analyses, stool will be stored at 4°C with no preservatives prior to analysis within 24 hours of specimen collection. After the final round of stool collection at age 24 months, all household members will be offered deworming medication.

Blood collection

At 6, 12, 18 and 24-month follow-ups, field staff will collect dried blood spots from the index child. After blood spots are dried for 24 hours, they will be transported to the icddr,b laboratory in Dhaka and archived at −80°C for analyses in future studies.

Environmental sample collection

At 6, 12, 18 and 24-month follow-ups, field staff will collect dust from floors in a subset of households (n=400). In a smaller subset (n=110), the staff will also collect a floor

swab and child hand rinse from index children. To collect dust from floors, staff will use a 0.5×0.5 m sterilised metal stencil to mark up to eight adjacent floor areas (total 2 m^2), starting next to the head of the bed where the index child usually sleeps. They will sweep the area within the stencil with a sterilised brush once vertically and then once horizontally. They will collect the resulting dust using a sterile scoop and place it in a sterile Whirl-Pak bag. Staff will then mark an adjacent 0.5×0.5 m floor area and swab the area within the stencil with a sterile prehydrated sponge once vertically and then once horizontally and place the sponge in a sterile Whirl-Pak bag. To collect index child hand rinses, staff will ask the caregiver to place the child's hands, one at a time, into a sterile Whirl-Pak bag prefilled with 250 mL of sterile water. They will massage each hand for 15 s from outside the bag, then shake the Whirl-Pak bag for 15 s with the hand submerged.

At the 6-month follow-up only, field staff will collect additional samples in a subset (n=110). This will provide an early assessment of intervention effectiveness on a wider range of matrices as well as detect additional sources of contamination in the domestic environment. The additional sample types include: drinking water (for index child or other children<5 years), prepared food (for index child or other children<5 years), floor soil (in control arm only), courtyard soil, and cow and chicken faeces from animals that stay in the compound. To collect drinking water, field staff will ask the caregiver to bring them a glass of water the same way they would give it to the index child or to another child<5 years if the index child is not yet drinking water. Staff will pour approximately 250 mL of water from the glass into a sterile Whirl-Pak bag. To collect prepared food, staff will ask the caregiver to bring them a small portion of food the same way they would give it to the index child or to another child<5 years if the index child is not yet eating food. Staff will use a 50 mL sterile tube with a sterile spoon to collect approximately 50 g of food. To collect floor soil, field staff will use a sterilised metal stencil to mark an additional 0.5 m × 0.5 m floor area near the child's sleeping area as described above. They will scrape a 5 mL sterile tube along a horizontal line within the stencil to collect approximately 5 g of sample for sequencing. They will then use a 50 mL sterile tube with a sterile spoon to scrape the remaining area within the stencil once vertically and once horizontally; they will repeat these steps until the tube is full to obtain approximately 50 g of sample to determine moisture content and soil type. To collect courtyard soil, field staff will use a sterilised metal stencil to mark a 0.3 m × 0.3 m area at the entrance to the household where the index child lives and follow the same procedure as floor soil collection. To collect cow and chicken faeces, field staff will ask the caregiver to identify faeces from recent defecation by their animals, then use a 50 mL sterile tube with a sterile spoon to collect the faecal sample. Zymo DNA/RNA Shield (Zymo Research, Irvine, California, USA) will be added immediately after collection to sample aliquots that will be used for metagenomic sequencing. All samples will be transported on ice to the icddr,b laboratory in Dhaka. Samples that will be used for molecular analyses will immediately be stored at −80°C until DNA extraction. Samples that will be used for culture-based analyses will be stored at 4°C overnight prior to analysis by the next day.

Laboratory assays

We will test for STH in stool samples and household floor dust samples using qPCR using previously published sequences for the following species which had prevalence>5% in our prior research in rural Bangladesh: *Ascaris lumbricoides,*[61] *Trichuris trichiura* and *Necator americanus*[62]. DNA will be extracted from stool samples using the QIAamp Fast DNA Stool Mini Kit (51604, QIAGEN GmbH, Hilden, Germany). Extractions will occur following the manufacturer's suggested protocol with the following changes: (1) Rather than vortexing, homogenisation will occur using the Mini-BeadBeater-24 (BioSpec Products). (2) Immediately following homogenisation, 1 µL of a 100 pg/µL stock of an internal recovery and amplification control (IAC) plasmid[63] will be added to each sample. DNA will be extracted from floor dust samples using the DNeasy PowerSoil Pro kit following the manufacturer's suggested protocol, again with the addition of IAC plasmid. Following DNA extraction, all samples will be tested for the presence of IAC. Amplification of plasmid target will indicate successful recovery of DNA during the extraction procedure and will demonstrate recovered DNA as amplifiable. DNA extracts that fail to produce an IAC result that falls within 3 SD of the mean of all sample IAC results will be eliminated, and the parent sample will undergo re-extraction. Testing for the presence/absence of IAC will occur in accordance with previously published protocols.[64]

The presence/absence of STH targets will be determined via the use of previously described small volume, multiparallel qPCR assays. Testing will occur in accordance with published protocols and cycling procedures.[60 61] Single-well reactions will be used to test all DNA extraction products for the presence of each pathogen of interest, and a qPCR result will be deemed 'positive' if testing produces an amplification curve with a cycle threshold value<40.

In a random subsample (n=110) stratified by geographical block, we will determine whether STH ova are larvated using our previously validated method of incubation followed by microscopy since larvated ova can transmit infections to humans, whereas non-larvated ova cannot.[65]

In the same subsample (n=110), we will use IDEXX Quanti-Tray/2000 with Colilert-24 (IDEXX Laboratories, Westbrook, Maine, USA) to enumerate the most probable number (MPN) of *E. coli* in floor swab and child hand rinse samples. Swabs will be eluted by adding 100 mL of sterile water to the Whirl-Pak bag containing the sponge, massaging the swab from outside the bag for 15 s, then swirling the Whirl-Pak bag for 15 s. This step will be repeated three times to generate 300 mL of eluate.[66] 5 mL

of the eluate will then be diluted with 95 mL of sterile water to generate a 100 mL aliquot for IDEXX testing. 50 mL of child hand rinse water will be diluted with 50 mL of sterile water to generate a 100 mL aliquot for IDEXX testing. For floor swab samples, a second 100 mL aliquot will be processed after adding 80 µL of filter-sterilised 5 mg/mL cefotaxime solution (final concentration of 4 µg/mL in the 100 mL aliquot) to enumerate the MPN of cefotaxime-resistant *E. coli*.[67]

In the same subsample (n=110), we will also detect and enumerate ESBL-E in the following sample types: child stool, cow and chicken faeces from the same compound, floor swab, courtyard soil, child hand rinse, drinking water and prepared food. We will use CHROMagar ESBL media to isolate and identify ESBL-E.[68] Selected colonies from each plate will be analysed by qPCR for major ESBL genes (CTX-M, SHV, TEM, OXA) following previously published protocols.[69] Isolates from previous studies will be used as positive controls. For selected isolates, antibiotic susceptibility will be determined using the Kirby-Bauer disk diffusion method following guidelines of the Clinical and Laboratory Standards Institute and European Committee on Antimicrobial Susceptibility Testing.[70 71]

In the same subsample (n=110), we will perform metagenomic sequencing of child stool, floor soil, cow faeces and chicken faeces samples from each follow-up round. Floor soil will only be collected from control arm households (n=55) because we expect that the quantity of soil needed for DNA extraction (10 g) will not be available on concrete floors. We will combine 10 faecal samples of each type and 5 floor soil samples to generate 11 composite samples of each type. We will extract DNA from each composite sample using DNeasy PowerMax Soil Kits for soil samples and Qiagen QIAamp PowerFecal Pro DNA Kits for stool samples. Metagenomic shotgun sequencing will be performed using the Illumina platform. Bioinformatics analysis will be completed using the Chan Zuckerberg ID platform[72] to identify pathogens and bacterial antimicrobial resistance genes in each sample.

Maternal measures

We will measure maternal stress, depression and time use at child ages 3 and 12 months and maternal bandwidth at child ages 6 and 18 months. This sequencing will minimise participant fatigue by reducing the number of measures collected per round and will ensure that mediators are measured prior to each child cognitive measurement at 12 and 24 months.

Maternal bandwidth measures will include visual-spatial working memory, executive function, inhibitory control, and cognitive flexibility and attention shifting. To measure visual-spatial working memory, we will use an analogue version of the Corsi Block Span Task[73] since mothers may be unfamiliar with computers or tablets. The analogue version is a customised set of blocks located in fixed positions on a board. An enumerator will tap on a sequence of blocks, and mothers will be asked to recall the sequence by tapping the blocks. Sequence length will increase in each round, with a maximum sequence length of nine blocks for the forwards Corsi task and eight blocks for the backwards Corsi task, where the mother recalls the sequence in the reverse order. Field staff will record the maximum sequence length correctly recalled by the mother.

We will measure perception, abstraction capacity, analogical reasoning and metacognitive executive function except emotion using Raven's Progressive Matrices.[74 75] Each booklet will contain 48 patterns with a missing tile inside. Mothers will have 45 min to choose the missing tile that best completes each of the 48 patterns. At the end of the task, the total raw score will be converted to an Ability Score and Standard Score.

We will also measure cognitive inhibition, which refers to the ability to suppress the processing of stimuli that are irrelevant to the intent of the task and inhibit a prepotent response. We will use an adapted version of The Hearts and Flowers task[76] using images of cats and dogs, which are recognisable to the study population. This task takes into account both accuracy and speed and captures individual differences in inhibition and cognitive flexibility.[44 76] This task has three rounds, each with 20 trials. In the first round, dogs will appear randomly on either the right or left side of a page, and respondents (mothers) will be asked to respond to one rule: to place their hand over an arrow on the same side of the page as a dog image (congruent task). In the second round, cats will appear on either side of the page, and mothers will be asked to place their hand on an arrow on the side opposite to where the cat appears (incongruent task). In the third round, dogs and cats will appear intermixed (mixed task), and mothers will be asked to respond accordingly. Usually, no executive demands are required in the dog task, thus it is used as a control task to compare performance on the cat and mixed tasks. The percentage of correct responses and response time will be recorded for each respondent.

To measure cognitive flexibility and attention shifting, we will use the Dimensional Change Card Sort test presented as stimuli on flip charts instead of a screen.[77] Two target pictures will be presented that will vary along two dimensions (eg, shape and colour). The participants will match the picture at the top of the displayed page with two pictures with varied dimensions (eg, shape and colour) at the bottom. To match the picture according to the requested dimension spoken by the tester, participants will place their hand on an arrow at the side of the correct corresponding picture. Following practice trials with colour-matching and shape-matching, 29 mixed trials will be offered. We will record the percentage of correct responses and response time for each participant.

To measure maternal discretionary time, we will use a hybrid time diary adapted to our setting in Bangladesh.[78] Enumerators will invite mothers to summarise the prior day's activities chronologically and allocate hours by placing tokens next to photos of nine common activities. This approach does not require mothers to perform

calculations or be literate. We will calculate total time spent on each activity to determine discretionary time.

Child development assessment

The Ages and Stages Questionnaire Inventory (ASQ:I) will be administered at child ages 12 and 24 months to evaluate problem solving, communication, fine motor, gross motor and personal social development in index children. The ASQ:I is a continuous sliding scale with questions for each domain and starts with the child's chronological age followed by establishing a basal and ceiling level of a child's performance. Although it is a tool based on parents' reports, in Bangladesh, the ASQ:I was adapted by researchers to include a subset of items that are administered through direct assessment with locally available materials that the parents may not observe. Administration of the ASQ:I requires adequate training and around 45 min to administer. The adapted version of this instrument has been validated in Bangladesh.[79] The Family Care Indicator instrument will be used to measure the amount of stimulation the child receives at home at 12 and 24 months. This instrument measures stimulating activities, the availability of a variety of play materials, caregiver responsiveness and evaluates the child's surrounding environment. This instrument has been validated in Bangladesh.[80]

Quality assurance for psychosocial measures

Child development and maternal bandwidth data will be collected by trained physicians and psychologists from icddr,b. All measurements will begin after pretesting in the community on non-study mother–child dyads (n=40), once an interobserver agreement value of 90% is achieved between testers and trainers. Refresher training will take place every 6 months or when correlation coefficients for tester–supervisor pairs fall below 0.85. In a random sample of 5–10% of tests, testers' evaluations will be compared with evaluations completed by trained psychologists.

Video recording and analysis

Field staff from icddr,b will record 6-hour video observations in a random subsample of 60 children (30 children per arm). Recording start times will vary from 07:00 to 12:00 between households to capture a wider range of activities and will be conducted in the household, courtyard or near the courtyard. Observations will be paused during breastfeeding, bathing and sleeping times. To minimise Hawthorne effects, field staff will spend time acclimating themselves with household members prior to starting the recording, and they will use unobtrusive recording equipment. Additionally, field staff conducting video recordings will be local staff members who are familiar with the social and cultural norms of study participants. Videos will be coded by icddr,b research staff to measure the duration, time and location of relevant child activities, such as soil contact and ingestion and animal contact, using LiveTrak software.[81]

Data management

Data will be collected on tablets using customised CommCare software, which facilitates longitudinal data collection. Data will be securely stored on CommCare servers and at icddr,b, with access limited to the study Principal Investigator and the data manager. Paper records will be digitised and destroyed, and personal identifiers will be removed. Digitised materials will be stored indefinitely, with identifiable information password-protected and encrypted. Hard copies will be stored in locked cabinets. To ensure data quality, supervisors will observe interviews, conduct reinterviews, cross-check data and provide feedback to enumerators. Field staff will maintain a field tracking form to track daily data collection activities. Stata and R scripts will regularly be used by the data manager, investigators and statisticians to identify inconsistencies and errors, and errors will be resolved prior to analysis.

Statistical analysis

To assess randomisation, we will compare the means and percentages of baseline characteristics between arms including maternal age, maternal education level, paternal education, paternal employment, housing wall and roof materials, household assets, acres of homestead land owned, household WASH infrastructure and access, open defecation practices and deworming in the prior 6 months, animal ownership and animal cohabitation.

The primary analysis will compare prevalence of any STH between study arms using an indicator for whether a child tested positive at the 6, 12, 18 or 24-month follow-up rounds. We will estimate the unadjusted prevalence ratio comparing intervention to control using generalised estimating equations[82] with a binomial family and log link and an exchangeable correlation matrix to account for repeated measures within the same child. If log-binomial models do not converge, we will use modified Poisson regression with robust SEs.[83] Secondary analyses will include indicators for follow-up rounds in order to estimate the prevalence ratio at each follow-up to assess whether effects vary over different child ages. All models will condition on geographical block and estimate robust sandwich SEs[84] to account for the matched design.[85 86] To assess whether the intervention effect is sustained over 2 years, we will also fit a model with an interaction term between treatment and follow-up time. All statistical tests will be conducted using a two-sided significance level of 0.05, consistent with the level used in our sample size calculations.

We will also compare secondary outcomes (table 1) between study arms. For repeated measures outcomes, we will use generalised estimating equations[82] with an exchangeable correlation matrix; we will estimate mean differences for continuous outcomes using an identity link and Gaussian family and prevalence ratios for binary outcomes using a log link and binomial family.[85] For measurements analysed at a single time point, we will fit generalised linear models[85] with a Gaussian family and identity link for continuous outcomes and a binomial

family and log link for binary outcomes. If log-binomial models do not converge, we will fit models with a Poisson and log link.[83 85]

Primary analyses will be unadjusted for covariates. A secondary analysis will adjust for baseline covariates to reduce bias associated with any chance imbalances between study arms at baseline and possibly increase efficiency.[87] We will prespecify a potential covariate adjustment set of baseline variables and only adjust for covariates among this set that are associated with each outcome (likelihood ratio test p value<0.2).

Analyses will be intention-to-treat. The following households will be considered non-compliant: (1) control households that instal concrete floors that cover at least one entire room inside the mother's household; (2) households that cover at least one room's floor with a cement-based finish; (3) intervention households that remove any part of the concrete floor installed as part of the trial; (4) intervention households in which a substantial portion of the concrete floor is damaged. If non-compliance exceeds 10% in either arm, we will perform a per-protocol analysis as well. We will not adjust for multiple comparisons because the number of outcomes is relatively modest, and the analysis will follow a prespecified analysis plan.

We will compare attrition rates at each follow-up and across follow-ups between randomised arms and compare baseline characteristics of those lost to follow-up to those who complete the study. If there is evidence of systematic differences in attrition between arms and attrition exceeds 20%, we will explore whether study drop-out resulted in selection bias using inverse probability of censoring weights with flexible machine-learning based estimation.[88]

For STH measured in floor dust samples, the primary analysis will impute STH prevalence as 0 for floors that do not contain enough dust for nucleic acid extraction (0.1 g). The imputation assumes that floors with no dust do not harbour STH eggs. Our pilot data indicate that concrete floors in 40% of households may yield insufficient dust for nucleic acid extraction. We will conduct a secondary analysis by comparing STH outcomes in floor dust between intervention and control groups only using data from households where sufficient dust was obtained. We expect this analysis to yield a conservative estimate of intervention effectiveness because it will exclude intervention households with dust-free floors which are less likely to harbour STH eggs.

We will explore potential effect modification by the following baseline variables: household wealth, household WASH infrastructure, presence of animals inside the household, primary play location of children<2 years, index child sex, household distance to nearest permanent water body[89] and ordinary Portland cement versus green cement. We will also assess effect modification by monsoon versus dry season using a data-based definition and precipitation, temperature and humidity levels[90] using weather station data from the Government of Bangladesh Meteorological Department. We will test for effect modification on the relative scale by including interaction terms between these variables and treatment group indicator variables in regression models. We will estimate additive scale interactions from log-linear models using the relative excess risk due to interaction (RERI).[91] To test for effect modification, we will estimate p values on the interaction terms for relative scale interaction in log-linear models and for additive scale interaction RERIs.[91 92]

To assess whether any post-treatment variables mediate intervention effects, we will perform causal mediation analyses[93] for the following potential mediators: deworming or antimicrobial consumption of birth cohort or other household members in the past 6 months, and floor coverings. Interim reductions in STH could result in reduced deworming use, which in turn further reduces STH at the final follow-up measurement. Additionally, installation of concrete floors may alter the type and frequency of floor coverings used, which may influence health outcomes. We will also use causal mediation analysis to assess whether health and child development outcomes are mediated through environmental versus maternal pathways. For the environmental pathway, mediators will include contamination of the home with *E. coli* and STH. For the maternal pathway, mediators will include maternal discretionary time use; maternal bandwidth (measures of executive function, inhibition and working memory); and maternal quality of life, stress and depression.

For the ASQi outcome, if child age varies substantially at each follow-up round, we will use age-specific Z-scores for each test within 2-month age bands and will control for age in the analysis. We will create reference distributions for each ASQi domain (communication, fine motor, gross motor, problem solving and personal social) and the overall global scale. The sum of age-specific raw scores from the control group will be standardised with a mean of 0 and a SD of 1 for each 2-month age band. For the intervention arm, we will calculate standardised Z-scores using the reference distribution from the control arm in each age band. We will summarise the distribution of continuous outcomes (eg, ASQi Z-scores) using Gaussian kernel density smoothers. We will estimate mean differences in ASQi scores or Z-scores between study arms using generalised linear models that condition on geographical block. To compare rates of attainment for each growth milestone, we will estimate HRs using a semiparametric generalised additive model with a complementary log–log link and baseline hazard fit with a monotonic cubic spline.

Cost-effectiveness analysis

We will conduct cost-effectiveness analysis to examine both the costs and health outcomes of the concrete floor intervention. We will collect data on floor installation costs from a programme perspective, separating material and labour costs, since in the future households may instal

floors themselves. Using an ingredients-based approach, we will record costs for individual line items within categories including capital costs, materials, transportation, personnel and operations. We will then adapt our previously published natural history and cost-effectiveness models of childhood helminth infections and enteric fever to project the health impacts and cost-effectiveness of floor installation.[94–97] We will populate the model with outcome rates from the control and intervention arms of this trial, simulate age-specific risk over a 10-year period and project disability-adjusted life years (DALYs) for each health outcome for households with concrete floors and soil floors.

We will calculate DALYs for child STH infections, child diarrhoea, child wasting and maternal depression using published disability weights.[98] While we expect the intervention to influence a broad range of outcomes, disability weights are only available for the subset listed above. We will calculate disability weights for hookworm-associated anaemia as the product of the disability weight for anaemia due to hookworm disease by the probability that an individual infected with hookworm develops anaemia.[23] For each STH infection, we will estimate the probability of mild, moderate and severe infections based on Ct values from qPCR using data from a prior study of children in rural Bangladesh.[99] For diarrhoea, we will calculate weights assuming the distribution of mild, moderate and severe diarrhoea is the same as found in the MAL-ED (Malnutrition and Enteric Disease) study in Bangladesh.[58]

We will perform simulations under different scenarios for the durability of intervention effects and intervention coverage, adjusting for inflation. The model will predict costs and health outcomes, deaths and DALYs averted over a 10-year period; we will obtain 95% credible intervals for uncertainty. We will estimate the incremental cost-effectiveness ratio for concrete versus soil household floors. Parameter draws from variable distributions will be performed through Latin Hypercube sampling.[100] We will perform a probabilistic sensitivity analysis with prespecified ranges of key parameters (eg, disability weights, costs, intervention effects) supported by our study findings and the literature.[101 102] If we find that the cost of concrete floors made with the fly ash mix differs from that of traditional concrete floors, we will repeat the cost-effectiveness analysis specifically for green concrete floors using the same methods.

ETHICS AND DISSEMINATION

The trial protocol was approved by the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) Ethical Review Committee (PR-22069) and the Stanford Institutional Review Board (63990).

The US- and Bangladesh-based PIs will be responsible for safety oversight. PIs will meet twice each year. The study's data collection phase will end after the final measurements are taken when children are approximately 2 years of age. The PIs will continue to monitor the study population for two weeks after offering deworming to household members at the end of the data collection period in case of adverse events. Interim analyses will only be conducted at the discretion of the PIs to ensure safety of participants and to plan for future data collection and analyses.

The results of the study will be presented at stakeholder workshops in Bangladesh, which will include community members, local, regional, and national stakeholders. In addition, results will be presented on ClinicalTrials.gov, in scientific manuscripts, and at scientific conferences. De-identified study data and replication scripts will be made publicly available online at the time of manuscript publication.

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