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Assessing the setting-specific individual and joint roles of water contact and sanitation practices on the prevalence of *Schistosoma haematobium* prevalence in Kano, Nigeria

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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ABSTRACT

Assessing the setting-specific individual and joint roles of water contact and sanitation practices on the prevalence of *Schistosoma haematobium* prevalence in Kano, Nigeria

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BACKGROUND: Nigeria has the highest cases of schistosomiasis in sub-Saharan Africa and accounts for a quarter of the global population requiring treatment. Factors influencing transmission are complex, context-specific, and need to be understood for adequately designed control strategies. This thesis examined the individual and combined roles of water contact and sanitation practices on *Schistosoma haematobium* prevalence in Kano, Nigeria.

METHODS: A cross-sectional study was carried out in five endemic Local Government Areas of Kano in June and July 2019. Urine samples from school-aged children (4 – 18 years) were screened for *S. haematobium* and follow up questionnaires were administered to assess participants' awareness, behavior, and practices. The analytic dataset used 272 participants who had valid laboratory data. Multivariate log-binomial models were used to estimate prevalence ratios (PRs) adjusted for participants' age, gender, water source, and farming practices.

RESULTS: The prevalence of urinary schistosomiasis for this population was 37.5%; 33.7% of whom reported unimproved sanitation use and 84.6% engaged in at least one of six water contact activities. The majority of participants were male (n=221, 81.6%), and mean age was 11.2 (SD = 4.1). After adjusting for covariates of interest, any degree of water contact (moderate or high) was significantly associated with prevalence, aPR = 3.94, 95%CI [1.68, 9.25]; there was no significant association between unimproved sanitation use and prevalence, aPR = 0.99, 95 CI [0.72, 1.37]; and the observed joint effect of water contact and unimproved sanitation use was significantly associated with infection prevalence; aPR = 3.91, 95%CI [1.68, 9.10].

CONCLUSION: These findings not only suggest that water contact might be the key limiting factor on *S. haematobium* prevalence for this population when compared to poor sanitation infrastructure alone. The study further highlights complexities in the measurement of WASH constructs within urinary schistosomiasis transmission and provides novel direction for more robust causal research that considers the embedded roles of WASH exposures.

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I. BACKGROUND

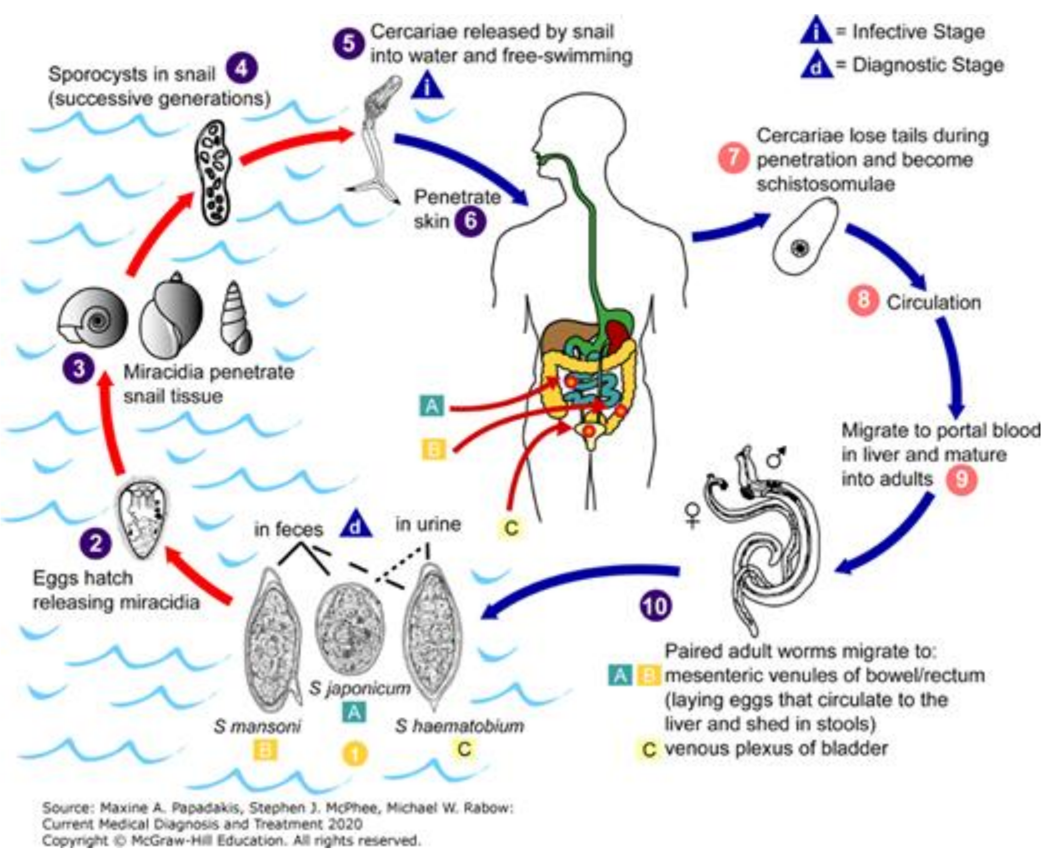
Rationale

Schistosomiasis - historically termed bilharzia – is a parasitic disease currently estimated to affect over 200 million people globally, causes mortality in about 100,000, and results in chronic illnesses for over 20 million(Rosenthal, 2020). An infectious disease especially associated with poverty, schistosomiasis is considered as one of the targeted Neglected Tropical Diseases (NTDs) - "a group of diseases that cause substantial illness and affect the world's poorest people"(Center for Global Health . Division of Parasitic & Malaria, 2011, p. 1). Recent estimates show that approximately 90% of people who are infected and in need of treatment reside in sub-Saharan Africa. Over a quarter of this population, about 26%, are Nigerians (WHO, 2019a).

The parasitic species implicated in schistosomiasis are trematode blood flukes that belong to the genus, Schistosoma (Colley, Bustinduy, Secor, & King, 2014). There are 6 main species commonly known to cause disease in humans. Five of these – *Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi*, *Schistosoma intercalatum*, and *Schistosoma guineensis* result in intestinal schistosomiasis; while the sixth, *Schistosoma haematobium,* causes urinary schistosomiasis (Rosenthal, 2020). Beyond relatively fewer instances of an acute febrile illness, the hallmark of the disease caused by all species is chronicity and significant morbidity usually as a result of inflammatory host immune responses to the presence of eggs laid by parasite worms in the body tissues (McManus et al., 2018).

In urinary schistosomiasis, typical acute – to – chronic presentations include haematuria (blood in the urine), dysuria (painful urination), anemia, anorexia, weight loss, weakness, fluid in the ureters, fluid in the kidneys, urinary tract infections, chronic kidney disease, and bladder wall carcinoma (Rosenthal, 2020). Urogenital schistosomiasis has also been associated with an increased risk for HIV transmission (Kjetland et al., February 2006). In areas of endemicity, the highest infection prevalence is usually recorded among children, especially school-aged between 4 and 17, and young adults in typically poor communities (WHO, 2019a).

Figure 1. Life Cycle & Schistosome Transmission (Rosenthal, 2020).



The cycle of schistosome transmission begins when water bodies are contaminated with miracidia which hatch from eggs shed in the feces and urine of infected individuals. Miracidia develop & multiply exponentially in intermediate - host freshwater snails which then excrete the infective free-living cercariae that penetrate the human skin upon water contact (Colley et al., 2014). Apparent, therefore, in the transmission pathway and life cycle of schistosomes, is an intricate link with Water, Sanitation, and Hygiene (WASH). Moreover, a peculiarity of schistosomiasis as a water-borne disease is evident in how humans get infected by schistosome cercariae; through skin penetration from contact with rather than ingestion of contaminated water (Braun, Grimes, & Templeton, 2018). Sanitation in WASH refers to the containment of human excreta. Its peculiarity in schistosomiasis can also be appreciated by its relatively indirect contribution to infection; in that water bodies have to be contaminated and fresh-water snails penetrated rather than waste matter directly ingested (Grimes et al., 2015).

Problem Statement

While the role of sanitation might be obvious for intestinal schistosomiasis, understanding its role in urinary schistosomiasis would be rewarding; seemingly a more indirect pathway to measure for *S. haematobium*. Outside of control of the intermediate host snails, WASH public health interventions that target schistosome transmission could concentrate on preventing human contact with contaminated water and/or prevention of water contamination in itself (Evan Secor, 2014).

Many WASH interventions have aimed at demonstrating a reduction of schistosomiasis prevalence by focusing on the provision of safe water sources and have documented a consequent reduction in water contact (Grimes et al., 2015). A few other interventions, such as one reported in a Ghanaian study (2012), have been created to specifically reduce contamination with contaminated water (Kosinski et al., 2012). However, countries that have accomplished large strides in reducing schistosomiasis prevalence and transmission are places where robust economic development occurred over time. These developments naturally incorporated all aspects of WASH – including safe water & adequate sanitation (Secor & Colley, 2018).

Grimes et al.(2015) highlight the complex role that sanitation plays in their review; portraying it as a perplexing one to determine, not only as a result of disproportionate reproduction ratio of miracidia to cercariae, but also due to the important contribution of the population setting or context in determining its role and that of water contact for schistosome transmission in that setting. They conclude that the roles of water and sanitation pathways in schistosome transmission among a population are usually specific to that setting (Grimes et al., 2015, p. 5).

In the last ten years, there has been increased awareness and intensification of the global commitment towards the control of NTDs generally by donor bodies, national and international health programs. An example of this commitment is communicated in the London Declaration on Neglected Tropical Diseases (2012). A recurring theme, however, is the need for data to inform the nature and sustainability of programs (Development, 2012). The current control strategy championed by the World Health Organization(WHO) in the last WHA resolution (2012) is focused on providing preventive chemotherapy with praziquantel to at-risk populations in endemic regions that have a disease prevalence of 10 – 50% like Nigeria. They recommend the incorporation of additional measures like health education and WASH only after some level of transmission reduction has been achieved (Freeman et al., 2013).

In the time since, it has become increasingly apparent that whether it be chemotherapy alone or a more integrated approach, “emphasis has to be put on laying the groundwork necessary” (Secor & Colley, 2018, p. 1). For endemic areas, there is always a risk of rapid reinfection which renders unsustained MDA counterproductive. International praziquantel supply, albeit increased in the past decade, has not been sufficient to meet the need even for one-time campaigns. (WHO, 2013). Moreover, context-specific data is needed to determine what the minimal WASH levels are needed for a setting. And for this data to be generated, “interventions beyond MDA must become widely available” (Secor & Colley, 2018, p. 1). Provision of safe water and adequate sanitation have been key game changers in successful schistosomiasis control programs and are always options for an integrated approach; one that allows for efficient use of the resources available to achieve a more sustainable schistosomiasis control (M. D. French et al., 2018).

Nigeria, Africa’s most populous country, has the largest number of people infected with schistosomiasis – about 26% of all infected sub-Saharan Africans (Dawaki et al., 2016). Although both *S. mansoni* & *S. haematobium* are prevalent; a recent review documented *S. haematobium* as the most prevalent species in Nigeria. (Ezeh, Onyekwelu, Akinwale, Shan, & Wei, 2019). If “sub-Saharan Africa could lose US $3.5 billion of economic productivity every year as a result of schistosomiasis”

(Tanser, Azongo, Vandormael, Bärnighausen, & Appleton, 2018), then about 26% of this loss is realized in Nigeria alone. The WHA 65.21 resolution named 2018 as the milestone for all top 10 endemic countries to initiate control programs. Nigeria is yet to take up this mantle; most probably due to a lack of more suitable data that could guide the development of a national strategy (WHO, 2013). Praziquantel campaigns targeting schistosomiasis in Nigeria have been sporadic at best, with no improvement in consistency since the last WHA resolution. (Ojurongbe et al., 2014). For Nigeria to tackle schistosomiasis headlong, there is a need for ownership and commitment to what would is sure to be a long undertaking. This would be made feasible by a strong foundation of situational data (M. French & Evans, 2019).

Purpose Statement

This pilot study for this thesis was carried out in five endemic Local Government Areas (LGAs) Kano, Nigeria – a northern state in which both intestinal and urinary schistosomiasis are endemic (Abdulkadir et al., 2017). The population surveyed was school-aged children from ages 4 to 18 years. Nested in primary research to discriminate between tools for optimal urinary schistosomiasis diagnosis, this survey specifically aimed to create a background for much stronger epidemiological assessment of the individual and joint roles that contact with contaminated water and sanitation behaviors play in this population. With the recent robust research into S. mansoni and *S. haematobium* in Kano residents by Dawaki et al (2016), this pilot study ultimately hopes to create traction that draws attention to this population and aid implementation of adequate schistosomiasis control programs for this setting.

Research Question

What are the individual and combined effects of human water contact and sanitation practices on the prevalence of *Schistosoma haematobium* (Urinary blood fluke) among school-aged children in Kano, Nigeria?

Null Hypothesis: There is no difference between the individual and combined effects of water contact and sanitation practices on the prevalence of *Schistosoma haematobium* for this population.

Significance Statement

A highly diverse and "multi-ethnic country" with 380 languages, Nigeria, more than any other, needs suitably designed programs to tackle myriads of health issues, including schistosomiasis (Adedini, Odimegwu, Bamiwuye, Fadeyibi, & De Wet, 2014). Setting-specific data to guide initiation of, commitment to, and efficient delivery of any health program is necessary for the different affected regions. Several prevalence studies carried out in different states of Nigeria are currently being used to provide statistics as needed. However, the consensus is that Nigeria does need more situational data for the promise of any successful control strategy. There is a call for more targeted data to inform the best use of resources for the Nigerian context; in the event of favorable political will and available funding (Ezeh et al., 2019).

It is indisputable that water and sanitation contribute considerably to the transmission of schistosomiasis. It has been argued that the more indirect role of sanitation, and probably some of the complexity in effecting it as a public health intervention might relegate it to the background in the design of WASH programs targeting schistosomiasis (Grimes et al., 2015). The demand for long term commitment in the combat of schistosomiasis necessitates understanding all possible tools and approaches possible for the undertaking. A country like Nigeria with not only the highest cases of schistosomiasis, but also repeatedly unsustained or failed myriad public health interventions can benefit from every foresight (Muhammad, Abdulkareem, & Chowdhury, 2017).

What is an estimate of the role water contact plays in urinary schistosomiasis for this population? What does the estimate for sanitation look like? Is there a combined effect worth noting? Ultimately, one role isn't magnified over the other – water contact over sanitation or vice versa and allocated resources are efficiently used. This pilot investigation aims to provide these estimates for Kano, Nigeria. It hopes to highlight the WASH roles in transmission for this setting and leverage its findings for stronger and more robust causal investigations that a national strategy or programs can run with.

II. LITERATURE REVIEW

Introduction

Urinary or urogenital schistosomiasis alludes to *Schistosoma haematobium's* characteristic invasion of the urinary system, unlike other species that cause intestinal schistosomiasis (Gryseels, Polman, Clerinx, & Kestens, 2006). Nevertheless, like other schistosomes, the hallmark of the infection with *S. haematobium*, usually irrespective of intensity, is characterized by chronicity that culminates in significant morbidity (C. H. King, Sturrock, Kariuki, & Hamburger, 2006). A case burden of around 250 million and an at-risk population of about 779 million people convey how substantial the healthy years of life lost to the disease is – 90% of which is shouldered by sub-Saharan Africa (SSA) and 26% of this 90% by Nigeria (Hajissa et al., 2018; Tanser et al., 2018). In this regard, schistosomiasis has been referred to as "the most important water-based disease"(P. Steinmann, J. Keiser, R. Bos, M. Tanner, & J. Utzinger, 2006).

Unfortunately, the age-old battle against schistosomiasis has neither been easy nor straightforward (Bergquist, 2013). Albeit waterborne, schistosomiasis demonstrates one of its major complexities in that humans are not infected after ingesting contaminated water, but rather after infective worms penetrate the human skin (Grimes et al., 2015). The processes involved in water contamination by miracidia from human excreta, development of miracidia to cercariae in intermediate-host snails, and infection of human hosts with cercariae tend to overlap

(Holveck et al., 2007). Ambiguity persists when both urinary and intestinal schistosomiasis are prevalent in a population (M. D. French et al., 2018).

Possible Areas of Intervention Within the Transmission Cycle

In order to combat urinary schistosomiasis, four main areas that could inform the choice of intervention have been identified. I) The major strategy employed for "morbidity control", the worm burden in the human body could be targeted for reduction. The lone medication for this is praziquantel. 2) Targeting intermediate *Bulinus* snail hosts. 3) Preventing contamination of water bodies with the urine of infected human hosts. 4) Preventing contact between contaminated water and human skin (Rollinson et al., 2013).

Morbidity control with praziquantel is the programming approach recommended by the World Health Organization for many endemic countries, especially because it is invariably the quickest and easiest to carry out on a large scale (WHO, 2013). This has generally been implemented as school-based mass drug administrations. However, for many reasons, including the short-sightedness of treating symptoms instead of the source, there has been mounting evidence portraying the need for more integrated and sustainable approaches (C. H. King, 2009).

To name a few challenges documented in SSA, cure rates after drug administration have been demonstrated to be often suboptimal (Doenhoff et al., 2009; N'Goran et al., 2001); Infection levels return to baseline magnitudes after a maximum of two years(Gray et al., 2010); funding has been unsustainable; and there are looming issues of praziquantel resistance (Hotez, Engels, Fenwick, & Savioli, 2010). Research into the few instances of mass drug administration that have taken place in endemic regions within Nigeria has also proven the paucity, inconsistent programming and return-to-baseline infection levels (Chiamah, Ubachukwu, Anorue, & Ebi, 2019; Garba et al., 2013).

Any move toward the second area of intervention, which involves targeting intermediate host snails biologically, chemically or environmentally could arguably be the most rewarding approach (Angelo et al., 2018). This is because the absence of intermediate host snails is nearly equivalent to the absence of the infection. More affluent countries have been able to anchor schistosomiasis elimination on annihilating the implicated snail species (Sokolow et al., 2016). One lesson that stands out from China's 50-year war against *S. japonicum*, a species that causes intestinal schistosomiasis, is that the "snail control" undertaking requires substantial commitment - an intensive and very expensive commitment (Wang, Utzinger, & Zhou, 2008).

Few countries such as Saudi Arabia, Tunisia, Mauritius, and Egypt that have achieved significant control and/or elimination of *S.haematobium* have occasionally in their integrated schistosomiasis programming, supplemented with snail control when feasible (Knopp et al., 2013). Notwithstanding, the bulk of strategies employed in these countries have revolved around development, behavioral modification and political commitment toward local water, sanitation and hygiene structuring (Secor & Colley, 2018).

Water Sanitation and Hygiene in *S.haematobium* Transmission

In 2010, Bartram and Cairncross began to develop the idea that in spite of being an obvious necessity, Water, Sanitation and Hygiene (WASH) had become one of the "forgotten foundations of health" (p. 1). This points to the characteristic tie of neglected diseases like schistosomiasis to an inherent detriment in WASH systems within any affected population. And in that the disease is neglected, WASH systems are typically found lacking (Charles H. King, 2017). A notable occurrence is that many successes against schistosomiasis have been achieved due to a natural improvement in WASH structures concurrent with economic development while most others have been intentional commitments (Bergquist, 2013).

Egypt, Tunisia, and Algeria stand out in Africa as countries that have made huge strides in the intentional control and/or elimination of *S.haematobium*. In all, minimal progress is being realized in endemic areas of Africa to the south of the Sahara (Rollinson et al., 2013; J. Utzinger et al., 2009). After assessing the near-stagnant cycles of schistosomiasis control in SSA, Stothard, Chitsulo, Kristensen, and Utzinger (2009) emphasize the inescapable need for integration of WASH focused interventions with morbidity control to achieve more sustainable outcomes (p. 1).

For a simple sketch, the "water" component of *S.haematobium* transmission is rooted in water contamination and exposure to contaminated water. Sanitation, which is the containment of human excreta, is also related to water contamination; from direct urination into the water body to more complex mechanisms that might link a lack of sanitation to water contamination (Grimes et al., 2015). Water contamination and contact are both human acts. Therefore, hygiene, which is contingent on human behavior, could very much be the backbone of both water and sanitation (Lansdown et al., 2002). The strength of this behavioral determinant in transmission has become a propellant of the need to understand socio-ecological and eco-epidemiological contexts within which frailties in WASH structures act to determine infection prevalence and intensity so as to tailor behavioral interventions appropriately (J. Russell Stothard, French, Khamis, Basáñez, & Rollinson, 2009).

The Importance of Eco-epidemiological and Socioecological Context

The century-long fight against schistosomiasis is in complete agreement of the fact that the "infection is highly focal, often with substantial heterogeneity between neighboring communities (M. French & Evans, 2019)." Clements et al (2009) were able to apply Bayesian geostatistical prediction tools to evaluate the variations of local *S.haematobium* infection in Burkina Faso, Mali, and the Niger. They provide evidence that local infection or transmission patterns are not always representative of the whole and that variability should be expected within the same geographical location. (pp. 921 - 927).

This setting-specific approach to research and control also extends to praziquantel delivery and snail management. The underpinnings of other major lessons from China's incredible success against *S. japonicum* is found in the significance of adapting strategies to different settings within the country (Wang et al., 2008). Findings from an assessment of drug response and reinfection rates after praziquantel treatment of *S.haematobium* infection in an endemic region of the Ivory coast supports the reasoning that even a seemingly straightforward approach could require population-specific knowledge (N'Goran et al., 2001). Within integrated control, therefore, is the importance of local context.

Creating WASH solutions for urinary schistosomiasis has likewise been neither clear cut nor seamless (Freeman et al., 2013). Usual directions have involved doing what seemed obvious – providing safe water sources. However, due to several factors, specifically hinged on understanding the setting-specific roles of water contamination and water contact, results have varied for different interventions with varying indicators measuring impact in varying populations (Aagaard-Hansen, Mwanga, & Bruun, 2009).

As the response to the urge for more research into transmission dynamics that pertains to WASH increases, the most basic of questions that arise revolve around determining which factor limits transmission in a population and the extent to which it does (Colley & Secor, 2007; Grimes et al., 2015). Is water contact a sole limiting factor? What role does poor sanitation play in the setting? And how unprofitable might focusing on one over the other be?

Understanding the Role of Contact with Contaminated Water

Human contact with contaminated water is the frame of reference within which both schistosome penetration of the human skin occurs and contamination of water with infected urine is most likely to occur. For this reason, "water contact" has remained a prime determining factor of infection intensity and prevalence (Bruun & Aagaard-Hansen, 2008). Because most endemic regions like those in Nigeria typically lack potable water sources, water contact is almost inevitable, even besides recreational reasons (Espino, Koops, Manderson, Research, & Training in Tropical, 2004). Therefore, research has sought to prove this association in myriad settings. In addition, different water–based interventions have been evaluated to quantify their effects on *S. haematobium* transmission in different settings. What has proved most apparent, outside of unavoidable research limitations, are the intricate complexities of estimating indices for water contact or the factors associated with it and then providing context-appropriate interventions that are impactful enough to prevent it (Aagaard-Hansen et al., 2009).

Many studies in sub-Saharan Africa have been able to prove an association between proximity of an affected population to the prevalence of urinary schistosomiasis (J. Utzinger et al., 2009). Others have linked infection incidence with the development of large water dams or irrigation systems (P. Steinmann et al., 2006). Studies in Kenya that modeled the adjusted odds of infection based on estimated water contact with snail infested water bodies have proven increased odds (Clennon, Mungai, Muchiri, King, & Kitron, 2006). Rudge et al. (2008) assessed high-risk behaviors involved in transmission for a Zanzibar setting. They reported the significance of evaluating water contact patterns as a platform for further estimating behavior (pp. 45 - 53). In some instances, null associations have been found and in others, ambiguity (J. Russell Stothard et al., 2009). One study explored water contact practices among girls in rural South Africa but could not estimate any differential effects between those who reported exposure and those who did not (Thomassen Morgas, Kvalsvig, Taylor, Gundersen, & Kjetland, 2010).

Water-based interventions have varied in their impact as much as the type of intervention and settings have varied. It is accepted that the peculiarities of schistosome transmission and behavioral context have manifested as difficulty in reducing water contact by simply providing safer water sources (Grimes et al., 2015). Consequently, some interventions have focused on and recorded a reduction in water contact as a proxy for the reduction in infection burden (Tchuem Tchuenté, Southgate, Webster, De Bont, & Vercruysse, 2001). One Ghanaian intervention was able to measure significant reduction in prevalence of *S.haematobium* after the provision of a safe water recreation area. This is an example of a tailored intervention (Kosinski et al., 2012).

Understanding the Role of Poor Sanitation

Uncertainties surround the role that lack of sanitation plays in transmission and prevalence of urinary schistosomiasis, including how to measure its effect (Asaolu & Ofoezie, 2003). The proportion with which miracidia from water contamination multiplies into cercariae from intermediate host snails is usually exponential, reasoning that might be behind focusing on provision of safe water sources alone. However, this reproductive potential has mainly been measured for intestinal schistosomiasis (Grimes et al., 2015). Furthermore, the effect of sanitation on direct urination into water bodies is vague. While some findings suggest that this gives sanitation a pivotal influence, others simply have not estimated its role (Bruun & Aagaard-Hansen, 2008).

Another interesting challenge is that intestinal and urinary schistosomiasis are typically co-endemic within countries like Nigeria and so how proportionate could keeping stool from contaminating water bodies be with preventing urine contamination (Rollinson, 2009)? Also, the urge to urinate is increased in urinary schistosomiasis and reportedly relieved with the cooling effect of immersion in water (Rudge et al., 2008). Besides, the provision of sanitation infrastructure has not always translated into use or sustained use which is due to several interwoven factors that have to be considered in choosing the type of sanitation solution that would be beneficial. This has been a narrative in many sanitation programs within Nigeria (Asaolu & Ofoezie, 2003).

A detailed study in Zanzibar found significantly increased odds of *S. haematobium* infection due to the actual act of urinating in water (J. Russell Stothard et al., 2009). An ensuing study found reduced odds of infection among those who had latrines in their homes (Knopp et al., 2013). Some other estimations have been indirect, such as simply demonstrating correlations in areas that lack sanitation (Liao et al., 2011). A review of control and elimination strategies all over the world found a few effects of sanitation improvements alone on prevalence comparable to the provision of safe water sources together with sanitation improvements (Asaolu & Ofoezie, 2003). A post sanitation behavioral intervention in Tanzania was able to achieve a secondary effect of reduction in water contact and a review of WASH improvements with economic developments noted more significant reductions in prevalence when both sanitation access and water sources were improved (Mwanga & Lwambo, 2013).

Overview of Situational Analyses in Nigeria

S.haematobium is documented as the more prevalent species in all regions of Nigeria – Northwest, Northeast, Northcentral, Southwest, and Southeast (Abdulkadir et al., 2017). However, *S.mansoni* tends to exist concurrently in many states, including Kano in the Northwest (Dawaki et al., 2015). Across both species, a 2015 review estimated about 29 million infected people; 55% of whom were children (Adenowo, Oyinloye, Ogunyinka, & Kappo, 2015). The distribution of urinary schistosomiasis is characteristic in that it has mostly been reported among the rural and peri-urban poor who have limited to no potable water sources and improved sanitation. Populations in Northern Nigeria are generally the most representative of this description (Muhammad et al., 2017).

Per the last WHA resolution by the world health organization, Nigeria released a strategy for control, elimination, and strategy in 2012 (WHO, 2013). The strategy highlighted the urgent need for situational analysis and mapping of the disease across all local endemic sites to generate data suitable enough to guide a national control plan. It also took care to specify the need for integrating WASH measures along with the recommended praziquantel chemotherapy as the latter was not sustainable (Onyebuchi, 2012).

Notably, the bulk of research carried out in the past two decades has mainly sought to estimate prevalence and demographics within the settings studied – seeking to generate data that displays endemicity in Nigeria (Ezeh et al., 2019). Studies estimating prevalence levels after praziquantel administration have portrayed this control measure as unreliable (Chiamah et al., 2019; Garba et al., 2013). Some have estimated correlations between *S.haematobium* and other infections involving the urinary tract (Eyong, Ikpeneme, & Ekanem, 2008; Nmorsi, Kwandu, & Ebiaguanye, 2007). Others have focused on mapping out snail populations in some settings (Abe et al., 2018; Akinwale et al., 2011).

Amongst the wealth of prevalence studies are a few investigations into determinants of infection, particularly to establish risk associated with water sources. A 50-year review of urinary Schistosomiasis by Ezeh, Onyekwelu, Akinwale, Shan, and Wei (2019) surveyed 47 out of 323 Nigerian dams and reported that 96% of surveyed dams were located in hyperendemic regions of the country (pp. 1 - 2). One study in southwestern Nigeria was also able to model an association between infection and proximity to a local water source (Ugbomoiko, Ofoezie, Okoye, & Heukelbach, 2010). Eight years after the provision of a safe water source to a community in the South, Ekanem et al. (2017) were able to demonstrate a significant reduction in *S.haematobium* prevalence from 51% to 15% (p. 1).

In Northern Nigeria where Kano state is, research that estimates correlations between water contact activities among school children and prevalence of *S.haematobium* has increased over the past decade (Amuta & Houmsou, 2014; Atalabi, Adoh, & Eze, 2018; Singh, Muddasiru, & Singh, 2016). One of these was able to report the actual increase in odds of infection with water contact activities (Umar et al., 2017). So far in Kano, a relatively comprehensive mapping was carried out between 2005 and 2007 which revealed an *S.haematobium* prevalence range of 18%

to 64%. Dawaki et al. (2016), in response to the need for more research that directly estimates risk patterns in Kano, further carried out a hypothesis-generating analysis of some risk factors correlated with combined Schistosoma infections in 5 endemic kano districts (p. 1).

Most studies in Nigeria that have assessed risk factors for *S.haematobium* have mainly reported correlations or prevalence estimates among those who engage in water contact activities. Strengths of association were rarely determined as valid estimates that could inform much-needed programming or more in-depth research. Furthermore, hardly any evaluation of the role of poor sanitation among affected populations is documented.

Conclusion

Urinary Schistosomiasis is a neglected disease and a disease of poverty particularly confined to the rural poor in sub-Saharan Africa who disproportionately lack access to safe water sources and improved sanitation (Freeman et al., 2013; Kullmann et al., 2018). Strikingly, it has been found that "disparities between the rich and poor are much greater in sanitation than in water" (Moe, 2009). Nigeria aptly models this narrative in that only 26% of the population have access to improved sanitation sources and twice of that, some access to safer water sources. What might be more important to note, however, is that populations who lack access to safe water typically lack access to sanitation (Akpabio, 2012).

The "neglect" of diseases like schistosomiasis occurs at both global and national levels in the world (Holveck et al., 2007). This reality, in addition to the level of integration and commitment required for disease control and elimination, creates an inevitable need for the efficient use of limited resources available sustainably. Nigeria, just like many other endemic nations, is in the race against time and disease complications to develop current and practical guidelines for its different settings (Ezeh et al., 2019).

Within *S. haematobium* transmission, the overlapping intricacies of water contamination, poor sanitation and contact with contaminated water lend credence to a possible need for combined research and combined WASH interventions (C. H. King et al., 2006). It is without reasonable doubt that endemic areas such as Kano Nigeria are not only characteristically proximate to unsafe water bodies but also tend to be areas lacking in sanitation (Jürg Utzinger, N'Goran, Caffrey, & Keiser, 2011).

III. METHODOLOGY

Introduction

This thesis aims to investigate the individual and joint roles of two major exposures - water contact activities and sanitation on the prevalence of urinary schistosomiasis (*S. haematobium*) in Kano, Nigeria.

To this effect, data were taken from a study designed to compare different diagnostic tests for urinary schistosomiasis with a secondary aim to analyze WASH factors associated with infection. This cross-sectional pilot was carried out between June and July of 2019 in select Local Government Areas (LGAs) of Kano.

Study Area

Kano state (11^{o}30'N 8^{o}30'E), located in the central part of Northern Nigeria, is the most populous of the Nigerian states with 13,076,872 people (Portal, 2020). It has an altitude of 400 – 800m above sea level, average annual rainfall of about 800 to 900mm, Sudan Savannah vegetation and widely distributed open water bodies. Its climate is tropical with two predominant seasons – wet (June to September) and dry (October to May). The Hausa and Fulani are the main tribes and they practice agriculture as one of their major occupations (Dawaki et al., 2015).

All of Kano's 44 Local Government Areas (LGAs) were comprehensively mapped between 2005 – 2007 to estimate schistosomiasis prevalence and found to be endemic for *S. haematobium* (Abdullahi, Bassey, & Oyeyi, 2009). Four of the highly endemic LGAs were chosen for this study - Kura with the highest documented prevalence (62%), Minjibir, Gwarzo, and Bebeji. The kano Municipal area, expected to have relatively lower prevalence, was chosen as a fifth study site (Bassey & Umar, 2004) – Figure 1.

Study Population and Sample

Pre-school and school-aged children between 4 to 18 years of age were the participants from whom urine samples were collected and screened laboratory diagnosis of *S. haematobium*. Follow up questionnaires that mainly assessed a few participant characteristics, WASH - related behavior, disease awareness, and previous praziquantel campaigns were administered to every participant, along with their guardians.

A priori simple random sample size of 275, accounting for a likely 10% loss of data, was estimated based on recently documented prevalence from a survey that had been conducted in three of the LGAs being assessed (Dawaki et al., 2016). Notably, this survey had sampled individuals of all age groups and their reported prevalence of 17.8% used in our sample size calculation was for both *S. haematobium* and *S. mansoni* infections.

The main pediatric General Hospital or Primary Health Center (PHC) in each LGA was chosen as enrollment site.

Data Collection

Data collection was implemented on an on-going basis until the sample size was attained. One extra day of collection was added after attaining 275 urine samples for one LGA where mild errors in the collection had been noted during iterative process monitoring and evaluation.

Outpatient days specific to each Healthcare center were used as enrollment days. Two research assistants assigned to each LGA used a randomly selected number to determine recruitment within the healthcare facility. For instance, a random number of '3' meant that every third outpatient between the ages of 4 – 18 who came in during the clinic hours would be screened for willingness to participate and enrolled after they or their guardian consented. Every child less than 18 years of age could only be enrolled if they had a guardian with them. Consent and assent forms were signed by the guardian and participants after the study was explained to them. Children less than 6 years of age gave verbal assent.

Following consent and assent, identification numbers were assigned. The participants were instructed on how to pass urine into 50 ml universal sample containers labeled with their identification numbers. Those who could comprehend were asked to pass "terminal urine" if feasible, but otherwise as much urine as they could. The time of urine collection was between 10:00 am and 2:00 pm which is the reported window for optimal *S. haematobium* egg passage (WHO, 1991, pp. 41-44).

After urine samples were obtained, electronic questionnaires built on the Open Data Kit (ODK) platform were administered to participants, with input from their guardians as required. The interviewers asked the questions and input the answers supplied.

***S.haematobium* Diagnosis**

Each viable sample (intact bottle with at least 12 ml of urine) was initially assessed macroscopically and tested for microhematuria with the dipstick test. 10 ml of urine was thereafter filtered, using the standard nucleopore filtration technique. Each filter paper was then stained with Lugol's iodine before the identification of *S. haematobium* eggs under the microscope (WHO, 1991). Diagnosis of *S. haematobium* infection was recorded as the presence or absence of eggs. One trained Research Assistant and a Graduate microbiologist viewed all the samples. An expert microbiologist subsequently viewed 20% of the samples for validation.

Ethical Considerations

The ethical approval for this study was provided by the Institutional Review Board of Emory University (IRB00111157). Secondary permission was also obtained from the Kano State Ministry of Health. This study included a non-invasive collection of urine samples from human subjects, therefore expedited IRB approval was granted on June 18, 2019, after protocol and research instruments were submitted.

Full procedures, potential risks, and benefits were explained to every participant and guardian, after which informed consent and assent were obtained from guardians and participants before data collection. Consent forms were transcribed to the Local Hausa language and back-translated as recommended by the IRB. Every urine sample and questionnaire entry was de-identified; labeled only with the participant IDs. Finally, every child who tested positive for *S.haematobium* was contacted and prescribed a dose of praziquantel through the hospital management.

The Data

Laboratory data recorded and validated by all three lab scientists were doubly entered into excel. The survey data collected electronically on the ODK platform was automatically uploaded to a server and available in excel format, resulting in two major datasets.

Data preparation and subsequent analyses were done using **SAS 9.4** (**SAS Institute, Inc., Cary, NC**). Individual lab and survey excel files were imported into, cleaned and merged to a final analytical dataset. Further coding, cleaning, and manipulation were performed on this final dataset to prepare the variables needed for analyses.

Missing Data

During questionnaire design, most question options included "don't know" and "refused" in addition to "yes" or "no". For consistency across variables, the approach adopted in the manipulation of variables for this thesis was to recode "don't know" and "refused" data values as "missing" (Winters & Netscher, 2016).

Outcome Measure

For this analysis, the outcome of interest was whether *S. haematobium* was present or not. This measure was already specified in this format from the microscopy results.

The Main Exposures

Six ***water contact activities*** were assessed in the survey: playing, swimming, laundering, working, fetching, and fishing. Participants answered "yes" or "no" to each of these. In consideration of potential correlation between all these binary variables, a scale was created from 0 – 6; ‘0’ representing participants reporting no water contact and ‘6’ representing participants reporting all water contact activities. From this scale, a measure for “exposure intensity” was created as a variable with three levels – 0, 1 and 2. An intensity of ‘0’ was for a scale of 0; ‘1’ was for a scale of 1 – 3 water contact activities; and ‘2’ was for a scale of 4 – 6 water contact activities. The three levels of intensity were labeled as “none”, “moderate/some” and “high” (Table 1).

Sanitation was assessed in this survey by asking for what type of sanitation facility the participants had access to. Participants could choose as many that applied, and the choices ranged from “no facility” to numerous unimproved and improved sanitation types. A dichotomous exposure variable to represent sanitation for analysis was created from this question. This variable was named “unimproved”; coded ‘1’ for those who used unimproved sanitation and ‘0’ for those who did not (Table 1). Unimproved sanitation was created from positive answers to “no facility/open”, “bucket”, “hanging latrines” and “pit latrine without slab” (WHO/UNICEF, 2019).

Confounding Assessment

Other covariates associated with both outcome and either exposure were considered a *priori* as potential confounders:

i. Participant’ age (Osakunor, Woolhouse, & Mutapi, 2018).
ii. Participant’ gender (Zida et al., 2016).
iii. If a guardian had formal education or not (Donohue et al., 2017).

iv. If participant or guardian had heard of schistosomiasis (Folefac et al., 2018).
v. Participant' involvement in subsistence rice farming (Yapi et al., 2005).
vi. Unprotected household water source (Hajissa et al., 2018).

The prevalence of urinary schistosomiasis in this study was not rare (> 10%). Therefore, log-binomial regression was used to estimate Prevalence Ratios (PRs) to more accurately reflect the observed relationships between exposures and disease.

Confounding assessment was carried out to inform which variables would remain in the final model as confounders. With the *gold standard* model containing all six potential confounders above, repeated log-binomial regression models were run to assess different combinations of these variables (*sub-models*); when one or more variables were dropped from the *gold standard* model. PRs for individual exposure-outcome associations from each *sub-model* were compared to the estimates from the *gold standard* to show if there was evidence of confounding (a meaningful >10% change in PR) by the dropped variables. The PRs of the chosen model were meaningfully different from that of the *gold standard*. This model contained four confounders – age, sanitation, farming, and water source.

Modeling Effects

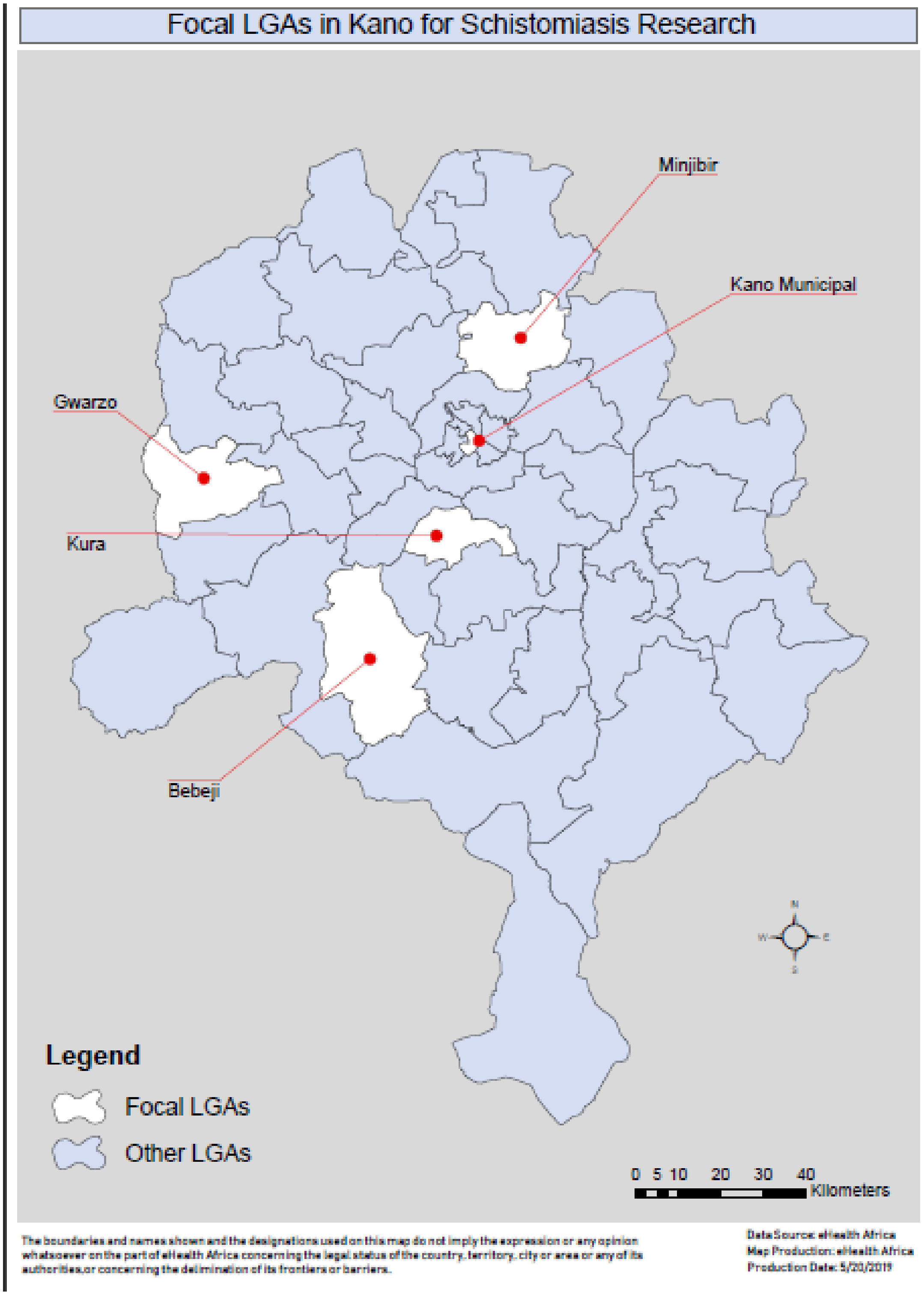
$$\text{Ln (probability of } \textit{S. haematobium}) = \alpha + \beta 1(\text{Water Contact}) + \beta 2(\text{Sanitation}) + \gamma 1(\text{Age}) + \gamma 2(\text{Gender}) + \gamma 3(\text{Farming}) + \gamma 4(\text{Source of Water}) + \delta_1(\text{Water Contact * Sanitation})$$

This analyses modeled the effect of two exposures (water contact and sanitation) on a health outcome (*S. haematobium* infection). The only interaction considered was that between the two exposures of interest. A chunk test was used to access statistical interaction – as one exposure, intensity of water contact, had three levels and was included in the model using dummy variables. An exposure assessment was thereafter conducted for statistical purposes. However, none of the exposures were dropped from the model, as the research goal was to estimate the effect of multiple exposures. Finally, estimate statements were used to determine crude and adjusted effects.

Table1. Variable Specification

VARIABLE DESCRIPTION	CATEGORY	COMPOSITION/ DESCRIPTION	CODING
***S. haematobium* Infection**	OUTCOME	Microscopic diagnosis of S. haematobium	1: present 0: Absent
Intensity of water contact exposure	EXPOSURE 1	Of the water activities assessed, exposure is high if the participant engages in 4 to 6 activities and moderate for 1 to 3 activities.	2: High exposure 1: Some/Moderate exposure 0: No exposure
Type of sanitation	EXPOSURE 2	Various types of sanitation facilities	1: Unimproved 0: Improved
Age	CONFOUNDER	_____	Participants' age
Gender	CONFOUNDER	_____	1: Male 0: Female
Source of water	CONFOUNDER	Reported sources of water for everyday use	1: Unprotected 0: Protected
Farming as a domestic occupation	CONFOUNDER	If participants engaged in farming activities (such as rice farming for this population)	1: Farm 0: Do not farm

Figure1. Local Government Areas



IV. RESULTS

Distribution of Outcome and Exposures

Table 1 shows the overall prevalence of *S. haematobium* for this study. Of the 272 screened urine samples, 102 (37.5%) participants had the infection.

The water contact activities had a total of 242 valid responses after creating the combined intensity scale (Table 2.1). No water contact was recorded for 81 (33.5%) participants. 100 (41.3%) participants had some water contact, while 61 (25.2%) had a high intensity of water contact. Table 2.2 shows that out of a total of 265 participant responses on sanitation type, 80 (30.2%) used unimproved sanitation facilities. 185 (69.8%) used improved facilities.

Of the participants who were positive for *S. haematobium*, 33.7%(n = 34) reported unimproved sanitation use. 84.6% (n = 77) reported engaging in at least one of playing, swimming, laundering, fishing, fetching, or working in local water bodies (Table 3).

Other Participant Characteristics

Table 3 describes the overall participant characteristics of interest and then stratified by the two main exposures. Of the 272 participants screened and surveyed, the mean age was 11.2 (SD = 4.1). Majority of participants (n= 221, 81.6%) were male, while 50 (18.5%) were females. About half of the participants (n=133, 49.1%) got their household water from an unprotected source. Only 39 (14.3%) reported participating in farming as a domestic occupation.

Analytic Sample

The values which were coded as "missing" during variable preparation were excluded from the final analytic sample by the SAS Genmod procedure. The final sample size from which effects were estimated was 242 participants. (Figure 1)

Final adjusted model

At an alpha level of 0.05, the interaction term was found to be insignificant and dropped from the model.

$$\text{Ln (probability of } S.\ haematobium) = \alpha + \beta 1(\text{Water Contact}) + \beta 2(\text{Sanitation}) + \gamma 1(\text{Age}) + \gamma 2(\text{Gender}) + \gamma 3(\text{Farming}) + \gamma 4(\text{Source of Water})$$

The general formulas used for estimating effects were:

- PR for the effect of water contact on *S. haematobium* prevalence: **exp($\beta 1$)**
- PR for the effect of sanitation on *S. haematobium* prevalence: **exp($\beta 2$)**
- PR for the effect of both exposures on *S. haematobium* prevalence: **exp($\beta 1 + \beta 2$)**

Estimated Effects of Individual Exposures

Tables 4 and 5 show the observed measures of association (prevalence ratios) between individual exposures - water contact and sanitation type – and the prevalence of *S. haematobium*. The number of outcome and summary measures for each effect group is also reported in the tables. Table 4 contains crude effects, while the effects in table 5 have been adjusted for age, gender, water source, and domestic farming practices.

For the crude effects, participants who had moderate contact with water bodies were 3.03 times more likely to be infected, 95%CI [1.81, 5.07]. Those who had a high intensity of water contact were 2.41 times more likely to be infected, 95%CI [1.35, 4.32]. However, there was no statistical difference in the association when comparing the levels of water contact (High vs Moderate) with *S. haematobium* prevalence, PR = 0.80, 95 CI [0.55, 1.16]. Also, those with unimproved sanitation were equally likely to be infected with *S. haematobium* compared to those with improved sanitation, PR = 0.93, 95 CI [0.65, 1.35]. When considering the effect of any intensity of water contact alone, these participants were 7.32 times more likely to be infected with *S. haematobium*, 95%CI [2.61, 20.54].

For the adjusted estimates, moderate contact with water bodies was 2.14 times more likely to be associated with prevalence compared with no water contact, 95%CI [1.41, 3.23]. A high intensity of water contact was1.84 times more likely to be associated with prevalence, 95%CI [1.12, 3.03]. Again, there was no statistical difference in the association when comparing the levels of water contact (High vs Moderate) with *S. haematobium* prevalence, PR = 0.86, 95 CI [0.62, 1.21]. And those with unimproved sanitation were equally likely to be infected with *S. haematobium* compared to those with improved sanitation, PR = 0.99, 95 CI [0.72, 1.37]. Regardless of intensity, contact with contaminated water alone was associated with a 3.94 times increased likelihood of infection, 95%CI [1.68, 9.25].

Estimated Effects of Joint Exposure

The crude and adjusted effects of being exposed to both contaminated water and unimproved sanitation on *S. haematobium* prevalence compared to being exposed to neither are also highlighted in tables 4 and 5 respectively. As noted for individual effects, there was no statistical difference in the association when comparing high degree of water contact to some degree of water contact. Therefore, the overall combined effect of both exposures represented by any degree of water contact and the use of unimproved sanitation was also estimated.

For the crude prevalence ratios (table 4), the association of both moderate water contact and unimproved sanitation on prevalence compared to neither was 2.83 times more, 95%CI [1.54, 5.21]. The effect of high intensity of water contact and unimproved sanitation was 2.25, 95%CI [1.22, 4.17]. Overall, having any degree of water contact and unimproved sanitation had 6.83 times increased association with *S. haematobium* prevalence compared with having neither exposure, 95%CI [2.42, 19.30].

For the adjusted prevalence ratios (table 5), the association of both moderate water contact and unimproved sanitation on prevalence compared to neither was 2.11 times more, 95%CI [1.29, 3.48]. The effect of high intensity of water contact and unimproved sanitation was 1.83, 95%CI [1.10, 3.05]. And overall, having any degree of water contact and unimproved sanitation had 3.91 times increased association with *S. haematobium* prevalence compared with neither exposure, 95%CI [1.68, 9.10].

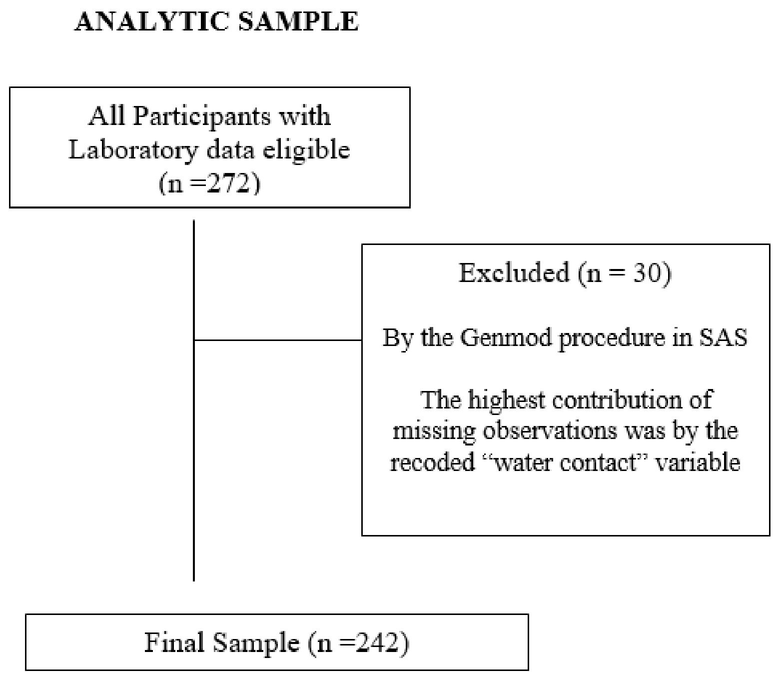


Figure 1. The final sample size utilized in the multivariate modeling.

Table 1. Prevalence of *S. haematobium* infection in this Study Population

***S. haematobium* Infection**	**N (%). Total = 272**
Present	102 (37.5)
Absent	170 (62.50)

Table 2.1. Distribution of water contact activities reported by the participants

Intensity of Water Contact	Water Activity Scale (0 – 6)*	N (%). Total = 242
None	None	81 (33.5)
Some / Moderate	1 – 3 activities	100 (41.3)
High	4 – 6 activities	61 (25.2)

Water activities assessed: playing, swimming, fetching, fishing, laundry, & working*

Table 2.2. Distribution of Sanitation type that participants have access to

Type of Sanitation	N (%). Total = 265
Unimproved	80 (30.2)
Improved	185 (69.8)

Table 3. Participant Characteristics by degree of water contact and type of sanitation

		Intensity of Water Contact / Exposure			Sanitation Type	
Characteristic	**Total (272)** **N (%) or Mean (SD)**	**None** **N (%) or Mean (SD)**	**Some/Moderate** **N (%) or Mean (SD)**	**High** **N (%) or Mean (SD)**	**Improved** **N (%) or Mean (SD)**	**Unimproved** **N (%) or Mean (SD)**
***S. haematobium* Infection**						
Present	102 (37.5)	14 (15.4)	52 (57.1)	25 (27.5)	67 (66.3)	34 (33.7)
Absent	170 (62.5)	67 (44.4)	48 (31.8)	36 (23.8)	118 (72.0)	46 (28.1)
Participant' age	11.2 (4.1)	9.0 (4.1)	11.9 (3.9)	12.9 (3.4)	11.2 (4.3)	11.2 (3.6)
Participant' gender						
Male	221 (81.6)	51 (26.6)	84 (43.8)	57 (29.7)	144 (67.3)	70 (32.7)
Female	50 (18.5)	29 (59.2)	16 (32.7)	4 (8.2)	40 (80.0)	10 (20.0)
Source of Water						
Unprotected	133 (49.1)	31 (26.3)	51 (43.2)	36 (30.5)	85 (66.9)	42 (33.1)
protected	138 (50.9)	50 (40.3)	49 (39.5)	25 (20.2)	100 (72.5)	38 (27.5)
Farming Occupation						
Farm	39 (14.3)	6 (16.2)	22 (59.5)	9 (24.3)	34 (87.2)	5 (12.8)
Do not farm	233 (85.7)	75 (36.6)	78 (38.1)	52 (25.4)	151 (66.8)	75 (33.2)

Table 4. Table of crude effects. Individual and joint associations between exposures and *S. haematobium* prevalence

Exposures		N	Number of *S. haematobium* cases	Crude PR (95% CI)*	P value†
Intensity of Water Contact	**Type of sanitation**				
None	Improved	71	11	Ref. (1.00)	---
Moderate	Improved	80	43	3.03 (1.81, 5.07)	<0.0001
High	Improved	31	13	2.41 (1.35, 4.32)	0.0030
High vs Moderate	Improved	131	65	0.80 (0.55, 1.16)	0.2301
None	Unimproved	10	3	0.93 (0.65, 1.35)	0.7139
Moderate	Unimproved	20	9	2.83 (1.54, 5.21)	0.0008
High	Unimproved	28	11	2.25 (1.22, 4.17)	0.0097
Any (Moderate or High)	Improved	131	65	7.32 (2.61, 20.54)	0.0002
Any (Moderate or High)	Unimproved	128	63	6.83 (2.42, 19.30)	0.0003

Note: Crude model contained both exposures (water contact and sanitation) with no other covariates of interest.

*PR: Prevalence Ratios
†Absolute p values generated by the statistical software (SAS 9.4)

Table 5. Table of adjusted effects. Individual and joint associations between exposures and *S. haematobium* prevalence

Exposures		**N**	**Number of *S. haematobium* cases**	**Adjusted PR (95% CI)***	**P value**
Intensity of Water Contact	**Type of sanitation**				
None	Improved	71	11	Ref. (1.00)	---
Moderate	Improved	80	43	2.14 (1.41, 3.23)	0.0003
High	Improved	31	13	1.84 (1.12, 3.03)	0.0161
High vs Moderate	Improved	131	65	0.86 (0.62, 1.21)	0.3912
None	Unimproved	10	3	0.99 (0.72, 1.37)	0.9593
Moderate	Unimproved	20	9	2.11 (1.29, 3.48)	0.0031
High	Unimproved	28	11	1.83 (1.10, 3.05)	0.0205
Any (Moderate or High)	Improved	131	65	3.94 (1.68, 9.25)	0.0016
Any (Moderate or High)	Unimproved	128	63	3.91 (1.68, 9.10)	0.0016

Note: Adjusted model contained all covariates: exposures and confounding factors.

*Adjusted for participant' age, gender, source of water for domestic use, and engagement in farming activities.
†Absolute p values generated by statistical software (SAS 9.4)

V. DISCUSSION

Key Findings

This thesis examined data from a pilot cross-sectional study that was carried out among school-aged children in Kano Nigeria to estimate the individual and joint effects of water contact and sanitation practices on *S. haematobium* prevalence.

The results of the analyses suggest that water contact *at any degree or intensity* is not only significantly associated with *S. haematobium* prevalence, but also singularly confers the highest magnitude of association with the infection for this population (aPR = 3.94, 95% CI [1.68, 9.25]). Compared to improved sanitation, unimproved sanitation by itself is not significantly associated with prevalence (aPR = 0.99, 95% CI [0.72, 1.37]). Lastly, unimproved sanitation in combination with *any degree of water contact* is significantly associated with *S. haematobium* prevalence with an effect size of 3.91times the likelihood of infection (95% CI [1.68, 9.10]).

Joint Association

This thesis hypothesized that the joint effect of two key constructs, water contact and poor sanitation, which are embedded in the transmission of *S. haematobium* would be significantly higher than the effect size of either singular construct. However, this hypothesis was not confirmed. Although the joint effect of both exposures was significant (aPR = 3.91, 95% CI [1.68, 9.10]), the association remained slightly lower compared to the lone effect of water contact after adjusting for participants' age, gender, farming practices, and water source (aPR = 3.94, 95% CI [1.68, 9.25]).

Comprehensive reviews of previous literature document that the limiting factor for schistosomiasis transmission may differ from setting to setting. They elucidate that while contact with contaminated water is undeniably important, sanitation might play a more pivotal role in some settings and so, figuring out the limiting factor specific to a setting is pertinent for adequate control (Grimes et al., 2014).

The hypothesis tested here considered that regions still endemic for the disease are typically areas lacking in both 'safe' water and 'adequate' sanitation. Also, regions that have achieved significant control or disease eradication are notably those in which significant developmental changes occurred over time, including WASH improvements (Rollinson et al., 2013). Therefore, for WASH-poor Kano, Nigeria, focusing on one limiting factor over another might be counterproductive for significant and sustainable control. This thesis, therefore, sought to generate evidence that might highlight a stronger combined effect of multiple exposures compared to either individual exposure.

Perhaps, the finding of a weaker joint association compared to the effect of water contact alone does not deter from depicting the interwoven connections between the individual Water, Sanitation and Hygiene (WASH) components of schistosomiasis transmission. Indeed, it might serve to underscore this complexity. For instance, investigations into pathophysiologic mechanisms of infection chronicity report that bladder changes result in increased urgency and frequency of micturition. Those infected describe a consequent desire to urinate into water bodies due to the cooling effect of water on the genitals. (Rudge et al., 2008). In this, the co-occurrence of water contamination and poor sanitation behavior can be appreciated within the complex construct of water contact and possibly lends credence still to the call for integrated measures in the battle against schistosomiasis transmission (Akinwale et al., 2011; Gray et al., 2010).

WASH interventions have shown that the provision of safe water sources, while somewhat impactful, has not been synonymous with adequate prevention of contact with contaminated water. Also, the sole provision of hygiene education or sanitation facilities might only cause negligible effects in *S. haematobium* prevalence (Aagaard-Hansen et al., 2009; Grimes et al., 2015; Knopp et al., 2013). So, the reasoning is that the provision of accessible, safe, and functional sanitation facilities should reduce water contamination even during inevitable water contact. However, this needs to be backed by the provision of safe water sources and behavioral interventions that reduce contact with contaminated water (J. R. Stothard et al., 2009).

While this analyses could not generate absolute novel evidence to prove the reasoning above, the intertwined complexion of WASH exposures is still quite apparent and might need to be investigated and measured in a more direct or causal replication of this pilot.

Contact with Contaminated Water

This study was able to reiterate the established consensus that contact with contaminated water remains a principal determinant of schistosomiasis infection

(WHO, 2019a). In analyzing the individual exposures for this setting, water contact was the sole limiting factor. It is apparent from underlying infection mechanisms that this is the most direct pathway in schistosome transmission; in that the infective schistosome cercariae that are excreted into water bodies by intermediate host snails have to penetrate the human skin when it comes into contact with the water (Colley et al., 2014).

In analyzing the association between water contact and prevalence, a scale denoting the degree of water contact was created from six water activities to preclude shrinking the construct of water contact in its quantification. Categories of high and moderate water contact intensities were created from this scale and used in effect estimation. Interestingly, this led to an additional finding that the prevalence of urinary schistosomiasis in this population statistically remained the same regardless of how many water contact activities the participants reportedly engaged in. This might support a strong correlation between the individual water contact activities, in that they aren't necessarily mutually exclusive (Afiukwa et al., 2019; Angelo et al., 2018). It also conveys the possibility that any contact with contaminated water puts individuals at similar levels of risk compared to a cumulative exposure index; thereby portraying a high infection potential of water contact behavior. With this finding, the need for more causal estimation of risk, that incorporates frequency of water contact, for instance, becomes apparent (Grimes et al., 2015).

Also, the collection, preparation, and analysis of "water contact" as a construct support suggestions that the underlying determinants of this behavior might be complex. This ambiguity is repeatedly reported in the evaluation of various water-based interventions that have aimed at reducing *S. haematobium* prevalence. Interventions have differed and underlying indicators of impact measurements have also differed (Aagaard-Hansen et al., 2009). For example, some have provided piped or bore-hole water as a safe water alternative for domestic use and irrigation at the community level. With this, a secondary mitigation of water contact is usually anticipated, but sustainable impact is highly dependent on inherent behavioral practices and how readily available or accessible water sources are (Peter Steinmann, Jennifer Keiser, Robert Bos, Marcel Tanner, & Jürg Utzinger, 2006). A few interventions have directly provided alternate sources of water recreation to detract from continued water contamination and contact. However, the impacts have largely hinged on hygiene behavior and / or functional sanitation infrastructure (Evan Secor, 2014; Kosinski et al., 2012). These lessons need to be incorporated in designing any intervention to reduce or eliminate contact with contaminated water.

Sanitation

In estimating the individual role that sanitation plays on *S.haematobium* prevalence for this population, the measured index was the use of unimproved sanitation compared to improved sanitation facilities and this demonstrated no significant association with prevalence. Notably, preliminary descriptive analysis of this data had shown that a high proportion (70%) of participants infected with *S. haematobium* reported the use of improved sanitation facilities as opposed to unimproved facilities. This is a remarkable finding since endemic regions such as

Kano, Nigeria are also typically deficient in adequate sanitation (Liao et al., 2011) (Akpabio, 2012) (Kullmann et al., 2018).

Relatively few studies have been carried out and able to demonstrate lower odds of infection with improved sanitation (Grimes et al., 2014). In particular, those that have collected adequate data to demonstrate that those with improved sanitation had the facilities in their homes (Knopp et al., 2013). Overall, however, investigations into the role that sanitation plays has majorly involved evaluating combined sanitation and hygiene interventions (Rollinson et al., 2013).

Peradventure, the insignificant finding here does more to support the complexity of measuring sanitation as a construct and in the context of schistosomiasis transmission (Grimes et al., 2015). Reviews of many schistosomiasis related interventions have found it difficult to estimate the role of sanitation due to differing indicators. In Nigeria, for instance, the availability of improved sanitation infrastructure has repeatedly unequaled its use because said infrastructure might be inaccessible or nonfunctional (Asaolu & Ofoezie, 2003).

Furthermore, the construct of sanitation might be embedded within the measurement of “water contact” wherein initial water contamination occurs. There is an increasing need to define “use” and “access” as regards sanitation infrastructure. The latter could include safety, privacy, facility cleanliness, distance to facility, functionality during the rainy season, shared access, and so on (Hulland et al., 2015). There are also calls for more nuanced approaches in collecting information about sanitation due to interviewer biases and stigma that could be related to inadequate facilities (WHO, 2019b).

Strengths and Limitations

Context is highly important and informs relevant data–driven strategy for schistosomiasis interventions. The factors influencing prevalence have been known to vary within regions of a country (Clements et al., 2009). This study exhibited strength in highlighting the roles played by the investigated exposures on disease for the specific context of Kano Nigeria. The simple random sampling strategy employed reduced bias; electronic coding and collection minimized data entry errors, and the population of school-aged children used is suitable for inference comparable to other studies. Albeit a small study, it was able to generate transparent and directly applicable evidence that highlights the interwoven intricacies of the WASH factors on schistosomiasis transmission.

However, due to several limitations, caution should be employed in interpreting the findings of this study. This pilot could only cover five Local Government Areas (LGAs). Furthermore, the simple random sampling strategy employed would be limited in the generalizability of findings to the entire region of Kano. For better inference, complex sampling methods would be more representative – weighted based on previous prevalence estimates for the different LGAs. Self - reported answers to the survey questions are liable to recall and interviewer biases. Also, the cross-sectional and observational nature of this study limits adequate measurements of exposures and causal inference from results. Ffinally, there is an apparent weakness in the way data on sanitation was collected. The questionnaire assessing type of sanitation facility did not account for customary use of, actual access to, and functionality of sanitation infrastructure. In addition, a pertinent assessment of sanitation behavior for this peculiar water-borne disease, such as the occurrence and frequency in which participants urinated into water bodies was not collected (Grimes et al., 2015). Future research would benefit from the rigorous application of principles and guidelines for the collection of WASH information (Gine, Jiménez Fdez de Palencia, & Pérez-Foguet, 2013).

Implications for Practice and Research

The findings of this study emphasize the significant role of water contact in the prevalence of urinary schistosomiasis for the Kano population of Nigeria. It particularly goes further to portray that this exposure - disease association is possibly the key limiting factor for this setting when compared to poor sanitation. Although the estimated role of joint water contact and sanitation exposures was slightly lower than the singular role of water contact, its significant effect size is not hastily discarded as it presents a novel leverage for further research that could support the need for integrated WASH research and interventions in the battle against schistosomiasis.

Nigeria, the country with the most cases of infection, is in dire need of more relevant data to inform a targeted national strategy (Ezeh et al., 2019). Without a doubt, highly endemic regions such as in Kano, are lacking across all WASH indices (Akpabio, 2012). For these data and in this setting, although water contact was demonstrated as a limiting factor and sanitation was not, we interpret these observational findings with care and recognize that while solutions to poor sanitation alone may not be pivotal for control, sanitation behavior is still embedded in water contact. Robust research is therefore necessary to investigate if disease transmission would likely continue if both constructs are not attended to concurrently or if adequately designed programs targeting water contact alone might end up killing two birds with one stone (Rollinson, 2009).

In conclusion, this pilot does not only begin to highlight the complex inter-relations between individual WASH components in *Schistosoma haematobium* infection. It also provides direction for more focused causal research to estimate risk and control strategies that consider the combined roles of WASH exposures.

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