Determinants of Population Variability in HIV across West Africa: Ecological and Mathematical Modelling Analyses.

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Abstract

Introduction

Mathematical models of HIV transmission have played an important role in helping to understand the drivers of the HIV epidemic, and shape the global HIV response. The underlying approaches, assumptions and structures used in HIV modelling have the potential to fundamentally influence the conclusions of any modelling analyses. For this reason, it is important that approaches to modelling HIV transmission in different contexts carefully consider how best to 'characterise' a populations distribution of risk and networks of sexual interaction based on data, and the implications of incorporating different levels of epidemiological complexity into their modelling.

Across West Africa there are substantial variations in population HIV prevalence - ranging from 0.5-6%. To date, there has been limited exploration of the potential factors influencing this population variation.

This PhD aims to inform our understanding of the determinants of population variations in HIV prevalence across West Africa, using a combination of ecological analysis of population data, and both simple and more complex epidemiological modelling. The findings are used both to explore the determinants of HIV transmission across West Africa, and to discuss the implications for future modelling and epidemic appraisal approaches.

Methods

A range of modelling and epidemiological analytical approaches were used. Firstly, an existing policy model, The Modes of Transmission (MoT) model, designed to predict patterns of HIV incidence, was revised and re-parameterised using data from Nigeria, to explore the effect on overall conclusions of adding additional heterogeneity into the model, and considering more explicitly how to model HIV risk amongst lower-risk subgroups.

Secondly, population data from 13 West African countries were compiled. Linear regression analyses were used to assess potential relationships between HIV prevalence in high-risk groups and population HIV prevalence and the size of high-risk population subgroups and HIV prevalence in the general population.

Based on the findings from the MoT and ecological analysis, a dynamic deterministic model was developed to explore the variations in HIV prevalence across West Africa. The population model not only included sex work, client and general population sub-groups, but also included a category of adolescent females (15-24) and a category of males with multiple sexual partners, with a mixing formulation being used to vary the degree the adolescent females form partnerships with clients of female sex workers and the subgroup of males who have multiple partnerships

Input parameters were sampled from ranges relevant for West Africa, using Latin Hypercube sampling. The model was fitted to equilibrium prevalence in the general population.

Results:

A critique and revisions to the MoT, identified high levels of infections in previously unrecognised subgroups. These included 16% of new infections occurring in young females engaging in transactional sex.

Findings from the ecological analysis, showed that across West Africa HIV prevalence in FSWs and their clients is not associated with higher HIV prevalence in the general population. Instead, the size of groups of males and females with multiple partners is correlated with higher HIV prevalence levels.

The deterministic model generated 11000 fits. Grouping fits, based on epidemic size (with 1% incremental increases from 0-6%), the findings revealed that population sizes of key subgroups is the predominant driver of the epidemic. For epidemics where prevalence is less than 3%, FSW population size is the most important determinant of HIV prevalence. For epidemics above 3%, it is the size of the group of adolescent females with multiple partners and their level of interaction with clients of FSWs that is the most significant variable related to higher HIV prevalence. When the limiting effects on HIV transmission of male circumcision are removed from the model, the findings are less clear, with both sex work and the role of adolescent females with multiple partners being important determinants of the epidemic.

Circumcision is however shown to significantly limit the magnitude of an epidemic and epidemic categorisation should account for these variations accordingly.

Conclusions

Behavioural heterogeneity has long been recognised as an important component of model development. The results from this thesis show the importance of carefully considering how to compartmentalise population HIV models. Even for simple static models, the inclusion of additional subgroups change model conclusions and suggests different intervention priorities.

The use of results and findings from ecological analyses, whilst unable to provide strong evidence of causality, can provide useful insights into the relationship between population level factors or behavioural variables and HIV prevalence in the general population. These findings may then be used to inform model development.

Deterministic dynamic modelling used in this thesis demonstrates that the size and sexual networks of vulnerable subgroups in the population may be of key importance in determining levels of HIV epidemics in West Africa. In-particular, adolescent females engaging in non-commercial multiple partnerships, often associated with transactional exchange are an important determinant of the HIV epidemic in West Africa. An improved understanding of this group, their size and motivations for engaging in multiple partnerships, through the use of epidemic mapping techniques and social research, will be important to future HIV intervention activities.

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Contents

Tables and Figure

1. Introduction

1.1 Outline and structure of the thesis

The format of this thesis is paper-based and includes a literature review (Chapter 1), and overview of the methods (Chapter 2), four research Papers (1-4, chapters 3-6) and a discussion. The first research paper has been published in the journal AIDS (2013), the second paper has been accepted for publication in PLOS ONE (2015) and is pending publication. The third research paper is under review at PLOS Medicine.

The literature review (Chapter 1) explores the history of the HIV epidemic in Sub-Saharan Africa and the development of mathematical models for infectious disease transmission and HIV. The inclusion of behavioural heterogeneity in mathematical models of HIV is examined, along with the concept of the core group and population subgroups associated with the core. Using the ideas from the literature a conceptual framework for the thesis is developed.

Chapter 2 provides an over-view of the methods included in the thesis and additional information and justification for the selection of the different technical methods that are included in the research papers.

Chapter 3 (research paper 1), explores the implications of including additional behavioural heterogeneity in the UNAIDS Modes of Tranmission (MoT) model in Nigeria and whether this affects predicted patterns of incidence produced by the MoT. In particular I examine the role of including additional groups and their 'risk' and assess the implications of subdividing the large subgroup categorised as 'low-risk' into smaller subgroups that explicitly include discordant couples, boyfriend/girlfriend relationships and those with no risk of acquiring HIV.

Chapter 4, (research paper 2), is an ecological analysis of population and HIV data from 13 West African countries. In this chapter I explore what factors are associated with population variations in HIV prevalence across the region and begin to identify the characteristics of population subgroups that are associated with this variation. Groups that emerge as important include, men who pay for sex (assumed to be clients of female sex workers) and subgroups of females and males with two (2+) or more partners (in a 12 month period), stratified by age (15-24 and 25-49 year olds). The results from the linear regression conducted are used to inform the development of a dynamic deterministic compartmental model used in research paper 3 and 4, to explore the importance of behavioural heterogeneity, population subgroup size and sexual networks for HIV endemic prevalence.

In Chapter 5, (research paper 3), I formulate a dynamic transmission model, based on the findings from Chapters 3 and 4. The model includes subgroups of adolescent females with 2+ partners and males (15-49) with 2+ partners, in addition to female sex worker (FSW) subgroups and clients who partner with FSWs. I include in the model structure a sexual network pathway between client groups and adolescent females 2+. This includes a mixing formulation which describes the proportion of partnerships adolescent girls with 2+ partners have with clients of FSWs versus other lower-risk men. The results assess the importance of different population subgroups and networks of sexual risk in predicting variations in HIV prevalence for parameter sets reflective of West Africa.

In Chapter 6 (research paper 4) I explore model projections for West Africa when the limiting effect on transmission of male circumcision is removed from the model. I assess the importance of the size of the adolescent female 2+ group and if this is an important factor for classifying and categorising epidemics.

The discussion (Chapter 7) draws together the ideas from the literature review and the findings from the research papers, that will be later developed into a conceptual paper. Key themes on the importance of incorporating adequate levels of behavioural heterogeneity into mathematical HIV transmission models and effectively using the available data to inform model parameterisation and identify key network pathways is discussed. The strengths and limitations of the research are examined and the implications for future research and policy are assessed.

1.2 An overview of the HIV epidemic in Sub-Saharan Africa

Human Immunodeficiency Virus (HIV) was first identified in the United States amongst a cohort of previously healthy homosexual men presenting with multiple viral infections (Gottlieb et al., 1981). The first report on AIDS in patients in central Africa was published in 1983 (Clumeck et al., 1983). By 1986, there was strong evidence for its extensive spread into populations across many countries in sub-Saharan Africa and there was recognition the disease was beginning to pose a major problem to public health. It was recognised that in this region the primary route of transmission was heterosexual rather than homosexual sexual partnerships (Quinn et al., 2001). The HIV epidemic continued to spread at a rapid pace, facilitated by changing demographics, slowing economic growth throughout the 1980s and structural adjustments to programmes that imposed cuts that effected social services including education and health services (The World Bank, 2001).

By 2012, there was approximately 36 million people living with HIV, with over 75 million estimated to have been infected since the start of the epidemic. Sub-Saharan Africa continues to be the region most affected, constituting just 12% of the global population, it accounts for

25 million reported infections, equating to 71% of the global burden of infections (UNAIDS, 2012). However, since 2001, there has been an estimated 33% reduction in the number of AIDS related deaths, with 2.3 million new infections in 2012 (globally), down from 3.4 million in 2001. In 26 countries the decline in new infections was approximately 50% (UNAIDS, 2012). AIDS related deaths have also fallen by around 30% since 2005, with more people able to access treatment and revisions to the WHO guidelines in 2013 allowing people to become initiated on treatment earlier (UNAIDS, 2012). Figure 1 below shows variations in the global prevalence of HIV, for countries where data are available.

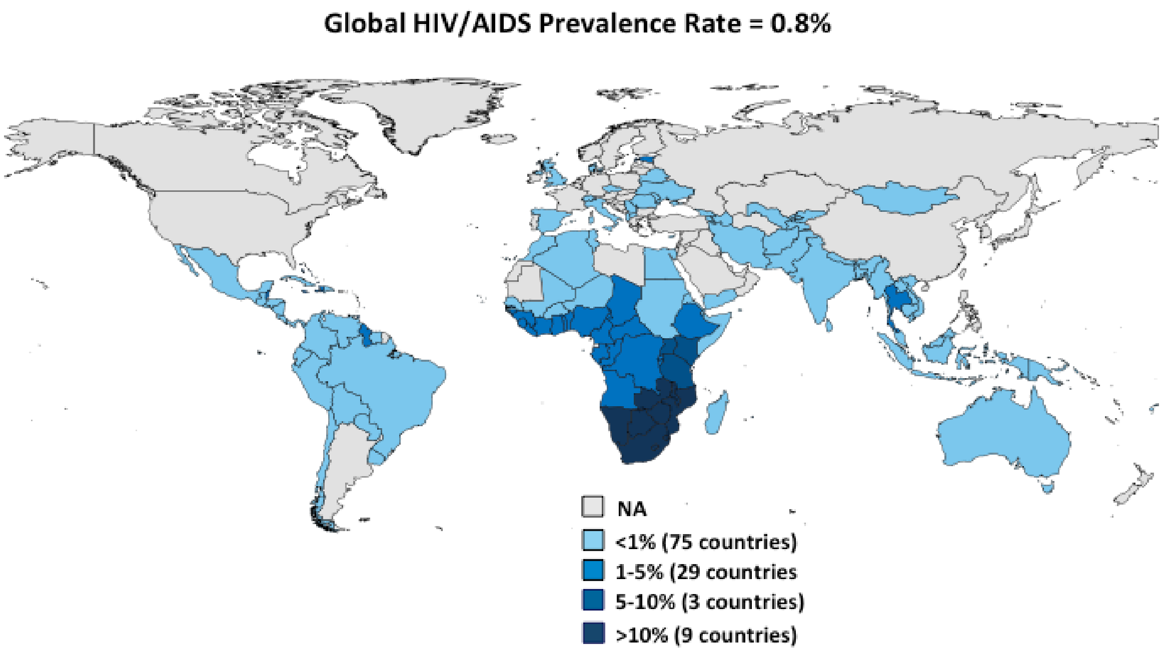


Figure 1: The global prevalence of HIV in 2014 (from www.globalhealthfacts.org)

Poverty has been an important mediator in the spread of infection; with limited access to schooling for future prospects, many turn to sex work as a survival strategy (McClarty et al., 2014, Fielding-Miller et al., 2014). Rapid urbanisation has also been an important factor. Time spent away from the family, often exposes individuals to periods of loneliness in which they are more likely to become exposed to higher sexual risk taking behaviour (Brockerhoff and Biddlecom, 1999). Gender power differentials may also play an important role, with the economic dependence of women on men and women entering into marriage at an earlier age (with partners often five or more years older than themselves) (Gregson et al., 2002).

However, despite the rapid spread of HIV across sub-Saharan Africa, there exists large disparities between HIV prevalence levels in East and Southern Africa compared to West and North Africa.

The study of four cites, two with higher prevalence levels of HIV in East Africa and two with lower prevalence levels in West Africa, surprisingly showed no significant differences in key sexual behaviours thought to be associated with HIV prevalence (Ferry et al., 2001). An important reason for this difference may be the higher levels of male circumcision in North and West Africa. Early on in the HIV epidemic male circumcision was observed as potentially incurring a protective effect against transmission in males, through the macro-level analyses of the geographical distribution of HIV infection and circumcision in Africa (Bongaarts et al., 1989). This observation was later confirmed through a randomised control trial (Auvert et al., 2005). To date circumcision is cited as one of the main reasons for the differences in HIV prevalence across the African continent (Alsallaq et al., 2009).

Compared to Eastern and Southern Africa, research in West Africa (and also Central Africa) is limited to a few cities in a region consisting of over 350 million people in 24 different countries. It is estimated over 6.5 million people are living with HIV, constituting around 20% of the total global burden. Prevalence of HIV ranges from 1-5%, significantly lower than the rest of Sub-Saharan Africa (Wheeler et al., 2015). In many countries with HIV prevalence greater than 1%, the epidemic is classified as ‘generalised’. However, this crude classification has been bought into question with multiple studies still highlighting the importance of key populations such as females sex workers and their clients remaining of paramount importance in the transmission of HIV (Alary et al., 2013). This has led to the belief that resources may currently be ineffectively spent, with money diverted away from key populations towards the general population (Bautista-Arredondo et al., 2008).

In 2008, The World Bank conducted a rigorous analysis into the characterisation of the HIV epidemic in West Africa (The World Bank, 2008). This provided several key findings which has aided in characterising the HIV epidemic in this region:

1. Firstly, although spread of the infection was less than originally expected, the region still faces a serious epidemic. However, antenatal clinic (ANC) data which ranged from 2.8-6.7% was shown to overestimate the severity of the epidemic and in reality the epidemic is thought to be less 'generalised' in nature than suggested. The available data indicates a more "mixed" but complex set of epidemics which cannot be defined easily by numerical proxy methods.
2. Although the data and past research suggest strong evidence that male circumcision limits the epidemic in men, there is no evidence that it directly reduces the transmission in women.
3. The most important core and bridging populations in the HIV epidemics in West Africa are female sex workers (FSWs) and their male clients. Sex work in the region is very varied and has evolved over time (Tara Beattie et al., 2011). Whilst in the past many FSWs worked in a fixed location and were known as 'seaters', more women are migrating and taking up professional sex work or 'official' sex work, they identify as sex workers, tend to reside only in the larger cities and earn their main income through

sex work. ‘Clandestine’ or ‘unofficial’ sex work is also a growing trend, with younger local women who do not identify as sex workers and may supplement their main source of income with sex work entering the industry indirectly.

4. Whilst official sex workers account for a large volume of sexual activity, despite being a small minority of individuals involved in transactional sex. However, there is another end of the spectrum encompassing young women who exchange sex for “gifts and/or money” without regarding this as sex work. Despite having far fewer partners, partners are often older and relationships may be concurrent, making such partnerships a cause for concern.
5. Clients of FSWs come from all walks of life and it is notoriously difficult to estimate the percentage of the male population engaging in commercial sex. The estimates from DHS data are likely to be gross under-estimates due to selection and social desirability bias. Especially since males who work away from home are significantly more likely to be engaging is commercial sex.
6. Finally, educational campaigns have led to a decline in men engaging in partnerships with official sex workers, but instead seeking out females who are not so obviously sex workers and perceived as lower risk.

This summary shows that the HIV epidemic within West Africa, is both complex and developing. With a large raft of research already established in Eastern and Southern Africa where the HIV epidemic is more severe, attention is now shifting towards West Africa, where the nature of the “mixed” epidemics within this region are less well defined.

The limited research undertaken in West Africa, a region undergoing rapid development, but in recent years blighted by civil unrest, makes this area of particular interest for attaining a better understanding of the HIV epidemic and its routes of transmission. As such, this thesis will focus on the epidemiology of HIV transmission in West Africa, through the use of ecological and mathematical modelling techniques.

1.3 Mathematical models of infectious diseases

Disease epidemics have been present throughout history, with infectious disease epidemics dominating public health until the 20th century (Frederick F. Cartwright, 2004). However, the discovery of infectious disease agents and their routes of transmission, the dawn of antibiotics and vaccination programmes, has heralded a significant improvement in treatment and prevention, which has reversed the trend in deaths of what are now, curable or treatable infections (Frederick F. Cartwright, 2004). Whilst many infectious diseases are now either curable or preventable, several, including HIV are lifelong infections and have had a significant impact on the social and economic development of countries, with a large number of deaths resulting from the pandemic.

An epidemic is defined as a widespread disease or condition that affects many individuals in a population. It can be either endemic or non-endemic in nature, depending on the time period it occurs. An epidemic is described as endemic if it persists for an extended period of time without reintroduction from an external source, for example HIV. Conversely a disease is non-endemic if it occurs only for a prolonged period and its repeated introduction can produce similar patterns of infection, for example measles. A pandemic is an epidemic that is more widely distributed in space, for example an epidemic that occurs on a global level (Rothman K.J, 2012).

Mathematical models have been used for centuries to help physicians, large institutions, policy makers and international organisations develop strategies for improving our understanding of infectious disease epidemiology and designing intervention programmes.

Eykhoff (1974) defined a mathematical model as 'a representation of the essential aspects of an existing system (or a system to be constructed) which presents knowledge of that system in usable form'(Ukoba O.Kingsley et al., 2013). The aim of a mathematical model is to use an equation or a set of equations, to provide a solution for the physical behaviour of a state or system being modelled. Mathematical models are used extensively in the natural sciences and engineering as well as in social sciences, including both economic and political science.

A mathematical model usually describes a system through a set of variables and a set of equations. The set of equations establish and describe the relationship between the variables, with the variables being representative of the properties of the system. Depending on the *priori* information of the system, a model can be described as either a white box model, if all the information about the system are available, or a black box model if none of the important information is known (Kai Velten, 2009). In reality modelling systems tend to lay between these two extremes, with a greater amount of *priori* information significantly improving the accuracy of the model.

Mathematical models of infectious diseases, in the strictest sense, are tools used to describe the processes associated with the spread of infection. Models may take multiple forms, with their development largely dependent on data availability, knowledge of the biological transmission processes and the purpose they are intended to serve.

In practise there are inevitably trade-offs in the modelling approaches used. Simple models are relatively easy to develop, use and parameterise, and have the potential to give qualitative insights, threshold statements, robust approximations and identify key determinants of HIV transmission (Pisani E et al., 2003, Gouws and Cuchi, 2012). However, there is the risk that these models are overly simplistic, and omit key features that are important from an epidemiological standpoint (Case et al., 2012). More complex models will often require more detailed assumptions about the processes that are applied within the model and there are usually costs associated with increasing model complexity – with models becoming more difficult to construct, parameterise and interpret.

In disease modelling, models can take a statistical approach by describing the associations between variables, or the mathematical approach which describes the causal pathways and mechanisms linking exposures, interventions, and infection or disease (Garnett et al., 2011).

Mathematical models of disease can be classified is several ways (Vynnycky E and White R, 2010):

Firstly, linear and nonlinear models. Models are usually composed of variables and operators that act upon these variable. These can be algebraic operators, functions and differential operators. If all the operators in a model present linearity, the resulting model is described as linear, otherwise it is characterised as nonlinear.

Secondly, models may take either a deterministic or stochastic form. A deterministic model is one whereby every set of variable states that occur is determined by parameters in the model and by sets of previous states of those variables. Stochastic models, in contrast apply randomness, such that variable states are not described by unique values but rather by probability distributions.

Finally, models are described either as static or dynamic. A static model does not include time as an element, whilst a dynamic model does. Dynamic models generally take the form of either difference or differential equations.

Mathematical disease models can be used to predict a disease course once that disease has entered a susceptible population of individuals, as well as having the ability to evaluate the effectiveness of both intervention and control strategies. Mathematical models allow the ability to describe a system such as the spread of an infectious disease, using the available data and additional insights provided by a given scenario or situation (Eaton et al., 2014, Anderson et al., 2014). This can then be tested against either experimental or observed patterns of disease. The ability to understand such systems, allows for the potential to analyse and evaluate the impact of proposed interventions (Garnett, 2002). Models are thus able to assist in identifying successful interventions, the scale at which they are applied and their benefits to general population health (Panovska-Griffiths et al., 2014).

Insights from mathematical modelling range from those that can be gained from analytical and simple numerical approximations of key epidemiological measures of disease potential (Dietz, 1993); analyses of the determinants of the probability of HIV transmission (Garnett and Anderson, 1995); insights from static models, that do not seek to capture trends in infection over time, but simply seek to approximate the potential short term impacts of HIV transmission (Pisani E et al., 2003), through to complex, multi-compartmental dynamic transmission models, with the ability to incorporate a more advanced understanding of the HIV epidemic's complexity (Garnett, 2002, Diez Roux and Aiello, 2005, Kretzschmar and Dietz, 1998, Bezemer et al., 2010, Shirreff et al., 2010).

One of the earliest models was formulated by Bernoulli in 1760, to assess the effectiveness of vaccinating healthy individuals against smallpox (C.C. Heyde and E. Seneta, 2013). Since then, model development has progressed significantly. Further concepts on modelling were developed by Ronald Ross in 1911, who formulated a mathematical model for the spread and control of malaria (Smith et al., 2012) and later Kermack and Mackendrick developed the concept of the *SIR* (susceptible-infectives-removed) models, used initially to understand the cholera epidemic (Kermack and McKendrick, 1927). The significance of this model is that it has duration dependent infectivity, such that the rate of infection is dependent on the duration of those infected and their infectious status, with the infection occurring only once in the life time of the individuals. Since its development, the model has been re-examined by Diekmann (Diekmann, 1977) and Metz (Metz and Diekmann, 2014). The importance of this kind of *SIR* structured model is that it is important for modelling epidemics in which the disease has a long incubation period such as HIV/AIDS.

In general, the development of dynamic models is often dependent on using a series of differential equations which take the form *SI*, *SIR* and *SIS*. Within these, the term *S(t)* is the number of susceptibles at time *t, I(t)* is the number of individuals who are infected (and usually presumed therefore to be infectious, although in the case of some infections we see an incubation period. This is the time when levels of the infectious agent increase in the host before they themselves become infectious, this is generally accounted for in models) and *R(t)* are those in the removed or recovered class at time *t*. Removed or recovered may represent those who have gained temporary or permanent immunity, have died or have been isolated or quarantined, depending on the aetiology of the disease being modelled.

In the next section, I will explore the more recent development of mathematical models for the transmission of HIV and the parameters and conditions that determine the spread of a sexually transmitted infection (STI). I look at importance of mathematical models in the context of the HIV epidemic and their evolution and applications.

1.3.1 The use of Mathematical Models in HIV Epidemiology

Mathematical models of HIV transmission have played an important role in helping to understand the drivers of the HIV epidemic in different locations, and shape the global HIV response (Hollingsworth, 2009).

Over the course of the epidemic, approaches to HIV modelling have continued to evolve and develop (Anderson R M et al., 1986), in response to new evidence about the importance of different behavioural and epidemiological factors (Anderson R. M et al., 1990) and the emerging and developing arsenal of HIV intervention options (Anderson et al., 2014). The use and purpose of mathematical models is both wide and varied.

One useful epidemiological measurement derived from mathematical models and also used in HIV modelling, is the concept of R_0, the basic reproduction number (Andersen and May R, 1991). R_0, is a measure of transmissibility and an epidemiological concept which describes the number of secondary cases a single infectious case would produce in a totally susceptible population (Dietz, 1993). It is an epidemic threshold which helps quantify the amount of effort required to control a disease. The variables associated with R_0, are assumed to be those that have the biggest impact on transmission.

1.3.2 Describing the spread of HIV infection; R_0 and the *risk of infection*

Both HIV incidence and prevalence are determined by the value of *Ro* and are dependent upon the characteristics that define it. In the case of a sexually transmitted infection such as HIV, classically and in its simplest representation:

$$R_0 = \beta c d \qquad (1)$$

Where;

c, represents the rate at which individuals form new partnerships in the population.

β, is the transmission probability for HIV per sex act or per sexual partnership.

d, is the duration of the infectious stages of HIV.

Whilst both the concept and formula are simplistic, each individual term of the equation has its own hidden complexities and each of these is applicable to the success, growth and propagation of an HIV epidemic.

Firstly, β, the transmission probability per act or partnership is initially dependent on type of sex act, with the highest risk for infection being receptive anal intercourse (Baggaley RF et al., 2010). Evidence suggests that male-female heterosexual transmission may be slightly higher than female-male (Boily MC et al., 2009), although this is still widely debated and other factors may account for the differences seen in HIV prevalence (Glynn et al., 2001). Other routes of transmission were established early in the emergence of the HIV epidemic and include contaminated needle sharing, blood transfusions and perinatal transmission from mother to foetus (Friedland and Klein, 1987). Additionally, the presence of sexually transmitted infections in either or both partners is associated with an increased risk of HIV transmission

(Fleming and Wasserheit, 1999), whilst male circumcision has been shown to have a protective effect in males for heterosexual transmission (Weiss HA et al., 2000). The value of β is also reduced through the protective role of condoms, although the consistency of use is an important factor (Weller S and Davis K, 2003). More recent trials have shown that the use of ART drugs as prophylaxis can significantly reduce the chances of infection for the uninfected partner (Celum and Baeten, 2012) and that earlier diagnosis and treatment of HIV infected individuals can significantly reduce the likelihood of onward transmission (Cohen et al., 2011).

Such evidence for reducing the transmission and acquisition rate of HIV has meant that, over the years, intervention policies have tended to focus directly on reducing the probability of transmission, β. From early interventions such as condom promotion campaigns (Solomon and DeJong, 1989, Rojanapithayakorn and Hanenberg, 1996), to more recent initiatives of distributing HIV drugs as pre-exposure prophylaxis (PrEP) (Okwundu, 2012) or using as a means of early treatment as prevention (TasP) (World Health Organization and Joint United Nations Programme on HIV/AIDS, 2012).

Secondly the rate at which individuals form new partnerships for R_0 is c. The implications of how fast an individual changes partners is important, particularly because high rates of partner change during the acute or high viraemia phase of HIV infection increases the exposure of uninfected individuals to a higher titre of the virus in their infected partners blood or semen. The implications of this for an epidemic is that HIV may spread at a very high rate initially, amongst individuals with high numbers of partners, but then the progression of the disease may slow down as it takes longer to spread into lower-risk individuals and as the course of the infection enters a less transmissible asymptomatic phase (Pilcher et al., 2004).

However, this theory has been disputed, with more recent evidence suggesting the acute phase of infection may be less severe than initially thought (Bellan et al., 2015).

Finally, the duration of infection for HIV is variable depending on the time after an individual is infected. The initial six month period following infection, commonly known as the “acute phase” where the level of virus is high is the most likely phase in which an individual will transmit the virus (Miller et al., 2010). Individuals may be as much as 25 times more infectious during this period. However, this is a high estimate with a systematic review of the data and meta-analysis suggesting the estimate to be lower (Boily MC et al., 2009). The implications of this are that high rates of partner change during this period may lead to a rapid dissemination of the disease (Pinkerton, 2008). An initial modelling study of the epidemic spread in San Francisco suggested that as a result of the short initial high vireamia phase, the virus spread rapidly in high-risk groups, causing a saturation effect in prevalence which then limited the spread of the infection as individuals became less infectious (Jacquez et al., 1994). In other settings variations in the total duration of infectiousness may limit the magnitude of the epidemic. Whilst the initial growth rate is likely to be similar under comparable conditions, in settings where total duration of the infectious period is shorter, the epidemic peaks at lower levels, partly because infected individuals are alive for a shorter period of time to transmit the infection (Garnett, 1998). The objective of policy makers is to prolong the lives of those infected with HIV, whilst aiming to limit the number of new infections. The discovery and roll out of anti-retro viral therapy (ART) (Sande et al., 1993, Jablonowski, 1995), has proved highly effective at achieving the goal of prolonging life. More recently a randomised control trail showed that the earlier treatment of HIV infection is also highly effective at a reducing the risk of onward transmissions and prolonging life (Cohen et al., 2011).

Another factor relating to the duration but also the number of partners, is the number of over-lapping or concurrent partners individuals have at any one given point in time. When individuals have multiple partners at any given time, the length of partnership duration becomes an important component of transmission, because it serves to link individuals together through sexual networks that they would otherwise not be exposed to if they were part of a monogamous relationship. Previous modelling has shown that increasing levels of concurrency can lead to increases in R_0 (Morris and Kretzschmar, 1997), but that sexual mixing amongst groups is key to facilitating the impact of concurrency (Doherty et al., 2006). When the number of overlapping partnerships is high enough, any infection is capable of spreading very fast, within an existing sexual network of partnerships that are linked. Beyond this, the subsequent spread of infection is slower, relying on the formation of new partnerships to widen the epidemic (Watts and May, 1992).

Building on these concepts mathematical models of HIV transmission use, what is termed, a *risk of infection* equation to represent the probability (π) that a susceptible individual becomes infected with HIV over a fixed time period. This is relevant in the context of an *SIR* model since it represents the probability an individual will become infected. For a simple static model, this is represented at a given moment in time and therefore, the equation may be multiplied by the total size of the population at risk. For a dynamic system that models the probability of infection at a given moment in time, the risk of infection is the risk relative to the individuals at time *S(t),* in the susceptible class. In its simplest form, an established Bernoulli equation may be represented as:

$$\pi = 1 - [1 - p + p[1 - \beta(1 - E)]^n]^m \qquad (2)$$

Where:

P is the probability that the sexual partner is infected with HIV

β is the probability of HIV transmission per sex act.

E is the probability that an individual is protected by a biological intervention (such as condoms or microbicides) and represents the consistency of use and the efficacy of the individual product.

n is the average number of sex acts per partnership over a fixed time period

m is the average number of sexual partners the individual has over that time period.

Whilst the variables included in the R_0 equation (1) relate to the propensity of an epidemic to occur, the risk of infection equation, describes the probability of individual infections (or total infections in a population in some cases, if the model is static in nature). For the risk of infection equation, here we see the importance of the terms *n* and *m,* which are both exponent terms in the equation and the multiplicative effect of β. The simple form of this equation thus highlights the importance of reducing both the average number of sexual partners (*m*) an individual has over a given time period, as well as the number of sex acts that an individual has with those partners (*n*). Reducing the multiplicative effects of the transmission probability is also significant, this is especially true if the HIV prevalence in the population is high because the probability that an individual partner is infected is greater (*p*).

This is the reason why multiple interventions focus on reducing the number of partners people form relationships with, as well as encouraging the use of condoms, which reduce the value of β, if used both consistently and correctly.

The risk of infection for an individual within a population is represented through the mathematical modelling process. In the next section I explore the different types of mathematical models that exist and their applications.

1.3.3 Mathematical models of HIV infection

The first model used for the explicit study of a sexually transmitted disease, namely gonorrhoea, was a one-sex model (Cooke and Yorke, 1973). A two-sex model was later developed by Lajmanovich and Yorke (Lajmanovich and Yorke, 1976). Dietz and Hadeler (Dietz and Hadeler, 1988) and Waldstätter (Waldstätter, 1989) also studied epidemiological models of sexually transmitted diseases using a simple two-sex model.

The start of the HIV epidemic heralded the further development of models on the sexual transmission of HIV/AIDS in heterosexual populations. These have included models by Anderson and May (Anderson et al., 1988), LePont and Blower (Le Pont and Blower, 1991) Lin *et a*l (Lin et al., 1993) and Busenberg *et al* (Busenberg and Castillo-Chavez, 1991). However, a large proportion of the earliest models for HIV were also based on homosexual transmission, these included models by Gabriel *et al*, Gupta *et a*l and Jacquez *et al* (Gabriel et al., 1990, Gupta et al., 1989, Jacquez et al., 1994).

The suitability of a model and the appropriateness of the assumptions on which it is based depend entirely on its purpose and available data. The different classes of model span a wide spectrum. At one end are highly detailed individual-based simulation models (Tolentino et al., 2013, Orroth et al., 2007). These include a large number of individuals, units or entities each with their own characteristics, who interact with one another, often in the presence of a contact network and infectious disease agent. At the other end of the dynamic modelling spectrum are compartmental models, in which states for individuals (rather than individuals themselves) are aggregated into compartments in which everyone shares the same average characteristics and interaction is uniform. In this case, only the time evolution of the compartments is described, for example the number of individuals susceptible to infection versus those who are already infected, at a given point in time (Heesterbeek et al., 2015).

One type of compartmental model is a deterministic model. In these types of model the input parameters are fixed and therefore the model output such as number of incident cases or HIV prevalence is predetermined. A further subdivision of deterministic models are 'static' and 'dynamic' models. Dynamic models incorporate contact between individuals over time and are therefore able to estimate changes in both prevalence and incidence, since the risk of transmission will depend on how many individuals are infectious at any time point (Garnett, 2002). They can therefore be used to approximate the effect of an intervention (Pickles et al., 2013). However, in a static model 'risk 'is predetermined, so such models are often only used when the risk of infection is known or can be estimated. This type of model is therefore not capable of measuring impact over time.

Dynamic deterministic compartmental HIV transmission models use systems of differential equations to describe how rates of HIV infection and disease progression will evolve over time (Andersen and May R, 1991, Hethcote, 2000), with the population commonly being divided into sub-categories, determined by their 'disease state', these may be represented as 'susceptible' individuals, 'infected' individuals and 'recovered' individuals. This classical model construct, as described earlier, is known as the *SIR* model (Kermack and McKendrick, 1991). Because HIV infection is life-long and the severity of infection and levels of infectious agent in the body vary over the course of the disease's life-time (Hollingsworth et al., 2008), more typically such a model will instead include states such as; susceptible, newly HIV infected, HIV infected with low viraemia, HIV infected with high viraemia and more recently HIV infected on ART treatment (Stover et al., 2014). These systems of differential equations are then solved numerically, using computational algorithms applied in a programming language.

Historically, deterministic mathematical models of HIV transmission have used the compartmental approach of dividing populations into multiple subgroups dependent on their level of risk for acquiring HIV (Pisani E et al., 2003, Shafer et al., 2011, Boily MC et al., 2007). The division of populations into the model compartments is often based on evidence of the distribution in sexual risk behaviours and epidemiology in a population. The uncertainty of the model is reflected by generating uncertainty ranges around each parameter input. Often thousands or millions of input parameter sets are generated by sampling from this parameter space, with model runs for different combinations of inputs being used to generate a measure of uncertainty around the models projection (Vynnycky E and White R, 2010).

There are also stochastic models (which can be compartmental or individual based), in which the model allows for a probabilistic distribution of model inputs within any compartment, and for individuals to move between compartments as a result of chance i.e. infection and recovery rates may vary randomly (Vynnycky E and White R, 2010, Steen et al., 2014) (Sani et al., 2007, Mode and Sleeman, 1999). To date, a large proportion of policy focused HIV modelling uses deterministic modelling. For MSM modelling, for example, a systematic review found that 80% of models used a deterministic approach (Punyacharoensin et al., 2011). There may be several reasons for this. Firstly, stochastic models require far more computer operating power to run and generate results, which can be slow. This may have historically affected their development since it is only more recently with the development of high powered computers, this been made possible. They may also take more time to construct, adapt and require more parameters which are difficult to source. In addition to this the large number of parameters can also make it more difficult to elucidate the overall contribution of a single input parameter on the overall outcome of interest. For infectious disease dynamics, chance events often play an important role in the course or process of individuals becoming infected. This is often particularly important at lower levels of biological aggregation, such as disease outbreaks. At higher aggregation levels, when many more individuals are coming into contact, the effects of chance may be averaged out, meaning deterministic descriptions tend towards being as equally valid as stochastic representations. Both deterministic and stochastic models are not mutually exclusive in this regard and models exist that are a mixture of the two. Although the role of chance is often a reality in transmission dynamics of infection, its role in modelling may be less significant on influencing the model outcome than the selection of model parameters and assumptions around risk (Heesterbeek et al., 2015).

In essence, a deterministic model may provide equivalent findings under certain conditions.

The above section summarises the types of models that can be applied in HIV transmission dynamics. In section 1.3.2, R_0, was presented as the basic reproduction number highlighting the importance of the duration of infection, the transmission probability of infection and the number of partners an individual has, as key parameters for the spread of infection. The risk of infection equation (2), represents the risk an individual has of acquiring infection, with a static model calculating this risk at a given point in time. For a dynamic model, the equation translates to be a *force of infection*, representing the risk of infection for an individual or individuals at a given moment in time. In the next section a basic dynamic transmission model for HIV is presented, showing the movement of individual through different infection states.

1.3.4 Basic model structure for HIV transmission

Here I present a simple HIV transmission model to familiarise the reader with basic ideas behind HIV models. A basic model for the transmission of HIV (Anderson R. M et al., 1990, Vynnycky E and White R, 2010, Kaplan, 1990), contains three compartments into which individuals fall; susceptible, infectious and AIDS cases (in many models this represents the cessation of sexual activity). The models assumes constant AIDS mortality rate, μ.

Because the model represents the long-term dynamics of a persistent infection that ultimately leads to death, a variable for the rate of recruitment into the sexually active group 'α' is included to ensure the number of susceptibles in the population is not depleted. A variable for non-AIDS mortality amongst the sexually active population is also included, *m.* This may also represent individuals who leave the population for other reasons if the model is representative of a specific population, for example migration out of the population.

Different assumptions can be made about the given variables in the model, for example recruitment into the sexually active groups or population may vary over time. The compartment model is shown in Figure 1.2.

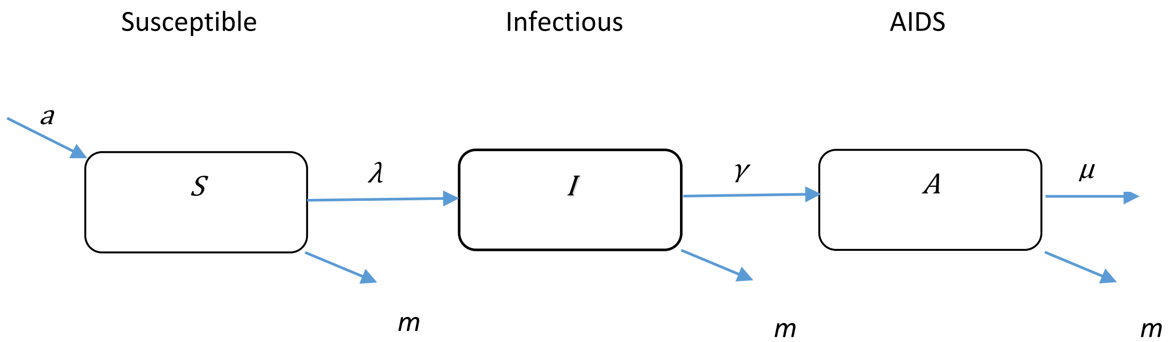


Figure 1.2: Compartmental model of HIV transmission and progression

The model equations are as follows:

$$
\begin{cases}
\frac{dS}{dt} = \alpha N - \lambda S - mS & (3.1) \\[2ex]
\frac{dI}{dt} = \lambda S - \gamma I - mI & (3.2) \\[2ex]
\frac{dA}{dt} = \gamma I - \mu A - mA & (3.3)
\end{cases}
$$

S is the number of individuals who are susceptible to HIV at time t in the population

I is the number of individuals infectious with HIV at time t in the population

A is the number of individuals who have AIDS at time t in the population

N is the total population size

$\lambda = \beta c \left(\frac{I}{N}\right)$ is the force of HIV infection on the population at time t

α is the rate of recruitment into the sexually active age group per unit of time (i.e. per annum)

α is the recruitment rate into the population per unit of time

m is the non-HIV mortality or leaving rate amongst those sexually active per unit of time

γ is the progression rate to AIDS per unit time

μ is the death rate due to AIDS per unit time

The basic reproduction number R_0 for the basic HIV model is given by:

$$R_0 = \frac{\beta c}{\gamma + m}$$

However, the above system of equations (3.1-3.3) is fairly simplistic. For example, it is known that HIV has an additional high-viraemia phase, lasting around 3-6 months, before a longer asymptomatic phase, thus dividing the infectious stage into two component stages. More recent models also incorporate compartments for those receiving treatment such as anti-retroviral drugs, in which case additional states must be also be incorporated (Eaton et al., 2014).

The above model structure also makes a very large assumption regarding the sexually active population, i.e. that everyone in this model behaves in a homogeneous way and is subject to the same *force of infection*. In reality we know that this is not the case, for example at a very basic level, we know that individuals in different age categories behave differently, based on population level data, with younger individuals tending to change partners more frequently than those in the older age categories and mix predominantly with individuals of the same age (Mercer et al., 2013).

Thus, behavioural heterogeneity is an important aspect of modelling. Sexual mixing patterns within populations tend to have some level of organisation and as such mathematical models must incorporate differences in individuals and subgroups in regards to their behaviour.

In the next section, I explore the different types of behavioural heterogeneity that have been observed and incorporated into models.

1.4 Behavioural Heterogeneity and challenges in HIV modelling

The earliest models of HIV transmission considered the spread of HIV within a population which was homogenous in regards to sexual behaviour (Anderson R M et al., 1986), These early models often explored the epidemic amongst groups of men who have sex with men (MSM) (Jacquez JA et al., 1988, Gupta et al., 1989, Sattenspiel et al., 1990), the group in which the virus was first detected. Later models began to explore greater levels of behavioural heterogeneity amongst individuals (Anderson R M et al., 1986, Knox, 1986, Pickering et al., 1986), as well as the importance of modelling pair formation (Dietz and Hadeler, 1988), which renders two non-infected individuals temporarily non susceptible to infection. As specific behavioural subgroups with elevated risks in the population were identified, such as homosexual and bisexual males, IDUs, patients receiving blood transfusions and children of HIV positive mothers, models that included these different subgroups were developed (Pickering et al., 1986).

Later models began to recognise the importance of further stratification, including by age (Garnett GP and Anderson RM, 1994) and/or other behavioural characteristics such as rates of partner change (Anderson R. M et al., 1990). Along with the inclusion of this behavioural heterogeneity, mathematical models began to explore how patterns of HIV transmission may vary according to the patterns of 'mixing' between these different sub-groups. A tendency to form partnerships with others who have similar characteristics (Bohl et al., 2011, Doherty et al., 2011) is termed 'assortative' or 'like with like' mixing (Vynnycky E and White R, 2010). 'Disassortative' mixing instead refers to individuals who preferentially form partnerships with individuals who have dissimilar characteristics to their own, such as females who engage in 'cross generational sex' (Adegbenro et al., 2010), or those who have high numbers of sexual partners mixing preferentially with those who have low numbers of partners (Vynnycky E and White R, 2010). Mixing patterns are of great importance in the projected course of HIV epidemics. Assortative mixing patterns have a tendency to generate a rapid growth in incidence in the early stages of infection, with multiple peaks in the epidemic possible at later stages as HIV infection spreads among different groups (Jacquez JA et al., 1988, Sattenspiel et al., 1990). In contrast, disassortative patterns tend to result in a higher magnitude of infections but over a longer period (Gupta et al., 1989, Hethcote et al., 1991).

More recently, with the advancement in treatment options and the recognition that a multi-faceted approach towards the epidemic is required, current model development focuses both on patterns of mixing and behavioural heterogeneity as well as taking more of a 'therapy orientated approach' (Punyacharoensin et al., 2011). Models have also explored the effect of other emerging biological interventions such as circumcision and microbicides (Cox AP et al., 2011, Foss et al., 2009).

Differences in rates of partner change, choice of partners and varying levels of concurrency amongst individuals is what gives rise to behavioural heterogeneity within a population. Model development and parameterisation is reliant on such observations. However, interpretation of the evidence can often be complicated by, for example, an apparent difference in the reported number of sexual partners between men and women (Ferry et al., 2001). This disparity is usually common to most studies and may be a result of rounding error with individuals failing to recall exact number of partners. Alternatively sampling frames may fail to detect some of the women with the highest sexual activity, or simply men may over-report and women under-report partner numbers as a result of social desirability bias (Nnko et al., 2004).

Despite these possible inaccuracies, one key observation that can be drawn from studies is that the majority of individuals have only one or no sexual partners in any one year (Mercer et al., 2013), with a small subset of the population having multiple partners. This was a phenomenon first identified by Hethcote and Yorke (Yorke et al., 1978) who used epidemiological data to show that the prevalence of gonorrhoea adjusts significantly as a result of social behaviour and that the incidence of the disease is described by them as; "theoretically limited by saturation in a sexually active core population (Yorke et al., 1978)."

1.4.1 Core group theory

Core group theory is one of the central concepts of STI and HIV transmission dynamics and primarily describes groups of individuals with higher rates of sexual partner change (Brunham, 1997), compared to the rest of the population. Hethcote and Yorke observed that for infectious diseases such as measles, once the prevalence of infection reaches a certain threshold, individuals who are newly infected begin to make contacts with other infected individuals, resulting in a saturation of the disease in the population as infected individuals gain immunity and are not susceptible to reinfection. However, gonococcal infection does not confer immunity and once individuals are treated they are again susceptible. Saturation, thus only occurs when already infected individuals contact other individuals who are infected from a different source. This was defined as the 'pre-emption effect.' This effect tends to only occur in a very small subset of high-risk individuals; this group has much higher prevalence rates of the infection and is termed the 'core' group of individuals. This group alone is thought to be capable of sustaining sexually transmitted infections within a population, in which sexual mixing patterns are heterogeneous. Whilst high rates of partner change are fundamental to the existence of a core group, sexual networks are also important. When high activity individuals mix with one another, the speed at which an infection such as HIV will spread is accelerated (Garnett, 1998).

The presence of a core group in propagating and sustaining an STI infection is likely to be important in most settings. Infection from the core, is likely to be transmitted to lower risk individuals through extended networks, although the process of infection is often slower because contact rates are not as high as within the core.

Based on the theory of the core group, a mathematical model may divide a population into subgroups, constituting both individuals who are at lower risk of acquiring HIV as well as groups such as female and male sex workers, clients of sex workers, MSM, people who inject drugs (PWID) and other vulnerable groups such as prison populations. This division is amenable for model fitting and evaluation, and the findings have provided important insights for policy (Pisani E et al., 2003, Pickles et al., 2010). In some cases, different sub-groups may be further sub-divided, although especially for population models, this level of heterogeneity may not be included, as it can add to the model's complexity.

1.4.2 Core groups in HIV epidemiology

Classic epidemiological theory identifies female sex workers (FSW) as a core group in HIV epidemiology (Estebanez et al., 1993). The behavioural characteristics of these groups make them particularly vulnerable to the rapid acquisition and spread of HIV. High numbers of sexual partners and rates of partner change are cited as important risk factors. In addition, FSWs may often be associated with other high-risk behaviours for the transmission of HIV including alcohol use, injecting drug use, high prevalence of STIs and in some settings low levels of condom use (Estebanez et al., 1993, Hunter, 1993). They also tend to be small population subgroups (Vandepitte et al., 2006) that form clusters in regions where the demand for sexual exchange from client groups, such as truck drivers (Oruboloye I.O et al., 1993), the military and police force (Akinnawo EO, 1995) is high. Since clients are also likely to have regular long term female partners, this group is often referred to as a 'bridging' population, that connects a 'core' group of FSW who have a high prevalence of HIV, with the general population, who tend to have lower levels of prevalence (Lowndes et al., 2002).

Men who have sex with men (MSM) are also a distinct population who tend to have higher than average sexual partners compared to the general population. In addition to the higher transmission probability of HIV (β) through receptive anal intercourse versus heterosexual sexual transmission (Boily MC et al., 2009, Baggaley RF et al., 2010), distinctive behavioural heterogeneity within homosexual male populations is likely to play a significant role in transmission. In India, evidence from surveys suggests males who are predominantly the 'receptive' or 'passive' partner in anal sex tend to have higher numbers of sexual partners (Phillips AE et al., 2008) and are more likely to participate in sex work than males who typically take the 'insertive' or 'active' role (Phillips et al., 2009). This pattern of behaviour in many ways is similar to sexual networks between FSWs and clients, with receptive males forming the 'core' group and males who are the 'active' partners acting more like a bridging group, with sexual contact with females more likely amongst this group (Phillips et al., 2010).

A third group with high-risk behaviour in the spread of HIV are people who inject drugs (Platt et al., 2009). Needle exchange between users is associated with a risk of HIV infection that is likely to be higher than both vaginal and anal intercourse (White et al., 2007). Populations of injecting drug users are often clustered, and in areas where clean needle exchange is unavailable, risk of transmission through sharing contaminated syringes is often high (Uuskula et al., 2014).

1.4.3 The role of core groups in categorising HIV epidemics

The concept of core groups in HIV epidemics has been a key defining feature for the categorisation of different epidemic states within countries (Brunham, 1997). The definitions in general are quite broad, but have important implications for how policy is implemented and funding for HIV treatment and prevention distributed.

The implementation of the definitions followed a UNAIDS report from 2000, on Guidelines for Second Generation HIV Surveillance (World Health Organization and Joint United Nations Programme on HIV/AIDS, 2000). With recognition of the growing diversity of different countries HIV epidemics globally, there was an awareness within the report that many in-country surveillance systems were ill-equipped to understand the nature of the epidemic or to explain more comprehensively changes that were occurring over time.

Countries were encouraged to strengthen their surveillance systems and to tailor them towards the pattern of the epidemic that existed within that setting. The guidelines encouraged the use of both biological and behavioural data collection to generate a more informative picture.

Biological indicators included HIV and STI serological prevalence data as well as the number of new adult AIDS cases. Behavioural indicators were recommended to collect data on the percentage of individuals who had sex with a non-regular partner in the past 12 months, condom use at last sex act with that partner and age at first sex. For drug users, reported sharing of unclean needles was cited as a key indicator of risk and for female sex workers, the number of clients reported in the last week.

Other socio-demographic indicators were also highlighted as important for HIV surveillance. These included, age, sex, social economic status and educational status, migration status and marital status.

With the use of these indicators UNAIDS recommended different categorisations for epidemic states using a numerical proxy method, with the intention to help countries prioritise surveillance efforts and interventions. The categorisations are as follows (World Health Organization and Joint United Nations Programme on HIV/AIDS, 2000):

Low-level

• "Principle: Although HIV infection may have existed for many years, it has never spread to significant levels in any sub-population.

• Recorded infection is largely confined to individuals with higher risk behaviour: e.g. sex workers, drug injectors, men having sex with other men. This epidemic state suggests that networks of risk are rather diffuse (with low levels of partner exchange or sharing of drug injecting equipment), or that the virus has been introduced only very recently.

• Numerical proxy: HIV prevalence has not consistently exceeded five percent in any defined sub-population."

Concentrated

• "Principle: HIV has spread rapidly in a defined sub-population (core groups), but is not well-established in the general population. This epidemic state suggests active networks of risk within the sub-population. The future course of the epidemic is determined by the frequency and

nature of links between highly infected sub-populations and the general population.

• Numerical proxy: HIV prevalence consistently over five percent in at least one defined subpopulation.

• HIV prevalence below one percent in pregnant women in urban areas."

Generalised

• "Principle: In generalised epidemics, HIV is firmly established in the general population. Although sub-populations at high risk may continue to contribute disproportionately to the spread of HIV, sexual networking in the general population is sufficient to sustain an epidemic independent of sub-populations at higher risk of infection.

• Numerical proxy: HIV prevalence consistently over one percent in pregnant women."

Since their inception these categorisations have been important for policy decision making and for the distribution of funding (Lazarus JV et al., 2010, Pisani E et al., 2003). Mathematical models, developed by UNAIDS and others have used surveillance data to help guide this decision making process (Stover et al., 2012, Gouws and Cuchi, 2012).

Such a model is the Modes of Transmission (MoT) model which seeks to approximate the distribution of new incident infections (UNAIDS, 2007). The model was developed in order to help countries estimate the proportion of new infections occurring among adults through key modes of transmission, such as sex work, multiple partnerships, men who have sex with men, injecting drug users and individuals in long-term stable partnerships. It is a static model, developed using an Excel Spreadsheet, with the intention that the structure makes it accessible to non-mathematicians and policy makers in the field. To date it has been employed in 29 countries (Shubber et al., 2014), but there are concerns over the assumptions underlying the model structure, particularly the homogeneity in the selected risk groups, the data available for deriving the model input parameters and how the results and findings are interpreted and applied to policy in different settings (Case et al., 2012).

More generally the limitations to both WHO/UNAIDS numerical proxy method and the MoT include: (i) that there is insufficient information contained on the behavioural factors that drive the epidemic, (ii) both are difficult to apply to more localised epidemics, and (iii) the MoT is highly sensitive to input parameters and relies on information and assumptions from other sources (Mishra et al., 2012a).

Another limitation is the reliability in the interpretation and accuracy of data. One report from 2006, showed that ante-natal clinic (ANC) data often over-estimates HIV prevalence in the general population. Therefore, the WHO/UNAIDS numerical proxy terminology is flawed because it is not a transmission-based definition, but rather one that classifies countries "arbitrarily as concentrated or generalised", which limits any further analysis of transmission dynamics (Wilson D, 2006).

The report suggested the following revisions to the categorisation:

Concentrated

"An HIV epidemic is concentrated if HIV transmission is primarily attributable to HIV-vulnerable groups and if protecting HIV-vulnerable groups would protect the wider population."

Generalised

"An HIV epidemic is generalised if the converse is true – HIV transmission is not primarily attributable to HIV-vulnerable groups and protecting HIV-vulnerable groups would not in itself protect the wider population."

Using specific examples, the report demonstrated the misuse and interpretation of the terms. Firstly, in Ghana, where the HIV prevalence is 2%, HIV prevalence in sex workers is about 80% and 76% of new infections in adult males are attributed to sex work. In this case, a highly concentrated epidemic was classified as generalised by the WHO/UNAIDS numerical proxy method and a disproportionate amount of funding was being transferred away from sex workers and client interventions and into more general population interventions.

As suggested, this example shows how classification should be based on an understanding of the source of infections as well as having a clearer perspective on the environments in which HIV is transmitted and acquired and under what circumstances. Transmission dynamics, depending on partnership numbers, effective use of condoms and duration of contact with infected individuals, provide a clearer understanding of the nature of an epidemic. Behavioural heterogeneity is also important. Sexual behaviours within a population are not homogeneous and an understanding of the size and networking of different groups would provide a more comprehensive outline of disease transmission and the nature of the epidemic.

Whilst key indicators relating to transmission should provide a means of assessing epidemic potential, comparisons between countries using these measures is often unclear and may be contradictory. For example, one study compares behavioural risk factors in four countries with concentrated epidemics to Zimbabwe, with a generalised epidemic (Group, 2007). The study found that over twice as many individuals in Russia reported 2-5 partners per year, compared to Zimbabwe and in India and China those who reported ‘never’ using condoms was 87% and 93%, compared to 53% in Zimbabwe.

It means that ultimately, countries that are classified as having 'generalised' epidemics don't necessarily have the highest measures for HIV-associated risk behaviours, that we might expect to see.

A second important study conducted was The Four Cities Study (Buve et al., 2001). The aim of this study was to explore whether differences in the rate of spread of HIV in different regions in sub-Saharan Africa (East versus West) could be explained by differences in sexual behaviours or other factors that could influence the probability of HIV transmission through sexual intercourse. Surprisingly, the study found that high rates in change of partners, contacts with sex workers, concurrent partnerships and large age differences were no different when the high and low prevalence settings were compared (Ferry et al., 2001). These findings illustrate the challenges in characterising and categorising epidemics in different settings. Evidence from numerical proxy measures, MoT modelling and studies on individual risk behaviours, whilst providing policy makers with some level of insight, do not truly provide sufficient evidence to describe variations in HIV prevalence levels.

A recent major development in the field has been the emergence of programme science, defined by Blanchard *et al* (2010) as "the systematic application of theoretical and empirical scientific knowledge to improve the design, implementation and evaluation of public health programmes" (Blanchard and Aral, 2010). The approach is far more holistic, focusing on the total prevention programme, including impact evaluation methods. Whilst focusing on multiple approaches, of importance to modelling may be the emergence of epidemic mapping strategies which aim to both map the location of high-risk groups as well as enumerating their population size. A fundamental idea behind this approach is that without knowing your denominator (e.g. the number of sex workers within a particular region), you are not able to plan and properly implement effective intervention strategies. The application of Programme Science for future modelling and providing a more comprehensive approach to understanding HIV epidemics will be important.

In the next section, I assess further the importance of behavioural heterogeneity and the role of the core group in propagating infections, with a particular focus on the importance of sexual networks or subgroups that link core groups to individuals with lower sexual risk behaviour.

1.5 Sexual networks and HIV

The theory of core groups in the transmission of HIV is an established principle. Assortative sexual mixing amongst high risk individuals, such as those who are a member of a core group, is associated with a rapid increase in infections amongst those individuals. However, as alluded to by Garnett, the size of an HIV epidemic will be relative to how far out of the core the virus is able to spread and how efficiently this occurs (Garnett, 1998). Jolly *et al.* (2001) used a process of social network analysis to describe and illustrate the effects of sexual networks on STI transmission, using the spread of chlamydia in Winnipeg and Colorado Springs as examples. The results showed that smaller more sparsely linked networks peripheral to the core were more likely to form the mechanism through which chlamydia was able to remain endemic in the population, in contrast to the densely connected networks of the core, associated with very steep rises in incidence (Jolly et al., 2001).

In a further study, Ghani *et al*. (1997) developed a stochastic individual-based model to understand pair formation and dissolution rate between individuals (Ghani et al., 1997). Their approach included attempting to understand the role that network structures play in the transmission dynamics of STIs, using as an example the spread of gonorrhoea in a closed population. In the results the author categorised individuals into four activity groups, those with 1, 2, 3-4 and 5 or more partners. They used three modelling approaches to assess which was the best measure of estimating the establishment of infection in the population and the prevalence. This including developing models to assess the distribution in the number of sexual partners, sexual mixing patterns in the population and measures of network structure.

The findings show that population size was the most important variable both in relation to the establishment of infection and prevalence. However, the establishment of infection was made more likely when individuals had an increased number of partners. Sexual mixing was also important and particularly the number of non-monogamous pairs that were formed in the networks, since they are the only route through which infection can spread. This in turn is linked to how well connected the population is i.e. the number of vertices or links between sexual activity groups and the level of cohesion, which represents how densely connected individuals are. The prevalence is also associated with the mixing of the highest sexual activity group (the core); when this group's mixing becomes more disassortative, infection is more likely to spread into other groups and become established.

These studies and the insights gained from them, show that the presence of a core group is likely to be fundamentally important to the outbreak and sustainability of infection in a population, but that peripheral networks linked to the core are also likely to be important in maintaining the epidemic in the wider population.

This is also a phenomenon that was observed in earlier work, assessing the initial spread of HIV in Sub-Saharan Africa. Whilst theory points to the importance of FSWs in the HIV epidemic as the core group through which HIV spreads, there has been some research questioning whether they are always the most central group to the HIV epidemic in concentrated HIV epidemic settings (Watts C et al., 2010). High-rates in the formation of new partnerships amongst FSWs, with a larger population of male clients is likely to have led to the initial spread of the epidemic in many African settings (Oruboloye I.O et al., 1993, Pickering et al., 1997). However, the relative size of populations of sex workers compared to the general population is likely to be small (Vandepitte et al., 2006), so that in higher prevalence settings the establishment and persistence of infection may actually be supported through larger peripheral sexual networks outside the core, that are more diffuse, but are intrinsically linked to the core.

Advancing this concept further, Garnett *et al* (Garnett and Anderson, 1996) showed that individuals in the population who have an *intermediate* number of sex acts with each partner (i.e. tend to form slightly longer-term relationships with individual partners) and fewer numbers of partners, as opposed to sex workers who are more likely to have one-off encounters, may actually contribute the greatest to the spread and persistence of an STI - especially when the STI has a low transmission probability, such as HIV.

Using the theory of R_0, Dietz (1993) observed that an important element in transmission is the number of new partners a newly infected individual acquires (c), the total number of contacts with these individuals and how they are distributed across the population (Dietz, 1993). He derived a series of formulae to show how R_0 depends both on the number of partners (N) and the number of contacts (C).

Dietz denoted the reductions in the per-contact infection probability, β, and the number of partners (N) as r_N and r_β, respectively, assuming the total number of contacts (C) is held constant. The objective was to understand under what circumstances, one is more efficient than the other; a proportionate reduction in N, or the equivalent proportional reduction in β.

Dietz showed that for scenarios where $N > \beta C$, the best approach is to reduce β, whereas when $N < \beta C$, a given proportional reduction in the number of partners would have a greater impact on reducing R_0. Dietz's findings are important in that they show that for a group of FSWs, reducing β, by increasing condom use may be the most effective intervention approach. However, as Garnett observed, for individuals in the population who are having more sex acts with fewer partners, a reduction in N, i.e. their total number of partners, may be more beneficial. Since this later group are likely to constitute a proportionately larger group in society, an understanding of this dynamic may help to make more informed decisions as to how to target certain population subgroups at risk of acquiring HIV.

In the next section I review the characteristics of core groups and their '*peripheral'* networks that Ghani refers to. I seek to understand whether these '*peripheral'* networks may include individuals with *intermediary* numbers of partners, and if so, what the implications of this may be.

1.5.1 Core groups and their sexual networks

People who inject drugs: HIV epidemics amongst drug users are of paramount importance in certain regions where this route of transmission is capable of sustaining epidemics (Uuskula et al., 2014). One study examined the probability that injecting drug use was likely to be the major source of HIV that led to a wider-spread heterosexual epidemic (Des Jarlais et al., 2012). The findings from this study show that such an epidemic was more likely to occur in a low- versus a high-income setting, probably as a result of fewer resources being available to initiate an intervention programme, such as free exchange of clean injecting equipment. In addition, the researchers also identified that continual high levels of incidence amongst people who inject drugs was associated with higher levels of HIV amongst the heterosexual population. Again this was likely to be associated with the lack in provision of safe injecting equipment but also potentially a rapid turnover in new injecting drug users, who maintain a pool of new susceptible individuals. For high level epidemics amongst drug users, the population size of this group was also associated with higher levels of HIV prevalence in settings, such that large numbers of individuals participating in the practice of injecting inflated prevalence levels, a finding that we would naturally expect to observe (Rhodes et al., 1999).

The propensity of an HIV epidemic amongst people who inject drugs, to spread to members of the wider non-injecting population, is likely to be associated with their level of risk behaviour and their number of contacts. Transmission may occur through either injecting or sexual transmission (anal and/or vaginal). One study showed that in individuals co-infected with Hepatitis C and HIV, around one fifth of HIV infections were acquired through sexual transmission (Vickerman et al., 2013). It has also been shown that in settings such as St Petersburg in Russia, where HIV prevalence amongst people who inject drugs is high, the non-injecting partners of injecting drug users may play a crucial role in bridging infection to the non-injecting population through heterosexual transmission, thereby sustaining a heterosexual epidemic (Mills et al., 2013).

Another study has shown that an increased risk of infection amongst people who inject drugs may be associated with also being members of other core groups. For males who inject drugs, this involved having sex with other men, and for females, it involved being a sex worker (Kral et al., 2001). These additional associations are important in that they may extent the transmission network of HIV from injecting drug users to other core groups.

In turn, the social links between people who inject drugs, men who have sex with men, and females who trade sex, is often mediated by high levels of poverty and homelessness. This is illustrated by Gorbach (2009), who suggests an “embedded core group of drug using men who have sex with men and women”, may not contribute necessarily to the spread of HIV to the wider general population but that infections in this group are “driven by their pressing need for drugs and money”, and this may concentrate the epidemic among men and women in similar situations to themselves where resources are scarce (Gorbach et al., 2009). In this sense, injecting drug use may be capable of sustaining rather than elevating HIV infection amongst the general population. However, in general it is unclear how important the sexual behaviour of HIV infected drug users is in the dissemination of infection, with studies also reporting lower levels of sexual activity amongst this group (Uuskula et al., 2014).

In summary, the capacity for individuals who inject drugs to initiate a more wide-spread epidemic is unclear. The evidence suggests that population size of the group may be an important variable (Des Jarlais et al., 2012). High-risk MSM and individuals (men and women) who trade sex for money (who themselves may form members of core population groups), as well as other non-injecting sexual partners are possible groups that may extend the network of infections in people who inject drugs to lower-risk individuals.

Men who have sex with men: HIV epidemics amongst populations of MSM continue to be a major public health concern. Such epidemics occur on a global level both in developing and more developed countries, with high and increasing HIV prevalence in certain regions (van Griensven et al., 2009). The high probability of transmission per act through anal intercourse plays a central role in the high burden of infection seen in this population (Baggaley RF et al., 2010). Molecular epidemiological data also show clustering of HIV infections amongst networks of MSM and higher rates of dual-variant and multiple-variant HIV infection in MSM than heterosexual populations, suggesting multiple exposure of the infection amongst certain individuals (Beyrer et al., 2012).

However, HIV risk amongst MSM is not homogeneous, with males who predominantly take the receptive/passive role during anal sex tending to be disproportionately affected by higher prevalence levels (Brahmam. Ginnela NV et al., 2008, McLean et al., 2015). However, role segregation (individuals taking either the passive or active role but not both) within populations of MSM, has been shown to yield a lower incidence of HIV, compared to role versatility (Goodreau et al., 2005). This is because, with role segregation, infection is more likely to occur in receptive partners but these individuals in turn are less likely to transmit the infection further because they are unlikely to take the insertive/active role in anal sex (which is associated with a higher probability of onward transmission to the receptive partner) (Baggaley RF et al., 2010). Non-segregated sexual role behaviour amongst MSM carries a lower individual level risk of acquiring HIV compared to always taking the passive role, but a higher population level risk since, when MSM practice both passive and active roles, they can acquire infection through passive role behaviour and then transmit it when the active role is assumed (Goodreau et al., 2007).

The high levels of sexual activity and elevated probability of transmission through anal sex, give MSM characteristics associated with core groups. However, heterogeneity in sexual behaviour is diverse. In developing country settings, such as India, the role of the passive partner may be associated with cultural beliefs and traditions. For example, *Hijras*, are born biologically male, but reject this identity over time, and are equivalent to transgendered persons (Venkatesan Chakrapani et al., 2002). In contrast a *panthi* identity is the description given by *Hijras* to males who predominantly take the insertive role during sex but do not necessarily self-identify as 'gay'. Social economic factors may distinguish sexual roles, with *Hijras* tending to have lower levels of literacy, be more likely to rely on sex work as their main source of income and live with other male partners (Phillips et al., 2010).

Role segregation such as this often results in variations in levels of risk, with HIV infection more likely to be concentrated in predominantly passive/receptive MSM. This group are less likely to form or have relationships with females in the wider population (Phillips et al., 2010), meaning HIV infections are more likely to remain concentrated amongst this group of MSM. Insertive/active MSM and their female partners, could be considered as a peripheral network through which HIV is spread from the core to the wider population (Friedman et al., 2014), particularly because this population are estimated to be larger than the smaller networks of high-risk passive MSM and because they are likely to have an intermediate number of partners (Prudden HJ et al., 2012).

HIV epidemics in developed settings may display a different form of heterogeneity, with age-stratification being of common importance (Grey et al., 2015, Wilson, 2009, Service and Blower, 1995). However, despite being less explicit than in developing country settings, the dichotomy of MSM is still evident, with the phrases ”top” or “bottom” more commonly used to describe sexual role. Social economic status in role description and preference may also be important here with the term “versatile” being recognised and used more by middle class MSM in some settings (Wei and Raymond, 2011).

Individual settings, their laws and cultural practices influence the structure of MSM networks. Where homosexual practises are outlawed, large and hidden diverse networks of MSM may exist, which could create a greater propensity for the formation of peripheral networks, through which HIV is able to spread to the general population. However, to date, no strong evidence has been identified to suggest that epidemics amongst heterosexual individuals are necessarily associated with HIV epidemics initiated amongst MSM. It is likely that the structure and sexual networks that would need to support a growth in the heterosexual epidemic are not large enough.

Clients of female sex workers and their long-term female partners: Classical epidemic theory of HIV amongst FSWs suggests transmission occurs between this group and their client population who then act as a “bridging” group through which HIV is transmitted to casual or long-term partners (Mishra et al., 2012b). It is assumed that the more infections that occur in the FSW group and their clients, the more infections are likely to be spread to the general population. Ghani and *et al*. (2005) showed that higher levels of HIV prevalence are achieved when clients form non-repeating partnerships with FSWs (as opposed to FSWs having regular client partners), and that prevalence levels are higher when the FSW population is larger, because this increases the total number of FSW-client contacts per unit of time (Ghani and Aral, 2005).

In certain circumstances, such as the epidemics seen in Sub-Saharan Africa, when HIV prevalence reaches a level of above 1% in ante-natal clinics, the epidemic is re-classified from *concentrated* to *generalised*, on the premise that HIV infection has become self-sustaining in the general population, with the core groups playing a less significant role in maintaining higher prevalence levels in the general population (UNAIDS, 2011). However, the establishment of HIV infection in the general population is less well understood. In Thailand and Cambodia a reversal of the HIV epidemics occurred in the 1990s with laws implemented to enforce the use of condoms in brothels and empower sex workers (Rojanapithayakorn, 2006). In India, the Avahan HIV-intervention programme in Southern India resulted in changes in sexual risk behaviours amongst FSWs that is projected to have averted a high percentage of future HIV infections (Pickles et al., 2013). In these examples it would appear that a reduction in levels of infection amongst female sex workers and their partners are imperative to reducing the epidemic.

However, in African settings it is less clear why similar interventions focused on the protection of FSWs and positive messages about the use of condoms have not had such a significant effect. Uganda is perhaps the exception in this case, with a decline in HIV prevalence being attributed to The ABC programme; abstinence, be safe and use condoms (Green et al., 2006). However, it is less clear as to what aspects, if any, of this programme were successful. Earlier studies would suggest the initiation of the epidemic in sex worker populations and their client partners, with a progression to the general population, potentially through wives or girlfriends of clients (Oruboloye I.O et al., 1993). If this were the case, abstinence, a reduction in partner numbers, concurrent relationships and condom use could all be attributed individually or in combination to reductions in HIV. As such, the peripheral network that extends beyond the core group of FSWs may be large and diffuse. The reversal in HIV prevalence, would therefore likely be attributed to a marked reduction in infections amongst these individuals.

Relationships between young adolescent females and high-risk males: A major objective of the 2001 United Nations Declaration of Commitment was to reduce HIV prevalence amongst young people by 2010 (International Group on Analysis of Trends in and Behaviours in Young People in Countries most Affected by, 2010). Adolescent girls are disproportionately affected by HIV/AIDS. Compared to their male counter-parts, young adolescent girls incur over 80% of all new HIV infections in the countries of Sub-Saharan Africa with the highest burden of disease. Every year, 380,000 adolescent girls and young women are infected with HIV (The DREAMS initiative, 2014). In 2014 The United States President's emergency plan for AIDs relief initiated a $210 million programme to reduce new HIV infections in adolescent girls and young women (The DREAMS initiative, 2014).

Previous research has suggested that a high proportion of high-risk men's (i.e. migrants and clients of FSWs) sexual partners, are likely to be adolescent girls (Luke, 2003, Morris et al., 2000). This observation could be important in the transmission of HIV. This group are young, faced with gender inequity and potentially vulnerable to HIV infection. The formation of partnerships with higher-risk males may create a larger peripheral sexual network that is linked, through a transmission pathway, to the core population of FSWs. The Four Cities study found an association between earlier sexual debut and transactional sex to higher HIV prevalence, suggesting potentially an increased vulnerability amongst young females (Ferry et al., 2001). In addition, in Uganda, if the message of abstinence, having fewer sexual partner and higher levels of condom use were effective, then it is likely that such measures may have had a significant impact on reducing new infections in young adolescent females.

A core theme of this thesis will be to understand in greater detail the role of adolescent girls in the context of HIV epidemics in West Africa and if this population could form a peripheral network to the core, which is important to the transmission dynamics and epidemiology of

HIV. Below, I summarise previous studies that provide evidence for the potential relevance of this group.

1.5.2 Adolescent Females

Several reasons have been cited for a heightened risk of HIV infection in young adolescent women. There include engaging in unprotected sexual intercourse, having multiple partners, lacking skills to correctly and consistently use condoms, inadequate knowledge about condom use, unavailability of condoms, transactional sex and perceived vulnerability. In addition, HIV/STD prevention programmes are less tailored or designed for the purpose of adolescents and the structural support within communities is lacking (Kennedy et al., 2012).

I now turn to examine the prevalence of multiple partnerships amongst young females and the potential factors associated with this in West Africa and more broadly in other regions. I then focus on the evidence for the existence of non-commercial transactional sex amongst this group.

Evidence from the literature indicates that sexual behaviour amongst young men and women, is influenced by the context of sexual debut, social status, relation to peers and family as well as attitudinal, normative and behavioural control constructs (Boileau et al., 2009). Reports of multiple partnerships are varied and often context specific, depending on where and how the data were collected. For example, one study amongst young slum dwellers in Nigeria, found that 12% of females had multiple partners (Adedimeji et al., 2007) and a study from urban centres in Mali showed that 32% of women reported multiple partners in the past 6 months (Boileau et al., 2009). A more thorough review of the available literature and data on the prevalence of multiple partnerships amongst young people in West African countries is included in this PhD, in Appendix 5, Table 5.2. In summary, the estimates range from less than

1% to over 20% of the population of young females reporting multiple partnerships in the past 6 months or one year, in the different surveys that were sourced.

The importance of multiple partnerships is that it is likely to expose young people to a greater risk of HIV. One particular factor related to multiple partnerships is age of sexual debut. This individual variable may be a proxy for having a higher number of sexual partners throughout adolescence, with a greater length of time to form relationships before entering marriage. It is consistently cited as a risk factor for HIV, with one study finding that if first sexual intercourse occurs before the age of 14, individuals had a 2.7 times greater risk of HIV relative to their older (20-24 years) peers. Those aged 15-24 with two or more sexual partners in the past 12 months had a 1.6 times ($p<0.05$) higher risk of HIV infection (Kembo, 2012). This was also one of the few parameters from the Four Cities study that showed a significant relationship with higher HIV prevalence (Ferry et al., 2001).

A second important factor may be age asymmetry in sexual partnerships. Findings from several studies revealed that between 27-50% of adolescent girls had partners that were six or more years older than them and many of these men were married (Luke, 2003). Despite this, the evidence on age asymmetry and risk of HIV infection is mixed. Some studies have shown evidence for an increased risk of HIV infection with partners 10 or more years older (Kelly et al., 2003), whilst another study has shown an increased risk when partners are five or more years older (Gregson et al., 2002). However, other studies have shown no significant effect (Jewkes R et al., 2012, Glynn et al., 2001, Harling et al., 2014).

For young females, an important distinction between whether an older partner may be at higher-risk of being infected with HIV is dependent on that individual's sexual behaviour more generally. From Jewke's study an association between having an older partner and HIV infection was not evidenced, although engaging in any form of transactional exchange for sex was shown to be significantly related to being infected with HIV (Jewkes R et al., 2012). One study has shown that adolescent girls younger than 20 years constitute between 31 to 66% of men's non-marital partners (Glynn et al., 2001) and that 32% of all extramarital sex partners of men involved an element of transactional exchange (Lagarde et al., 1995). Two of these studies also found approximately half of all partners of men with 'high-risk' sexual behaviours, such as travellers or those involved in economic transactions are likely to be adolescent girls (Luke N and Kurz KM, 2002, Morris et al., 2000).

Synthesising the literature, an important element of multiple partnerships and HIV risk appears to be the associated with what is termed 'non-commercial' transactional sex. Below I explore the evidence for this and look at the motivations associated with it.

1.5.3 Transactional sex

An important facet of the vulnerability of young females relates to their motivations or social pressures for engaging in sexual partnerships, particularly those involving a transactional element. Typically, we equate meanings of sexual exchange towards subsistence rather than consumption. For example, the motivation for women entering sex work, tend to be related to survival strategy and poverty alleviation as opposed to a desire to obtain non-essential material goods. Interestingly, one study identified up to 25 different forms of sex work, categorising these as either 'direct' or 'indirect' forms of transactional exchange, with a wide range of geographical distribution (Harcourt C and Donovan B, 2005). This highlights the broad definition of what the material exchange of goods or money for sex may encompass.

A large multi-country study examined factors influencing transactional sex. Out of the 12 countries included in the study, 11 estimated that the odds of women engaging in transactional sex are significantly higher among women in the younger age groups (15-24) compared to older women (25 years and older). In Burkina Faso, women in the 15-19 age range were 400 percent more likely to engage in transactional sex compared to those over 25. In Mali, Togo and Zambia, the odds are more than 100 percent higher and those in the 20-24 age range were significantly more likely to engage in transactional sex compared to older women (Chatterji et al., 2005). This suggests the demographic of those engaging in transactional sex for consumptive purposes tend to be adolescents and those aged under 25. Another study examined the motivational reasons for engaging in transactional sex within a high poverty setting in South Africa. These included pursuit of fashionable images, popular culture, increased availability of commodities, a high desire for global technologies and the general level of wealth inequality that exists (Zembe et al., 2013).

Reports of the incidence of transactional sex are quite varied. Only 8.3% of the cohort of women followed in the Eastern Cape province in the South African Stepping Stones study (mean age 18.6) reported transactional sex (Jewkes R et al., 2012). Those engaging in transactional sex were more likely to have experienced partner violence, had a higher level of inequitable relationships and were more likely to also be infected with HSV-2. The lower prevalence of transactional sex in the Stepping Stones study, compared with 21.1% of women attending an antenatal centre from a study in Soweto (Dunkle et al., 2004), showing how varied reports of transactional sex may be. In the Soweto study, transactional sex was associated with reporting a past experience of violence by intimate partners, substance use, urban residence, ever earning money or living in substandard housing. In both instances, transactional sex was positively associated with increased odds of being HIV positive.

A study conducted in post-conflict Liberia also examined the risk factors for transactional sex in young females. In this instance, 72% of the sample reported transactional sex. This unusually high percentage may be correlated with the long-term political instability of the country, where women engage in transactional sex equally as a means of survival as well as for consumptive purposes. Engagement in transactional sex was associated with a lack of education, reporting no earned income, longer duration of sexual activity, early sexual debut, a history of sexual violence and multiple sexual partnerships (Okigbo et al., 2014).

The above studies examine the risk factors for transactional sex, however, what motivates engagement in transactional sex may be quite different. Sexual exchange is also seen as a means used by women in order to pursue images and ideals created by both the media and globalisation (Zembe et al., 2013). What shapes such behaviour is equally embedded in an understanding of different contexts and what, according to Leclerc; "constitutes normative heterosexual activity in various socio-economic and cultural context" (Leclerc-Madlala, 2003). For many women, the exchange of sex for financial or life-style benefit is an important component of their attitude and orientation towards sexual relationships. The concept of 'prostitution' in such instances is misrepresented, with the motivational driver satisfying 'wants' as opposed to 'needs', and reflects a desire to acquire items representing higher social status (Leclerc-Madlala, 2003). However transactional sex may also be "part of a larger pattern of social interdependence in sub-Saharan Africa where women receive material goods whilst males obtain outward displays of power and prestige" (Leclerc-Madlala, 2003). In countries with high levels of economic instability and inequity, women may choose to engage in multiple concurrent transactional relationships as a means of providing essential resources (Atwood et al., 2011).

Transactional sex may therefore be an important component of the motivation by young females to engage in sexual partnerships with multiple individuals. If a large percentage of the female adolescent age group are engaging in transactional relationships, associated with higher HIV incidence, HIV prevalence within a setting is also likely to be higher, since the number of individuals exposed is greater. However, in West Africa, a factor which may limit HIV prevalence is the high levels of circumcision amongst males, which in turn may also mediate lower levels of ulcerative STIs, another factor associated with higher prevalence of HIV (Caldwell et al., 1995).

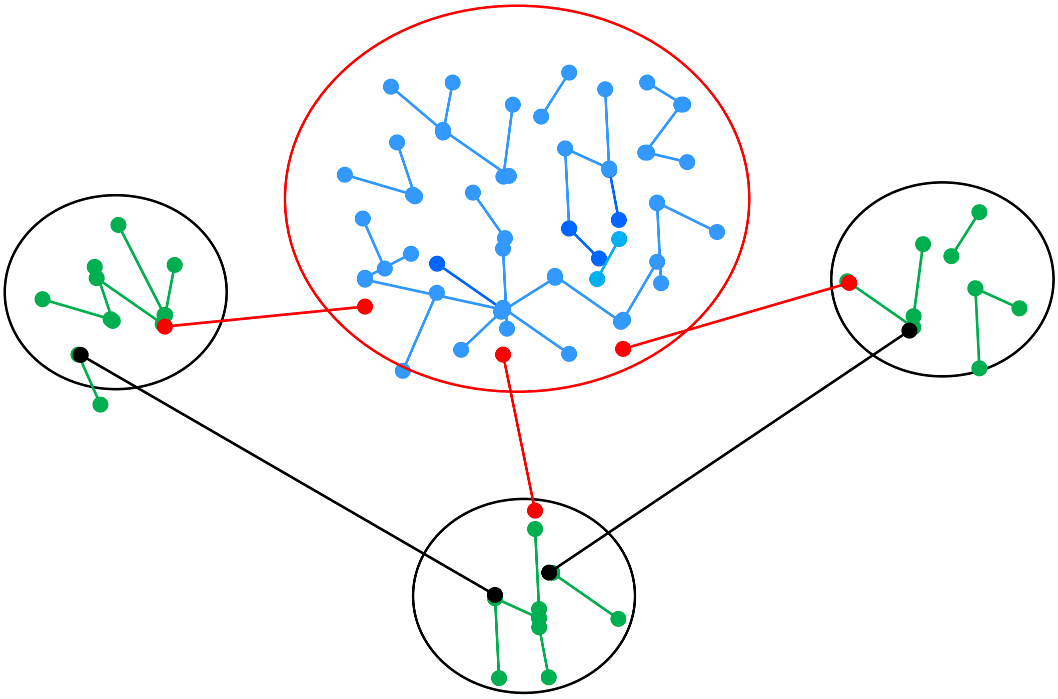
In the next section, I build on the ideas and knowledge gained from the literature and develop the outline for my conceptual framework.

1.6 Conceptual Framework

As discussed previously, a body of mathematical modelling research has demonstrated the importance of behavioural heterogeneity in explaining the transmission dynamics and epidemic characteristics of both HIV and STI epidemics in populations. Hethcote and Yorke established the idea of a "core group" and demonstrated the characteristics of this core group that enable epidemics to be sustained at a population level (Yorke et al., 1978). Modelling analyses have explained characteristics that are important. These include having high numbers of partners that are connected within a network, which alone, is capable of sustaining the persistence of an STI infection (Garnett and Anderson, 1996). Epidemiological studies have similarly established that a range of different groups of individuals form core groups. These include female (Alary and Lowndes, 2004) and male sex worker populations, groups of men who have sex with men and people who inject drugs (Gorbach et al., 2009, Plummer et al., 1991). Mathematical modelling of STIs and HIV has also shown the importance of sexual mixing patterns. Assortative (or 'like with like') mixing has a tendency to increase epidemic growth at a faster rate amongst individuals who form sexual partnerships others who have characteristics alike to themselves. Disassortative ('unlike with unlike') mixing conversely results in an epidemic that progresses at a slower rate, but ultimately reaches a higher prevalence level.

Modelling has also shown that larger 'core populations' lead to higher population endemic levels of HIV infection.

Modelling studies also show that high levels of assortative mixing, for example within core populations in combination with a level of disassortative mixing with 'peripheral groups' outside the network of the core, tends to increase and sustain HIV epidemics (Ghani et al., 1997). Additionally, the findings suggest that the greater the levels of cohesion between the peripheral groups are, ultimately results in higher population endemic levels of HIV infection within the population as a whole:



Sexual partnerships between individuals in the core

Sexual partnerships between individuals in ‘peripheral ‘network groups outside of the core

Sexual partnerships between members of the core and members of ‘peripheral’ networks outside the core

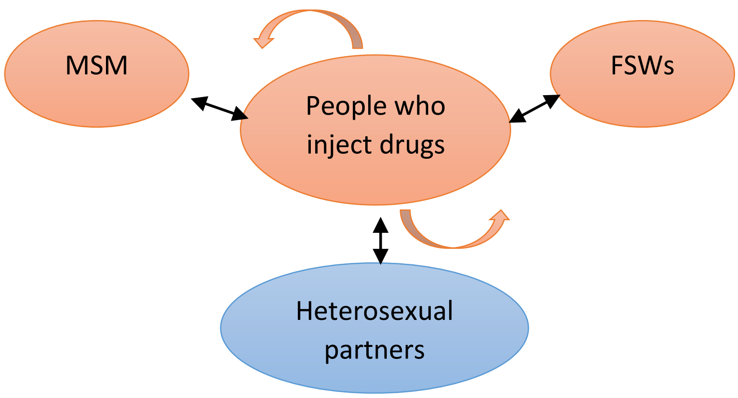
Sexual partnerships between member of different ‘peripheral’ networks (to the core) in the general population

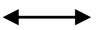
Figure 1.3: A large core group, with high levels of assortative mixing, may be linked to subgroups peripheral to the core, with partnerships that link these networks together.

This concept of cohesion and connectivity is important in understanding the drivers of HIV epidemics, showing that it is important for interventions to identify the networks of peripheral groups. Much of the previous modelling studies have sought to identify these individuals on the basis of partnership numbers, often without identifying key characteristics of these groups.

In my thesis research I seek to understand the relevance of behavioural heterogeneity when constructing a mathematical model, and how the modelling concepts translate to different epidemic settings, where there may be many subgroups of vulnerable populations of varying size and levels of connectivity. For example, do peripheral groups (i.e. those in green in figure 1.3) represent different types of individuals or could they, in fact, represent a single subgroup with similar characteristics, who are intrinsically linked through their sexual partners?

In 1.5.1 I reviewed core groups and their networks. For people who inject drugs (figure 1.4), their sexual networks may also include other core groups such as MSM and FSW as well as heterosexual partners (Gorbach et al., 2009). In this instance it may be more complicated to identify peripheral networks.

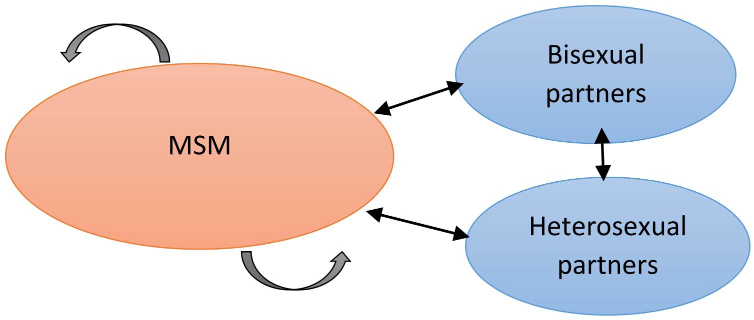



Black arrow shows sexual partnerships between groups


Curved arrow shows injecting partnerships formed within group

Figure 1.4: Peripheral sexual networks linked to the core population of people who inject drugs.

For MSM (figure 1.5), for example, heterogeneity amongst this group is evident from studies (Goodreau et al., 2005). Although high rates of partnership formation amongst this group often means that they are considered as a single core population, behavioural research shows that there are patterns of sexual mixing evident amongst them (Thomas et al., 2009). Partnerships external to the core may exist between bisexual men or partnerships with heterosexual partners. These may form peripheral networks, although it is unclear how inter-connected they are or how far the networks extend to the general population.

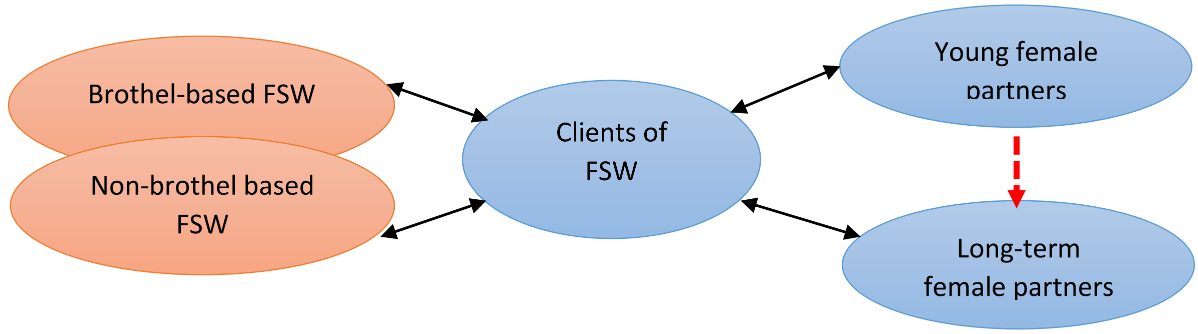


Black arrow shows sexual partnerships between groups

Curved arrow shows sexual partnerships formed within group

Figure 1.5: Peripheral sexual networks linked to the core population of men who have sex with men

Similarly, female sex worker groups are often highly heterogeneous with some FSWs being brothel-based and others either street-based, venue-based or home-based. The different subgroups may have very different numbers of partners and condom use. Behavioural research also shows that these groups change typology over the course of time in response to social economic and political pressures (Gorbach et al., 2006, Beattie et al., 2013). Similarly client populations are heterogeneous and may form partnerships with younger female partners as well as long-term partners or wives (Luke, 2003). In settings where sex work is widespread, the peripheral networks of FSWs and clients may constitute a larger proportion of the total population compared to those of MSM and IDUs, and so lead to larger HIV epidemics.



Black arrow shows sexual partnerships between groups

Red arrow shows aging and fluid movement of young females into females who are long-term partners of client.

Figure 1.6: Peripheral sexual networks linked to the core population of female sex workers

This PhD will explore the population drivers of heterosexual HIV transmission in West Africa, using ecological analysis, static and dynamic modelling to both explore key drivers of HIV in West Africa and discuss the simplification for model construction, epidemiological theory and epidemic classification.

Hypothesis

Epidemics in West Africa have previously been described as generalised or more "mixed" in nature. However, past modelling work has suggested that sex work remains to be the predominant driver of HIV infections in this region and is still of major importance. In this thesis I aim to explore this theory and seek to falsify the case that sex work and the behaviours associated with it (high partner numbers of sex workers, condom use and duration, for example) are the only major factor determining HIV prevalence in this region. I explore the importance of peripheral networks of high-risk adolescent girls, linked through clients of female sex workers and whether the size and sexual activity of this group may also have a key role in determining HIV prevalence, particularly in West African countries where prevalence is higher (3-6% versus 0-2%).

1.7 Aims and Objectives

The overall aim of this thesis is to use mathematical modelling and ecological analysis to gain an improved understanding of the determinants of the variability of HIV prevalence across West Africa and the potential implications for future epidemic appraisals and decision making.

Objectives:

1. To assess whether the incorporation of additional heterogeneity into the UNAIDS Modes of Transmission model affects predicted patterns of HIV incidence in Nigeria.

2. To explore whether variations in the size and HIV prevalence of different population subgroups is correlated with variations in female and male population HIV prevalence across West Africa.

3. To use dynamic modelling to explore the main determinants of variations in female and male endemic HIV prevalence across West Africa.

4. To use dynamic modelling to assess whether UNAIDS epidemic threshold categorisations for HIV epidemics should be revised to account for the presence of universal male circumcision in settings and if the categorisations should be updated to more accurately reflect pathways of HIV transmission.

5. Identify and report on key findings from this research thesis and discuss the implications for future modelling and epidemic appraisals

2. Overview of Methods

This PhD uses a combination of research methods. These include; a broad review of the published behavioural and epidemiological data from West Africa, the critique and revision of a UNAIDS static compartmental model and the development and application of a deterministic dynamic compartmental model. The appropriate choice of model structure and parameterisation are important underlying concepts to my thesis and approaches to inform model development is an important theme of the thesis.

The technical methods applied in the thesis are detailed in the chapters, which are in the format of four academic research papers (Chapter 3-6) and their accompanying technical appendices. The purpose of this section is to provide an overview of what these technical methods are and how they are related across the research papers.

This section also provides details of additional methods that were carried out, not included in the research papers, but instead used to inform the narrative, ideas and conceptual thinking related to the thesis. More detail of the exact methods in this section, relating to each of the technical methods are included in appendices at the end of the thesis.

2.1 Literature reviews for ecological analysis, mathematical model structure development and model parameterisation

This section outlines the research criteria for two different data reviews used in the ecological analysis (Chapter 4) and for model parameterisation (Chapters 3, 5 and 6). The reviews were carried out with the support of Natalia Bobrovia. We designed the research criteria together, Natalia sourced the literature and I scanned and reviewed the content and made the final decision on which to include.

The first review was to assess the size and behavioural characteristics of subgroups of female sex workers in West Africa, the results of which featured in all four Research Papers which included data to inform the ecological analysis (Chapter 4) as well as model parameterisation applied in Chapters 3, 5 and 6.

Quantitative and qualitative research studies were searched in Pubmed, Adolec, and Popline, using the following search terms:

‘sex work’, ‘sex worker’, ‘prostitute’, ‘prostitution’, ‘transactional sex’.

In addition, when no information was available using these search terms, the term ‘HIV’ was used. The search was limited to the 2010-2014 time period. Abstracts were further examined to determine eligibility for inclusion. In addition, grey literature and reports, such DHS, IBSS, UNGASS, UNAIDS, UNICEF, USAID, World Bank were studied as far as they were accessible.

Additional information on the methods is contained in Appendix 5.1 and the results from the review are in Appendix 2 table 2(c).

The second review was intended to provide parameter estimates for the size of a group of adolescent girls who have multiple partnerships for the ecological analysis (Chapter 4) and the dynamic model parameterisation (Chapters 5 and 6). From the above literature review aimed at assessing the size and behavioural characteristics of female sex workers, a significant number of the studies that were returned on transactional sex included within them the theme of non-commercial partnerships amongst younger females and male partners, which involved an element of transactional exchange. The females in the studies are not identified as female sex workers but except payment or gifts in return for sex. This prompted this second review to enable a better understanding of this group of younger females.

The intention of the review was later to provide estimates for the ecological analysis (Chapter 4) and model parameterisation (Chapters 3, 5 and 6). For chapters 5 and 6, data was instead acquired from a different source (the Demographic Health Surveys (DHS) across West Africa) and for Chapter 3 it was acquired from the NARHS 2007 survey (Nigeria only), because these source provided greater levels of consistency and comparability, with each of the individual country surveys in the DHS collecting data on females who reported multiple partnerships (2 or more partners) in the past year. Therefore, ultimately the review instead served as a guide to provide the highest possible estimates from the data for the percentage of adolescent girls engaging in multiple partnerships (per year). The review also provided additional insights into the characteristics and vulnerabilities of this group which helped to later justify their inclusion in the model structure.

The review included published and grey literature for 15 West African countries. Quantitative research studies were searched in Pubmed, Adolec, and Popline by country, using the following search terms:

‘young’, OR ‘adolescent’ OR ‘adolescent’ OR ‘youth’ AND ‘sexual behaviour’ OR 'sexual partners’ or ‘multiple partners’ or ‘number of partners’.

The search was limited to the 2000-August 2013 time period. Abstracts were further examined to determine eligibility for inclusion. In addition, grey literature and reports, such as IBBSS, UNGASS, UNAIDS, UNICEF, USAID, World Bank were studied as far as they were accessible. Manuscripts were reviewed in English and French, and reference lists from relevant articles and reports were hand-searched. The information obtained was used to provide guidance for an upper limit for the size of the female 2+.

Additional information on the methods is contained in Appendix 5.1 and the results from the second literature review are presented in Appendix Table 5.2.

2.2 Adaptation of the Modes of Transmission Model (MoT)

The adaptation of the MoT is included in the first Research Paper, Chapter 3. The literature review to assess the size and behavioural characteristics of subgroups of female sex workers in West Africa, provided an initial insight into the different typologies of sex work and how these could potentially be conceptualised and categorised in mathematical models. Sub-divisions based on the identification of "official" sex work versus "unofficial" provided the early thinking and a rationale, firstly for the stratification of commercial female sex workers into two different typologies; brothel-based and non-brothel based, but also the inclusion of a group of adolescent females who have multiple partners, for which the partnerships may be transactional in nature.

These ideas were used to guide the adaptation of the Modes of Transmission Model (MoT) to include new population subgroups. This was informed by the availability of the data from the National HIV/AIDS and Reproductive Health Survey (NARHS) 2007+ (Federal Ministry of Health Nigeria, 2008), for the model estimates on the adolescent female transactional group. Information to guide the stratification of the female sex worker groups into brothel-based and non-brothel based was extracted from the HIV Integrated Biological and Behavioural Surveillance Survey (IBBSS) from 2008 (Federal Ministry of Health, 2007). Data on men who have sex with men, injecting drug users and the characteristics of their sexual partners was also extracted from this same survey.

Additional information on the model and the revisions are contained in Appendix 6, including a figure showing the subdivision and revision of groups.

2.3 Linear regression analysis for ecological analysis

The results from the literature review were used to inform the approach for the linear regression analysis included in the second Research Paper, Chapter 4. The results from the MoT modelling demonstrated the importance of including behavioural heterogeneity in models and the size of population subgroups and their level of risk. The purpose of the regression analysis, was to build on these observations and to assess whether or not there was evidence for associations between the size, behavioural characteristics and HIV prevalence of different population subgroups from the demographic health surveys (DHS) data, which could be useful in identifying potential pathways of transmission in the population. Then to use these findings to guide the development of the dynamic deterministic compartmental model in Chapters 5 and 6.

The method of simple linear regression analysis was used because of the limitation in the number of data points available from the DHS across West Africa. In some instances data were only available for 10 countries. Consequently, other independent variables were not controlled for.

Additional information on this analysis including the rationale for the inclusion of behavioural subgroups are provided in Appendix 7.

2.4 Multiple risk to HIV infection in Mathematical Models

Additional analysis, which was initially intended for inclusion in Research Paper 1, but later omitted is presented here. The ideas and findings from this analysis helped to inform the concept for the development of the dynamic deterministic compartmental model, therefore justifying its inclusion here.

The methods in Research Paper 1, made revisions to the MoT model categories by introducing additional subgroups based on their sexual risk behaviour. However, an important observation in both the original and revised versions of the model, is that the risk of acquiring HIV is only possible from one partner group. For example, for male clients, risk of infection is from their female sex worker partners only and not their longer-term more stable female partners. In this instance the assumption may be valid, however, there are other examples that exist where an individual's risk of infection may be from multiple sources and that this observation is important for estimating new numbers of infection and HIV policy in general. This concept was examined for the subgroup of young females engaging in transactional sex to assess differences in the projected number of infections when the group partners only with their main partner group versus a scenario where they also partner with clients of female sex workers as well as their main partners. The worksheet of the model structure and the results are presented in Appendix 8.

2.5 Development of the dynamic deterministic compartmental model

The development of the dynamic model was guided by the findings from the MoT model and the work presented in Appendix 9, coupled with the findings from the ecological analysis and literature review. The over-arching aim was to develop a model that reflected important pathways for the risk of HIV in West African settings. The model design was intended to capture population HIV transmission in a heterosexual epidemic and therefore men who have sex with men and people who inject drugs were omitted from the model, justification for this is provided in Appendix 9, but is largely related to difficulties in sourcing data on these groups from the West Africa region.

I worked in collaboration with Zindoga Mukandavire to develop the dynamic model. I developed the concept and structure of the model and we jointly formulated the equations. The model was coded in R programme (The R Foundation, 2015) and this was carried out by Zindoga Mukandavire, who also ran the model and produced the output files. I carried out the full analysis of the model results.

Research Paper 3 includes details of the development and structure of the model as well as information on. Additional information on the model's development, including the section of population subgroups, behavioural heterogeneity and pathways of infection are presented in Appendix 9.

2.6 Model parameterisation and fitting, sensitivity and uncertainty analysis

Modes of Transmission Model

The MoT model was parameterised using multiple sources including the NARHS 2007 survey and IBBSS 2008 survey for population subgroups and high-risk groups, respectively. The model was calibrated to the ante-natal care (ANC) HIV prevalence for the state (Cross River) in Nigeria

A sensitivity analysis was used to test the robustness of the model input parameters and projections, using Latin Hypercube Sampling to generate 10 000 model input sets. The intention of this was to assess the variation in model outputs and results produced by the model, under different assumptions to understand which model input parameters, the model projections were most sensitive.

Additional information on the selection of parameters, model calibration methods and details of the sensitivity analysis are shown in Appendix 1 and 10.

Dynamic deterministic compartmental model

The model was parameterised using data from both the DHS surveys as well as the wider literature, Appendix 3, Supplementary Material (c). The parameter ranges acquired from the data and literature were sampled using uniform distributions and parameter input sets acquired using Latin Hypercube sampling.

For each model input, the model was run to equilibrium HIV prevalence and only the projections where HIV prevalence was among the literature-reported ranges were chosen. The model projected HIV prevalence of 0.5-6% in the general female population, 0.5-4% in the general male population, 15-48% in the brothel-based FSW group and 10-25% in the non-brothel based FSW group as potential model fits that reflect different West African epidemic trajectories. No fitting criteria were applied to the female 2+ group, male 2+ group or the brothel-based FSW clients and non-brothel based FSW client groups due to not having sufficient data for these subgroups (Chapter 3).

The behaviour of the model was explored for each of the scenarios sampled parameters using partial rank correlation coefficients (PRCC) as a sensitivity analysis technique (Blower et al., 1994). This allowed us to identify which input parameters were most influential on the prevalence values in different ranges.

Sampled model input parameters, that were independently related to the model outcome, HIV prevalence, were included in the analysis. The PRCC was carried out using Stata version 13 (http://www.stata.com/, 2013).

Additional information for the analysis are included in Chapter 5, Research Paper 3, Appendix 3 and more details on the specific calculations for the results figures are included in Appendix 10.

3. Can the UNAIDS modes of transmission model be improved? A comparison of the original and revised model projections using data from a setting in West Africa

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Research Paper Cover Sheet

Section A – Student Details

Student: Holly J Prudden

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Thesis Title: Determinants of population variability in HIV across West Africa: ecological and modelling analyses

Section B – Paper already published

Where was the work published? AIDS

When was the work published? 2013

If the work was published prior to registration for your research degree, give a brief rationale for the inclusion. NA

Have you retrain the copyright for the work? Yes

Was the work subject to peer review? Yes

Section D- Multi-authored work

For multi authored work, give full details of your role in the research included in the paper and in the preparation of the paper.

I was the lead author of this paper and worked with Charlotte Watts to develop the storyline for the paper. I was solely responsible for the re-parameterisation of the model and comparative analysis. I drafted the full manuscript and made revisions based on comments from Charlotte Watts and Peter Vickerman. Anna Foss and Lori Heise provided further comments and feddback

Amaka Momah, Natalia Bobrova, James Blanchard and Michael Ogungbomi provided advice and help in sourcing the data and comments to the final draft.

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3.1 Research Paper 1

Can the UNAIDS modes of transmission model be improved? A comparison of the original and revised model projections using data from a setting in West Africa

Abstract

Objective: The UNAIDS Modes of Transmission Model (MoT) is a user-friendly model, developed to predict the distribution of new HIV infections among different subgroups. The model has been used in 29 countries to guide interventions. However, there is the risk that the simplification inherent in the MoT produces misleading findings. Using input data from Nigeria, we compare projections from the MoT with those from a revised model that incorporates additional heterogeneity.

Methods: We revised the MoT to explicitly incorporate brothel and street-based sex-work, transactional sex, and HIV-discordant couples. Both models were parameterized using behavioural and epidemiological data from Cross River State, Nigeria. Model projections were compared, and the robustness of the revised model projections to different model assumptions, was investigated.

Results: The original MoT predicts 21% of new infections occur in most-at-risk-populations (MARPs), compared with 45% (40–75%, 95% Crl) once additional heterogeneity and updated parameterization is incorporated. Discordant couples, a subgroup previously not explicitly modelled, are predicted to contribute a third of new HIV infections. In addition, the new findings suggest that women engaging in transactional sex may be an important but previously less recognised risk group, with 16% of infections occurring in this subgroup.

Conclusion: The MoT is an accessible model that can inform intervention priorities. However, the current model may be potentially misleading, with our comparisons in Nigeria suggesting that the model lacks resolution, making it challenging for the user to correctly interpret the nature of the epidemic. Our findings highlight the need for a formal review of the MoT.

Keywords: HIV epidemic, mathematical modelling, most-at-risk-populations, Nigeria, UNAIDS

Introduction

Mathematical modelling has helped increase our understanding of the HIV epidemic and played a key role in decision-making (Anderson RM and Garnett GP, 2000, Anderson R. M et al., 1990, Boily MC et al., 2007, Regan and Wilson, 2008) . UNAIDS developed a series of simple mathematical models, to help countries understand their current epidemic (UNAIDS and The World Bank, 2010, Pisani E et al., 2003, UAC/UNAIDS, 2009). The Modes of Transmission (MoT) model is one such model. It is a deterministic static compartmental model, used to estimate the distribution of new HIV infections in different population subgroups based on information about their current HIV prevalence and behavioural patterns. So far, 29 countries have analysed their HIV epidemic using the MoT model [8], with the results being used to help guide interventions (Case et al., 2012, UNAIDS, 2007).

The MoT model divides the population into subgroups that represent the percentage of individuals in the population who ascribe to a certain type of behaviour or identity, related to their 'risk' of acquiring HIV. In this instance, 'risk' is dependent on: the degree of sexual contact or injecting drug use activity that is exchanged with their partner group; the HIV prevalence in their partner group; the probability of acquiring HIV through a single contact with that partner group and the percentage of sexual or injecting acts which are protected (through condom use or sterile needles). Some individuals have multiple partner groups, but in the MoT, acquisition of HIV is only characterised through the partner group with the highest transmission risk. The HIV transmission pathways were all predefined by the model's authors.

Although this compartmentalization of the population is a standard approach in deterministic modelling, most deterministic models usually take into account multiple exposures, unlike the current MoT. The predefined structure for the MoT may be overly simplistic, especially in settings with important heterogeneities within subgroups. For example, in many settings there are distinct subgroups of sex workers, such as ‘brothel-based’ and ‘street-based’, that have different numbers of sexual partners and condom use, and so potentially different HIV risks (Federal Ministry of Health, 2007).

Although there are many benefits to having a relatively simple MoT model, there is the risk that the model simplicity and inherent assumptions about patterns of sexual mixing, produces misleading findings (Case et al., 2012). The aggregation may also lead to a masking of key population subgroups that are particularly vulnerable to HIV infection, which should be targeted by HIV programming interventions. There is also a danger of it becoming a ‘black box’ process (Garnett, 2002), in which the findings are taken at face value, without sufficient appreciation of how the underlying assumptions and simplifications may influence the incidence projections obtained.

Given the widespread use of the MoT to inform decision making, the aim of this study was to compare the MoT model projections for Cross River, a Nigerian state with a low-level generalised HIV epidemic of 8%, with a revised MoT model that incorporates additional heterogeneity and updated parameters. An intermediate model, which employs the revised model structure, but retains the original model parameters, is used to illustrate the incremental effect of incorporating additional model complexity, and revising and updating the parameter estimates.

Methods

The modes of transmission model

The model is designed to calculate the number of new HIV infections within a 12-month period among different population subgroups, based on the current distribution of infections in the population. Biological and behavioural surveillance data, supplemented by the broader scientific literature are used to develop setting specific model input parameters.

To estimate the risk of infection for a susceptible individual, the model uses an established mathematical equation (Appendix 1.1), that estimates the probability of HIV acquisition if the individual has a given number of sexual partners from a particular (population) subgroup and a specified number of sex acts with those partners (UNAIDS, 2007). An estimate of the number of incident infections is generated by multiplying the risk of infection by the number of susceptible individuals at risk in a subgroup. In the original MoT model, the total adult population (commonly taken to be 15–49 year olds) is divided into 11 subgroups and disaggregated by sex. HIV transmission probabilities are per act estimates and are based on the published literature (Powers et al., 2008). The presence of sexually transmitted infections (STIs) in the partner group adds a multiplicative effect to an individual's risk of HIV acquisition (Gray et al., 2001). The partially protective effect of male circumcision is incorporated (Powers et al., 2008). Finally, the model is calibrated, by adjusting the HIV prevalence in certain risk groups to the antenatal care (ANC) prevalence for that particular setting, so the weighted average across all risk groups (men and women) matches the HIV ANC prevalence. The model therefore enables estimates for the total percentage of new infections in different population subgroups to be calculated.

'Original' modes of transmission modelling analysis for Cross River state

An MoT modelling analysis (Mbukpa M et al., 2010b), was conducted in 2009 in Cross River state, located in the south of Nigeria with a population of 2.1 million aged 15–49 years. Survey data from 2008 estimates an ANC HIV prevalence of 8%, making Cross River the fifth highest

HIV prevalence state in the country (UNAIDS and National Agency for the Control of AIDS (NACA), 2010). For this study, state level data were used where available, and otherwise data from states in the same geopolitical zone or national-level data were applied. The size of the population was based on the 2008 DHS (National Population Commission (NPC) [Nigeria] and ICF Macro, 2009) and 2007 NARHS (Federal Ministry of Health, 2008). The STI prevalence in different population subgroups was based on survey data on the reported presence of unusual genital discharge or genital ulcer in the past 12 months (Federal Ministry of Health, 2007, National Population Commission (NPC) [Nigeria] and ICF Macro, 2009). Total numbers of sex acts reported by one population subgroup were not equalized with their partner group. The original MoT indicates that sex acts between clients and FSW should be equal, in this case however this instruction is not followed. This limitation in the MoT may lead to an over-estimate of HIV infections for some subgroups and an under-estimate for others. Full details of the methods and data sources used are in Table 1, Appendix 1.2. The behavioural and biological parameter tables for the model are provided in Appendix 1.3. The original model was calibrated to ANC prevalence for Cross River state, 8%, for both male and female groups.

Revision of the modes of transmission model for Cross River state

The MoT model was revised to incorporate additional heterogeneity using data from the NARHS 2007 (Federal Ministry of Health, 2008), IBBSS 2007 (Federal Ministry of Health, 2007) and wider literature. Figure 1 summarizes the revisions made, showing how some of the original subgroups were divided into smaller subgroups or fed into different subpopulation categories.

Based upon a review of the literature, the revised model included a new group called 'women involved/engaged in transactional sex' to represent women 'who have sex for cash, gifts or favours' but who would not necessarily identity themselves as 'sex workers.' Research from Nigeria indicates that this type of behaviour is prevalent (Erinosho et al., 2012, Owoaje and Uchendu, 2009, Cooper et al., 2011). The subgroup is formed from the 'casual heterosexual sex (CHS)' group in the original model, although their involvement in the transactional exchange of money for sex and contact with multiple sexual partners place them at higher risk of HIV infection than those in the CHS group. In addition we subdivided the 'sex worker' group into 'brothel-based' and 'non-brothel based' FSWs because most surveys in Nigeria distinguish FSWs in this way. We established separate FSW client groups for each.

Revised size estimates for the subgroups from the original model led to an increase in the estimated size of the 'low-risk' population for women (26.5–38.6%) and men (18.8–34%), with estimates for 'partners of those engaged in casual heterosexual sex (partners CHS)' revised down because the NARHS 2007 survey suggested the percentage of individuals engaging in 'CHS' is lower than in the original model. Individuals who were originally in the 'partners CHS' subgroup were redistributed to the 'low-risk' group in the revised MoT. In the original model, those in the CHS subgroup were defined as individuals who report 'non-marital' sex, but in the revised model we reclassified them as individuals who report 'more than one marital or non-marital partner' in a 12-month period(Federal Ministry of Health, 2007), as many individuals have non-marital relationships but do not have multiple partners. For individuals in non-marital relationships with a single partner, we created additional subgroups called 'boyfriend' and 'girlfriend' relationships. The number of individuals receiving blood transfusions and medical injections was not revised.

The 'low-risk' group was divided into 'discordant' partnerships/couples, defined as heterosexual monogamous relationships in which one partner is HIV positive and the other

HIV negative. The estimate for the size of this population is based on a previous study (Chemaitelly et al., 2012). The remaining individuals in this subgroup are considered as being very 'low-risk'. They represent sexually active individuals in the population who are in stable relationships in which both partners are assumed to be either HIV negative or HIV positive. The prevalence in the 'low-risk' group may be adjusted to match the ANC prevalence in the setting, for model calibration purposes, but with no new infections being attributed to this subgroup.

In the revised model, the total number of sex acts offered by a subgroup was balanced between partner groups by adjusting the number of partners (*n*) in the corresponding subgroup, while assuming the number of contacts per partner (*a*) was equal between groups. As there is more data available on the number of partners of brothel-based and street-based FSW, we used a triangulation method to calculate the number of partners their client groups have. For the CHS groups, we used the estimate from the original MoT of two partners and 50 sex acts for men and calculated the number of female CHS partners based on the assumption that they too have 50 sex acts with male partners.

The revised model was calibrated to an 8% HIV prevalence from ANC data and incidence projections were cross-referenced with projections (0.0025 for Nigeria) from the UNAIDS global report (UNAIDS, 2010), which equates to approximately 5000–5500 new infections.

Modes of transmission: intermediate model

An intermediate MoT, with the revised model structure and original parameter estimates was developed. This model contains the revised population estimates for the stratified subgroups from the revised model but maintains the same behavioural and epidemiological estimates as the original model. Table 1(a) compares and summarizes the behavioural parameter estimates across all three models and Table 1(b) the epidemiological parameter estimates. As in the original model, for the intermediate model, balancing of sex act numbers between subgroups was ignored.

The revision to the model structure allows for a comparison of model projections between the original and revised MoT. As the intermediate model uses the revised structure and revised population size estimates it is not possible to draw a direct comparison of the effect of changing the structure because of changes to population sizes and additional risks. However, it does allow for an overview of additional heterogeneity present within individual subgroups. The comparison between the intermediate and revised model is more direct, because only parameter estimates are updated. Therefore, the effects of disaggregating subgroups and including different risk behaviours is shown here.

Categorisation of population subgroups

In order to assess the distribution of HIV infections in different key population subgroups from an HIV programming perspective, we grouped the population into categories in order to compare the findings from the original versus the revised MoT.

In the original model we classified sex workers, clients, men who have sex with men (MSM) and injecting drug users (IDUs) as 'most-at-risk-populations' (MARPs). In the revised model the MARPs included the brothel-based FSW, non-brothel based FSW, MSM, IDUs, clients and men and women involved in transactional sex. Subgroups that form partnerships with MARPs were termed 'partners of MARPs', these included female partners of MSM, sexual partners of IDUs and regular female partners of FSW clients in the original model. For the revised model, regular female partners of men involved in transactional sex were additionally included in this category. Subgroups not directly connected through sexual or injecting contact with high or medium-risk groups were categorized as 'general population' groups. In the original and revised model, these included the low-risk group, the CHS subgroup and partners of CHS subgroup. In the revised model, the 'boyfriend' and 'girlfriend' subgroups were also included as 'general population' groups. Finally, discordant couples, who are not explicitly recognized in the original model were assigned their own category in the revised MoT to assess the importance of this group for HIV programming purposes.

Evaluation of parameter estimates and methods for sensitivity analysis

In order to assess the robustness of model projections a detailed sensitivity analysis was conducted, for all parameter estimates. Latin Hypercube Sampling was used to generate 10 000 random parameter sets using uniform distributions for all parameters. For the majority of behavioural and epidemiological parameters estimated from surveys within the Nigerian setting (either state level or geopolitical zone) 95% CI from the survey data were used as uncertainty bounds. For parameter estimates obtained through alternative data sources or from the wider literature, we sampled each parameter relatively ±50% to reflect the higher levels of uncertainty. Parameter sets were included if the HIV prevalence projection fell within the 95% CI uncertainty range for the ANC estimate, obtained through the 2008 sentinel surveillance survey which collected HIV data from 300 women in Cross River. Additional sampling details for all parameter estimates are provided below in Table 2.

Results

Comparisons of the original and revised modes of transmission model projections Figure 2(a)–(c) show the projected overall distribution of HIV infections produced by the original, intermediate and revised MoT models respectively. Results from the original model show 73% of infections occur in general population subgroups, compared with 21%% in MARPs. HIV prevalence in the population is estimated to be 8% and the rate of HIV infection in the 15–49 population, 0.005 per year (500 infections per 100 000 population).

Following revisions to the MoT model structure through the introduction of additional subgroups, model projections are modified. The new 'discordant couples' group, are projected to account for 21% of all infections. The percentage of infections distributed amongst MARPs remains similar to the original model, partly as a result of maintaining the same parameter estimates. The percentage of infections in the general population subgroups is still significant, with 50% of infections occurring within this category. The overall population HIV prevalence for this model is 9.4%, 1.4% higher than the ANC HIV prevalence, with an HIV incidence rate of 0.0059 per year. The higher prevalence and incidence is largely due to infections being attributed to the 'low-risk' group, because of their large population size, despite the stratification of discordant partnerships away from this group.

Figure 2(c), shows the revised MoT model, including all parameter updates. The projected distribution of incident HIV infections is significantly different, with approximately 45% of infections now occurring amongst MARPs. In the revised model individuals in the low-risk group are assumed not at risk from transmitting or acquiring HIV. This lowered the number of infections in the population, resulting in a proportional redistribution to other subgroups, with discordant couples, now accounting for 34% of infections instead of 21% in the intermediate model. The stratification and re-parameterization of individuals involved in transactional sex, from the CHS group, is also important. We see that 23% of infections in the original MoT originate from casual heterosexual sex, whereas for the revised model the CHS and transactional sex groups combined contribute 25% of infections, but 16% of those infections arise from women engaging in transactional sex. The HIV prevalence for this scenario is 7.8% and the HIV incidence rate is 0.0031 per year.

Model sensitivity analysis

Figure 3 shows the distribution of infections amongst different subgroups as produced in the sensitivity analysis. In the revised MoT model, 18% of the sexually active 15–49 years old population were part of a MARP subgroup. Model projections suggest these groups contribute 40–75% (95% CrI) of incident HIV infections. This is in contrast to those in the general population subgroups which account for 6–24% of new infections but make up 78% of the sexually active population. Interestingly, discordant couples, who, constitute around 3.5% of the population may contribute 10–46% (95% Crl) of total infections.

We also analysed the number of infections amongst each female sex worker (FSW) group with their respective client groups to explore the percentage of infections derived from each type of sex work, including transactional sex. Our sensitivity analysis suggests that brothel-based sex work (FSW and clients) contributes the most infections (24–67%, 95% Crl) amongst MARPs, likely to be as a result of high numbers of partners and moderate condom usage (65%). In addition, a high percentage of infections (11–46%, 95% Crl) also occur amongst those involved in transactional sex. In contrast, although still significant, fewer infections occur as a result of non-brothel based sex work (7–30%, 95% Crl), IDUs (1–15%, 95% Crl) and MSM (1–16%, 95% Crl).

Discussion

Results from the original modelling analysis in Cross River state concluded that the HIV epidemic was generalised in nature, with the highest percentage of infections occurring through heterosexual sex amongst persons in the general population and that the majority of infections can only be curbed by targeting interventions towards general population subgroups.

Following model revisions to incorporate additional population subgroups, the conclusions about the distribution of new infections have changed substantially. The explicit inclusion of discordant couples into the model helps illustrate the burden of new infections that are likely to occur in these individuals. The incorporation of updated parameter estimates into the fully revised model, produces an epidemic profile with a significantly higher percentage of infections in MARPs, compared with the original modelling analysis. This more plausible scenario is due largely to the removal of the implicit assumption that all low-risk individuals have some risk of acquiring HIV, which results in high numbers of new infections occurring in the 'low-risk' group.

The results from the sensitivity analysis indicate that infections generated through brothel-based sex work in both FSW and their clients may be an important source of infections in this setting. However, with a high incidence of infections amongst this group, it is important to obtain better estimates of the size of the brothel-based FSW population. In the absence of more comprehensive mapping data, it is difficult to ascertain how accurate these projections are, as a smaller population may considerably lower this estimate. However, evidence from the modelling shows that continued surveillance and intervention programmes are essential for maintaining high rates of condom use and education amongst brothel-based FSW and their clients.

Transactional sex is also indicated to be an important source of new HIV infections, previously not included in the original MoT. Despite being well documented in the literature (Moore et al., 2007, Jewkes R et al., 2012, Gukurume S, 2011), until now mathematical models have rarely differentiated this as distinct from casual sex. However, identifying women engaging in transactional sex may be challenging because while one-off sex acts may take place within this context, quite commonly it may be the principal motivation for on-going relationship with primary or secondary partners.

There are also challenges identifying discordant couples. Discordant couples are often identified through ANC testing for women; however, this strategy relies on the attendance and willingness of the male partner to also test.

The high percentage of infections occurring in discordant partnerships illustrates the importance of identifying these individuals and providing effective prevention options – including condoms, early ART treatment and possibly pre-exposure prophylaxis treatment. The source of infection in a discordant couple also needs to be considered. Various studies indicate (Federal Ministry of Health, 2007, Federal Ministry of Health (FMOH), 2010) the duration of time that women spend selling sex may be short, and similarly, it may well be that girls only engage in transactional sex for a limited duration of time, before getting married. Therefore, it is possible that many of the infections within discordant partnerships arise from infections acquired from previous partnerships (Fazito et al., 2012, Mbukpa M et al., 2010a).

Our results highlight both the challenge and importance of appropriately parameterizing the MoT model to a particular setting. The introduction of greater model complexity provides a more comprehensive and realistic insight into which population subgroups are most vulnerable to HIV infection. The original MoT report for the state suggested focusing on primarily the general public groups, while also continuing to target high-risk groups such as FSWs (Mbukpa M et al., 2010a). For Cross-River State, our findings suggest most new HIV infections will occur among MARPs, and so effective prevention strategies need to be delivered to these groups as a priority. However, there is a requirement for sufficient data to be available before using the revised model. As demonstrated by the intermediate MoT analysis, unless more due care is taken in model parameterization, the user is likely to generate misleading results. In addition, the results of the analysis should be used as a guide rather than a platform on which to inform policy, as cost-analyses and epidemiological reviews of the setting must also be taken into consideration.

The UNAIDS MoT remains an accessible and potentially a useful model that can inform intervention priorities in different settings. However, our findings suggest that the current model may produce misleading findings, especially in concentrated or low-level generalised HIV epidemic settings, such as Cross River. Our analyses for Nigeria illustrate that the current model may underestimate the importance of different vulnerable groups, including girls involved in transactional sex and brothel-based sex work. We suspect that problems with the MoT model projections will be most significant for less generalised HIV epidemic settings, although further research to explore this question for other settings is needed. Nevertheless, our findings point to the need for UNAIDS to formally review and revise the MoT model.

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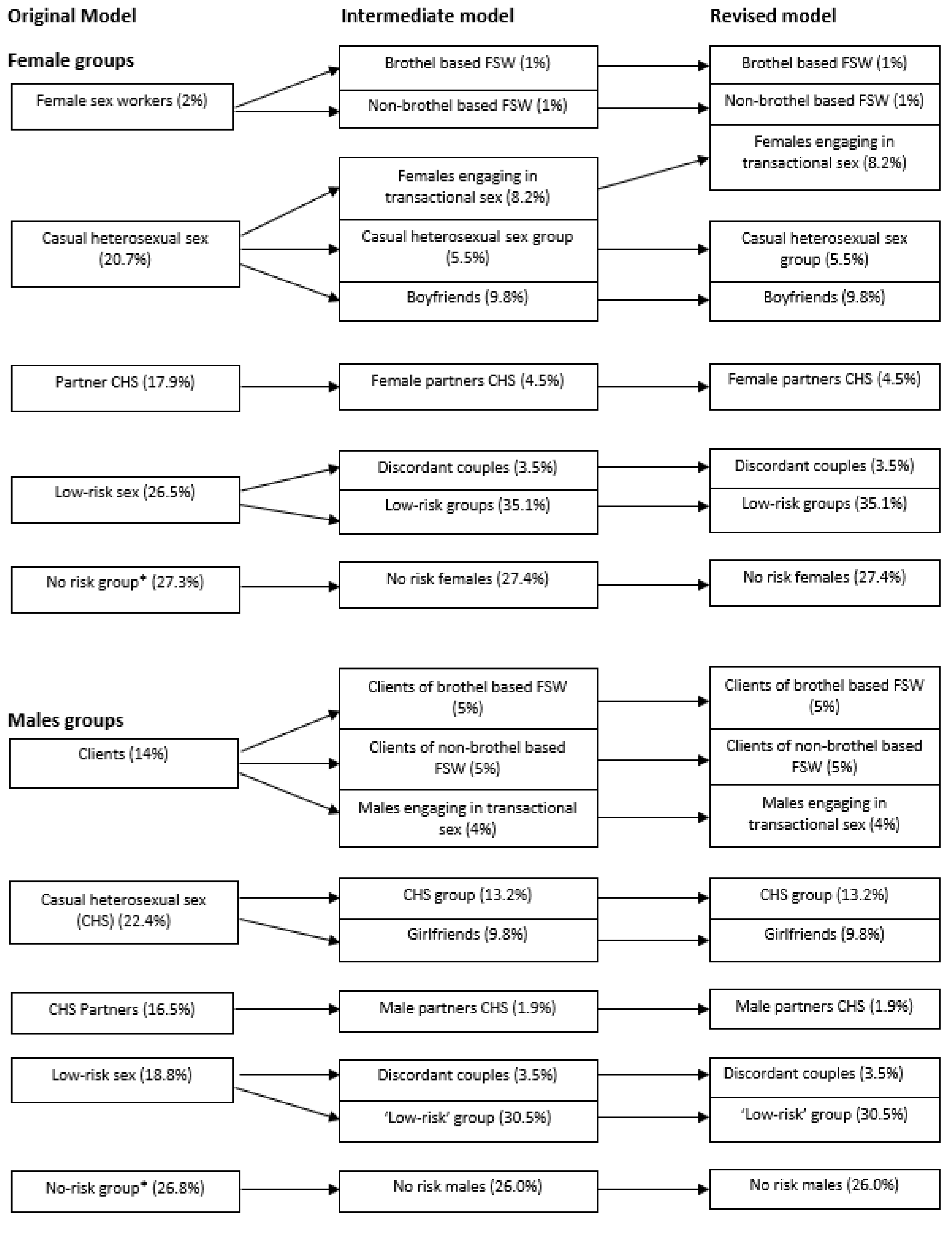
Figure 1: Schematic overview illustrating the structural changes to the MoT model, for the original model, intermediate and revised versions. Including revisions to subgroup sizes for each model.



*No risk individuals are those who report no sexual intercourse or injecting drug use in the past 12 months.
The figure does not include MSM, IDUs and any of the partners of the MARPs groups, since these were not revised.

Table 1a and Table 1b: Comparison of behavioural (Table 1a) and epidemiological parameter (Table 1b) estimates and population sizes for original MoT, intermediate MoT and revised MoT. For instances in which model revisions were made, the table represents the three model estimates as respective column headings. Population size estimates are depicted in blue, with original model estimates (no stratification) as the top row shaded in darker blue. Figures in white boxes, are those in which no stratification within the subgroup was made between the original, intermediate and revised models and for which parameter estimates are also unchanged. Light grey squares represent those parameter estimates from the original model, which are conserved in the intermediate and revised models, despite additional stratifications being applied to certain subgroups. Finally, dark grey squares correspond to revised parameter estimates, established through the stratification of subgroups in the intermediate and revised models.

Table 1(a):

Population subgroup	***Revised model stratification***	***Percentage of total population***		***Number of partners per year***			***Number of acts of exposure per partner per year***			***Percentage of acts protected* (%)***		
		Male (%)	Female (%)	Original MoT	Intermediate MoT	Revised MoT	Original MoT	Intermediate MoT	Revised MoT	Original MoT	Intermediate MoT	Revised MoT
Injecting drug users (IDUs)		0.32	0.27	2			224			79.0		
Partners of IDUs		0.26	0.31	1			80			26.1		
Female sex workers (FSWs)	Original MoT		2.00	175			4			61.6		
	Brothel based		1.00		175	250		4	4		61.1	65.5
	Non-brothel based		1.00		175	120		4	4		61.1	65.5
	Transactional sex (females)		8.70		2	6		50	20		46.8	28.0
Clients of FSWs	Original MoT	14.0		5			20			61.6		
	Brothel based	5.00			5	50[#]		20	4		61.1	65.5

	Non-brothel based	5.00			5	24#		20	4		61.1	65.5
	Transactional sex (males)	4.40			2	11#		50	20		46.8	28.0
(long-term) Females partners of clients	Original MoT		4.76	1			80			26.1		
	Brothel based clients		1.70									
	Non-brothel based clients		1.70									
	Transactional sex (males)		1.50									
Men who have sex with men (MSM)		0.9		3			38			56.3		
Female partners of MSM			0.22	1			80			26.1		
Casual heterosexual sex (CHS)	Original MoT	22.4	20.7	2			50			46.8		
	Casual heterosexual sex (males)	13.2			2	2		50	50		46.8	46.8
	Casual heterosexual sex (females)		5.50			4.8#						
	Boy/girlfriend relationships (males)	9.83				1#			80			26.1
	Boy/girlfriend relationships (females)		9.81			1#						
Partners of CHS	Original MoT	16.5	17.9	1			80			26.1		
	Revised MoT	1.87	4.49									
Low-risk heterosexuals	Original MoT	18.8	26.5	1			80			26.1		
	Low-risk	29.7	33.4									
	Discordant couples(positive partners)	1.75	1.75									
	Discordant couples(negative partners)	1.75	1.75									

No risk	Original MoT	26.8	27.3	0	0	-
	Revised MoT	26.0	27.4			
Medical injections		35.8	34.9	1.8	1	99.0
Blood transfusions		1.00	1.00	1	1	99.0

#Estimate for number of partners derived by balancing with corresponding partner group

**** sterile injecting equipment or condoms used***

Table 1(b):

Population subgroup	***Revised model stratification***	***Percentage of total population***		***HIV prevalence***			***STI prevalence***		
		Male (%)	Female (%)	Original MoT	Intermediate MoT	Revised MoT	Original MoT	Intermediate MoT	Revised MoT
Injecting drug users (IDUs)		0.32	0.27	3.1%			7.5%		5.5%
Partners of IDUs		0.26	0.31	8.0%	8.0%	4.3%	NA		
Female sex workers (FSWs)	Original MoT		2.00	23.4%			12.6 %		
	Brothel based		1.00		23.4%	27.8%		12.6%	4.6%
	Non-brothel based		1.00		23.4%	18.9%		12.6%	2.8%
	Transactional sex (females)		8.70		9.0%	3.2%		7.6%	3.3%
Clients of FSWs	Original MoT	14.0		10.4%			7.6%		
	Brothel based	5.00			10.4%	10.3%		7.6%	3.3%
	Non-brothel based	5.00			10.4%	10.3%			
	Transactional sex (males)	4.40			9.0%	7.4%			
	Original MoT		4.76	8.0%					

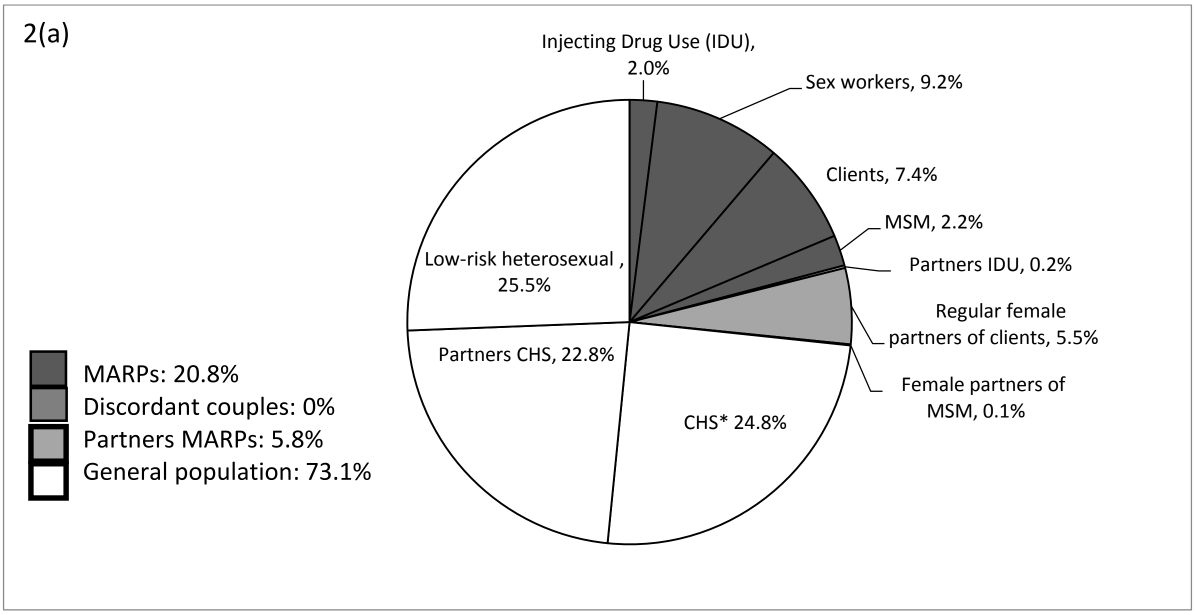
(long-term) Females partners of clients	Brothel based clients		1.70				NA		
	Non-brothel based clients		1.70						
	Transactional sex (males)		1.50						
Men who have sex with men (MSM)		0.9		2.8%			11.0 %	11.0%	1.9%
Female partners of MSM			0.22	8.0%	8.0%	4.3%	NA		
Casual heterosexual sex (CHS)	Original MoT	22.4	20.7	9.0%			7.6%		
	Casual heterosexual sex (males)	13.2			9.0%	3.5%		7.6%	0.2%
	Casual heterosexual sex (females)		4.50		9.0%	3.5%		7.6%	0.2%
	Boy/girlfriend relationships (males)	9.83			9.0	2.1%		7.6%	0.2%
	Boy/girlfriend relationships (females)		9.81		9.0	1.3%		7.6%	0.2%
Partners of CHS	Original MoT	16.5	17.9	8.0%	8.0%	4.3%	NA		
	Revised MoT	1.87	4.49		8.0%	4.3%			
Low-risk heterosexuals	Original MoT	18.8	26.5	8.0%			3.6%	3.6%	0.2%
	Low-risk	29.7	33.4		8.0%	8.0%			
	Discordant couples(positive partners)	1.75	1.75		100%	100%			
	Discordant couples(negative partners)	1.75	1.75		0%	0%			
No risk	Original MoT	26.8	27.3	6.0%	6.0%	7.9%	0%		
	Revised MoT	26.0	27.4		6.0%	3.8%			
Medical injections		35.8	34.9	8.0%			NA		

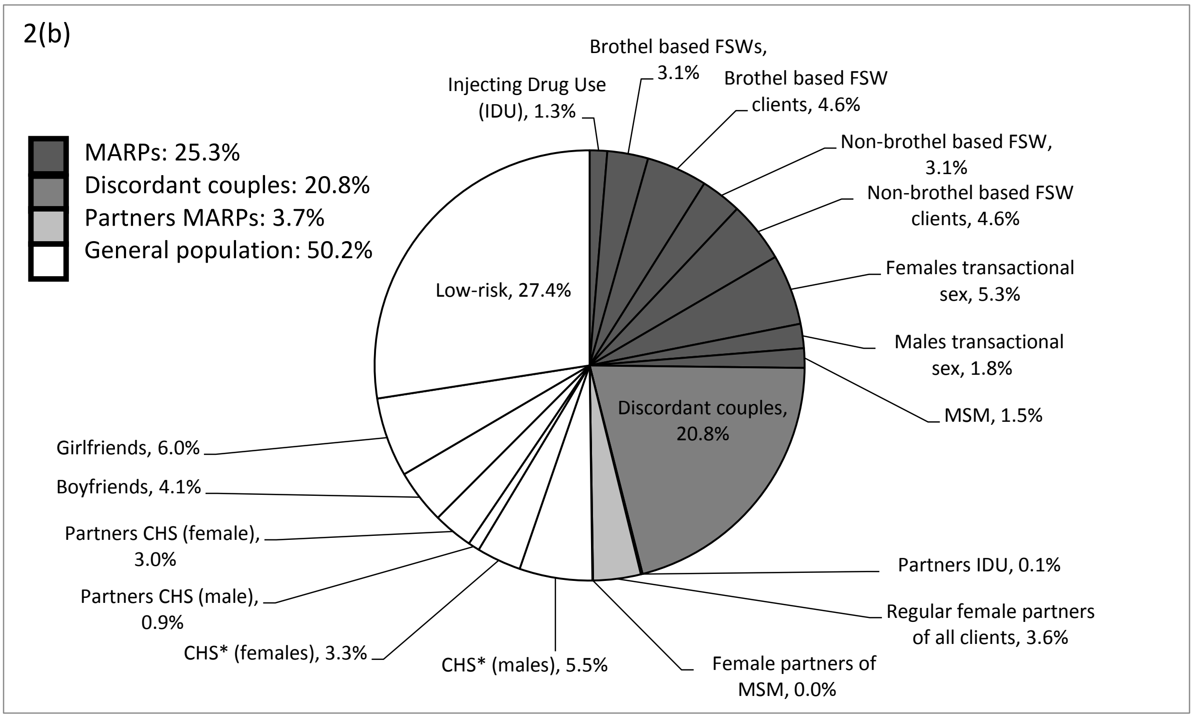
Blood transfusions		1.00	1.00	8.0%	NA

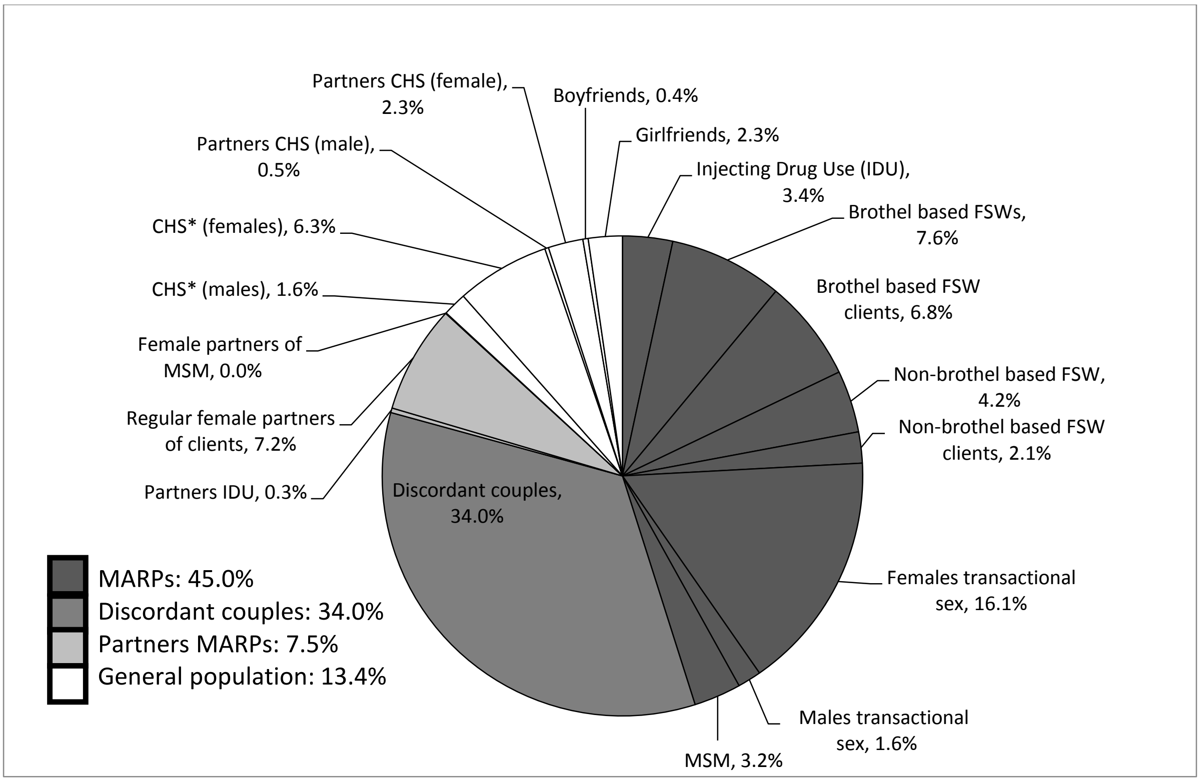
Table 2: Description of sampling methods used for the MoT revised model sensitivity analysis, including data sources and rationale.

Parameter	*Method of sampling uncertainty*
Population sizes	Population size estimates were sourced from the NARHS 2007+ surveys for general population subgroups. Details on high-risk group population estimates and additional calculations are contained in appendix D, with most of these estimates conserved from the original model. Owing to the high levels of uncertainty in the size of the population estimates we sampled each parameter relatively +/-50%.
HIV prevalence	For all HIV prevalence values estimated from survey data for Cross River state or regional estimates from NARHS+ 2007, 95% CI intervals were generated and applied in the sensitivity analysis, these included all risk-groups with the exception of females engaging in transactional sex and their partners, clients of brothel-based and non-brothel based FSW and their regular female partners. Because of the greater level of uncertainty in these estimated values each parameter was varied +/-50% relative to its original value.
STI prevalence	All estimates were generated from survey data for which 95% CI were available. For general population groups, the estimate was taken from the 2003 sentinel survey for individuals tested for syphilis. From this, 95%CI were derived based on the sample size for the south-south geopolitical zone. STI prevalence estimates for high-risk groups and clients were generated from the IBBSS 2010 for reported genital ulcer/sores. This estimate was selected because no serological data were available and since it was considered that genital ulcers/sores present as more visible forms of STIs and are more likely to reflect the presence of syphilis. 95%CI were generated from the data to reflect the uncertainty in these estimates.
Number of partners and number of sex acts with individual partners per year	To allow for the uncertainty in the number of partners and number of sex acts with each partner for individual subgroups all parameter estimates were varied +/-50%. This was to reflect the uncertainty in these estimates and the fact that some estimates were generated through triangulation methods based on population size estimates, whilst others were based on assumptions from the original MoT model.
Condom usage	Estimates for condom use for clients of brothel-based and non-brothel-based FSW come from the DHS for males who report 'payment for sex', the same value was assumed for brothel-based and non-brothel based FSW, since FSW in the IBBSS survey report 100% condom use and this estimate was deemed to be unrealistic. Estimates for condom use in MSM and sterile needle use for IDUs are taken from the IBBSS 2007 and all other subgroup estimates were generated using appropriate estimates from the NARHS 2007+, taking 95% CI on each occasion to generate uncertainty ranges for data sampling.

Figure 2: Comparison using the three different MoT models for the projected distribution of new HIV infections in the population. Figure 2(a) shows results from the original MoT model, figure 2(b), results from the intermediate MoT model and figure 2(c), modelling projections for the revised MoT model.

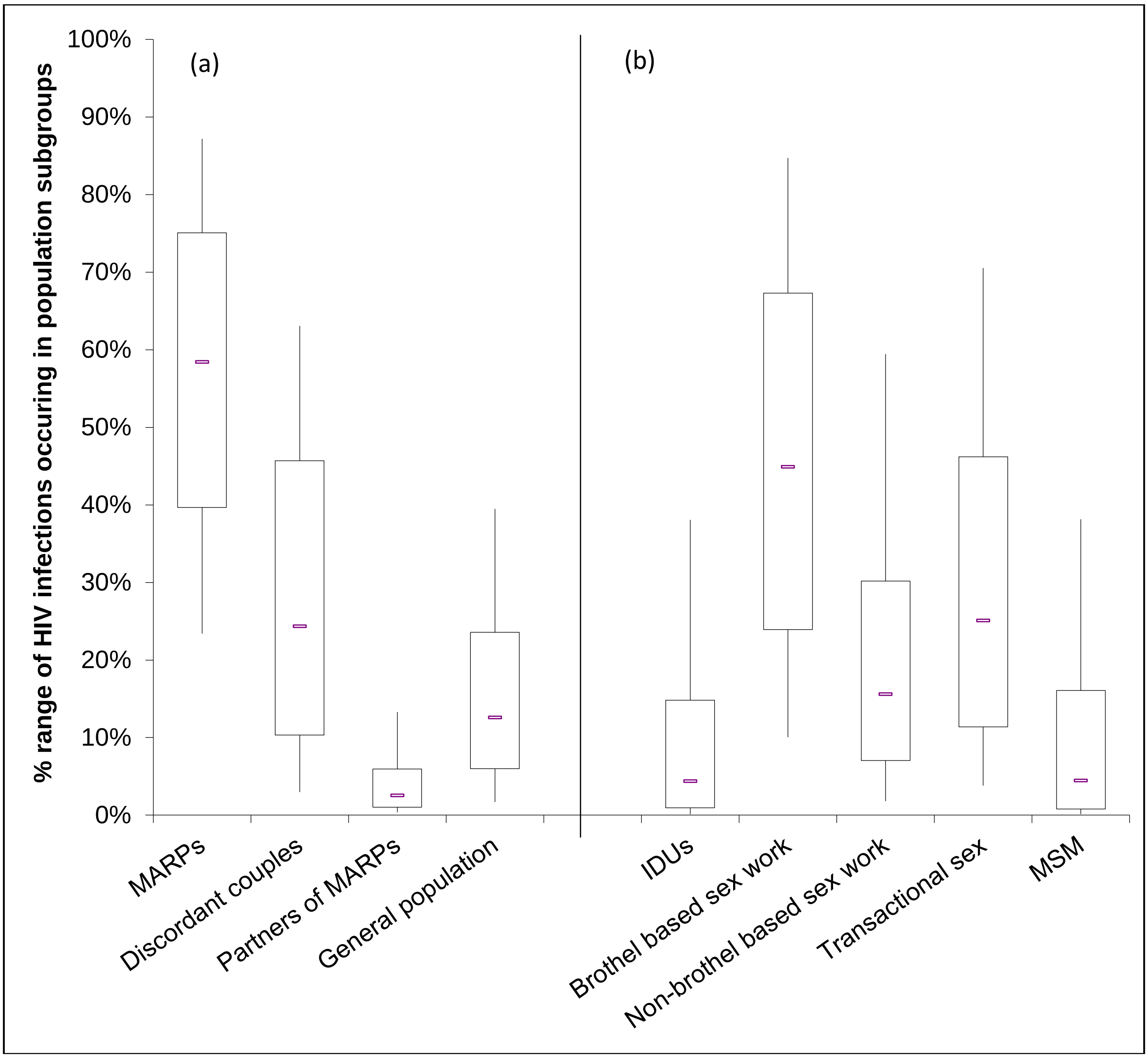






*CHS – Casual heterosexual sex

Figure 3: Results from the sensitivity analysis illustrating the projected percentage of infections likely to occur in different population risk categories on the left (a) and distribution of HIV infections amongst the MARPs only on the right (b).



3.2 Thesis discussion for Research Paper 1:

The inclusion of behavioural heterogeneity is critical to modelling STI/HIV infections. Core groups can sustain an epidemic in otherwise low-risk populations and the spread of HIV from 'core groups' to the general population may be facilitated through 'bridging' subgroups, such as the clients of female sex workers. A key question is however, how much heterogeneity is required in a model to give an accurate description of transmission dynamics and infection patterns? Which subgroups are most important to include and how can they best be identified? What are the underlying the patterns of sexual networks between groups and how may this change over time? (Kamazima and Kazaura, 2012, Alam SJ et al., 2010).

In Research Paper 1, I examine the importance of incorporating additional behavioural heterogeneity in a static model, the Modes of Transmission. There are several important findings. Firstly, the Modes of Transmission model inherently assumes the entre sexually active population is at risk of HIV, even though sexually active individuals are only ever at risk if they have a chance of coming into contact with an infectious individual. 'Core group members' generally have the highest risk, with individuals who form partnerships with members of core groups, also likely to be at risk of infection. In the MoT these groups (IDU, MSM and FSW) are included. For a setting such as Cross River state in Nigeria, where HIV prevalence is around 8%, it may therefore not be appropriate to assume that risk of infection is universal, particularly since we also know that HIV infections tend to be clustered within certain groups and/or geographical locations, with current research identifying potential "hotspots" of infection i.e. the existence of highly concentrated epidemics within generalised settings (Wand and Ramjee, 2010, Tanser et al., 2014).

In the revised model, the division of the low-risk group into component subgroups; discordant couples and 'low-risk' individuals not only distinguishes heterogeneity in risk amongst this group but is more helpful to policy makers since it allows more specific targeting of individuals, i.e. individuals who may form part of a discordant partnership. However, the inclusion of the separate 'low-risk' group is also to some extent necessary for the calibration of the model. The revisions to this group involved disabling any risk of infection (by reducing β to zero), meaning no new infections occurred within this subgroup, but at the same time observing that past infections meant that the prevalence in this group was around 8%, to allow for the model to be correctly calibrated. In the original version of the model structure, this failure to account for past infections naturally led to an over-estimation of new infections in the 'low-risk' group to allow for the model to be correctly calibrated.

A second important observation is that, being static in nature, the model is not able to identify the source of infection. For example, infections that occur within the discordant partnerships are likely to have a different source from whom the positive partner acquired the infection, yet importantly the largest proportion of all infections (34%) in the revised model arise from partnerships between discordant couples. Therefore, behavioural heterogeneity can distinguish groups who are at risk of acquiring HIV and is useful in highlighting the distribution of new infections in the MoT. However, pathways of infection and knowledge of where the source of infection has originated is also equally important in order to understand who has the highest risk of infection.

One important property of the MoT model is that it has the potential to give the user the ability to understand the importance of the size of population subgroups and their influence on the resulting number of incident infections. A key to understanding this, is the inclusion of sufficient levels of behavioural heterogeneity in the model. For example, in the original model the size of the low-risk group represents 26% of the female population and 19% of males and overall they account for 25% of total infections. Their rate of infection is 375 per 100 000. In the revised model however, this group is stratified into discordant partnerships and those who are not considered at risk (the 'low-risk' group). The total size of the discordant group is 3.5% of the population, yet they contribute over 34% of total infections, with an infection rate of 1496 per 100 000. In the original model the 'low-risk' group were vulnerable to acquiring infections, but at a comparably slow rate. However, by stratifying this group to identify approximately how many individuals may form part of a discordant partnership, we have a much better understanding of individuals within the so-called 'low-risk' group who are the most vulnerable.

This same message applies to core groups, where higher rates of infection make these groups important to identify.

The theme of population size is also important when considering the group of adolescent females in the revised MoT who engage in 'transactional sex.' This group, identified from the literature, are thought to represent younger females in the population (15-24), who themselves do not identify as FSWs, but who may exchange sex for gifts or money. Data from the National AIDS/HIV, Reproductive Health and Serological Survey 2007 (Federal Ministry of Health Nigeria, 2008), provides estimates of between 1.4% in the northern region of Nigeria and 12.4% in the southern region for the percentage of women who exchange in sex for gifts or favours. Since this was a household survey, we may assume the inclusion of FSW worker groups (who tend to be more mobile) was less likely, meaning the 12.4% figure represents only non-commercial females.

With the size of this group being significantly larger than the FSW groups in the revised model (8.7% versus 1%), but with lower numbers of partners and lower HIV prevalence levels; the model results indicate that such an intermediary group, who's sexual networks include higher-risk males, may be an important but previously unrecognised group, vulnerable to acquiring new HIV infections. This was an observation also previously made by Garnett *et al.* (Garnett and Anderson, 1996).

In summary, results from this paper have demonstrated the importance of behavioural heterogeneity and the risk of infection for individual subgroups. These importance concepts provide an improved perspective of the nature of an epidemic. As too, does evidence from the data suggesting groups of adolescent females who engage in transactional sex, may form a previously unrecognised but large subgroup who are potentially vulnerable to acquiring HIV infection.

The findings from this chapter support the hypothesis that high-risk behavioural groups including female-sex workers remain of fundamental importance as groups that are associated with a substantial number of new infections in the population. However, the analysis also emphasises the vulnerability of adolescent females with multiple partners. In-particular, their large sub-group size (compared to other high-risk groups) and their potential proximity within the sexual network of infections (as a peripheral group), places them at particularly higher levels of risk. However, the static nature of the model, in this instance, limits our understanding of the potential dynamic spread of infections and the importance of the group of adolescent females. Although, the model is able to demonstrate a high number of infections are acquired by this group, the potential of the group to also transmit infections cannot be proven. However, the relevance of the discordant couple in demonstrating the presence of an unknown source of infections may be representative of the likelihood of onward transmissions from both commercial sex and adolescent girls to members of the lower-risk general population.

Whilst the findings from this paper may provide helpful insights, one notable limitation is the lack of validation in the modelling results and hence it is not possible to prove conclusively which of the model structures gives a better approximation of the distribution of new infections. In order to achieve this, information on new incident infections per year would be required or the rate of acquisition of new infections for each of the risk groups. The newly revised model spreadsheet contains a validation tab that allows users to enter this information if it becomes available at a later date, which is a helpful new addition. Related to this limitation is the challenge of verifying sources of infections, for example in discordant couples or young females. Without this information it is difficult to inform policy measures, therefore adding additional heterogeneity is only useful if there is a means to identify and target risk groups.

However, the model findings from this research chapter have also helped to guide revisions to the original MoT model spreadsheet and processes for modelling. The spreadsheet model now includes an uncertainty analysis to help verify the sensitivity of model input values to model estimates. The low-risk group has been revised to a 'stable heterosexual' couples group, that includes both sero-concordant and discordant partnerships and additional developments have been added to ensure sex worker and client partnership numbers balance and the population prevalence is set to equal the adult prevalence for the setting by making the low-risk group a function of the other parameters for this calculation. Further revisions to the guidelines have stressed the importance of ensuring a measures are in place for reviewing the standard of data for inclusion as well as cautioning at over-interpreting model results. The insights made in this paper have thus contributed to future policy for using the MoT model. In the next research paper, I explore whether there is evidence for a relationship between the size of the group of adolescent females (15-24 years) with multiple partners (who may or may not themselves be engaging in transactional sex) and the HIV prevalence levels in countries across the West Africa region.

4. Factors associated with variations in population HIV prevalence across West Africa: Findings from an ecological analysis.

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Research Paper Cover Sheet

Section A – Student Details

Student: Holly J Prudden

Principle Supervisor: Charlotte Watts

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Section B – Paper already published

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Section D- Multi-authored work

For multi authored work, give full details of your role in the research included in the paper and in the preparation of the paper.

I was the lead author of this paper and worked with Charlotte Watts and Tara Beattie to develop the storyline for the paper. I designed the approach for the linear regression analysis and carried out the final analysis. Natalia Bobrova provided additional support for sourcing estimates for the female sex worker behaviour. I drafted the full manuscript and made revisions based on comments from Charlotte Watts and Tara Beattie.

David Wilson and Marelize Gorgens provided feedback on the policy implications. Zindoga Mukandavire and Jasmina Panovska-Griffths gave feedback on the implications of the finding and commented on drafts of the paper.

Student signature: Date: 05/10/2015

Supervisor signature: Date: 05/10/2015

4.1 Research Paper 2

Factors associated with variations in population HIV prevalence across West Africa: Findings from an ecological analysis.

Abstract

Background: Population HIV prevalence across West Africa varies substantially. We assess the national epidemiological and behavioural factors associated with this.

Methods: National, urban and rural data on HIV prevalence, the percentage of younger (15-24) and older (25-49) women and men reporting multiple (2+) partners in the past year, HIV prevalence among female sex workers (FSWs), men who have bought sex in the past year (clients), and ART coverage, were compiled for 13 countries. An Ecological analysis using linear regression assessed which factors are associated with national variations in population female and male HIV prevalence, and with each other.

Findings: National population HIV prevalence varies between 0·4-2·9% for men and 0·4-5.6% for women. ART coverage ranges from 6-23%. National variations in HIV prevalence are not shown to be associated with variations in HIV prevalence among FSWs or clients. Instead they are associated with variations in the percentage of younger and older males and females reporting multiple partners. HIV prevalence is weakly negatively associated with ART coverage, implying it is not increased survival that is the cause of variations in HIV prevalence. FSWs and younger female HIV prevalence are associated with client population sizes, especially older men. Younger female HIV prevalence is strongly associated with older male and female HIV prevalence.

Interpretation: In West Africa, population HIV prevalence is not significantly higher in countries with high FSW HIV prevalence. Our analysis suggests, higher prevalence occurs where more men buy sex, and where a higher percentage of younger women, and older men and women have multiple partnerships. If a sexual network between clients and young females exists, clients may potentially bridge infection to younger females. HIV prevention should focus both on commercial sex and transmission between clients and younger females with multiple partners.

Background: HIV in West Africa

In Sub-Saharan Africa, an estimated 23·5 million people are infected with HIV (UNAIDS, 2013). Whilst in West Africa HIV prevalence levels tend to be lower, Nigeria with a population of 178 million has an HIV prevalence of 3.1% and is the country with the second highest number of individuals infected globally. HIV prevalence in other countries in the region ranges from 0.5-4% (Avert, 2012).

There is substantial variation in population HIV prevalence within and between countries, with the almost universal practice of male circumcision in the region likely to be playing a central role in limiting the scale of the epidemic (Weiss HA et al., 2000). However, there are also substantial differences in the levels of infection between West African countries, with Nigeria, Cote d'Ivoire and Cameroon having estimated female population HIV prevalence levels ranging from 4-7%, compared to 0.5-2% more generally across the region (Tara Beattie et al., 2011).

Throughout West Africa, HIV remains largely concentrated in the most vulnerable populations (The World Bank, 2008), with transmission between female sex workers (FSWs) and their male clients thought to have a central influence on the scale of the epidemic (Alary and Lowndes, 2004, Morison et al., 2001). Although population HIV prevalence remains relatively low (Mishra Vinod et al., 2009), infection levels among brothel-based FSWs are far higher, ranging from 16% to 37% (Comite National de Lutte contre le SIDA, 2012, Bureau d'Appui en Santé Publique'96, 2011). In such 'concentrated' HIV epidemic settings, prevention programming is focused on FSWs and their male clients (Bureau d'Appui en Santé Publique'96, 2011, Sobela et al., 2009), with the latter conceived as the main 'bridging group' through which HIV spreads to the general population (Alary et al., 2003, Gomes do Espirito Santo and Etheredge, 2005).

However, such a simple programmatic focus may fail to respond to the complexity of sexual networks. Evidence suggests that a diverse group of women may exchange sex for money or resources, ranging from more formal commercial sex work that tends to be targeted by HIV programmes, through to informal transactional exchange, which may be more hidden (Harcourt C and Donovan B, 2005 , Moore et al., 2007, Jewkes R et al., 2012). Similarly, men who pay or provide resources for sex are a heterogeneous group (Owoaje and Uchendu, 2009, Odeyemi et al., 2009). As well as men who purchase sex from FSWs, men may provide money and/or resources to other long term and/or occasional sexual partners (Godin et al., 2008, Lowndes et al., 2002). Multiple sexual partnerships are an important risk factor for HIV infection, if condoms are not used consistently (Owoaje and Uchendu, 2009, Peltzer et al., 2013). Therefore, it is important to gain a clearer understanding of the relative epidemiological importance of commercial sex, versus the less visible dynamic of casual sex, which may or may not have a transactional element.

This paper presents the findings from an ecological analysis that explored whether the variations in population HIV prevalence observed across West Africa are associated with variations in the extent of formal commercial sex work, and/or the degree to which women and men of different ages report having multiple sexual partnerships in the past year. As the provision of anti-retroviral therapy (ARV) will also increase life expectancy (and so could potentially contribute to higher HIV prevalence levels), we similarly explore whether the variations in HIV prevalence may be associated with variations in national ARV coverage levels.

Methods

A review of demographic health surveys (DHS) was used to compile recent epidemiological and behavioural data on patterns of sexual behaviour and levels of HIV infection for 2010-2014 amongst members of the general population. Most data were available from 13 West African countries. No DHS data were available for Ghana or Guinea Bissau and therefore these countries were excluded from analyses. A 2013 preliminary report for Gambia was available but contained only data on sexual behaviour and no HIV prevalence data. Data on brothel-based FSWs, were sourced from publications published after 2010 from regional sites within country settings. We included data on brothel-based FSWs only, since this group was easier to identify and categorise from the literature (Appendix 2.1c).

For each country we extracted the most recent national estimates of the population prevalence of HIV among men and women nationally, and in urban and rural areas. Where available, we also extracted population data on the percentage of younger (15-24) and older (25-49) males and females reporting 2 or more (2+) partners in the past year (non-sexually active individuals were also included in the estimate), and the percentage of men reporting 'paying for sex' in the past year (assumed to be clients of FSWs). HIV prevalence among each sub-group was also compiled. In addition, we collected data on condom use. Reported levels of condom use were relatively similar across countries for partnerships between key subgroups (Appendix 2.1a) and FSW (Appendix 2.1c) and were therefore not considered within our analysis.

Estimates of the number of individuals receiving ART treatment (15-49) and the percentage of the population, 15 years or above who were HIV positive, were used to calculate the percentage of HIV infected people receiving ART treatment (Appendix 2.2). Population size estimates were sourced from the World Bank database (The World Bank, 2012), allowing for a 3% population growth rate (the average across West Africa).

Using this data, a series of linear regression analyses were conducted in STATA 13·1 to identify which factors or independent variables were associated with the observed variations in HIV prevalence across West Africa. For this, a systematic approach was adopted where we explored whether factors hypothesised as being associated with population HIV prevalence (dependent variable), were significant. The independent variables included HIV prevalence in FSW and in clients, assuming that these factors may be independently associated with higher prevalence levels seen in the general population. We also assessed whether the percentage of younger and older males and females reporting 2+ partners in the past year, were significantly associated with higher HIV prevalence levels in the general population. The rationale for this being, that if there are more individuals with 2+ partners and they are at higher risk of acquiring HIV, then overall more infections will occur in the population, leading to higher levels of HIV prevalence.

In addition, we explored whether HIV prevalence in younger and older females and males was associated with HIV prevalence in general population groups (of males and females). Here we wished to assess whether patterns of HIV observed in the younger age groups was correlated with general population prevalence, to understand patterns of infection and when infections are likely to occur. Finally, we analysed data on mean age at first sex to assess whether this variable was associated with the percentage of young males and females reporting 2+ partners.

Next we conducted regression analyses to explore patterns of association between different population subgroups. Our main objective for this was to explore whether the concept that

HIV is predominantly transmitted along a pathway from FSWs, to clients to the general population is supported by empirical data. Firstly, we assessed whether HIV prevalence in FSWs and clients, treated as independent variables, was associated with HIV prevalence in subgroups of younger and older males and females with 2+ partners (dependent variables), i.e. does higher prevalence in these core groups directly impact on HIV prevalence in other high-risk subgroups. Next we assessed whether the percentage of clients in the population and younger and older males and females with 2+ partners were independently associated with HIV prevalence levels in FSWs, clients and younger and older males and females in the general population, i.e. are larger risk populations associated with higher prevalence levels in all groups.

Finally, we assessed the previous round of DHS data sets from 2003-2009 for countries across West Africa, to assess whether sexual behavioural patterns that pre-date the analysis have a delayed impact on HIV prevalence in the later surveys.

Results

There is substantial variation in population HIV prevalence across the region for men (0.4-2.9%) and women (0·4-5.6%) respectively. Figure 1 shows how Cameroon, Cote d'Ivoire and Nigeria have the highest prevalence levels (4-5.6%) in general population females. For the remainder of countries, HIV prevalence tends to range from 0.4-2%. HIV prevalence is often higher in females than males and as expected, HIV prevalence is far higher among FSWs (15.9-36.7%).

Figure 2a shows the percentage of males reporting payment for sex (clients) in the past year and compares the older males with the younger male group. We see that overall, levels tend to be low across countries (0.4% - 4.8%) with similar levels of younger and older males reporting payment being generally relative to one another in each country.

Figure 2b compares the percentage of younger and older males who report 2+ partners in the past year. With the exception of Liberia and Nigeria, a higher percentage of older males consistently report 2+ partners in the past 12 months (p=0.002). For the male group the age of sexual debut ranges from 18.1-23.6 years with a negative correlation (p=0.001) between age at first sex and percentage of young males reporting 2+ partners (Appendix 2.1b). This may account for the lower percentage of younger males reporting 2+ partners in those countries.

A similar country pattern is seen amongst females (figure 2c). However, for females the reverse pattern is seen, with a higher percentage of the younger group reporting 2+ partners compared to the older females. For younger females, age at first sex ranges from 15.9-19 years and is also negatively associated (Niger is removed as an outlier) with having 2+ partners (p=0.03) (Appendix 2.3).

Exploring the potential influence of variations in ART coverage and national HIV prevalence

From the available ART data there is an increase in coverage of ART from 2008-2012. In 2008 Burkina Faso had the highest coverage rate with approximately 12.5% of HIV positive individuals receiving treatment and Niger the lowest rate at 2.1%. The mean coverage across countries was 6.7%. By 2012 the mean coverage had risen to 13.5%, ranging from 7.2%-23.4%. The results from the regression analysis (Appendix 2.2) indicate a weak negative relationship between HIV prevalence and the percentage of individuals on ART. This suggests that levels of ART treatment within countries are unlikely to be responsible for differences in HIV prevalence levels.

Associations between HIV prevalence among different-subgroups and male and female national, urban and rural HIV prevalence

Table 1 shows results from the linear regression analyses (p-values and R^2) that assessed whether variations in national, urban and rural population HIV prevalence are associated with variations in the HIV prevalence or size of different subgroups. Significant associations ($p<0{\cdot}05$) are highlighted in grey.

The findings show that brothel-based FSW HIV prevalence is not strongly associated with the HIV prevalence in any other population group. This is also true for the HIV prevalence in male clients. However, there is a significant association between the size of the client groups (in particular the younger group) and HIV prevalence in males at the urban and national levels.

As expected HIV prevalence among younger and older females and older males is significantly correlated with urban, rural and national HIV prevalence. However, there was only a very weak correlation between HIV prevalence among younger males and female HIV prevalence at a rural, urban or national level, and with only weak (ranging from p=0.03 for rural males to p=0.07 for urban males and at a national level) associations with male HIV prevalence levels.

Next, we considered the potential influence on variations in national, urban and rural HIV prevalence of the size of younger and older males and females reporting 2+ partners or buying sex (for men) in the past 12 months. For females, when all countries were included in the regression, the percentage of both younger and older females having 2+ partners was only significantly associated with urban male HIV prevalence. However, when the two outliers, Liberia and Sierra Leone, were removed from the analyses, the percentage of younger and older females reporting 2+ partners was significantly positively (p<0.005) associated with variations in national, urban, and rural HIV prevalence among males and females. For males, regression analysis for those including and excluding Liberia and Sierra Leone, gave similar results, showing that the percentage of both younger and older males reporting 2+ partners were significantly associated with HIV prevalence among all population groups.

Given the strong associations between population HIV prevalence and the size of the subgroups reporting 2+ partners in the past 12 months, we explored which factors were associated with variations in HIV prevalence among the different sub-populations considered (Supplementary Material 3). Tables 2a and 2b summarise these results. Table 2a shows the relationships between HIV prevalence in different groups. Firstly, there are no significant associations between the HIV prevalence in male clients (15-49) nor younger males and other population groups. FSW HIV prevalence is correlated with HIV prevalence among both older males and females, but not with any other groups. Finally, there is strong evidence for an association between HIV prevalence in young females (despite a lack of association in their young male counter-parts) and both groups of older males and females. As expected HIV prevalence in older males and females is correlated.

Table 2b explores the association between HIV prevalence in different sub-groups and their behaviour. The HIV prevalence in young females and in FSWs are associated with the size of both the younger and older group of male clients, and with the size of both younger and older groups of males and females who report 2+ partners in the past year. Yet, we see little evidence for an association with HIV prevalence in male clients or in the younger males reporting 2+ partners and the size of other population subgroups.

Exploring significant relationships between the sizes of population subgroups, we observe a strong association between the size of the older group of male clients and HIV prevalence among (i) FSWs, (ii) younger males and younger females. For the young male client group, there is only an association with HIV prevalence in FSWs and younger females reporting 2+partners.

Assessing evidence for a time lag in HIV prevalence as a result of earlier high-risk sexual behaviour

Because of the apparent time lag in high-risk behaviours impacting on HIV prevalence at a later date, we also reviewed the data from earlier DHS surveys from 2003 to 2009. We compared this with the data used in the analysis from 2010 to 2014. Due to revisions in the questionnaire, several of the earlier questionnaires did not include questions on 2+ partnerships. Despite this, two key observations are evident from the six country studies that could be compared. Firstly, HIV prevalence across this period tended to remain fairly constant in countries with lower prevalence levels, with the exception of Liberia where prevalence fell from 1.8% to 1.2% in general population females. For the countries where HIV prevalence is higher, Cameroon and Cote d'Ivoire, prevalence also declined from 6.8% to 5.6% and 6.4% to 4.6%, respectively. For the five countries with data available on 2+ partners in both rounds, either a decline in this behaviour or no change was also observed. In Liberia, the percentage of young females reporting 2+ partners declined from 9.5% to 8.6% and in Cote d'Ivoire from 6.2% to 4.8%. For the remaining countries (Benin, Guinea and Sierra Leonne) there was no reported change in behaviour. Here, we see that declines in HIV prevalence seem to mirror changes in high-risk behaviours, amongst the female 2+ group. However, there is no clear indicator of a delay in behaviour leading to a reduction in HIV prevalence, since both variables appear to decline concurrently.

Discussion

This study has sought to identify which ecological variables are associated with the 6-10 fold variation in population HIV prevalence across West Africa – a region where male circumcision is widespread.

Our analysis has several main limitations. The first is the ecological nature of the analysis, as we compare patterns of association using aggregated national data coming from multiple sources. In practise the multiple data sources are unlikely to be a major limitation, as most of the behavioural and HIV data used came from national DHS surveys, with some comparability internally and between countries. For each country we used the most recent data available, and the 4 year timespan will only have influenced our findings if HIV prevalence levels and/or patterns of population sexual behaviour changed substantially over this time. This is difficult to assess in the absence of data. However, given the ecological nature of this analysis, the findings should be seen as hypothesis generating, rather than providing strong evidence of causality.

Secondly, reporting bias is likely to have influenced our estimates of the size of different sub-populations. Questions on sexual behaviour - including on men's purchasing of sex or the numbers of sexual partners – are highly sensitive, and prone to under-reporting, especially among women (Fenton et al., 2001). For this reason, our values will be under-estimates (Peltzer et al., 2013). If there were no substantial differences in the degree of under-reporting between countries, the findings may nevertheless reflect true variations between countries. If there is also varying degrees of under-reporting between countries, we cannot rule out this hidden confounder. However, such misclassification is likely to weaken associations found in regression analyses, and so if anything, will lead to null findings. Given this, we expect that significant associations are meaningful, but caution against over-interpreting the lack of associations seen.

More broadly, the forms of analysis that we could conduct were limited by available data. There is multiple heterogeneity in patterns of sexual behaviour between countries. We were limited to using variables extracted from national DHS and other data sets. In particular, some variables (such as the size of the female sex worker population) was only available for a limited number of countries considered; HIV prevalence data on males reporting payment for sex was not disaggregated by age; we were not able to assess the degree to which men's reporting of purchasing sex related primarily to engagement in commercial sex, or other forms of sexual exchange; the degree to which young girls have sex with men with a history of multiple partners, consider whether sex worker and/or client migration may be important; or explore the influence of other factors, such as male sex work and injecting drug use.

Despite these limitations, we found several strong associations. Variations in population HIV prevalence across West Africa are strongly associated with variations in the extent that males and females in the general population report 2+ partners in a 12 month period. Stratification (into 15-24 and 25-49 year olds) by age and further analysis of these subgroups reporting 2+ partners in the past year reveals that HIV prevalence in younger females and female sex workers is strongly associated with the size of both male and female populations reporting 2+ partners in the past year. However, data on brothel-based FSWs within countries was collected mostly within specific locations or districts, often using different sampling criteria and parameters, so we must caution over-interpretation for this set of results.

Additionally, we see that the percentage of males in the population reporting payment for sex (in the past 12 months), especially amongst the older males is associated with HIV prevalence in younger males and females as well as FSWs.

From the earlier rounds of DHS data we did not observe any clear evidence for a time lag in sexual behaviour, impacting on HIV prevalence. A reason for this is that it is likely that behaviour changes involving multiple partners, increases in condom use and other preventative methods may pre-date these surveys and as such, here we observe the impact of these. Historical data suggests the HIV epidemic in West Africa peaked around 1999-2000 in most countries (The World Bank, 2015), although in the absence of reliable early data it is difficult to verify this behaviour change.

The findings have implications for the way in which epidemiologists understand the determinants of HIV epidemics. Figure 3(a) visually depicts the dominant epidemiological theory of HIV transmission in heterosexual concentrated epidemics (Mishra et al., 2012b, Garnett, 1998). Epidemiological models and HIV programmes are often constructed on the assumption that HIV is transmitted from FSWs to men who purchase sex (clients), with the multiple encounters of a large group of men with a small 'core' of sex workers providing a context in which rapid HIV transmission may occur (the core group theory) (Yorke et al., 1978). In turn, HIV then passes from these male clients to their steady or casual female partners in the general population, with clients being an important 'bridging population' for HIV transmission (Garnett, 1998).

Figure 3(b) shows a revised theory, emerging from this analysis. This is similar to 3(a), but also highlights that sexual activity between higher risk men (such as clients) and young girls may provide an important additional bridge of infection into the general population. In this revised theory, the proportion of adolescent females with multiple partnerships who have sex with high-risk men are at higher risk of HIV infection than other young females. Onward transmission may subsequently occur if girls also partner with lower risk men or re-infect higher-risk partners, either casually, or as they enter more stable partnerships. In this way, the higher HIV levels among these young women then leads to higher infection rates in all men. Over time also, adolescent females age into the general population, and so influence population HIV prevalence, especially if this group is large and survival is high.

In this revised theory, the size of the HIV epidemic is dependent on the extent that 'men pay for sex and/or have multiple partners', the extent that young girls have multiple partnerships, and the levels of 'connectivity' of these groups. Populations with large proportions of young females having multiple partners and large proportions of males reporting payment for sex or multiple partners would tend to have higher levels of HIV prevalence. It may also explain why there is a greater disparity between male and female HIV prevalence in countries with higher HIV prevalence levels, because of the higher incidence rate in young females. Conversely, in countries where HIV epidemics remain at lower levels and are more concentrated, it may be that the proportion of young females with multiple partners is not large enough or not 'connected' enough to higher risk men, to have a large contribution to the HIV epidemic. This may be the case for Liberia and Sierra Leone. For example, Liberia the only country in the analysis where male HIV population prevalence is greater than in females, suggesting possibly a different dynamic in the transmission pathway for HIV. We are currently conducting epidemiological modelling to explore these issue further.

Conclusion

The observed variation in population HIV prevalence across West Africa is strongly associated with national variations in the extent that men buy sex and individuals have multiple partners. The results from the regression analysis appear to show a linear trend between the percentage of individuals who report 2+ partners and HIV in the general male and female population. Interestingly, however, it is only the HIV prevalence in younger females and among brothel-based female sex workers that is associated with both multiple partnerships (2+ partners) in the population and males reporting payment for sex. This may highlight an important link between these population groups. Females with 2+ partners may form a critical bridge between high-risk men and the general population, that helps sustain larger HIV epidemics. In these countries prevention should focus both on commercial sex and adolescent girls with multiple partners.

The findings illustrate the importance of continually monitoring the distribution of HIV infection, and patterns of sexual behaviour, and the need to use this information to inform the efficient use of HIV prevention resources.

The results also support dominant epidemiological thinking about the important role of commercial sex to the HIV epidemic in West Africa, as highlighted in a recent modelling study (Boily et al., 2015). There is substantial programmatic experience with the provision of HIV prevention to sex workers and their clients, and multiple examples of where such programming has had marked impacts on the HIV epidemic (Laga et al., 2010, Rojanapithayakorn, 2006). It is important that such programmes are sustained and expanded, and that opportunities to achieve greater impacts, for example, through the additional provision of ART based prevention technologies, are explored.

Our findings also highlight that sexual activity between high-risk men and young girls is an important additional route through which HIV infection may spread to the general population. This poses major challenges for HIV programmes, as girls with multiple partners who may be involved in transactional exchanges (both monetary and material) but who do not identify themselves as sex workers, can be difficult to identify and reach. A number of potentially promising intervention models for adolescents are starting to emerge in other African regions. This includes the Zomba trial in Malawi, that showed an impact on HIV by providing cash transfers to keep girls in school (Baird et al.) interventions that provide information about the risks of 'risky male' partners (Dupas, 2011), and interventions which aim to socially and economically empower women (Kim et al., 2009). There is an urgent need for interventions to address HIV risk among adolescent girls and their sexual partners in the West African context, especially, where multiple partnerships are more commonly reported. With recent studies showing a lack of association between age disparate relationships between older males and younger females (Harling et al., 2014), it is important to understand the mechanisms through which young females become infected in such high numbers.

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Figure 1: HIV prevalence data taken from DHS and UNGASS reports in West African settings from 2010-2014.

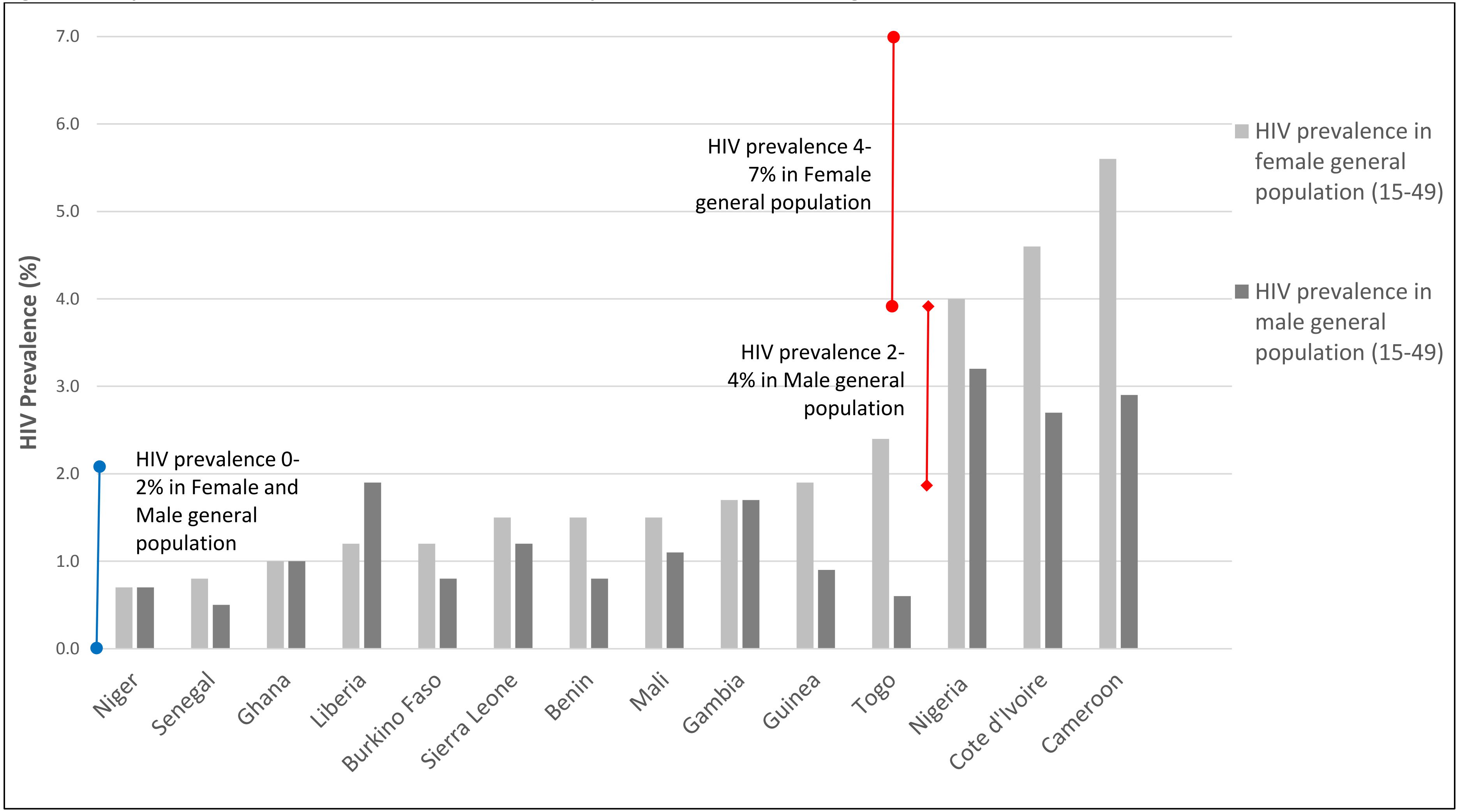


Figure 2(a): DHS Data from 10 West African countries, stratified by 15-24 and 25-49 year old males. Presented in ascending order of 25-49 year old males reporting payment for sex in the past 12 months, by country (2010-2014), data not available for Nigeria, Gambia and Togo.

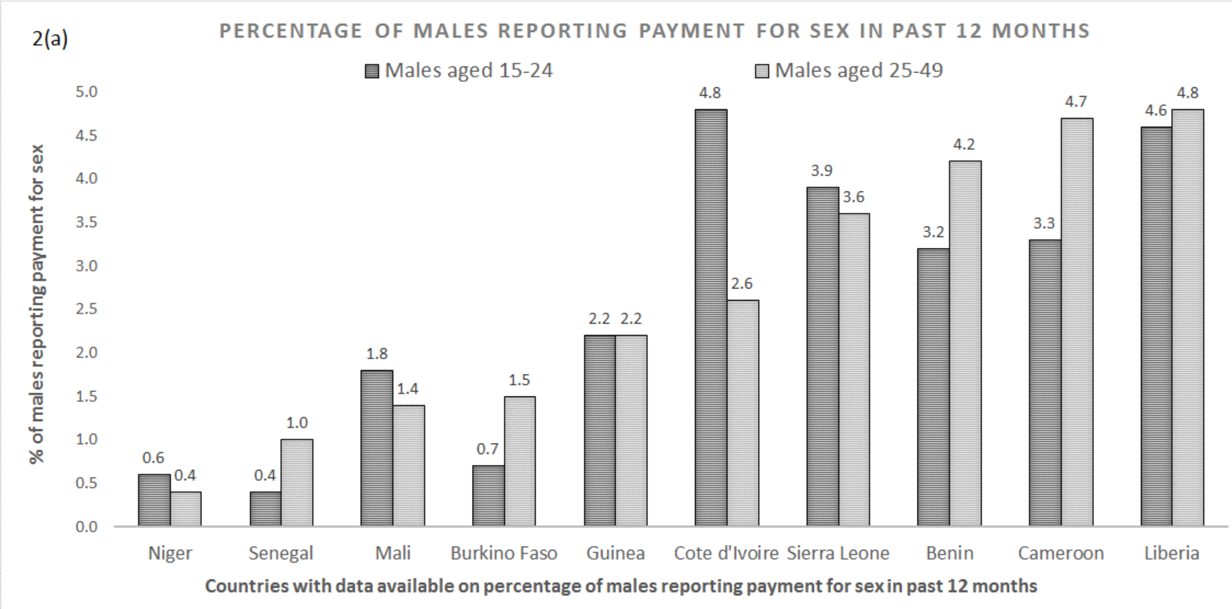


Figure 2(b): DHS data from 13 West African countries, stratified by age. Presented in ascending order of 25-49 year old males reporting 2 or more partners, by country.

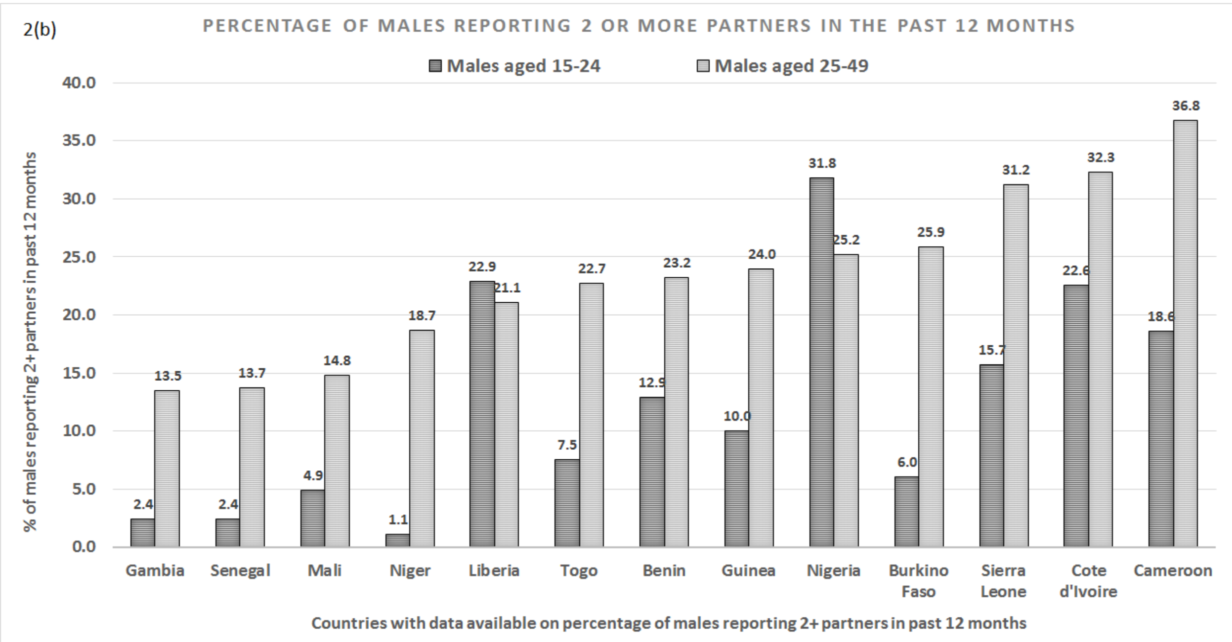
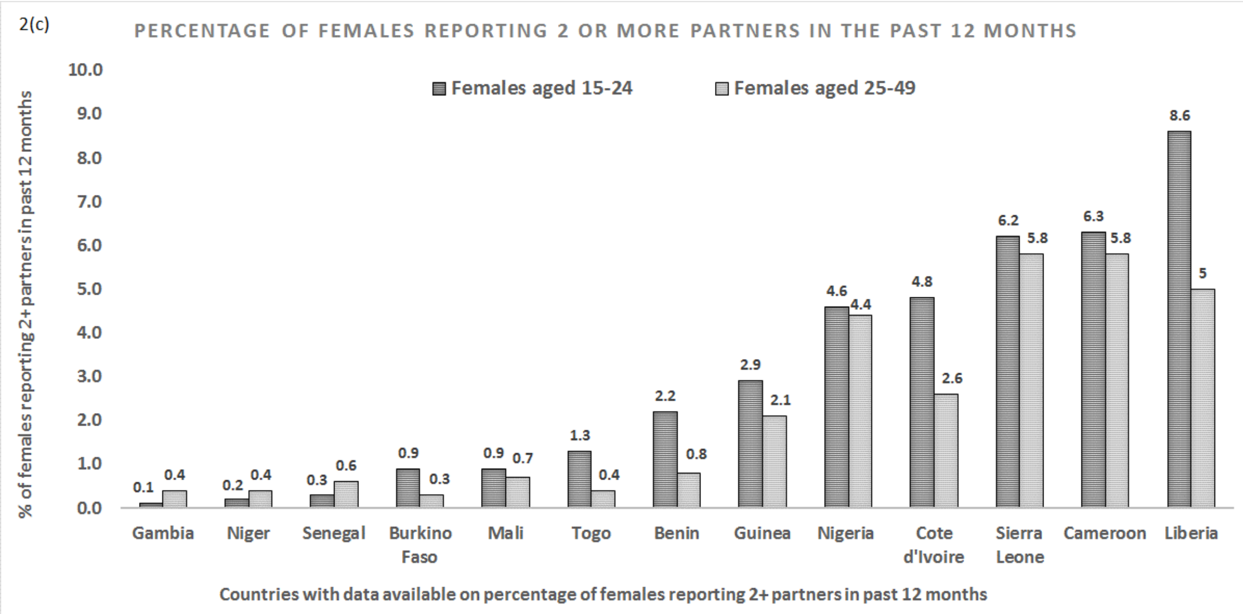


Figure 2(c): DHS data from 13 West African countries, stratified by age. Listed in ascending order of 15-24 year old females reporting 2+ partners in the past year, by country.



	Variable (n= number of countries included in regression analysis)	**Females**						**Males**					
		Urban HIV prevalence		Rural HIV prevalence		National population		Urban HIV prevalence		Rural HIV prevalence		National population	
		R^2	*p*	*R^2*	*p*	*R^2*	*p*	*R^2*	*p*	*R^2*	*p*	*R^2*	*p*
Brothel-based FSWs	HIV prevalence (10)	*0·39*	*0·08*	*0·31*	*0·11*	*0·44*	*0·06*	*0·31*	*0·11*	*0·25*	*0·17*	*0·34*	*0·10*
	% with risk behaviour	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*
Males reporting payment for sex in past year	HIV prevalence 15-49 (9)	*0·001*	*0·95*	*0·06*	*0·53*	*0·001*	*0·95*	*0·001*	*0·94*	*0·05*	*0·57*	*0·003*	*0·88*
	% with risk behaviour aged 15-49 (10)	*0.31*	*0.1*	*0.27*	*0.13*	*0.37*	*0.06*	***0.64***	***0.005***	*0.23*	*0.16*	***0.54***	***0.02***
	% with risk behaviour aged 15-24 (10)	*0.34*	*0.08*	*0.22*	*0·17*	*0.38*	*0.05*	***0.79***	***0.0005***	*0.28*	*0.12*	***0.58***	***0.01***
	% with risk behaviour aged 25-49 (10)	*0.24*	*0.16*	*0.26*	*0.13*	*0.31*	*0.09*	***0.46***	***0.03***	*0.12*	*0.23*	***0.43***	***0.04***
15-24 yr old females	HIV prevalence (12)	***0·44***	***0·01***	***0·76***	***0·0002***	***0·68***	***0·001***	***0·85***	***0·0001***	***0·85***	***0·0001***	***0·87***	***0·0001***
25-49 yr old females	HIV prevalence (12)	***0.93***	***0.0001***	***0.82***	***0.0001***	***0.97***	***0.0001***	***0.61***	***0.003***	***0.65***	***0.001***	***0.78***	***0.0001***
15-24 yr old males	HIV prevalence (12)	*0.01*	*0.79*	*0.25*	*0.10*	*0.08*	*0.36*	*0·30*	*0·07*	***0·40***	***0·03***	*0·30*	*0·07*
25-49 yr old males	HIV prevalence (12)	***0.79***	***0.0001***	***0.87***	***0.0001***	***0.95***	***0.0001***	***0.84***	***0.0001***	***0.83***	***0.0001***	***0.96***	***0.0001***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (12)	*0·21*	*0.12*	*0·22*	*0·13*	*0·30*	*0·06*	***0·49***	***0·01***	*0·18*	*0·16*	***0.44***	***0·019***
	% with risk behaviour (10)*	***0.64***	***0.005***	***0.88***	***0.0001***	***0.85***	***0.0002***	***0.76***	***0.001***	***0.78***	***0.0008***	***0.86***	***0.0001***

	% with risk behaviour (12)	***0·23***	***0·11***	***0·46***	***0·02***	***0·43***	***0·02***	***0·80***	***0·0001***	***0·57***	***0·0047***	***0·74***	***0·003***
25-29 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.31***	***0.09***	***0.70***	***0.003***	***0.56***	***0.01***	***0.83***	***0.0003***	***0.83***	***0.0003***	***0.82***	***0.0003***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	*0·19*	*0·15*	*0·31*	*0·06*	*0·31*	*0·06*	***0·44***	***0·01***	*0·27*	*0·08*	***0·44***	***0·01***
	% with risk behaviour (10)*	***0.46***	***0.03***	***0.86***	***0.0001***	***0.70***	***0.003***	***0.59***	***0.0094***	***0.78***	***0.0007***	***0.75***	***0.0013***
	% with risk behaviour (12)	***0·59***	***0·003***	***0·54***	***0·006***	***0·59***	***0·004***	***0·37***	***0·04***	***0·35***	***0·04***	***0·51***	***0·009***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.73***	***0.002***	***0.69***	***0.003***	***0.73***	***0.002***	***0.45***	***0.03***	***0.46***	***0.03***	***0.63***	***0.006***

Data shaded in grey for p<0.05.

* Subgroup population size data for Liberia and Sierra Leone were both significant outliers in the regression analysis for females 15-24 and 25-49 with 2 or more partners in the past 12 months. We therefore performed a second round of analyses for the 2+ partner groups where these were excluded, to compare results across both the male and female subgroups with 2+ partners

Table 1: Results from linear regression analysis. Associations between population subgroup HIV prevalence and relative population size, and levels of HIV infection in the general population (the number of countries included is shown in parenthesis)

Table 2a: Results from regression analysis showing level of association (p-values) from the linear regression analysis for associations between levels of HIV prevalence in different subgroups. Significant relationships (p<0.05) are shaded grey.

Table 2(a)		**HIV Prevalence**					
HIV Prevalence	(n= number of countries included in regression analysis)	Brothel Based Female Sex Workers	Men Who Report Payment for Sex (15-49)	15-24 year old females	15-24 year old males	25-49 year old females	25-49 year old males
	Brothel Based Female Sex Workers (10)	-	-	-	-	-	-
	Men Who Report Payment for Sex (15-49) (10)	**0.16**	-	-	-	-	-
	15-24 year old females (12)	**0.10**	**0.17**	-	-	-	-
	15-24 year old males (12)	**0.86**	**0.22**	**0.01***	-	-	-
	25-49 year old females (12)	**0.002**	**0.29**	**0.01**	**0.62**	-	-
	25-49 year old males (12)	**0.01**	**0.32**	**0.001**	**0.16**	**0.001**	-

*Nigeria data for male HIV prevalence is a significant outlier in the regression, removing this data point results in an association that is not significant at the p=0.05 level.

Table 2b: Results from regression analysis showing the level of association (p-values) from the linear regression analysis between the size of different subgroups in the population and HIV prevalence amongst the subgroups. Significant relationships (p<0.05) are shaded grey.

Table 2(b)		HIV Prevalence					
% of Population reporting Behaviour	(n= number of countries included in regression analysis)	Brothel Based Female Sex Workers^	Men Who Report Payment for Sex (15-49)	15-24 year old females	15-24 year old males	25-49 year old females	25-49 year old males
	Men Who Report Payment for Sex (15-49) (10)	**0.2**	**0.06**	**0.17**	**0.22**	**0.09**	**0.07**
	Men Who Report Payment for Sex (15-24) (10)	**0.05**	**-**	**0.01**	**0.06**	**0.18**	**0.08**
	Men Who Report Payment for Sex (25-49) (10)	**0.009**	**-**	**0.005**	**0.01**	**0.12**	**0.08**
	15-24 year old females 2+ partners (10)	**0.004**	**0.29**	**0.003**	**0.19**	**0.001**	**<0.001**
	15-24 year old males 2+ partners (10)	**0.05**	**0.28**	**0.001**	**0.01**	**0.05**	**0.003**
	25-49 year old females 2+ partners (10)	**0.04**	**0.93**	**0.001**	**0.11**	**0.008**	**0.002**
	25-49 year old males 2+ partners (10)	**0.001**	**0.06**	**0.04**	**0.48**	**0.003**	**0.008**

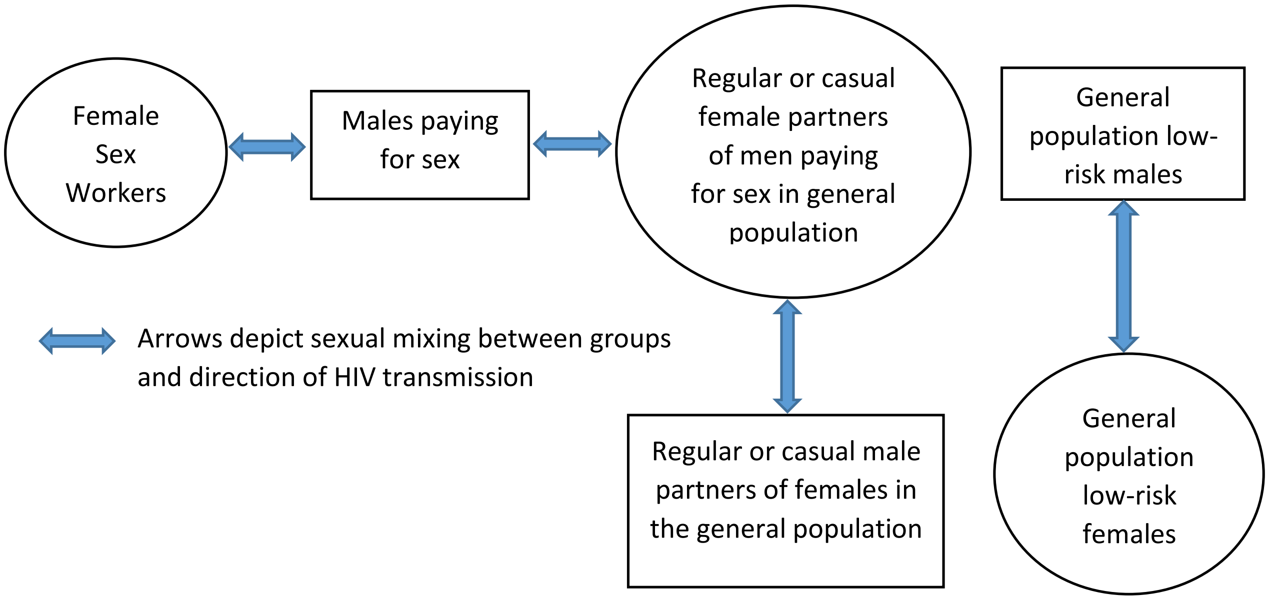


Figure 3a: Conceptual pathway of heterosexual HIV transmission from sex workers to the general population in West Africa

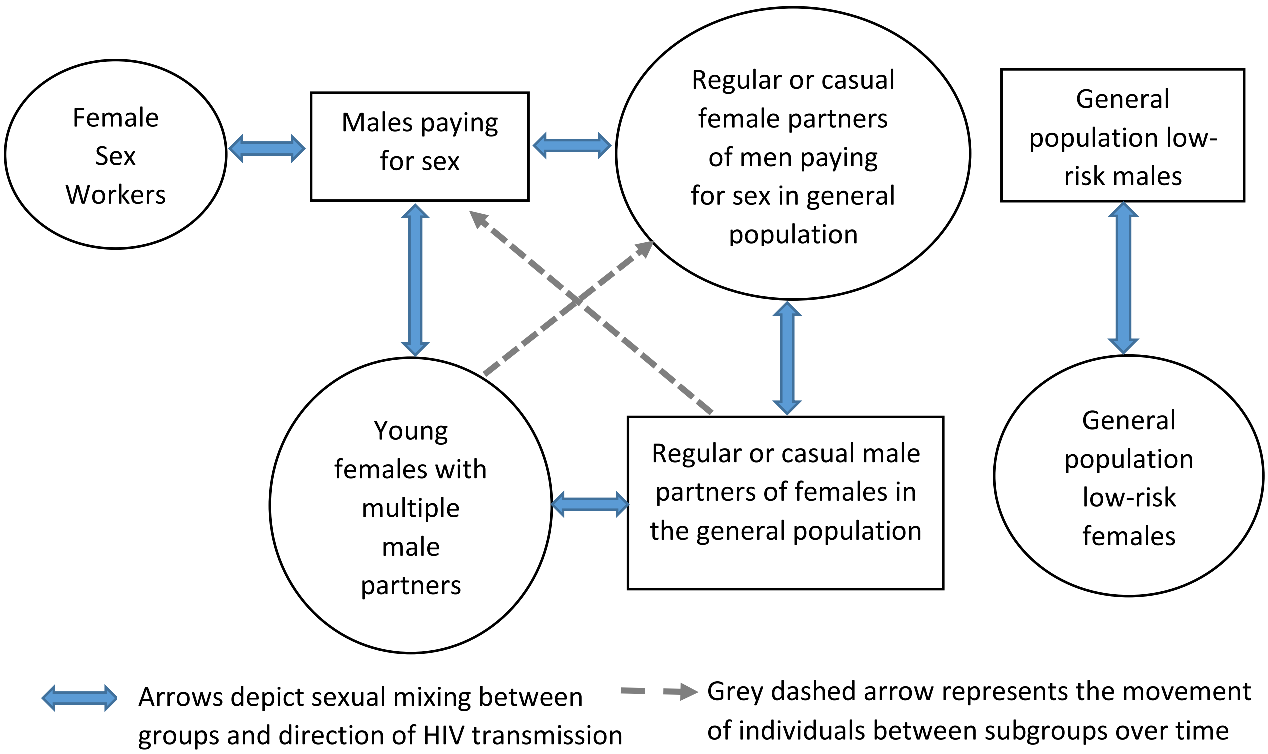


Figure 3b: Revised conceptual framework of HIV spread through sexual networks of individuals within the population

4.2 Thesis discussion for Research Paper 2:

Research Paper 1 highlighted the importance for modelling projections of assumptions made about the percentage size of different population subgroups and their level of risk of acquiring HIV. This Research Paper has used data acquired from the DHS and other sources (for FSWs) to help to identify associations between potential determinants of HIV infection and HIV prevalence. The findings from Research Paper 1 pointed to the danger of overestimating the risk of very large, lower-risk groups by failing to include additional behavioural heterogeneity. In research paper 2, I used behavioural and epidemiological data from West Africa to explore empirically what factors are associated with variations in population HIV prevalence across 13 West African countries and potential pathways of transmission. A logical assumption from core group theory is that where HIV prevalence is higher in high-risk groups such as FSWs, we are likely to see higher HIV prevalence in the general population. There is some evidence for this, with HIV prevalence in FSWs being associated with HIV prevalence in older males and females. However, surprisingly we do not see any correlation between HIV prevalence in FSWs and HIV prevalence in males who report paying for sex in the past year (clients). An additional association, which emerges from the findings is the association between the size of male and female subgroups who report having two or more partners in the past 12 months and HIV prevalence in FSWs and the general population.

Based on this ecological evidence alone, it is difficult to draw any conclusions in regards to transmission pathways. However, what the findings suggest is that within populations where a higher percentage of individuals are engaging in relationships with multiple partners, HIV prevalence is higher. These findings suggest that the size of 'risk groups' are a potentially important determinant of population HIV prevalence.

Although we did not have data on mixing patterns between subgroups, the higher HIV prevalence in the general population would logically suggest pathways of transmission between FSWs, their clients and individuals with 2+ partners. The pattern of association between subgroups provide some insights into these networks. For example, the size of the client group is associated with HIV in FSWs and adolescent females 2+, but to a lesser extent with other population subgroups. This suggests that a higher percentage of males in the population who are clients, partnering with both FSWs and adolescent females 2+ creates a broader sexual network in the population, which may then lead to a higher population prevalence of HIV.

We also observe that the size of the other male 2+ groups (15-24 and 25-49) are associated with higher HIV prevalence in adolescent females 2+ and FSWs, showing that larger networks in general may be associated with higher HIV prevalence levels. Reliable information on the size of FSW groups was not possible to obtain. This data would have helped provide further insights, such as whether larger population of FSWs are also correlated with higher population prevalence. Although it is well recognised that infection spread from higher to lower risk individuals, as suggested by core group theory, as network size increases and if HIV prevalence levels are higher, this concept may become less relevant.

This research chapter aims to address the hypothesis that sex work is the major driver of HIV in West Africa. Whilst, the findings are unable to falsify this claim, important insights are gained. Firstly, variations in HIV prevalence are not associated with higher prevalence levels in female sex workers or clients, suggesting that this is not a good indicator or measure of risk necessarily. Instead the size of risk groups, particularly those engaging in sex with multiple (2+) partners and clients of sex workers show stronger evidence of associations with HIV prevalence. Unfortunately, without accurate estimates of the size of female sex worker subgroups we are missing an important insight, which would strengthen this observation. And although we can make statements about potential transmission pathways of risk, the evidence is not substantial to conclude whether commercial sex is the predominant driver of HIV in West Africa, but the results are strongly suggestive of the importance of the size of risk groups. An importance question arising is what impact does network structure versus risk behaviours have on the magnitude of an epidemic, when both are also dependent on one another?

In conclusion, the findings are helpful for model development purposes, as it allows pathways of infection to be more empirically identified, as an initial starting point. In Chapter 5, Research Paper 3, I use these insights to inform the design of a dynamic model of HIV transmission.

For the results from the linear regression there are limitations associated with using R-squared and p-values as verification methods to indicate the adequacy of a model. Linear regression calculates an equation that minimizes the distance between the fitted line and all the data points, thereby representing the percentage of the response variable variation that is explained by a linear model. However, R-squared cannot determine whether the coefficient estimates and predications are biased and so cannot indicate whether the model is adequate. It is possible to have a high R-squared for a model that does not fit the data particularly well. Conversely, a graph with a lower R-squared and significant p-value show that it is possible even for noisy high-variability data to have a significant trend.

Both higher and lower values of R-squared can yield significant results, but lower values of R-squared indicate that the model has more error. An additional variable can be used which provides more information, S, the standard error of the regression. S, unlike R-squared is measured in the units of the response variable and represents the standard distance the data values fall from the regression line. It therefore, tells you how wrong the regression model is on average using the units of the response variable – with smaller values indicating that the observations are closer to the fitted line.

To add additional verification to the results, below I add an extension to Table 1 (Table 1 extended) below. In addition to p-values and R-squared, the standard error of the regression and the accompanying confidence intervals for the regression results is also presented. Only significant values are included ($p<0.05$). The same analysis is also included for the significant values in Tables 2(a) and 2(b).

	Variable (n= number of countries included in regression analysis)	**Females**			
		Urban Females (HIV prevalence)			
		R^2	*p-value*	*Standard Error*	*95% CI*
15-24 yr old females	HIV prevalence (12)	***0·44***	***0·01***	***0.399***	***0.24, 2.00***
25-49 yr old females	HIV prevalence (12)	***0.93***	***0.0001***	***0.064***	***0.59, 0.88***
25-49 yr old males	HIV prevalence (12)	***0.79***	***0.0001***	***0.179***	***1.48, 1.71***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.64***	***0.005***	***0.184***	***0.28, 1.12***
25-49 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.46***	***0.03***	***0.252***	***0.08, 1.24***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·59***	***0·003***	***0.050***	***0·08, 0.30***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.73***	***0.002***	***0.048***	***0.11, 0.33***
		Rural Females (HIV prevalence)			
15-24 yr old females	HIV prevalence (12)	***0·76***	***0·0002***	***0.200***	***0.68, 1.57***
25-49 yr old females	HIV prevalence (12)	***0.82***	***0.0001***	***0.079***	***0.35, 0.70***
25-49 yr old males	HIV prevalence (12)	***0.87***	***0.0001***	***0.104***	***0.64, 1.11***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.88***	***0.0001***	***0.079***	***0.43, 0.80***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·46***	***0·02***	***0.032***	***0.02, 0.16***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.70***	***0.003***	***0.027***	***0.06, 0.18***

25-49 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.86***	***0.0001***	***0.097***	***0.44, 0.89***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·54***	***0·006***	***0.0405***	***0.05, 0.23***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.69***	***0.003***	***0.039***	***0.07, 0.25***
		National Females (HIV prevalence)			
15-24 yr old females	HIV prevalence (12)	***0·68***	***0·001***	***0.280***	***0.68, 1.93***
25-49 yr old females	HIV prevalence (12)	***0.97***	***0.0001***	***0.036***	***0.62, 0.79***
25-49 yr old males	HIV prevalence (12)	***0.95***	***0.0001***	***0.084***	***0.92, 1.30***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.85***	***0.0002***	***0.113***	***0.49, 1.00***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·43***	***0·02***	***0.040***	***0.02, 0.20***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.56***	***0.01***	***0.041***	***0.04,, 0.23***
25-49 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.70***	***0.003***	***0.175***	***0.35, 1.16***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·59***	***0·004***	***0.047***	***0.07, 0.28***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.73***	***0.002***	***0.044***	***0.11, 0.31***
	Variable (n= number of countries included in regression analysis)	**Males**			
		Urban Males (HIV prevalence)			
		R^2	*p-value*	*Standard Error*	*95% CI*

Males reporting payment for sex in past year	% with risk behaviour aged 15-49 (10)	***0.64***	***0.005***	***0.119***	***0.04, 0.58***
Males reporting payment for sex in past year	% with risk behaviour aged 15-24 (10)	***0.79***	***0.0005***	***0.100***	***0.32, 0.78***
Males reporting payment for sex in past year	% with risk behaviour aged 25-49 (10)	***0.46***	***0.03***	***0.168***	***0.05, 0.82***
15-24 yr old females	HIV prevalence (12)	***0·85***	***0·0001***	***0.130***	***0.69, 1.27***
25-49 yr old females	HIV prevalence (12)	***0.61***	***0.003***	***0.095***	***0.17, 0.59***
25-49 yr old males	HIV prevalence (12)	***0.84***	***0.0001***	***0.096***	***0.49, 0.92***
15-24 yr old females 2+ partners in past 12 month	% with risk behaviour (12)	***0·49***	***0·01***	***0.087***	***0.08, 0.47***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.76***	***0.001***	***0.096***	***0.25, 0.70***
25-29 yr old females 2+ partners in past 12 month	% with risk behaviour (12)	***0·80***	***0·0001***	***0.999***	***0.32, 0.79***
25-29 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.83***	***0.0003***	***0.017***	***0.07, 0.15***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·44***	***0·01***	***0.113***	***0.07, 0.57***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.59***	***0.0094***	***0.138***	***0.15, 0.78***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·37***	***0·04***	***0.039***	***0.01, 0.18***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.45***	***0.03***	***0.043***	***0.01, 0.21***
		Rural Males (HIV prevalence)			
15-24 yr old females	HIV prevalence (12)	***0·85***	***0·0001***	***0.121***	***0.64, 1.18***

25-49 yr old females	HIV prevalence (12)	***0.65***	***0.001***	***0.083***	***0.18, 0.55***
15-24 yr old males	HIV prevalence (12)	***0·40***	***0·03***	***0.347***	***0.13, 1.67***
25-49 yr old males	HIV prevalence (12)	***0.83***	***0.0001***	***0.093***	***0.45, 0.86***
15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.78***	***0.0008***	***0.084***	***0.25, 0.64***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·57***	***0·0047***	***0.022***	***0.03, 0.13***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.83***	***0.0003***	***0.016***	***0.062, 0.14***
25-29 yr old females 2+ partners in past 12 month	% with risk behaviour (10)*	***0.78***	***0.0007***	***0.093***	***0.28, 0.70***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·35***	***0·04***	***0.037***	***0.01, 0.17***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.46***	***0.03***	***0.039***	***0.01, 0.19***
		National Males (HIV prevalence)			
Males reporting payment for sex in past year	% with risk behaviour aged 15-49 (10)	***0.54***	***0.02***	***0.11***	***0.02, 0.48***
Males reporting payment for sex in past year	% with risk behaviour aged 15-24 (10)	***0.58***	***0.01***	***0.120***	***0.12, 0.68***
Males reporting payment for sex in past year	% with risk behaviour aged 25-49 (10)	***0.43***	***0.04***	***0.144***	***0.03, 0.69***
15-24 yr old females	HIV prevalence (12)	***0·87***	***0·0001***	***0.103***	***0.61, 1.07***
25-49 yr old females	HIV prevalence (12)	***0.78***	***0.0001***	***0.061***	***0.22, 0.49***
25-49 yr old males	HIV prevalence (12)	***0.96***	***0.0001***	***0.037***	***0.56, 0.72***
15-24 yr old females 2+ partners in past 12 month	% with risk behaviour (12)	***0.44***	***0·019***	***0.077***	***0.04, 0.39***

15-24 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.86***	***0.0001***	***0.061***	***0.29, 0.57***
15-24 yr old males 2+ partners in past 12 month	% with risk behaviour (12)	***0·74***	***0·003***	***0.015***	***0.50, 0.12***
15-24 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.82***	***0.0003***	***0.015***	***0.06, 0.13***
25-49 yr old females 2+ partners in past 12 months	% with risk behaviour (12)	***0·44***	***0·01***	***0.096***	***0.06, 0.48***
25-49 yr old females 2+ partners in past 12 months	% with risk behaviour (10)*	***0.75***	***0.0013***	***0.092***	***0.23, 0.66***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (12)	***0·51***	***0·009***	***0.029***	***0.03, 0.16***
25-49 yr old males 2+ partners in past 12 months	% with risk behaviour (10)*	***0.63***	***0.006***	***0.030***	***0.04, 0.18***

Table 1 (extended): Additional information from the regression analysis to include the standard error ,S, and the respective 95% confidence intervals (CI).

	Variable (n= number of countries included in regression analysis)				
		Brothel-Based FSW HIV prevalence			
		R^2	*p-value*	*Standard Error*	*95% CI*
25-49 yr old females	HIV prevalence (12)	***0.77***	***0.002***	***0.362***	***0.89, 2.60***
25-49 yr old males	HIV prevalence (12)	***0.61***	***0.01***	***0.751***	***0.72, 4.27***
		15-24 year old female HIV prevalence			
25-49 yr old females	HIV prevalence (12)	***0.53***	***0.01***	***0.098***	***0.11, 0.55***
25-49 yr old males	HIV prevalence (12)	***0.77***	***0.001***	***0.108***	***0.40, 0.88***
		25-49 year old female HIV prevalence			
25-49 yr old males	HIV prevalence (12)	***0.87***	***0.001***	***0.179***	***1.10, 1.89***

	Variable (n= number of countries included in regression analysis)				
		Brothel-Based FSW HIV prevalence			
		R^2	*p-value*	*Standard Error*	*95% CI*
Males reporting payment for sex in past year (15-24)	% with risk behaviour (10)	***0.61***	***0.05***	***0.977***	***0.21, 5.23***
Males reporting payment for sex in past year (25-49)	% with risk behaviour (10)	***0.77***	***0.009***	***0.807***	***1.26, 5.41***
15-24 yr old females	% with risk behaviour (10)	***0.66***	***0.004***	***0.559***	***0.91, 3.49***
15-24 yr old males	% with risk behaviour (10)	***0.39***	***0.05***	***0.165***	***0, 0.76***
25-49 yr old females	% with risk behaviour (10)	***0.42***	***0.04***	***0.812***	***0.09, 3.84***
25-49 yr old males	% with risk behaviour (10)	***0.78***	***0.001***	***0.124***	***0.38, 0.95***
		15-24 year old female HIV prevalence			
Males reporting payment for sex in past year (15-24)	% with risk behaviour (10)	***0.57***	***0.01***	***0.121***	***0.11, 0.67***
Males reporting payment for sex in past year (25-49)	% with risk behaviour (10)	***0.41***	***0.005***	***0.147***	***0.004, 0.68***
15-24 yr old females	% with risk behaviour (10)	***0.82***	***0.003***	***0.079***	***0.29, 0.65***
15-24 yr old males	% with risk behaviour (10)	***0.84***	***0.001***	***0.016***	***0.07, 0.14***
25-49 yr old females	% with risk behaviour (10)	***0.83***	***0.001***	***0.084***	***0.33, 0.72***
25-49 yr old males	% with risk behaviour (10)	***0.40***	***0.04***	***0.042***	***0, 0.20***
		15-24 year old male HIV prevalence			
Males reporting payment for sex in past year (25-49)	% with risk behaviour (10)	***0.55***	***0.01***	***0.035***	***0.03, 0.19***
15-24 yr old males	% with risk behaviour (10)	***0.62***	***0.01***	***0.017***	***0.02, 0.10***
		25-49 year old female HIV prevalence			
15-24 yr old females	% with risk behaviour (10)	***0.78***	***0.001***	***0.186***	***0.57, 1.43***

15-24 yr old males	% with risk behaviour (10)	***0.44***	***0.05***	***0.064***	***0.01, 0.31***
25-49 yr old females	% with risk behaviour (10)	***0.60***	***0.008***	***0.278***	***0.33, 1.61***
25-49 yr old males	% with risk behaviour (10)	***0.78***	***0.003***	***0.056***	***0.17, 0.43***
		25-49 year old male HIV prevalence			
15-24 yr old females	% with risk behaviour (10)	***0.84***	***<0.001***	***0.101***	***0.42, 0.88***
15-24 yr old males	% with risk behaviour (10)	***0.69***	***0.003***	***0.030***	***0.06, 0.20***
25-49 yr old females	% with risk behaviour (10)	***0.72***	***0.002***	***0.149***	***0.33, 1.01***
25-49 yr old males	% with risk behaviour (10)	***0.69***	***0.008***	***0.042***	***0.08, 0.27***

Table 2(a) and (b) (extended): Additional information from the regression analysis to include the standard error,S, and the respective 95% confidence intervals (CI).

5. What factors drive variations in population HIV prevalence across West Africa? - the importance of adolescent girls and the effect of "*epidemic gearing*"

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Research Paper Cover Sheet

Section A – Student Details

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Section D- Multi-authored work

For multi authored work, give full details of your role in the research included in the paper and in the preparation of the paper.

I was the lead author of this paper and worked with Charlotte Watts and Zindoga Mukandavire to develop the storyline for the paper. I designed the concept for the mathematical model and I supported Zindoga Mukandavire in coding the model in R. I designed the approach for the multiple regression analysis and carried out the final analysis. I drafted the full manuscript and made revisions based on comments from Charlotte Watts and Zindoga Mukandavire.

Jasmina Panovska-Griffiths helped with the earlier development of the model structure and Marelize Gorgens and David Wilson provided comments and feedback on the final draft of the paper.

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5.1 Research Paper 3

What factors drive variations in population HIV prevalence across West Africa? - the importance of adolescent girls and the effect of "*epidemic gearing*"

Abstract

Background: The population HIV prevalence in West Africa varies between 0-6% in females and 0-4% in males. Male circumcision is almost universal, and it is unclear what explains the observed variations between countries.

Methods: A dynamic population model of HIV transmission among female sex worker (FSW) groups, their clients, adolescent males and females with 2+ partners in the past year, and other sexually active women and men in the general population was constructed. The model was parameterised using data from 13 countries in West Africa. Latin hypercube sampling was applied to identify parameter sets that fit HIV prevalence ranges for West Africa and a sensitivity analysis using partial-rank correlation coefficients was used to identify which model parameters were most sensitive to variations in HIV prevalence levels across West Africa.

Results: The key determinant of HIV in females when prevalence is between 0-3% is the size of the brothel and non-brothel FSW groups. When female HIV prevalence >3%, the percentage of sexually active adolescent females with 2+ partners has greater influence on HIV prevalence. The size of the FSW groups has the most significant impact on HIV prevalence for males.

Conclusions: The findings re-emphasise the continued prevention needs for FSWs in West Africa, with their population size being a key determinant of HIV risk. In addition, for more prevalent epidemics, our findings suggest that the percentage of adolescent girls with 2+ partners may enable the epidemic to be effectively "*geared up*" when partnerships are formed with higher-risk males, indicating additional prevention needs amongst this group.

Background

HIV in West Africa accounts for around 20% of all infections in sub-Saharan Africa with HIV prevalence here generally lower than in other African regions (UNAIDS, 2013) most likely as a result of the almost universal practice of male circumcision across West Africa(Weiss HA et al., 2000). However, within West Africa there are significant variations in HIV prevalence between countries (Figure 1) with National Demographic and Health Surveys (DHS) suggesting that Nigeria, Cote d'Ivoire and Cameroon have the highest HIV prevalence levels (4-6% among females and 2.5-4% in males) in comparison to other countries (0.5-2% amongst both females and males(Tara Beattie et al., 2011)).

Past epidemiological studies in this region confirm that commercial sex is a major driver of the HIV epidemic (Lowndes et al., 2002) and that interventions focused on female sex workers (FSWs) and their clients are highly effective at reducing the prevalence of sexually transmitted infections (STIs)(Lowndes et al., 2007). Similarly, a recent mathematical modelling study suggested commercial sex work in this region is a major driver of both the short and longer term epidemic trajectories in the region (Boily et al., 2015).

Our recent ecological analysis of variations in population prevalence levels across West Africa suggests that along with female commercial sex work, variations in HIV prevalence amongst general population males and females between countries is significantly ($p<0.05$) associated with national variations in the percentage of younger females (15-24 years) that have 2 or more (2+) partners (Prudden et al., 2015).

To explore this further and identify the potential determinants of population variation in HIV prevalence across the region, we developed and applied a dynamic model for HIV transmission between different cohorts of FSW, clients and the general population. Unlike previous studies, within our model we incorporated a cohort of sexually active adolescent females with multiple (2+) partners in the past year. The aim of our work is to explore the key parameters associated with different HIV prevalence levels in West Africa.

Methods

Model Structure and Development

We developed a deterministic compartmental model describing the transmission of HIV infection among sexually active 15-49 year olds (details in Appendix 3.1). In summary, the model stratifies the sexually active population into two groups of female sex workers (brothel-based and non-brothel based) and their respective client partner groups. In addition, the model includes a separate group of adolescent females with 2+ non-commercial sexual partnerships in the past year and a group of males (15-49) with 2+ non-sex worker partners in the past year, as well as subgroups representing other sexually active men and women in the general population. The mixing between different populations in the model is shown in Figure 2.

Based on the data from DHS surveys across the regions we assume the entire male population are circumcised(USAID). The probability of transmission per act is estimated using a wide range and this incorporates the potential presence of sexually transmitted infections, anal sex acts (as well as vaginal) and the effects of anti-retroviral therapy, which is introduced into the model 20 years after the start of the epidemic.

Model Parameterisation

Biological, epidemiological parameter data and published developmental indicators for West Africa were extracted from the literature. A full parameter table, including additional information on the computation and extraction of data is provided in Appendix 3.2. Table 1 below is a shortened version of the table showing only the parameters that were sampled and entered into the model. For each of these parameters a uniform range of plausible estimates was generated to account for variations across West Africa. Latin Hypercube sampling (Fenniak M, 2004) across these parameter ranges was used to generate 800,000 parameter combinations as model inputs.

Model Calibration and Fitting

For each model input, the model was run to equilibrium HIV prevalence and only the projections where HIV prevalence was among the literature-reported ranges were chosen. The model projected HIV prevalence of 0.5-6% in the general female population, 0.5-4% in the general male population, 15-48% in the brothel-based FSW group and 10-25% in the non-brothel based FSW group as potential model fits that reflect different West African epidemic trajectories. No fitting criteria were applied to the female 2+ group, male 2+ group or the brothel-based FSW clients and non-brothel based FSW client groups due to not having sufficient data for these subgroups.

Model mixing validation

In order to explore the population sexual mixing pattern that best represents West Africa, we tested two alternative mixing patterns within the model. The first was a standard proportional mixing matrix, whereby sexual partnerships between females 2+, clients and males 2+ were distributed proportionately based on their number of partners. The second mixing matrix was based on a “fixed proportionate” mixing scenario. Here, we created an additional parameter, ζ, to represent the proportion of partnerships females 2+ have who are clients (of either brothel-based or non-brothel based FSW). For both mixing matrices we ran the model using different model inputs and used least square difference to minimise the difference between the model projected outputs and the baseline HIV prevalence data from the DHS in West Africa. The mixing scenario for which the difference was smaller was considered a better fit and was used thereafter. Details are included in Appendix 3.3.

Analysis of fits

For the chosen model we firstly assessed the full range of model fits for males (0-4%) and females (0-6%). Given the wide range in HIV prevalence amongst females and males in West Africa, to assess whether determinants of HIV prevalence change as prevalence increases, we stratified the fits obtained into population prevalence ranges. These were based on the number of fits generated by the model to ensure there were more than 1000 fits for each range and the number of fits were approximately equivalent across ranges: generating six for females (0-2%, 2-2.5%, 2.5-3%, 3-3.5%, 3.5-4%, 4-6%), and five for males (0-2%, 2-2.5%, 2.5-3%, 3-3.5%, 3.5-4%). The behaviour of the model was explored for each of the scenarios sampled parameters using partial rank correlation coefficients as a sensitivity analysis technique(Blower et al., 1994). This allowed us to identify which input parameters were most influential on the prevalence values in different ranges.

Results

Model fits and verification

The model generated a total of 11,164 fits. The model which used a fixed proportionate mixing matrix was chosen as it gave a better fit to the baseline data in comparison to model which used a standard mixing matrix (with mean difference of 22.9 compared to 25.2 with further details in table 1 of Appendix 3).

Key determinants of HIV prevalence among female and male general population in West Africa

General population females

The first row of the table presents the model results for the full prevalence range for females. The population size of the female 2+ group is the parameter with the highest coefficient ranking, and therefore the most significant parameter in the 0-6% HIV prevalence range among the female general population. Other significant variables include the size of the non-brothel based and brothel based FSW groups and the duration of time they engage in sex work, with a shorter duration being more significantly associated with higher HIV prevalence. The number of sexual partners of both FSW groups and the female 2+ are also significant. The parameter (ζ) that describes the proportion of sex acts females 2+ have with clients of FSW versus males 2+ is also positively significant, suggesting that a higher proportion of sex acts with clients versus males 2+ results in higher levels of HIV. Condom use is important in all partnerships, but to a lesser extent than other model parameters (Table 2(a), first row).

For the 0-2% range, the size of all three female subgroups is important, although the FSW groups emerge as more important than the female 2+ group (Table 2(a); 2nd row). Between 2-3% HIV prevalence, the size of the non-brothel-based FSW remains the most important parameter, but the size of the brothel-based group becomes less important as prevalence increases beyond 2.5%. Other variables such as females 2+ size, partnership numbers and duration continue to be significant, although condom use is not (Table 2(a); 3rd row).

For female general population HIV prevalence above 3%, the influence of the size of the FSW groups remains significant but is replaced by the importance of the size of the female 2+ group and their number of sexual partners. The parameter (ζ) is also significant. As HIV prevalence increases above 4%, the partnership numbers of the FSW groups emerge as importance once again, indicating that sex work remains important for sustaining higher prevalence levels.

General population males

Table 2(b) presents the results of the PRCC analysis for the male general population. The population sizes of the FSW groups (both brothel and non-brothel based) have the highest correlation coefficient values and are thus the most influential variables associated with HIV prevalence among the male general population in the 0-6% HIV range. The number of sexual partners of females 2+ is also important but to a less degree, as is ζ, the level to which they form partnerships with clients of FSWs. Analogous to the female general population prevalence, partnership numbers of sex workers and their durations are significant, as is levels of condom use, but both to a lesser extent.

The findings remain similar for prevalence between 0-2%, with FSW population sizes, female 2+ partner numbers and duration of time as FSWs remaining important (Table 2(b); 2nd row). The results vary somewhat for prevalence levels between 2-3%. For 2-2.5%, duration of time spend as a brothel-based FSW is the most influential parameter – favouring longer duration periods rather than shorter (Table 2(b); 3rd row). However, between 2.5-3% HIV prevalence, shorter duration time spent for non-brothel based FSWs becomes the most important parameter (Table 2(b); 4th row). Population size of FSWs also remains significant, as does partnership numbers of females 2+. Finally, for prevalence levels between 3-4%, fewer parameters emerge as significant, with the size of the brothel-based FSW group being the most important parameter between this range, along with the size of the non-brothel based group, number of partners of females 2+ and shorter duration time spent as brothel-based FSW (Table 2(b); last row).

Discussion

Past studies have emphasised the importance of sex work and other vulnerable groups as key determinants of HIV prevalence. A recent modelling study showed that sex work alone is capable of sustaining higher level HIV epidemics in West Africa, within a range of 0-3% (in 2008)(Boily et al., 2015), whilst the model of Ghani *et al*.(11) demonstrated that the size of the FSW population (relative to the total population) is the most important determinant of HIV prevalence(Ghani et al., 2005).

The findings from this study show that the size of the female 2+ group is the parameter with the highest coefficient ranking for HIV prevalence in females in the 0-6% range. However, when we group model fits into different HIV prevalence ranges, we see that when prevalence is between 0-3%, it is the size of FSW groups that have the higher coefficient rankings – and in fact, there is evidence for a transition between determinants of risk that is masked by looking across the full range (0-6%) of HIV prevalence in females. This is an interesting observation which potentially highlights a change in nature of the HIV epidemic, from one being more dependent on the size and sexual activity of female sex workers, to an epidemic in which the subgroup size and sexual activity of young females, with multiple partners, is of greater importance. This same transition is not seen when the analysis is repeated for males, with the size of the FSW groups consistently having one of the highest ranked coefficient value, with their duration also being important. This may be explained in part, by lower levels of prevalence more generally in males, as well as the limiting effects of male circumcision, meaning sex work continues to be the major driver of infections. As expected, the model also confirms the importance of partnership numbers as important parameters in commercial sex and the duration of time that sex workers remain in the industry – with a faster turnover rate tending to favour higher levels of HIV prevalence.

These findings provide some interesting insights. Firstly, they confirm that commercial sex work plays a key role in HIV transmission, particularly in lower level epidemics (up to 3% HIV prevalence amongst females and up to 4% HIV prevalence among the male general population). However, our results also reveal that in higher level epidemics amongst females in the general population (>3%) other factors may also be important. In-particular, the percentage of females in the population who have two or more partners in a 12 month period and the proportion of this group that forms partnership with higher-risk males, that includes clients of FSWs.

The findings support the classic theory of STI epidemiology, where HIV is transmitted through a smaller core group of FSWs to their clients and onwards to the general population. When HIV prevalence is high amongst FSWs, this group may be capable of contributing a significant proportion of infections to the overall epidemic(Wilson D, 2006). As expected here, our results reveal the importance of behaviours that modify the risk of acquiring infection i.e. partner numbers, duration and condom use – that are also most commonly associated with higher HIV prevalence levels in empirical studies and mathematical modelling. However, for epidemics with higher levels of prevalence in females (>3%), the transmission pathways may be more complex and require a more advanced understanding of the underlying factors driving the epidemic. As well as behaviours that modify the risk of acquiring infections, conditions that shape sexual network structure, including the population size of higher-risk subgroups of adolescent females with 2+ partners and sexual partnership patterns in the population, are also shown to be important parameters that determine HIV prevalence and therefore should be considered in future model development.

This important result may support the idea of a type of "*epidemic gearing*" effect. Whereby, the epidemic has the propensity to grow, under the assumption that the epidemic is effectively "geared up", firstly, by smaller high-sexual activity groups of FSWs - and then secondly, through the larger subgroup of adolescent females 2+, which act as an additional larger "cog" in the epidemic chain enabling the epidemic to achieve higher-levels of HIV prevalence (Figure 4). Here the concept of behavioural heterogeneity and the importance of approaches that seek to identify high-risk individuals and understanding the structure of sexual networks emerge as important.

Our analysis does have several limitations. Firstly, estimates on the percentage of adolescent females reporting 2+ partners was mostly extracted from the DHS data. Whilst there is some comparability internally and between countries, typically questions on sexual behaviours are prone to under-reporting, especially amongst women. The results suggested a change in pattern of the determinants of HIV prevalence for females in the general population at around 3% prevalence. This finding potentially provides a more robust epidemiological measure for HIV classification compared to the numerical proxy method currently used (World Health Organisation). However, this should be seen only as an initial recommendation and not necessarily a specific guideline for changing policy. Further work needs to better quantify these findings.

Conclusion

Population data from DHS surveys suggests that the percentage of adolescent females with multiple partners, may comprise up to 9% of the total female population, with other studies reporting higher percentages (Atwood et al., 2012, Moore et al., 2007, Owoaje et al., 2009). This modelling study, shows the importance of the size and sexual activity of the female 2+ group and more broadly the need to assess and understand both behaviours that shape sexual network structures as well as those that modify the risks of acquiring infection, in determining variations in HIV prevalence. However, to date, very few mathematical models of HIV transmission in the general population explicitly include or recognise the importance of an adolescent female 2+ group, despite the high levels of incidence in this population. In addition, more accurate data on the estimated subgroup size for high-risk groups of female sex workers is often absent from modelling studies, despite demonstrating here the fundamental importance of this parameter. Future modelling studies should acknowledge the limitations of their findings, in cases where subgroup sizes cannot be accurately estimated.

The findings may also have important implications for future policy. The UNAIDS definition for a concentrated epidemic is one in which HIV prevalence is less than 1% in the general population and over 5% prevalence in key risk groups such as FSWs, with the caveat being that no subpopulation is fully self-contained and these thresholds should be interpreted with caution (UNAIDS, 2011). However, here we demonstrate the dangers of such rigid definitions, by highlighting the subtle maturity that may occur in epidemics from those driven predominantly by commercial sex work, to those in which both the role of commercial sex and the size and sexual behaviours of adolescent females with two or more partners in the population may be important determinants. In addition, the importance of understanding sexual network structure is highlighted, through the association of adolescent girls sexual partnership formations with high-risk males – an important observation that is evidenced in the literature (Luke, 2003, Luke N et al., 2002) but not incorporated within transmission models of HIV.

Finally, despite much focus on interventions being towards reducing the biological probability of transmission, our findings suggest that programmes which result in fewer women practicing sex work and fewer young females engaging in higher-risk partnerships, could play a key role in reducing the size of the HIV epidemics in West Africa.

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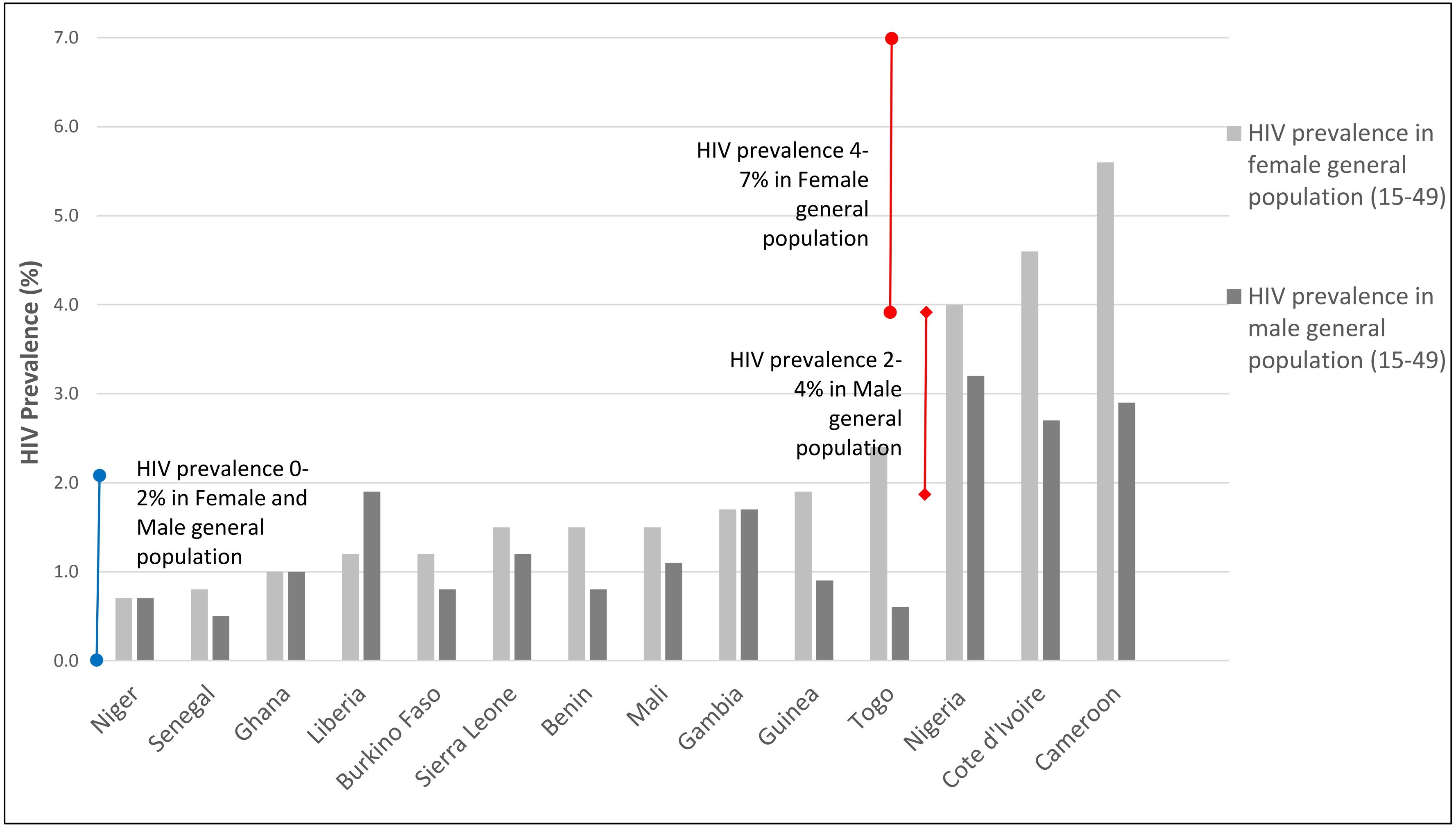
Figure 1: HIV prevalence in the general female and male populations of West African countries. HIV prevalence data taken from DHS and UNGASS reports in West African settings from 2010-2010



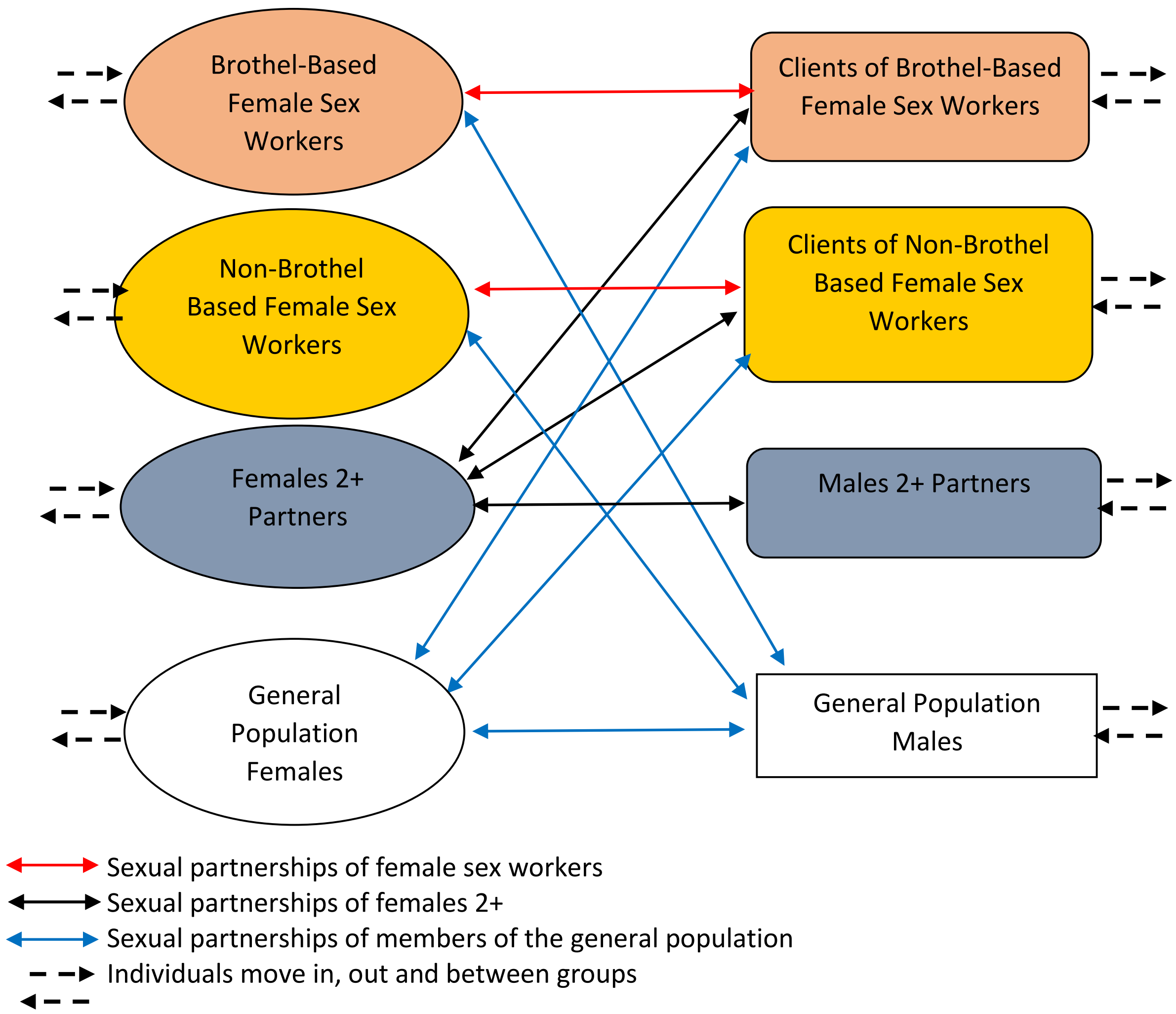


Figure 2: Sexual mixing patterns in the population. Black arrow denote partnership: Sexual partnerships exist between the two FSW groups and their respective client groups and between clients and females with 2+ partners. Younger females 2+ also partner with males 2+. Separate groups of general population males and females form partnerships with one another, with a given proportion also having longer term partnerships with clients (in the case of females) and FSW (in the case of males (to represent the wives of clients and husbands of sex workers, respectively).

Table 1: Biological and behavioural sampled model parameter estimate ranges.

Description	Symbol	Parameter value/range
Probability of HIV transmission	(β_{mf}, β_{fm})	0.006-0.06
Relative size of Brothel-based FSWs group	P_{FBB}	0-1.1%
Relative size of Non-brothel based FSWs group	P_{FNB}	0.15-3%
Relative size of Females with 2+ partners group	P_{FTS}	0.1-20%
Number of client partners of brothel-based female sex worker.	C_{FBB}^{c}	252-1092/yr
Number of client partners of non-brothel based FSWs	C_{FNB}^{c}	42-336/yr
Number of partners of Females 2+ partners (these include client partners of both brothel-based and non-brothel based FSWs as well as males 2+ partners)	C_{CTS}^{TS}	3-24/yr[1]
Number of brothel based FSWs, clients of brothel-based FSW form partnerships with.	C_{CBB}^{c}	12-48/yr
Number of non-brothel based FSWs, clients of non-brothel based FSWs form partnerships with.	C_{CNB}^{c}	12-48/yr
Consistency of condom use among Brothel-based female sex workers	f_{FBB}	41-83% (adjusted for efficacy)
Consistency of condom use among Non-brothel based female sex workers	f_{FNB}	41-68%
Consistency of condom use of females with 2+ partners	f_{FTS}	10-39%
Duration of brothel based female sex workers	$1/\alpha_{BB}$	0.5-6 yrs
Duration of non-brothel based female sex workers	$1/\alpha_{NB}$	0.5-6 yrs
Duration of Females 2+	$1/\alpha_{TS}$	1-15 yrs
Duration of brothel based clients	$1/\varphi_{BB}$	5-10yrs
Duration of non-brothel based clients	$1/\varphi_{NB}$	5-10yrs
Duration of Maless 2+	$1/\varphi_{TS}$	5-20yrs
Percentage of sex acts of females 2+ with client partners of brothel-based and non-brothel based FSWs	ξ	0-100%
(Percentage of sex acts of females 2+ with non-client male partners)	$1-\xi$	0-100%

Prevalence range	Number of model fits in range	Input parameter	PRCC	p-value	Most critical parameter affecting prediction precision of HIV prevalence
0-6%	11162	P_{FTS}	0.479	<0.0001	- Population size of female 2+.
		P_{FNB}	0.359	<0.0001	
		C_{FNB}^{C}	-0.2861	<0.0001	
		$1/\alpha_{NB}$	-0.2477	<0.0001	
		C_{CTS}^{TS}	0.2377	<0.0001	
		ξ	0.2248	<0.0001	
		P_{FBB}	0.1909	<0.0001	
		C_{FBB}^{c}	-0.1579	<0.0001	
		β_{mf}	0.1561	<0.0001	
		$1/\alpha_{BB}$	-0.155	<0.0001	
		f_{FNB}	0.1482	<0.0001	
		f_{FBB}	0.111	<0.0001	
		β_{fm}	-0.0833	<0.0001	
		f_{FTS}	-0.0315	0.0009	
		$1/\varphi_{BB}$	-0.0233	0.0138	
		$1/\alpha_{TS}$	0.0207	0.0288	
0-2%	2297	P_{FNB}	0.3359	<0.0001	- Population size of Non-brothel based FSW.
		P_{FBB}	0.2449	<0.0001	
		P_{FTS}	0.181	<0.0001	
		ξ	0.1652	<0.0001	
		$1/\alpha_{NB}$	-0.1527	<0.0001	
		C_{CTS}^{TS}	0.1313	<0.0001	
		$1/\alpha_{BB}$	-0.1105	<0.0001	
		C_{FNB}^{C}	-0.1094	<0.0001	
		f_{FNB}	0.0709	0.0007	
		β_{mf}	0.0385	0.0661	
2-2.5%	1772	P_{FNB}	0.0973	<0.0001	- Population size of Non-brothel based FSW.
		P_{FBB}	0.097	<0.0001	
		P_{FTS}	0.0966	0.0001	
		ξ	0.0723	0.0024	
		C_{CTS}^{TS}	0.0692	0.0037	
		C_{FBB}^{C}	-0.0626	0.0087	
		$1/\alpha_{NB}$	-0.0577	0.0156	
		$1/\alpha_{BB}$	-0.0557	0.0196	

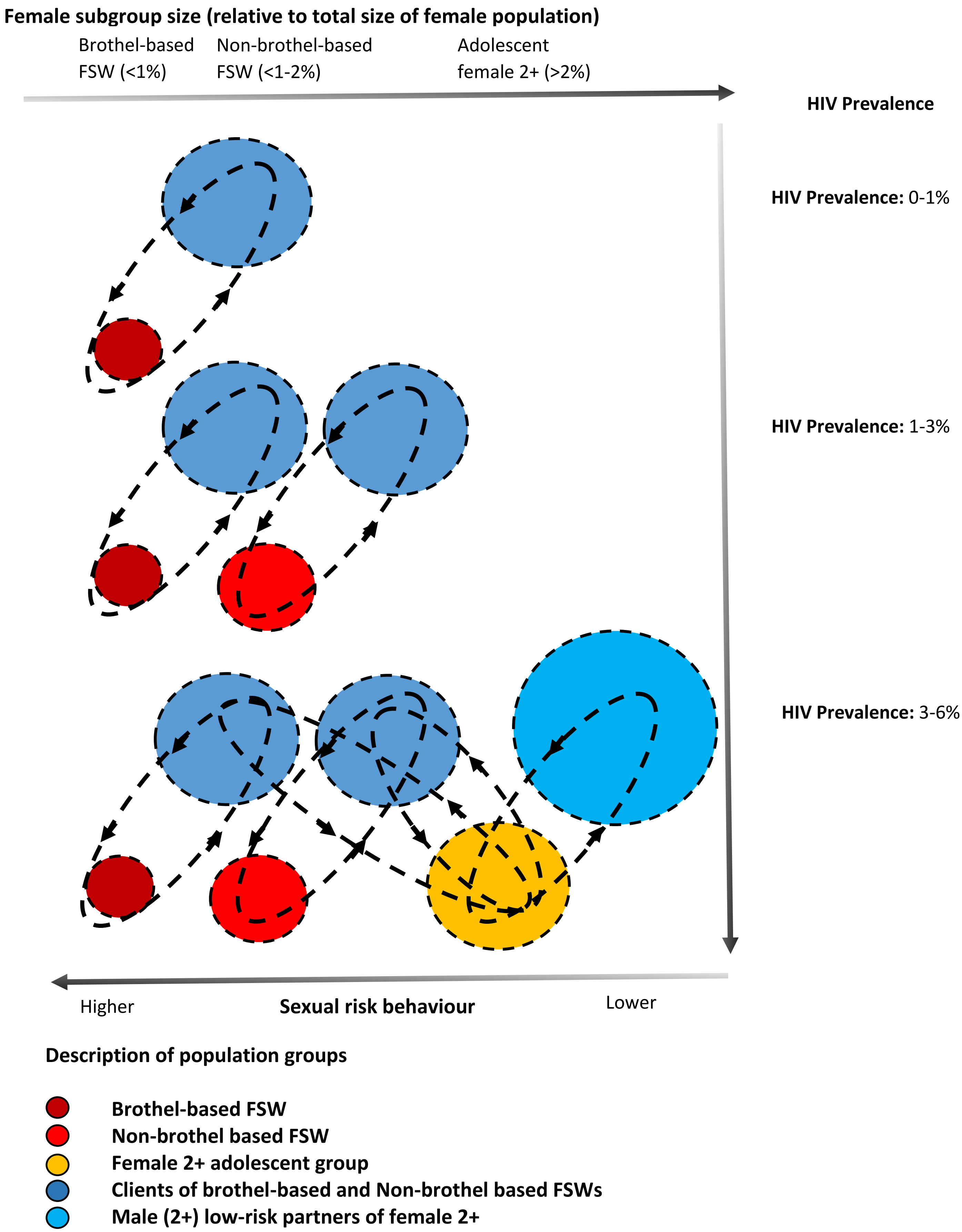
2.5-3%	1980	P_{FNB} C_{CTS}^{TS} P_{FTS} C_{FNB}^{C}	0.0562 0.0522 0.0515 -0.0457	0.0128 0.0207 0.0225 0.0429	- Population size of Non-brothel based FSW.
3-3.5%	1732	P_{FTS} C_{CTS}^{TS} P_{FNB} ξ β_{mf} $1/\alpha_{NB}$ P_{FBB} C_{FBB}^{C} $1/\alpha_{BB}$ C_{FNB}^{C} $1/\varphi_{TS}$	0.1112 0.0807 0.0784 0.0733 0.0731 -0.0724 0.0565 -0.0556 -0.0555 -0.0489 0.0474	<0.0001 0.0008 0.0012 0.0024 0.0025 0.0027 0.0192 0.0212 0.0215 0.0428 0.0498	- Population size of female 2+.
3.5-4%	1385	ξ P_{FTS} β_{mf}	0.1072 0.1025 0.0857	0.0001 0.0001 0.0015	- Proportion of female 2+ sexual partnerships formed with clients FSWs.
4-6%	1894	P_{FTS} C_{FNB}^{C} C_{FBB}^{C} β_{mf} β_{fm} f_{FBB} $1/\alpha_{NB}$ f_{FNB} ξ P_{FNB} P_{FBB} $1/\alpha_{BB}$ C_{CTS}^{TS}	0.3317 -0.232 -0.2155 0.2023 -0.176 0.01721 -0.1262 0.1188 0.1006 0.0912 -0.0665 -0.0586 0.0467	<0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 0.0001 0.004 0.0111 0.0432	- Population size of female 2+.

Table 2(a): Results from the Partial Correlation Coefficient sensitivity analysis for females in the general population.

Prevalence range	Number of model fits in range	Input parameter	PRCC	p-value	Most critical parameter affecting prediction precision of HIV prevalence
0-6%	11162	P_{FBB}	0.3646	<0.0001	- Population size of Brothel-based FSWs.
		P_{FNB}	0.3265	<0.0001	
		C_{CTS}^{TS}	0.2431	<0.0001	
		$1/\alpha_{NB}$	-0.1964	<0.0001	
		P_{FTS}	0.1859	<0.0001	
		ξ	0.1762	<0.0001	
		$1/\alpha_{BB}$	-0.1701	<0.0001	
		C_{FBB}^{c}	0.1342	<0.0001	
		β_{fm}	0.1015	<0.0001	
		β_{mf}	-0.1011	<0.0001	
		C_{FNB}^{C}	-0.099	<0.0001	
		f_{FBB}	-0.089	<0.0001	
		f_{FNB}	0.0878	<0.0001	
		f_{FTS}	-0.07	<0.0001	
0-2%	2225	P_{FNB}	0.3063	<0.0001	- Population size of Non-brothel based FSW.
		P_{FBB}	0.2981	<0.0001	
		C_{CTS}^{TS}	0.1578	<0.0001	
		$1/\alpha_{NB}$	-0.1248	<0.0001	
		ξ	0.1066	<0.0001	
		β_{fm}	0.1041	<0.0001	
		$1/\alpha_{BB}$	-0.1036	<0.0001	
		C_{FBB}^{c}	0.0783	0.0002	
		β_{mf}	-0.0691	0.0012	
		P_{FTS}	0.0648	0.0023	
		$1/\varphi_{BB}$	-0.0503	0.0181	
2-2.5%	1935	$1/\alpha_{BB}$	0.0787	0.0006	- Duration spent as Brothel-based FSW.
		P_{FBB}	0.0747	0.0011	
		C_{CTS}^{TS}	0.0702	0.0021	
		f_{FNB}	0.0653	0.0042	
		f_{FTS}	-0.0575	0.0118	
		P_{FNB}	-0.05	0.0287	

2.5-3%	2317	$1/\alpha_{NB}$ P_{FNB} P_{FBB} C_{CTS}^{TS} f_{FNB}	-0.0797 0.062 0.0588 0.045 0.0466	0.0001 0.003 0.0048 0.0308 0.0323	- Duration spent as Non-brothel based FSW.
3-3.5%	2402	P_{FBB} P_{FNB}	0.0467 0.0391	0.0225 0.0504	- Population size of Brothel-based FSWs.
3.5-4%	2282	P_{FBB} C_{CTS}^{TS} $1/\alpha_{BB}$	0.0685 0.0585 -0.0416	0.0011 0.0054 0.0476	- Population size of Brothel-based FSWs.

Table 2(b): Results from the Partial Correlation Coefficient sensitivity analysis for males in the general population.



Female subgroup size (relative to total size of female population)
Brothel-based FSW (<1%)
Non-brothel-based FSW (<1-2%)
Adolescent female 2+ (>2%)
HIV Prevalence
HIV Prevalence: 0-1%
HIV Prevalence: 1-3%
HIV Prevalence: 3-6%
Higher
Sexual risk behaviour
Lower
Description of population groups
Brothel-based FSW
Non-brothel based FSW
Female 2+ adolescent group
Clients of brothel-based and Non-brothel based FSWs
Male (2+) low-risk partners of female 2+

Figure 3: Conceptual idea of the "epidemic gearing" effect of HIV epidemics in West Africa (the black dashed lines represent the "gearing effect" of the epidemic, by representing the sexual network connections between risk groups in the population)

5.2 Thesis discussion for Research Paper 3:

This paper explored which behavioural and/or biological factors determine higher versus lower levels of population HIV prevalence in West Africa, within different prevalence ranges. This was done by constructing a dynamic deterministic compartmental model, to fit to plausible ranges for West Africa female and male population HIV prevalence at equilibrium.

The results from the MoT model in Research Paper 1 and the findings from the ecological analysis in Research Paper 2 were used to inform the development, structure and concept for the dynamic model.

The results from the MoT modelling, showed that behavioural heterogeneity is a crucial concept in mathematical models of HIV epidemics. Risk was also identified as an important concept and the assumptions made in relation to how HIV transmission is modelled. The ecological analysis in Research Paper 2, provided evidence that the size of a group of adolescent females 2+ and their patterns of partnership formation and sexual networking with clients of FSWs, may place them at elevated risk for acquiring HIV and lead to higher HIV population prevalence by broadening out higher-risk sexual networks.

In this third Research Paper, the development of the model attempted to incorporate the findings, lessons and insights from Research Papers 1 and 2. A recurring theme from the previous papers was the potential importance of the size of the group of females with 2+ partners and their proximity to higher-risk sexual networks such as FSWs and their clients. In this Research Paper, the design of the model and the way the model was parameterised allowed the size of this group and their level of interaction with higher-risk sexual networks of clients and their FSW partners to vary, in order to explore whether this may explain population variations in endemic HIV prevalence.

The results show that for HIV epidemics when the prevalence in the general population is at lower levels (0-3%), it is the size of the FSW groups that are the most significant determinant of variations in HIV prevalence. For epidemics, where prevalence is greater than 3%, the model projections show that it is the size of the group of young females with 2+ partners that is the most significant determinant of variation in HIV prevalence in the general female population. The size of this group is larger for epidemics where HIV prevalence levels are higher (approximately 9% for general female population prevalence in the 3-4% prevalence range, and 14% for epidemics in the 5-6% prevalence range).

In this way, the model results from this Research Paper suggest that the epidemic can be "geared up", so that small high-sexual activity groups of brothel-based FSWs are able to drive HIV epidemics when HIV prevalence is low. However, the larger group of non-brothel based FSWs and the subgroup of adolescent females 2+ are required as two additional larger "cogs" in the epidemic chain, to obtain higher-levels of female endemic HIV prevalence.

The modelling work in this chapter is able to address the hypothesis that sex work is the main driver of the epidemic by exploring different assumptions around variations in HIV prevalence. The modelling results show that population size of higher-risk subgroups (FSWs and Females 2+) are important to the overall HIV prevalence in the population, both for females and males. Here we see that it is the quantity of risk behaviour in relation to the size of higher-risk population subgroups that is potentially of greater importance than the behavioural risk factors (i.e. partnership numbers, condom use and durations) in determining prevalence. The hypothesis is supported for lower prevalence ranges, with the results suggesting it is both the size and sexual behaviour of female sex workers that important. However, for larger level epidemics (3-6%), although the size and sexual behaviour of female sex workers remain important, the size, partnership numbers and degree of sexual mixing of the females 2+ group with clients are shown to have the strongest association with HIV prevalence in general population females. In contrast the size and sexual behavioural of female sex workers is consistently the most significant determinants of HIV prevalence in males, when HIV prevalence ranges from 0-4%, hence supporting the hypothesis that commercial sex work is the main driver of the epidemic.

In conclusion, the findings from the paper present an important conclusion, with lower level epidemics in both males and females in West Africa, shown to be associated more strongly with commercial sex as suggested previously, whilst higher levels of prevalence in females being determined by the sexual behaviour of adolescent females with multiple partners.

In the final results paper, we use the mathematical model to explore the determinants of HIV prevalence across West Africa and assess the robustness of the UNAIDS categorisation of HIV epidemics, exploring in-particular whether there a transitional point or phase where epidemics, both in the presence, and in the absence of male circumcision transition from being primarily driven by the size and sexual behaviour of FSWs, to epidemics where the size and sexual behaviours of adolescent females 2+ is more important.

6. Epidemic categorisation of heterosexual HIV transmission in Sub-Saharan Africa: Insights from mathematical modelling of the importance of sex work and adolescent females with multiple sexual partners

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Status: Pending Submission

Research Paper Cover Sheet

Section A – Student Details

Student: Holly J Prudden

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Thesis Title: Determinants of population variability in HIV across West Africa: ecological and modelling analyses

Section C – For a 'research paper' prepared for publication but not yet published

Where is the work intended to be published? Lancet HIV

Please list the papers' authors in the intended authorship order:

Holly J Prudden (MSc), Zindoga Mukandavire (Ph.D), Charlotte Watts (Ph.D)

Stage of publication – submitted.

Section D- Multi-authored work

For multi authored work, give full details of your role in the research included in the paper and in the preparation of the paper.

I was the lead author of this paper and worked with Charlotte Watts and Zindoga Mukandavire to develop the storyline for the paper. I designed the concept for the mathematical model and I supported Zindoga Mukandavire in coding the model in R. I designed the approach for the multiple regression analysis and interpreted the results. I drafted the full manuscript and made revisions based on comments from Charlotte Watts and Zindoga Mukandavire.

Student signature: HJ Prudden Date: 05/10/2015

Supervisor signature: C. Watts Date: 05/10/2015

6.1 Research Paper 4

Epidemic categorisation of heterosexual HIV transmission in Sub-Saharan Africa: Insights from mathematical modelling of the importance of sex work and adolescent females with multiple sexual partners

Abstract:

Background: The most established method of HIV epidemic classification is the UNAIDS numerical proxy method, that classifies epidemics with HIV prevalence levels less than 1% in the general population as *concentrated* and those greater than 1% as *generalised.* However, it has been widely recognised that there are limitations to such an approach and a lack of understanding as to the exact epidemic characteristics that define these categorisations.

we developed a dynamic mathematical model for heterosexual transmission of HIV to explore the characteristics and determinants of HIV epidemics in the absence of male circumcision in West Africa, using

Methods: A deterministic compartmental deterministic model for HIV transmission was used to simulate epidemics in the absence of male circumcision in West Africa. . The sexually active population is sub-divided into 2 female sex worker (FSW) groups, their clients, adolescent males and females with 2+ partners in the past year, and other women and men in the population. A mixing parameter was used to model the degree to which adolescent females with 2+ partners have sex with male clients. Ranges for model parameters describing the sexual behaviour were developed using data from West Africa. We used Latin Hypercube sampling and partial-rank correlation coefficients as a sensitivity analysis. Potential thresholds for epidemic classification were explored.

Results: In the absence of male circumcision, at endemic levels, HIV prevalence in females ranges from 4-15% and in males from 6-17%, compared to 0-6% and 0-4% for model fits for west Africa. Between these ranges the size and sexual activity of both sex worker groups and females with 2+ partners are key parameters associated with HIV prevalence in both females and males in the general population.

Conclusions These results show that commercial sex work is an important determinant of HIV prevalence in the absence of male circumcision for both higher and lower prevalence epidemics. The vulnerability of adolescent females with 2+ partners are also an important group at different prevalence levels. Whilst there is no clear evidence for a prevalence level that lead to an “epidemiological switch” between concentrated and generalised epidemics, for setting where there is male circumcision, epidemics should be categorised accordingly.

Introduction

UNAIDS uses a system of epidemic categorisation to help inform intervention priorities. Concentrated HIV epidemics describe those where HIV prevalence is less than 1% in the general population and over 5% in defined sub-populations, typically known as “core groups”. Generalised HIV epidemics instead describe those where “HIV is firmly established in the general population” and “sexual networking in the general population is sufficient to sustain an epidemic independent of sub-populations at higher risk of infection” (World Health Organization and Joint United Nations Programme on HIV/AIDS, 2000). However, the descriptions are very broad, and so are of limited value for intervention priority settings, they also fail to describe individual behaviours and are therefore not particularly useful as epidemiological measures. For epidemics in Sub-Saharan Africa, in particular, where almost all epidemics are categorised as “generalised”, and despite large variations in HIV prevalence, the numerical proxy measure ends up putting all epidemics – be it in West, East or Southern Africa in the same epidemic category.

Where HIV epidemics may be higher than 1% often the epidemic is arbitrarily referred to as “mixed”, rather than generalised, meaning people are acquiring HIV in one or more subpopulations as well as in the general population (World Health Organisation). Whilst this provides some descriptive measure of a transitional state from a concentrated to a generalised epidemic, without additional information on the underlying epidemiology of the setting, it is of limited use as a tool for programming and prioritising interventions.

The rationale of epidemic categorisation is a potentially helpful tool in HIV policy and programming as it can be used to prioritise prevention activities. However, the approach must move beyond a numerical categorisation in HIV prevalence levels between settings to measures that reflect differences in population dynamics, behavioural heterogeneity, sexual networks and associated risks between epidemic settings. As the arsenal of HIV intervention tools expands, considerations of issues such as the impact of male circumcision in limiting the epidemic and the life-prolonging effect of ART treatment and its availability, now also need to be incorporated into thinking about epidemic classification and what this means for policy.

A recent mathematical modelling study in West Africa has demonstrated the importance of both the conditions of a sexual network structure, i.e. the size of high-risk subgroups and how they mix as well as behaviours that modify the risk of acquiring HIV, such as partnership numbers, condom use and duration of sexual activity. This paper aim to build on this work, by using mathematical modelling to investigate factors determining the variations in endemic HIV prevalence across West Africa in the absence of male circumcision, exploring in-particular whether there is a key level of HIV where the epidemic displays more characteristics of a generalised epidemic and what the West African parameters are that determine this.

Methods

Model Structure and Development

Similar to previous publications, a dynamic deterministic compartmental model, coded in R, was used to simulate population HIV prevalence that is reflective of patterns across West Africa (Prudden HJ et al., 2016). Briefly, the model stratifies the population into two groups of female sex workers, brothel-based and non-brothel based, and their respective client partner groups. In addition, the model includes a separate group of adolescent females with two or more (females 2+) non-commercial sexual partners in the past year and a group of males (15-49) with two or more (males 2+) non-sex worker partners in the past year, as well as other sexually active men and women in the general population.

Figure 1 shows the patterns of sexual mixing between sub-groups. Sexual partnerships exist between the two FSW groups and their respective client groups and between clients and females 2+. Females 2+ also partner with males 2+. Separate groups of general population males and females form partnerships with one another, with a given proportion also having longer term partnerships with clients (in the case of females) and FSW (in the case of males (to represent the wives of clients and husbands of sex workers, respectively).

The model formulation details and equations are provided in Appendix 3.1.

Model Parameterisation and Fitting

Parameter ranges and input values are shown in Appendix 3.2, with a shortened version of the table that includes only the sampled parameters shown in Table 1.

For each input a uniform range of plausible estimates across West Africa was generated using the available literature. Latin Hypercube sampling across these ranges of potential inputs was then used to generate 800,000 combinations of model inputs.

Model Calibration and Fitting

For each model input, the model was run to equilibrium HIV prevalence and only the projections where HIV prevalence was among the literature-reported ranges were chosen. The model projected HIV prevalence of 0.5-6% in the general female population, 0.5-4% in the general male population, 15-48% in the brothel-based FSW group and 10-25% in the non-brothel based FSW group as potential model fits that reflect different West African epidemic trajectories. No fitting criteria were applied to the female 2+ group, male 2+ group or the brothel-based FSW clients and non-brothel based FSW client groups due to not having sufficient data for these subgroups.

From these existing fits, the model was re-run omitting the effects of male circumcision to assess which behavioural or biological parameters induce a West African HIV epidemic.

Estimating the robustness of findings to situations with universal male circumcision

To assess the relative effect of different parameters on HIV prevalence, we first stratified the fits obtained into population prevalence ranges – from 4-5%, up to 13-15% for females (ensuring each range had a minimum of 500 model fits). The final range included a 2% prevalence increment. The same stratification was applied to the male data but starting from a slightly higher range – from 7-8% up to 15-17%. The behaviour of the model was explored for each of the scenarios sampled parameters using partial rank correlation coefficient as a sensitivity analysis technique, to identify which parameters are most important to variations in HIV prevalence (Blower et al., 1994).

Assessing the importance of the size of the Female 2+ group

For this analysis, we sought to determine whether there was an epidemic threshold level (HIV prevalence level) where the key parameters determining HIV prevalence change, and what the characteristics of these parameters are.

Results

The model generated a total of 11164 fits.

Table 2(a) and 2(b) in Appendix 4 shows the full analysis for the PRCC analysis. Figure 2(a) and 2(b), gives a simple breakdown of these results that compares the rank order of model parameters for each prevalence range projected by the model, to assess which parameters have the greatest impact on HIV prevalence.

Figure 2(a) shows the order of the PRCC for the female general population prevalence. The number of fits below 4% were not sufficient in number to include in an analysis, suggesting that when the effects of male circumcision are removed and with the current mixing pattern, under these conditions endemic HIV prevalence would reach a minimum of approximately 4% in females across West Africa, compared to less than 1% when universal circumcision is present. The maximum HIV in females is approximately 15%, although several fits gave higher projections these were few in number. This range is much wider than that of West Africa, 0-6% versus 4-15%. However, results from the PRCC shows no real evidence for a significant change in the model parameters that determine HIV prevalence levels between 4-15%. Both the population size of non-brothel based FSWs and females 2+ remain as high ranked coefficients for all HIV prevalence ranges. The importance of brothel-based FSWs appears to be greater for lower prevalence levels but also remains significant for higher prevalence levels. The partnership numbers of females 2+ is also an important determinant of prevalence across all ranges.

For males, the range in HIV prevalence of model projections is significantly different from those in West Africa, 0-4% versus 6-17%, when the effects of male circumcision are removed. Below 6% the number of model fits were not sufficient in number to include and between 6-7% none of the model parameters were identified as significant determinants of HIV ($P<0.05$). The results for the PRCC show a similar pattern to that of females. The size of the non-brothel based and female 2+ groups consistently have a high ranked PRCC vale as does the size of the brothel-based FSW group and the partnership numbers of females 2+. However, in a similar way to females, the size of the brothel-based FSW group becomes less significant as prevalence levels increase.

Discussion

The categorisation of HIV epidemics aims to identify the point at which HIV transitions from a more concentrated, in key vulnerable groups, to when HIV is more established in the general population and sexual networking is sufficient to sustain an epidemic independently of higher-risk subpopulations.

There are several important findings from this study. Previous modelling work of the epidemic in West Africa, has demonstrated the importance of both the size and sexual activity of female sex workers as well as the role of adolescent girls in the HIV epidemic in this region. Removing the effects of male circumcision, shows how these parameters remain important determinants of prevalence, but in addition the significant limiting effect that male circumcision has on prevalence levels. Under both scenarios commercial sex remains important and the distinction between epidemics which are more concentrated in nature, versus those that are more generalised does not demonstrate a clear threshold level, such as the 1% prevalence threshold currently endorsed. The policy message arising from this finding is that programmes should continue to focus on the importance of commercial sex, as well as addressing the vulnerability of adolescent girls and other groups. In addition, epidemic categorisation should account for levels of male circumcision within a region, with this study demonstrating the extent to which this limits transmission and may lead to misclassification and incorrect policy messages in low level regions such as West Africa.

There are several limitations associated with the results from this study. Firstly, we only consider HIV determinants for the endemic phase of the epidemic and not the transient phase, where the minimum HIV prevalence is around 4% in females and 6% in males. This means that the importance of other determinants may be under-estimated if this assumption is incorrect.

A second limitation is the known localisation of epidemics. HIV prevalence levels projected by our model were in the range 4-15% for the West African region in the absence of male circumcision, whereas many HIV epidemics (in areas of with no circumcision) have significantly higher levels. Here we are attempting to capture the epidemic at a population level, whereas in fact most epidemics within countries or states occur at a more localised level. In recent years there has been recognition that certain geographical locations may represent potential “hot-spots” of infection (Wand and Ramjee, 2010). Here, larger more concentrated groups of FSWs and their partners generate high levels of infection, a dynamic which we have not captured.

Finally, the wide availability of ART drugs for HIV treatment and methods of prevention, may also be an important factor for epidemic categorisation. We modelled, low levels of ART coverage within a range (approximately 20%), however we made the same assumption for the results where circumcision was omitted from the model. Because ART has a similar effect to male circumcision, in that it lowers the transmission probability of HIV during sexual contact, differences in coverage levels may lead to different results. With the newly revised WHO guidelines recommending that all infected individuals receive treatment (Cohen J, 2015) and as epidemics enter an endemic phase in which incidence levels are generally declining, epidemic prevalence levels may remain more stable and so epidemic categorisation and the policy messages that arise from it, need to evolve.

In summary, epidemic categorisation is a concept which must evolve with time as we gain more knowledge on the effectiveness of treatment and the uptake in some settings of male circumcision programmes (WHO and UNAIDS, 2011). Changing dynamics within epidemic settings in regards to treatment and the source of infections must be closely observed and monitored so that intervention programmes and policy messages can remain effective.

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Figure 1: Sexual mixing patterns in the population. Black arrow denote partnership: Sexual partnerships exist between the two FSW groups and their respective client groups and between clients and females with 2+ partners. Younger females 2+ also partner with males 2+. Separate groups of general population males and females form partnerships with one another, with a given proportion also having longer term partnerships with clients (in the case of females) and FSW (in the case of males (to represent the wives of clients and husbands of sex workers, respectively).

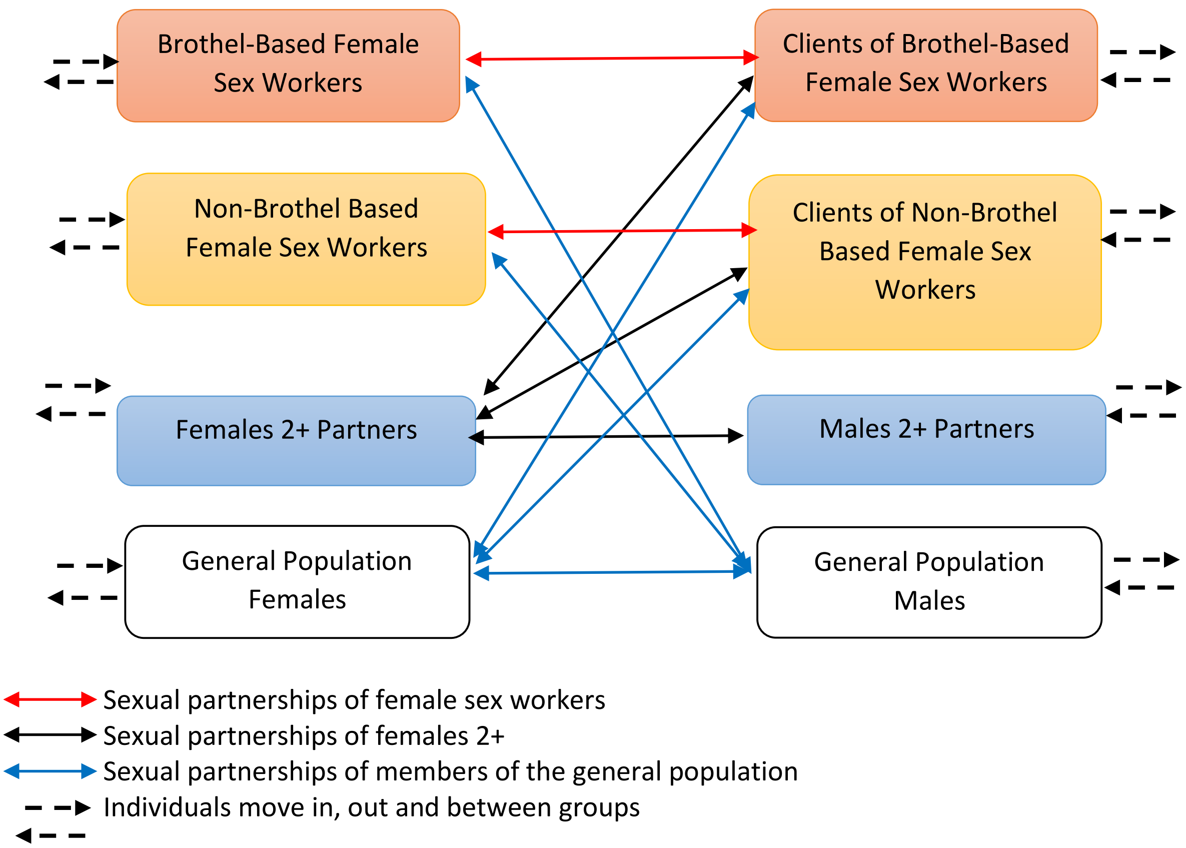


Table 1: Biological and behavioural sampled model parameter estimate ranges.

Description	Symbol	Parameter value/range
Probability of HIV transmission	(β_{mf}, β_{fm})	0.006-0.06
Relative size of Brothel-based FSWs group	P_{FBB}	0-1.1%
Relative size of Non-brothel based FSWs group	P_{FNB}	0.15-3%
Relative size of Females with 2+ partners group	P_{FTS}	0.1-20%
Number of client partners of brothel-based female sex worker.	C_{FBB}^{c}	252-1092/yr
Number of client partners of non-brothel based FSWs	C_{FNB}^{C}	42-336/yr
Number of partners of Females 2+ partners (these include client partners of both brothel-based and non-brothel based FSWs as well as males 2+ partners)	C_{CTS}^{TS}	3-24/yr[1]
Number of brothel based FSWs, clients of brothel-based FSW form partnerships with.	C_{CBB}^{c}	12-48/yr
Number of non-brothel based FSWs, clients of non-brothel based FSWs form partnerships with.	C_{CNB}^{c}	12-48/yr
Consistency of condom use among Brothel-based female sex workers	f_{FBB}	41-83% (adjusted for efficacy)
Consistency of condom use among Non-brothel based female sex workers	f_{FNB}	41-68%
Consistency of condom use of females with 2+ partners	f_{FTS}	10-39%
Duration of brothel based female sex workers	$1/\alpha_{BB}$	0.5-6 yrs
Duration of non-brothel based female sex workers	$1/\alpha_{NB}$	0.5-6 yrs
Duration of Females 2+	$1/\alpha_{TS}$	1-15 yrs
Duration of brothel based clients	$1/\varphi_{BB}$	5-10yrs
Duration of non-brothel based clients	$1/\varphi_{NB}$	5-10yrs
Duration of Maless 2+	$1/\varphi_{TS}$	5-20yrs
Percentage of sex acts of females 2+ with client partners of brothel-based and non-brothel based FSWs	ξ	0-100%
(Percentage of sex acts of females 2+ with non-client male partners)	$1-\xi$	0-100%

4-5%	5-6%	6-7%	7-8%	8-9%	9-10%	10-11%	11-12%	12-13%	13-15%
P_{FNB}	P_{FNB}	P_{FNB}	P_{FTS}	P_{FNB}	P_{FTS}	P_{FNB}	C_{CTS}^{TS}	P_{FTS}	P_{FTS}
P_{FTS}	P_{FBB}	P_{FTS}	P_{FNB}	P_{FTS}	P_{FNB}	P_{FTS}	P_{FTS}	P_{FNB}	β_{mf}
P_{FBB}	P_{FTS}	C_{CTS}^{TS}	β_{mf}	P_{FBB}	β_{mf}	$1/\alpha_{NB}$	C_{FBB}^{C}	C_{CTS}^{TS}	C_{CTS}^{TS}
β_{mf}	ξ	P_{FBB}	P_{FBB}	C_{CTS}^{TS}	C_{CTS}^{TS}	β_{mf}	β_{mf}	β_{mf}	P_{FNB}
ξ	C_{CTS}^{TS}	β_{mf}	C_{CTS}^{TS}	β_{mf}		P_{FBB}	f_{FBB}	f_{FTS}	ξ
	β_{mf}	f_{FBB}	$1/\alpha_{BB}$				P_{FNB}	$1/\alpha_{NB}$	f_{FTS}
	f_{FNB}	ξ	f_{FTS}					P_{FBB}	
	$1/\alpha_{BB}$	C_{FBB}^{C}							

Table 2(a): Rank order of partial coefficients from analysis for each prevalence range for females in the general population. Parameters that are consistently shown to be significant (p<0.05) are in highlighted to emphasise any patterns in the data.

6-7%	7-8%	8-9%	9-10%	10-11%	11-12%	12-13%	13-14%	14-15%	15-17%
	P_{FNB}	P_{FBB}	P_{FBB}	P_{FNB}	P_{FNB}	P_{FTS}	C_{CTS}^{TS}	β_{fm}	P_{FTS}
	P_{FBB}	P_{FTS}	P_{FNB}	C_{CTS}^{TS}	P_{FTS}	C_{CTS}^{TS}	P_{FTS}	P_{FNB}	C_{CTS}^{TS}
	C_{CTS}^{TS}	C_{CTS}^{TS}	P_{FTS}	P_{FBB}	C_{FNB}^{C}	P_{FBB}	β_{fm}	C_{CTS}^{TS}	f_{FTS}
	P_{FTS}	P_{FNB}	C_{CTS}^{TS}	P_{FTS}	C_{CTS}^{TS}	P_{FNB}	$1/\varphi_{NB}$	P_{FTS}	P_{FNB}
	$1/\alpha_{BB}$	f_{FBB}	C_{FBB}^{C}	C_{FNB}^{C}	P_{FBB}	C_{FNB}^{C}	ξ		β_{mf}
		C_{FBB}^{C}	$1/\varphi_{BB}$		β_{fm}	β_{mf}	f_{FTS}		β_{fm}
		$1/\varphi_{BB}$	β_{mf}		β_{mf}		$1/\alpha_{TS}$		P_{FBB}
		β_{mf}					C_{FNB}^{C}		ξ
									$1/\varphi_{NB}$
									$1/\alpha_{TS}$

Table 2(b): Rank order of partial coefficients from analysis for each prevalence range for males in the general population. Parameters that are consistently shown to be significant (p<0.05) are in highlighted to emphasise any patterns in the data.

7. Conclusion

The overall aim of this thesis was to use mathematical modelling and ecological analysis to gain an improved understanding of the determinants of variability of HIV prevalence in West Africa and to then use this information to discuss the potential implications for epidemiological theory, future epidemic appraisals and decision making. The hypothesis that commercial sex work is the main driver of HIV prevalence in West Africa, as previously suggested by past modelling studies was addressed.

Objective one aimed to assess whether the incorporation of additional heterogeneity into the UNAIDS Modes of Transmission model affects predicted patterns of HIV incidence. I used data from NARHS 2007+ survey to generate a new group of adolescent females who engage in transactional sex and include the estimates from the survey into a revised MoT model.

Another important revision to the model was the subdivision of the 'low-risk' group into those who have no-risk or very low risk and discordant partnerships. The revised projections have very different conclusions, showing a very high incidence of infections in the discordant partnerships with no new infections in the other groups. The findings point to the dangers of 'averaging out' the very large 'low-risk' population as this leads to a distortion in the projected incidence of infections. The results from Research Paper 1 show that the MoT model should incorporate additional behavioural heterogeneity, which should be tailored to the setting and the availability of reliable data. The limitations of the findings for the use of the model in Cross River, Nigeria relate to the lack of available data on men who have sex with men, a highly stigmatised group in this setting, and also people who inject drugs. In addition, to this data on the size of female sex worker populations was not available. As such, there is a need to caution on over interpretation of specific projections of the model.

Objective two set out to explore whether variations in the size and HIV prevalence of different population subgroups is correlated with variations in female and male general population HIV prevalence across West Africa. The results from the regression analyses show that only HIV prevalence in groups of adolescent females (15-24) 2+ and HIV prevalence amongst FSWs are correlated with HIV prevalence in older males and females (25-49) in the general population. Whilst no data was included on the size of the FSW group, the size of the male client group was associated with HIV prevalence amongst adolescent females with 2+ partner and FSWs, but to a lesser extent with other subgroups in the population. This finding suggests that there may be a possible pathway of transmission between FSW, clients and adolescent females 2+. HIV prevalence in all population subgroups included in the analysis, with the exception of male clients and younger (15-24) males was associated with the percentage size of higher-risk subgroups – providing evidence for an association between the percentage of individuals engaging in higher-risk behaviour (multiple partnerships) and HIV prevalence in the general population.

As discussed in more detail in Research Paper 2, the limitations of this analysis was firstly the availability of the data, which in some instances only included 10 countries data in some of the regression analyses. This meant that I was limited to looking at linear associations, without the ability to control for other factors using multiple regression analysis. The strength and reliability of some data in some instances, such as HIV prevalence in FSW, was difficult to assess. In this case, estimates were extracted mostly from the literature or institutional surveys, with a potential lack of comparability or consistency between collection sites, sampling frames or number of participants included. To reduce this bias, I only included data on brothel-based FSWs, so that the data has more chance of reflecting similar populations across countries. However, this could not be guaranteed.

Although ecological analyses are always exploratory in nature, with the aim of generating hypotheses. The findings provide empirical evidence of the potential importance of variations in the percentage of adolescent females with multiple partners as an important determinant of population HIV prevalence.

The third objective of the thesis was to use dynamic modelling to explore what the main determinants of variation in general population males and female endemic HIV prevalence across West Africa.

This objective was achieved through the structural design and development of a dynamic deterministic compartmental model, influenced by the findings and insights from the earlier Research Papers. The model was used initially to assess the most plausible mixing scenario between groups, proportionate mixing or a 'fixed' proportionate mixing method, in West Africa. Model fits were collated and used in a multiple regression analysis to explore the most important determinants of variations in HIV prevalence in general population males and females across different prevalence ranges. For the female general population the main determinants varied depending on the levels of HIV prevalence in the female population; between 0-3% prevalence the size of the FSW groups was the most important determinant and for HIV prevalence levels between 3-6%, the size of the adolescent female 2+ group were the most important determinant of HIV prevalence. Other factors, relating to R_0, including consistency of condom use and partnership numbers in the three female groups were also important determinants of HIV prevalence. In males, the percentage size of the FSW groups was the main determinant of HIV prevalence, when prevalence is between 0-4%. The levels of HIV prevalence are likely to be limited in males as a result of the effects of male circumcision (Weiss HA et al., 2000). Of course, the percentage size of subgroups does not have a direct effect on determining HIV prevalence, but rather is mediated by other variables such as consistency of condom use, duration and partnership numbers. This is evidenced by the fact that once HIV prevalence levels in the female general population become greater than 3%, the median percentage size of their population does not vary very much but instead their behavioural factors such as partnership numbers become more significant as determinants of HIV prevalence. This is an important message for policy makers since it suggests interventions to reduce vulnerability amongst FSW are still important in limiting the size of epidemics.

The final objective was to use a dynamic model to understand the limiting effects of male circumcision in West Africa and the importance of the percentage size of the female 2+ group on epidemic projections and epidemic classification.

The model results show the importance of male circumcision in limiting the HIV epidemic in West Africa. In the absence of male circumcision, the model projected HIV prevalence to be in the 4-15% range for general population males and females, compared to 0-6% for female and 0-4% for males when circumcision is included in the model. The results suggest that male circumcision may reduce levels of prevalence by 3-4 times, under the assumptions made in the model for HIV epidemic spread in West Africa.

I also assessed whether there was a threshold level for the size for the female 2+ subgroup, where we see a change in the main determinants of HIV prevalence, from being more dependent on the size and behavioural characteristics of FSWs, to behavioural characteristics of the female 2+, such as their number of sexual partners and the degree to which they form partnerships with clients of FSWs becoming more important. The model projects that this transition occurs when the size of the female 2+ subgroup is approximately 7% of the total female population, when the universal effects of male circumcision are included and omitted from the model. This epidemiological approach, which uses threshold values to categorise HIV epidemics, could be applied as an alternative approach to the current UNAIDS numerical proxy measures for helping policy makers to improve their understanding of epidemic classification.

Whilst this analysis recognises the potential importance of male circumcision in epidemic categorisation, other interventions may also be important. New technologies in HIV are constantly evolving and showing levels of success. For example, the impact of limiting new infections from ART, is potentially now another factor that also need to be considered the context of epidemic classification. The ambitious 90-90-90 treatment target set out by UNAIDS (UNAIDS, 2014) is aimed at significantly changing the profile of the HIV epidemic globally. This means policy terms, such as epidemic categorisation, need to be in line with these developments.

8. Discussion

Metrics such as the number of sexual partners, consistency of condom use and duration of time spent in high-risk groups are well recognised as important determinants of HIV risk. The findings from this thesis also show that the percentage size (relative to the size of the general population) of higher risk groups, such as female sex workers for lower level epidemics and adolescent females with multiple partners for higher levels epidemics, are important determinants of endemic HIV prevalence in the general population and merit more informed attention. Of course, the effect of subgroup size is indirect and is mediated by other factors related to R_0 – that is to say, the size of the subgroup alone is not capable of leading to higher prevalence levels without other factors playing a role.

The proximity of individuals within sexual transmission networks also are important, especially for larger groups of adolescent females with multiple partners who form partnerships with higher-risk males. The findings provide new insights into more historical studies, such as the four cities study (Ferry et al., 2001), which found no association between multiple partnerships or differences in age between partners (older males partnering with younger females) and HIV prevalence. Jewkes *et al.* (Jewkes R et al., 2012) study also showed that multiple partnerships were not associated with higher incidence of HIV but that transactional sexual relationships amongst adolescent females were. In combination, with the findings from the modelling work in this thesis, this suggests that, it is not multiple partnerships or age differences between partnerships that are direct risk factors for HIV, but that these factors are mediated by the dynamic sexual network in which such relationships take place. For example, multiple partnerships or age differences between partners that occur within networks associated with higher-risk groups and their immediate partners.

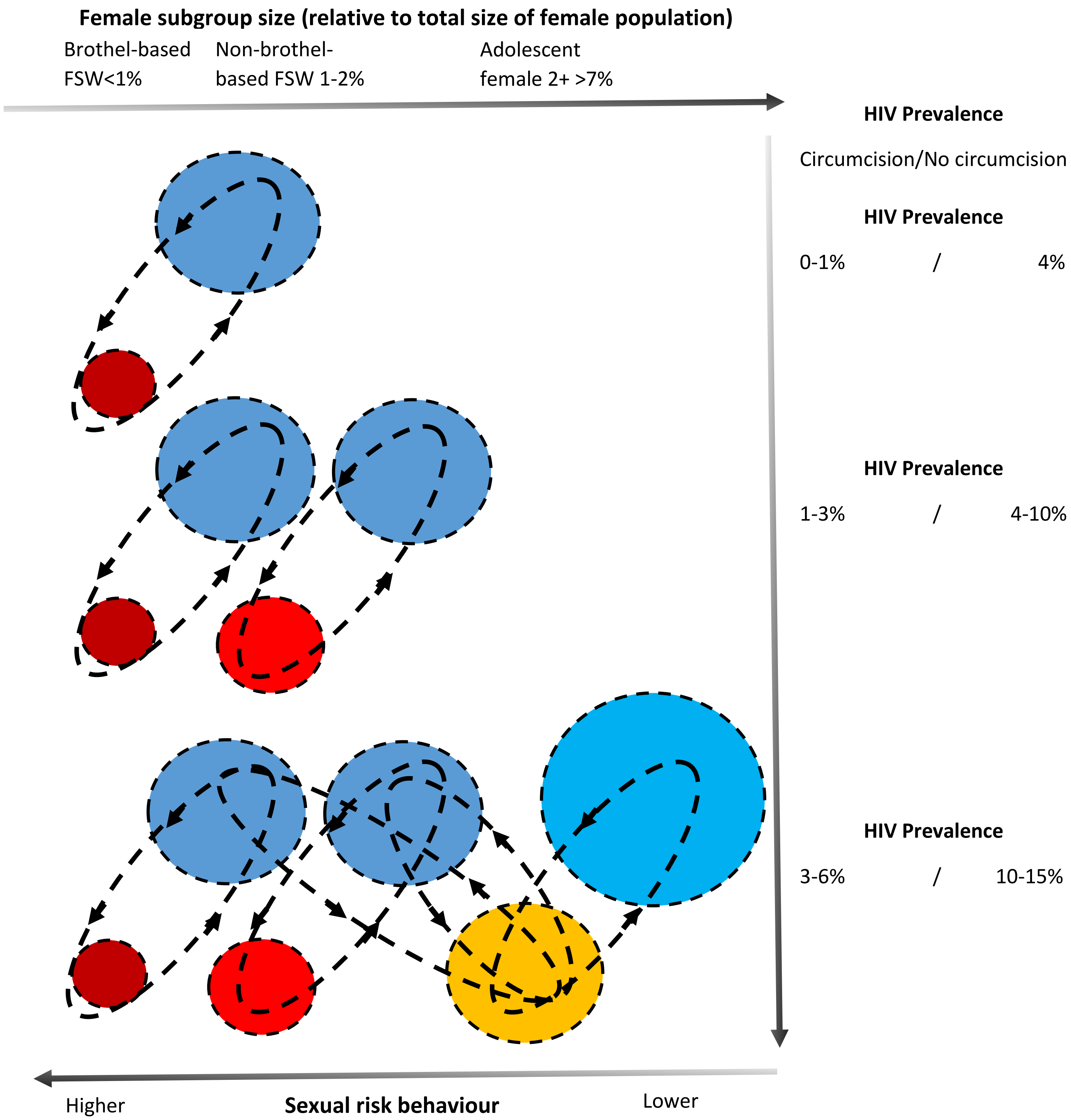
These finding show how the pathways through which infection may occur are complex. Empirical evidence has previously sought to establish associations between key parameters and higher HIV prevalence levels, in an attempt to show which factors are most important for mediating higher levels of infection within groups of adolescent girls as well at the general population.

However, a critical aspect of HIV transmission that is perhaps less well understood, is how conditions that shape network structure are correlated with other behaviors that modify the risks of acquiring infection. Behaviors that shape sexual network structure would include factors such as the size of high-risk subgroups, the presence and nature of sex work, levels of marriage, transactional sex, migration, the characteristics of sexual relationships as well as the strength of connections between networks – i.e. here represented by the degree to which females 2+ form partnerships with clients of female sex workers. Whilst, behaviors that modify risk of infection are more typically factors that are measured within behavioural and biological surveys and include condom use, ART use, violence, STI infections, duration of sexual activity and number of sex acts with partners, as examples.

Mathematical models of disease transmission rely strongly on behaviours that modify the risk of infection – particularly since they are most strongly associated with the basic reproduction number, R_0, which is used to estimate the key drivers of HIV transmission. However, behaviors that shape network structure may be equally as important, but are often less well understood – in part because the nature of these factors as well as their quantification is important. To date the approach to mathematical modelling is to assume a network structure and assess how behavioral risk data effects transmission. However, since network structure is influenced by the behavior of the population and the behavior of the population is determined to some extend by the network structure, an alternative approach to modelling would be to use the behavioural data to inform the structure of the model. Of course, such an approach requires highly informed data collection, that goes beyond information on risk factors alone and also explore the structure of the population network, which is why this approach is rarely adopted.

The importance of structural network conditions is illustrated through the important influence of the size of different risk populations and the potential idea of an “epidemic gearing” effect. This is depicted below in Figure 1, which represents the epidemic in West Africa. Small subgroups high-sexual activity groups of brothel-based FSWs (comprising less than 1% of the female general population in West Africa) are able to drive HIV epidemics when HIV prevalence is low (<1% in the general population). However, the larger groups of non-brothel based FSWs (<2% of the general female population) are required to “gear” the epidemic up to higher prevalence levels (1-3% in West Africa) – the gearing up occurs because this subgroup are larger and able to generate more infections than brothel-based FSWs alone. A third gearing effect occurs when adolescent females 2+ (>7% of the general population) also form part of the sexual network of FSWs, by partnering with some of their clients. Additional analysis in Appendix 11, figure 11.1 suggests around half female 2+ partners to be clients. These could be past or present clients, since the system is dynamic, but essentially they represent a subgroup of males who have higher levels of HIV infection and HIV prevalence. This additional cog in the chain is what shifts epidemics from being more concentrated in nature among different subgroups of FSWs and their clients, to being more generalised, by introducing HIV infection into a larger group of adolescent females through whom the infection can spread to the general population. In addition, because the system is dynamic, as infected adolescent girls age, they sustain higher levels of endemic HIV within the population.

We see that this effect is potentially even more important when male circumcision is not universal, with the FSW groups alone able to sustain epidemics up to approximately 10% prevalence. From this point, the size of the adolescent 2+ group becomes directly associated with the level of HIV in the population, showing the importance for policy makers of effectively targeting this subgroup.



Description of population groups

- Brothel-based FSW
- Non-brothel based FSW
- Female 2+ adolescent group
- Clients of brothel-based and Non-brothel based FSWs
- Male (2+) low-risk partners of female 2+

Figure 8.1: Conceptual idea of the "epidemic gearing" effect of HIV epidemics in West Africa (the black dashed lines represent the "gearing effect" of the epidemic, by representing the sexual network connections between risk groups in the population)

Although my modelling focused on a limited number of vulnerable groups, the concept may also apply similarly to other networks of partnerships. For example, where there are large subgroups of people who inject drugs in populations (Mills et al., 2013) or hidden populations of MSM who have female partners (Phillips et al., 2010).

Mathematical modelling of HIV has evolved over the decades, as our knowledge of the virus and its transmission dynamics have advanced. Model development has tended to move from attempting to understand population dynamics, towards estimating the impact of different forms of interventions, assuming our earlier knowledge on population dynamics is well established.

However, the early models that sought to understand the drivers of HIV transmission dynamics are still of great value and useful to inform modelling and policy. Particularly understanding the importance of heterogeneity within the population and how differences in individual's behaviour impacts on the epidemic.

As mathematical models play an important role in HIV policy planning and implementation. However, their reliability is strongly associated with their structural design and the data used to parameterise them, in accordance with a satisfactory understanding of the nature of the HIV epidemic that is being modelled. Especially given the number of patterns of risk and evidence of high HIV incidence among young females in some countries of Sub-Saharan Africa. Future model development should consider not only the standard focus of model inputs such as information on sex partners, condom use, duration etc., typically collected in surveys; but also ensure additional information on sexual network patterns, subgroup sizes, factors which influence and determine the presence of non-commercial transactional sex, and other potentially important feedback loops are included. Whilst the 'one model, fits all' solution, such as the MoT model was convenient for policy, the reality is that such an approach is imperfect. Whilst the resources are limited and models cannot be developed for every individual epidemic, better approaches should be sought in future, that are more transferable. Potential "gearing" effects need to be more explicitly mentioned and included.

Of importance for policy is the evidence produced by this research that suggests the percentage size of groups, of different levels of risk, such as female sex workers may be an important determinant of HIV prevalence. Past policies relating to sex work range from range from enforcing 100% condom use to supply and demand side restrictions. These include changes in the laws or culture in society, in an attempt to reduce the number of women entering the sex industry, that often instead lead to structural changes in the organisation of sex work and greater restrictions within the industry (Beattie et al., 2013) (Shahmanesh et al., 2009). The consequence of this is that sex work may change its form, from being more visible i.e. the presence of brothels to becoming more hidden, i.e. street based.

Likewise, the findings illustrate the importance of adolescent girls who have sex with high-risk men. The reason for young females engaging in multiple partnerships with high-risk individuals, may be complex with some research suggesting the motivation behind multiple partnerships may be more orientated towards subsistence than consumption, with the practice often perceived as a 'normal' component of modern life, allowing women the power and agency to assert themselves in order to pursue 'needs (Leclerc-Madlala, 2003).' With aspirational images of wealth and success generated by the media and globalisation, the approach to reducing the desire for multiple partners is challenging. Such relationships may also be the consequence of a lack of economic empowerment and gender inequality leading to inequitable power divides between men and women. Such issues are indirect structural factors, resulting in behavioural and biological outcomes that make individuals more susceptible to HIV infection. They are not the direct cause of HIV but may be seen as strong social mediating factors. Past research has shown positive effects using conditional and unconditional cash transfer programmes in reducing risk of HIV infection in young females (Remme et al., 2014) and such initiatives may be important as future intervention measures.

In summary the lessons learnt through a combination of different approaches in this thesis have wider implications for how we approach policy issues in the future.

In conclusion, the thesis set out to test the hypothesis that sex work is the major driver of HIV prevalence in West Africa, in a setting where the epidemics, despite being classified as generalised or more mixed in nature are actually thought to remain concentrated with the majority of infections arising from commercial sex. Through my findings I illustrated the importance of high-risk subgroup size as a key parameter and indicator of “risk.” The first results chapters showed the importance of recognising behavioural heterogeneity within populations and in particular a group of adolescent females in the population who have multiple partners and who’s sexual networks may include high-risk male partners of female sex workers. The results from the final two chapters were seen to falsify the claim that commercial sex is the main driver of HIV prevalence in this region, in women, when HIV prevalence levels are in the higher range (3-6%). However, there is strong evidence from the modelling results to suggest that commercial sex is still highly important when prevalence levels in females are less than 3% and across the range of prevalence levels in males (0-4%).

For setting where universal circumcision in males is not present, there prevalence value ranges are likely to differ. These findings provide important insights to both future modelling studies as well as policy. The need for a more robust approach to model development that also includes information on network conditions as well behavioural risk factors should be considered, as too should the role of circumcision in classifying epidemics to ensure policy messages are appropriate and consistent.

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Appendix 1

Technical Appendix 1.0, contains additional technical data accompanying Research Paper 1.

Appendix 1.1

Equations for estimating HIV transmission in individual risk-groups:

1) **Probability of HIV transmission via sexual contact:**

$$\boldsymbol{I = S\{[1 - pB[1 - \beta']^{\alpha(1-v)} + p(1 - B)[1 - \beta]^{\alpha(1-v)} + (1 - p)]c^{n}\}}$$

$\boldsymbol{I}$= incidence
$\boldsymbol{S}$= number susceptible
$\boldsymbol{p}$= HIV prevalence in partners
$\boldsymbol{B}$= prevalence of STIs in partners
$\boldsymbol{\beta}$= probability of transmission (with STI ($\boldsymbol{\beta'}$)), without STI ($\boldsymbol{\beta}$))
$\boldsymbol{\alpha}$= contacts per partner
$\boldsymbol{v}$= proportion of acts protected by condom use
$\boldsymbol{n}$= number of partners

*$1 - \beta'$ = Probability of no transmission when partner has STI
$1 - \beta$ = Probability of no transmission when partner does not have an STI
$1 - v$ = Proportion of acts not protected by condom use.

2) **Probability of HIV transmission in Injecting Drug Users:**

$$\boldsymbol{I = S\left\{1 - \left[p[1 - \beta']^{\alpha(1-v)} + [1 - p]\right]^{n}\right\}}$$

$\boldsymbol{p}$= HIV prevalence in needle sharing partners
$\boldsymbol{\beta}$= probability of transmission
$\boldsymbol{\alpha}$= needle contacts per partner
$\boldsymbol{v}$= use of sterile needles
$\boldsymbol{n}$= number of partners

3) **New infections from unsafe medical injections:**

$$\boldsymbol{\pi = p\{1 - (1 - P_s\beta P_c)^{n}\}}$$

$\boldsymbol{\Pi}$ = Number of new infections
$\boldsymbol{P}$ = Population
$\boldsymbol{Ps}$ = Prevalence (total population)

β = Transmission probability
Pc = Prevalence*% unsafe needles (estimates the number of needles contaminated)
n = Number of injections per year per individual.

4) New infections from blood transfusion:

$$\pi = B_t P_s v$$

Π = Number of new infections
B_t =Totoal number receiving blood transfusions
Ps = Prevalence (total population)
v = proportion of acts protected[#]

[#] proportion of acts protected = number of units screened*sensitivity of test for HIV.

Appendix 1.2

Table 1: Data sources and explanation for parameter selection in the original modes of transmission analysis in Cross River state.

Model subgroup	
IDUs	Percentage of individuals identifying as IDUs came from NARHS 2003, a national survey, no stage level data was available so this estimate was used. The value was deducted from those having low-risk sex.
Sexual partners of IDUs	Population size for this group was based on the percentage of IDUs who reported being sexually active in the past 12 months in the IBBSS 2007. HIV prevalence data were not available, so ANC prevalence was used as a default estimate, despite this being higher than the prevalence in IDUs.
Female sex worker population	Population size estimates were inferred from estimates of the number of FSWs in West Africa[26]. This value was subtracted from females who report non-marital sex. To estimate the number of partners per year, weighted data for brothel-basedFSWs and non-brothel based FSWs from the IBBSS 2007 was combined and, because the sample sizes of these two groups was almost equal, it was assumed the FSW population was composed of equal numbers of brothel-basedFSWs and non-brothel based FSWs. The estimate also allows for the fact that FSWs, on average, take 10 weeks off per year due to menstrual periods and 5 weeks off per year for personal reasons. The model estimates that FSW have 175 clients per year and 4 acts per client per year, whilst clients have 5 FSW partners per year and 20 acts per partner per year. However, FSW and their clients should have an equal number of sex acts per partner, i.e. either 4 or 20 each, respectively. This is not dealt with in the original model. Prevalence estimates for HIV and STIs came from two sources [11, 18]
Clients	Calculated by subtracting those reporting exchanging gifts, favours and money for sex from males who reported non-marital sex from NARHS+ 2007.
Female partners of clients	Estimated from DHS 2008, 34% of males who reported consorting with FSWs were married or co-habiting. HIV prevalence data were not

	available, so ANC prevalence was used as a default parameter estimate.
MSM	The percentage of the population who behave as MSM was determined using two high-risk group surveys, the BSS 2005 and the IBBSS 2007. The value was deducted from those ***men reporting*** casual heterosexual sex.
Female partners of MSM	MSM who had sex with a female in the past 12 months. HIV prevalence data were not available, so ANC prevalence was used as a default estimate, despite this being higher than the prevalence in MSM.
Casual heterosexual sex (CHS)	Those reporting only marital sex were assumed to have one partner and those reporting non-marital sex, more than one partner. Because more males than females reported more than two partners, the authors assumed the average person engaging in non-marital sex had two or less partners per year. No balancing of sex acts between males and females in this group is considered.
Partners of CHS	Assigned as a 'default' value, although it is unclear how this was calculated. HIV prevalence data were not available, so ANC prevalence was used as a default parameter estimate
Low risk	This group was defined as those individuals remaining once all other groups had been subtracted from the whole population.

Table 2: Data sources and explanation for parameter selection for the revised modes of transmission analysis in Cross River state.

Original MoT subgroups	Subgroups in revised MoT	Explanation and description of revisions
- Female sex workers	**- Brothel based female sex workers (BBFSWs)** **- Non-brothel based female sex workers (NBBFSWs)** **- Young females engaged in transactional sex (YFs)**	- HIV prevalence estimates for **brothel-based FSWs and non-brothel based FSWs** were taken from IBBSS 2007 as well as average number of client partners per week for both subgroups. Number of sex acts between **brothel-based FSWs and non-brothel based FSWs** and their respective client partners was fixed at 4 per year as in the original analysis. We estimated 1% of the population were brothel-based FSWs and 1% non-brothel based FSWs based on the assumptions from the original modelling study which used data on the sample from the survey. Condom use for both groups was assumed to be

		the same as in the original model, based on reported condom use by 15-49 year old males reporting payment for sex in past 12 months from DHS 2008. - Population size for YFs was calculated by deducting **brothel-based FSWs and non-brothel based FSWs** populations away from those reporting 'sex in exchange for gifts or favours' from the NARHS+ 2007, and this was verified using a population size estimate for the total number of students aged 15-19 engaged in transactional sex through a study by Moore et al 2007[27] and further verified from a study by Jewkes[28], as this was thought to be a high risk group. HIV prevalence estimates and condom use for the female transactional sex group were based on the 15-19 year old group from the south-south geopolitical region who reported having sex for gifts/money and those in non-marital relationships who report using a condom with their last partner. Estimates for number of partners and number of sex acts per partner was based on anecdotal evidence from the literature, showing females engaged in transactional sex have multiple partners at any one time[29-31].
- **Clients**	**- Clients of BBFSWs** **- Clients of NBBFSWs** **- Men who engage in transactional sex with young females (MYF)**	14.4% of males from the NARHS 2007+ in the south-south region reporting 'exchanging money, gifts or favours for sex'. Using the DHS 1999, 10% of males report 'payment for sex,' we assumed 5% of these were clients of brothel-based FSWs and 5% were clients of non-brothel based FSWs. The remaining 4.4% (from NARHS 2007+) of males we attributed as being males engaging in transactional sex, since there is strong evidence for the existence of different male groups engaged in transactional sex dependent on age, social status and mobility[32]. Number of sex acts per partners was the same as their female partner group. Number of partners was calculated based on the size of their population and their female partners population, so that total numbers of partners for females and males was different (because of different population sizes) but total number of sex acts was equal. Estimates for total number of client partners was verified using additional studies[32, 33]. HIV prevalence for clients of **brothel-basedFSWs and non-brothel based FSWs** was estimated from the IBBSS 2010 for those who report genital warts/ulcers from the three high-risk male populations. For males engaging in transactional sex prevalence estimates came from NARHS 2007+ for men aged 20-25 who engaged in sex for gifts or favours, with the assumption based on females aged 15-19 reporting an average of six years between them and their partners.

		Condom use for Clients of **brothel-basedFSWs and non-brothel based FSWs** was the same as in the original model and for males engaged in transactional sex, with was assumed to be the same as their female partners
- Female partners of clients	**- Female partners of clients of brothel based FSWs** **- Female partners of clients of non-brothel-basedFSWs** **- Female partners of males involved in transactional sex**	Each of these three groups collectively represent the "partners of clients" group from the original model. Population size estimates were maintained as 34% of the size of their partner groups, based on DHS 2008, for male (who exchange sex for gifts/favours/money) who report having a co-habiting partner. All other biological and behavioural estimates from the original model were kept the same.
- Casual heterosexual sex (CHS)	**- Casual heterosexual sex** **- Boyfriend/girlfriend relationships**	In the revised model this group was divided by gender, since different percentages of males and females report casual heterosexual sex in the NARHS 2007+. To ensure the number of sex acts both males and females have balanced, females, whose population size was smaller were assigned a greater number of partners. In this way the number of sex acts was balanced by assuming males have 2 casual partners per year and therefore females, whose population size for this group is smaller, require a greater number of partners. This was based on the estimates from the original model in which males had an average of 2 partners and 50 sex acts with each. Population size estimates were revised since only 13.2% of males in the south-south report having more than one non-marital sexual partner, we discounted those males who have more than one marital partner because of polygamous marriages. Size estimates for females were calculated in the same way from the NARHS 2007+. Boyfriend/girlfriend relationships are defined within the NARHS 2007+ as a 'non-spousal partner that is more stable than a casual sex partner,' but were not included in the original MoT model. This group was created on the basis that certain individuals have sex with only one non-marital partner in a 12 month period and are therefore at lower risk than the CHS group. The population size for this group is estimated from the NARHS 2007+, for the south-south region. 39.2% of males report at least one non-marital partner. Deduct from this, 14% who report exchanging sex for gifts or favours, 13.2% who report more than one non-marital partner in the past 12 months and the estimated percentage of males who are the partners of those having casual heterosexual sex. The value remaining after assigning estimates for these other groups was used as the estimate for the boyfriend subgroup. The percentage of females was assumed to be equivalent, on the basis that females who report at least

		one non-marital partner was an under-estimate. This group were presumed to have the same behaviour as the low-risk group from the original model. Since these partnerships are likely to involve younger individuals we estimated HIV prevalence from the NARHS 2007+ for males, 2.1% and females, 1.3% in the 15-19 age category. Condom use was assumed to be the same as for the partners of the CHS group in the original MoT model.
- Partners of CHS	**- Partners of CHS**	The population size for males and females was estimated as 34% of the total size of those having CHS, based on males reporting exchange of sex for gifts/favours/money from DHS 2008 who report having a co-habiting partner. Because male clients are also individuals who have more than one non-marital partner, we assumed those having CHS to have similar characteristics. All other parameter estimates from the original model were kept the same.
- Low risk group	**- Discordant couples** **- Low risk**	In the original model this group is those in a 'marital or co-habiting relationship', with the entire group to having an HIV prevalence of 8%. Because it is unlikely all individuals in this group are at risk, but that some will be at very high risk (if their partner is HIV positive) and some at very low risk or no risk at all if the relationship is monogamous and both individuals are negative or both positive, we subdivided this group into 'discordant couples' and 'low risk' individuals. A study was used to estimate the percentage of the population in a discordant relationship. When HIV prevalence is less than 10%, 0-4 individuals out of every 100 sexually active individuals are likely to be in a discordant relationship[34]. For Cross River, with an ANC HIV prevalence of 8%, we assumed an average of 3.5 individuals out of every 100 to be the positive partner in a discordant relationship, with an additional 3.5% of the sexually active population acting as negative partners (1.75% females and males combined) . We also presumed half those positive were males and the remaining 50% females[34]. All parameter estimates remained the same as in the original model for the low risk group. The low risk group were all individuals in the model who were not accounted for in any other subgroup. Parameter estimates for this group were the same as in the original model, with an estimate for the HIV prevalence being calibrated to give an overall 8% prevalence in the total population. .
- No risk	**- No risk**	Defined as individuals who had not had sex or injected drugs in the past 12 months. NARHS 2007+ data on percentage of males and females in the south-south

		zone who had not had sex in the past 12 months were used as estimates. HIV prevalence also came from NARHS 2007+, for females this was 7.9% and males 3.8%. The estimates are quite high compared to other groups. This may be because divorced/widowed or separated individuals or those who no longer practice sex work, whose HIV prevalence is higher than the general population form a subset of this group. Since the group are not part of any transmission pathway, the estimates only affect the prevalence estimates and not the incidence.
- MSM **- Female partners of MSM** **- IDUs** **- Sexual partners of IDUs**	**- MSM** **- Female partners of MSM** **- IDUs** **- Sexual partners of IDUs**	Population sizes, behavioural and biological parameter estimates for these groups were unchanged, apart from females of MSM and sexual partners of IDUs, whose HIV prevalence was revised to be the same as partners of CHS, since they have similar behavioural characteristics. A lack of data on MSM who are predominantly receptive versus those who are predominantly insertive meant this group was difficult to subdivide, however, it was noted as a limitation in the model estimates because the transmission probability for HIV in this group is for the receptive partner only.

Appendix 1.3

Behavioural parameter estimates from original MoT analysis

Population group	Percentage of total population		Number of partners per year	Number of acts of exposure per partner per year	Percentage of acts protected (sterile injecting equipment or condoms used)
	Males	**Females**			
Injecting drug users (IDUs)	**0.32%**	**0.27%**	**2**	**224**	**79.0%[11](always used sterile injecting equipment last month)**
Partners of IDUs	**0.26%**	**0.31%**	**1**	**80**	**26.1% (same behaviour as low-risk group)**
Female sex workers (FSWs)		**2.00%**	**175**	**4**	**61.1%[17] (based on reported client use)**
Clients of FSWs	**14.00%**		**5**	**20**	**61.1%[17] (as above)**
Partners of clients		**4.76%**	**1**	**80**	**26.1% (same behaviour as low-risk group)**
Men who have sex with men (MSM)	**0.90%**		**3**	**38**	**56.3%[11](page 97 last act use with males)**
Female partners of MSM		**0.22%**	**1**	**80**	**26.1% (same behaviour as low-risk group)**
Casual heterosexual sex (CHS)	**22.40%**	**20.70%**	**2**	**50**	**46.8%[17](with non-marital partners. Female/male average)**
Partners of CHS	**16.56%**	**17.92%**	**1**	**80**	**26.1%[11]**
Low-risk heterosexuals	**18.76%**	**26.53%**	**1**	**80**	**26.0% (figure for South-South)**
No risk	**26.80%**	**27.30%**	**0**	**0**	**0.0%**
Medical injections	**35.80%**	**34.90%**	**2**	**1**	**99.0%**
Blood transfusions	**1.00%**	**1.00%**	**1**	**1**	**99.0%**

Epidemiological parameter estimates from original MoT analysis

Population group	HIV prevalence	Comments	STI prevalence	Comments
Injecting drug users (IDUs)	**3.1%[11]**		**7.5%[11]**	
Partners IDUs	**8.0%**		**-**	**NA**
Female sex workers (FSWs)	**23.4%[11]**	**Average of BBSWs and NBBSWs**	**12.6%[11]**	
Clients of FSWs	**10.4%**	**Average of low-risk and sex worker prevalence**	**7.6%**	**Same as CHS**
Female partners of clients	**8.0%**	**Assumed similar to those engaged in low-risk sex**	**-**	**NA**
Men who have sex with men (MSM)	**2.8%**		**2.8%[11]**	
Female partners of MSM	**8.0%**	**Assumed similar to those engaged in low-risk sex**	**-**	**NA**
Low-risk	**8.0%**	**2008 ANC survey**	**3.6%[17]**	**Self reporting, not disaggregated by sex (table 13.13)**
Casual heterosexual sex (CHS)	**10.0%**	**Secondary analysis from NARHS 2007 and adjusted**	**7.6%**	**Self reporting STIs (table 13.13)**
Partners of CHS	**8.0%**	**Assumed similar to those engaged in low-risk sex**	**-**	**NA**
Medical injections	**8.0%**	**ANC prevalence**		
Blood transfusions	**8.0%**	**ANC prevalence**		

Behavioural parameter estimates for revised MoT analysis

Population group	Percentage of total population		Number of partners per year	Number of acts of exposure per partner per year	Percentage of acts protected
	Males	**Females**			
Injecting drug users (IDUs)	**0.32%***	**0.27%***	**2***	**224***	**79.0%***
Partners of IDUs	**0.26%***	**0.31%***	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
BBSWs		**1.00%[16]**	**250[11]**	**4***	**61.1%[17]* (based on reported client use)**
Clients of BBSWs	**5.00%[17, 18]**		**50#**	**4#**	**61.1%[17]* (as above)**
Female long-term partners of BBSW clients$		**1.70%***	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
NBBSWs		**1.00%[16]**	**120[11]**	**4***	**61.1%[17]* (based on reported client use same as BBSWs)**
Clients of NBBSWs	**5.00%[17, 18]**		**24#**	**4#**	**61.1%[17]* (assume same as BBSW clients)**
Female long-term partners of NBBSW clients#		**1.70%***	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
Young females engaged in transactional sex (YFs)		**8.20%[17, 18, 27]**	**6(1 partner every 2 mths)**	**20 (2 acts per week)**	**28.0%[11]**
Males engaged in transactional sex with young females (MYF)	**4.40%[18]**		**11#**	**20#**	**28.0%[18]**

Female long-term partners of MYF		**1.50%***	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
Men who have sex with men (MSM)	**0.90%***		**3***	**38***	**56.0%[11]*(page 97 last act use with males)**
Female partners of MSM		**0.22%**	**1**	**80**	**22.9%[18] (section 6)**
Casual heterosexual sex (CHS) males	**13.20%[18]**		**2***	**50***	**46.8%[17]*(with non-marital partners. Female/male average)**
Casual heterosexual sex (CHS) females		**5.50%**	**4.8#**	**50***	**46.8%[17]*(with non-marital partners. Female/male average)**
Partners CHS (males)	**1.87%**		**1***	**80***	**26.0% (figure for South-South)**
Partners CHS (males)		**4.49%**	**1***	**80***	**26.0% (figure for South-South)**
Boyfriend/girlfriend relationships (males)	**9.83%**		**1***	**80***	**26.1%* (assume same behaviour as low-risk group)**
Boyfriend/girlfriend relationships (males)		**9.81%**	**1#**	**80***	**26.1%* (assume same behaviour as low-risk group)**
Discordant couples	**3.50%[34]**	**3.50%[34]**	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
No risk (males)	**26.00%[18]**		**0***	**0***	**-**
No risk (females)		**27.40%[18]**	**0***	**0***	**-**
Low risk	**29.27%**	**33.41%**	**1***	**80***	**26.1%* (same behaviour as low-risk group in original)**
Medical injections	**35.80%**	**34.90%**	**1.8**	**1**	**99.0%**
Blood transfusions	**1.00%**	**1.00%**	**1**	**1**	**99.0%**

***Estimates from original model maintained in revised model.**
 # Estimate calculated based on balancing of sex acts with partner group.
$ Subgroup combined in final model to form "long-term female partners of males engaged in transactional sex"

Epidemiological parameter estimates for revised MoT analysis

Population group	HIV prevalence	Comments	STI prevalence	Comments
Injecting drug users (IDUs)	**3.1%[11]**		**5.5%[24]**	**Reporting of genital warts/ulcers**
Partners IDUs	**8.0%**		**-**	**NA**
BBSWs	**27.8%[11]**		**4.6%[24]**	**Reporting of genital warts/ulcers**
Clients of BBSWs	**10.4%***	**Assume same as clients in original model**	**3.3%[24]**	**Reporting of genital warts/ulcers**
Female long-term partners of BBSW clients[$]	**8.0%***		**-**	**Reporting of genital warts/ulcers**
NBBSWs	**18.9%[11]**		**2.8%[24]**	**Reporting of genital warts/ulcers**
Clients of NBBSWs	**10.4%***	**Assume same as clients in original model**	**3.3%[24]**	**Reporting of genital warts/ulcers**
Female long-term partners of NBBSW clients[#]	**8.0%***		**-**	
Young females engaged in transactional sex (YFs)	**3.2%[18]**		**3.3%[24]**	**Assume same as male partner group**
Males engaged in transactional sex with young females (MYF)	**7.4%[18]**		**3.3%[24]***	**Reporting of genital warts/ulcers**

Female long-term partners of MYF	**8.0%***		-	
Men who have sex with men (MSM)	**2.8%***		**1.9%[24]**	**Reporting of genital warts/ulcers**
Female partners of MSM	**8.0%***		-	
Casual heterosexual sex (CHS) males	**3.5%[18]**	**Individuals with 2+ partners in south-south in past 12 months**	**0.2%[35]**	
Casual heterosexual sex (CHS) females	**3.5%[18]**	**Individuals with 2+ partners in south-south in past 12 months**	**0.2%[35]***	
Partners CHS (males)	**4.3%[18]**	**Individuals with 1 non-marital partner in past 12 months**	-	
Partners CHS (males)	**4.3%[18]**	**Individuals with 1 non-marital partner in past 12 months**	-	
Boyfriend/girlfriend relationships (males)	**2.1%[18]**	**Males 15-19 in south-south region**	**0.2%[35]***	**Assume same as low-risk group in original model**
Boyfriend/girlfriend relationships (females)	**1.3%[18]**	**Females 15-19 in south-south region**	**0.2%[35]***	**Assume same as low-risk group in original model**
Discordant couples	**50.0%**	**Assume half of risk group infected**	**0.2%[35]***	

No risk (males)	**3.8%[18]**		**0.2%[35]**	**Assume same as low-risk group in original model**
No risk (females)	**7.9%[18]**		**0.2%[35]**	**Assume same as low-risk group in original model**
Very Low risk	**0%**		**0.2%[35]**	**Assume same as low-risk group in original model**
Medical injections	**8.0%***			
Blood transfusions	**8.0%***			

**Estimates from original model maintained in revised model*

Appendix 1.3: Original MoT model for Cross River State, Nigeria

Country:	Nigeria
Adult (15-49) population size:	2,129,536
Adult (15-49) HIV prevalence (%):	8.00

Blue cells: Input necessary
Peach cells: Input optional
Orange cells: Output
Green cells: Need to check data

Transmission per act	
Male -> female	0.0011
Female -> male	0.0003
% men circumcised	98.0%
STD cofactor	5.3

Cross River	***Use either method 1 or 2 to determine number with risk behaviour for each group (column F).*** **Method 1: Percent of population with risk behaviour (%)**		**Method 2: Population with risk behaviour**									***Transmission probability per risky exposure act***				
Adult Risk Behaviour	***Male***	***Female***	***Male***	***Female***	***Total number with risk behaviour***	***Prevalence of HIV (%)***	***Number HIV+***	***Prevalence of STI (%)***	***Number of partners per year***	***Number of acts of exposure per partner per year***	***Percentage of acts protected (%)***	***with STI***	***No STI***	**Incidence**	**% of incidence**	**Incidence per 100,000**
Injecting Drug Use (IDU)	0.32%	0.27%			6,282	3.1%	195	7.5%	2	224	79.0%	NA	0.01	141	2.00	2,250
Partners IDU	0.26%	0.31%			6,027	8.0%	482	NA	1	80	26.1%	0.0058	0.0011	14	0.19	229
Sex workers	0.00%	2.00%			21,295	23.4%	4,983	12.6%	175	4	61.6%	0.0058	0.0011	652	9.20	3,061
Clients	14.00%	0.00%			149,068	10.4%	15,503	7.6%	5	20	61.6%	0.0015	0.0003	525	7.41	352
Partners of Clients		4.76%			50,683	8.0%	4,055	NA	1	80	26.1%	0.0058	0.0011	390	5.51	769
MSM	0.90%				9,583	2.8%	268	11.0%	3	38	56.3%	0.0530	0.0100	157	2.22	1,642
Female partners of MSM		0.22%			2,342	8.0%	187	NA	1	80	26.1%	0.0058	0.0011	5	0.08	227
Casual heterosexual sex	22.40%	20.70%			458,915	9.0%	41,302	7.6%	2	50	46.8%	0.0036	0.0007	1,759	24.83	383
Partners CHS	16.56%	17.92%			367,132	8.0%	29,371	NA	1	80	26.1%	0.0037	0.0007	1,612	22.75	439
Low-risk heterosexual	18.76%	26.53%			482,233	8.0%	38,579	3.6%	1	80	26.1%	0.0041	0.0008	1,809	25.54	375
No risk	26.80%	27.30%			576,039	6.0%	34,562	0.0%	0	0	0.0%			0	0.00	0
Medical injections	35.80%	34.90%			752,791	8.0%	60,223	NA	2	1	99.0%	NA	0.004	4	0.05	1
Blood transfusions	1.00%	1.00%			21,295	8.0%	1,704	NA	1	1	99.0%	NA	0.9	15	0.22	72
TOTAL ADULT POPULATION	**100.00**	**100.01**			**1,553,560**	**7.96**	**169,487**						Total incidence	7,083		456
										Total incidence in **partners** of high-risk individuals				2,021	28.527	474

Appendix 1.4: Intermediate model for Cross River State, Nigeria

Country:	Nigeria
Adult (15-49) population size:	2,129,536
Adult (15-49) HIV prevalence (%):	8.00

Blue cells: Input necessary
Peach cells: Input optional
Orange cells: Output
Green cells: Need to check data

Transmission per act	
Male -> female	0.0011
Female -> male	0.0003
% men circumcised	98.0%
% reduction in transmission for circumcision	60.0%
STD cofactor	5.3

Cross River	*Use either method 1 or 2 to determine number with risk behaviour for each group (column F).* Method 1: Percent of population with risk behaviour (%)		Method 2: Population with risk behaviour									*Transmission probability per risky exposure act*					
Adult Risk Behaviour	***Male***	***Female***	***Male***	***Female***	***Total number with risk behaviour***	***Prevalence of HIV (%)***	***Number HIV+***	***Prevalence of STI (%)***	***Number of partners per year***	***Number of acts of exposure per partner per year***	***Percentage of acts protected (%)***	***with STI***	***No STI***	**Incidence**	**% of incidence**	**Incidence per 100,000**	**Balance sex act**
Injecting Drug Use (IDU)	0.32%	0.27%	3,407	2,875	6,282	3.1%	195	7.5%	2.0	224	79.00%	NA	0.01	141	1.74	2,250	
Partners IDU	0.26%	0.31%	2,768	3,301	6,069	8.0%	486	NA	1.0	80	26.10%	0.0058	0.0011	14	0.17	229	
Brothel based sex workers	0.00%	1.00%	0	10,648	10,648	23.4%	2,492	12.6%	175.0	4	61.10%	0.0058	0.0011	330	4.06	3,100	7,453,376
BBSW Clients	5.00%		53,238	0	53,238	10.4%	5,537	7.6%	5.0	20	61.10%	0.0015	0.0003	192	2.36	361	5,323,840
Partners of BBSW		1.70%	0	18,101	18,101	8.0%	1,448		1.0	80	26.10%	0.0058	0.0011	139	1.71	769	
Non-brothel based sex workers		1.00%	0	10,648	10,648	23.4%	2,492	12.6%	175.0	4	61.10%	0.0058	0.0011	330	4.06	3,100	7,453,376
NBBSW Clients	5.00%		53,238	0	53,238	10.4%	5,537	7.6%	5.0	20	61.10%	0.0015	0.0003	192	2.36	361	5,323,840
Partners of NBBSW		1.70%	0	18,101	18,101	8.0%	1,448		1.0	80	26.10%	0.0058	0.0011	139	1.71	769	
Students (15-19)		8.70%	0	92,635	92,635	9.0%	8,337	7.6%	2.0	50	46.80%	0.0058	0.0011	570	7.00	615	9,263,482
Clients	4.40%		46,850	0	46,850	9.0%	4,216	7.6%	2	50	46.80%	0.0015	0.0003	77	0.95	165	4,684,979
Partners of clients		1.50%	0	15,929	15,929	8.0%	1,274		1.0	80	26.10%	0.0058	0.0011	106	1.30	666	1,274,314
MSM	0.90%		9,583	0	9,583	2.8%	268	11.0%	3.0	38	56.30%	0.0530	0.0100	157	1.93	1,642	
Female partners of MSM		0.22%	0	2,342	2,342	8.0%	187	NA	1.0	80	26.10%	0.0058	0.0011	5	0.07	227	
Casual heterosexual sex (males)	13.20%		140,549	0	140,549	9.0%	12,649	7.6%	2.0	50	46.80%	0.0015	0.0003	232	2.85	165	14,054,938
Casual heterosexual sex (females)		5.50%	0	58,562	58,562	9.0%	5,271	7.6%	2.0	50	46.80%	0.0058	0.0011	360	4.42	615	5,856,224
Partners CHS (male)	1.87%		19,911	0	19,911	8.0%	1,593	NA	1.0	80	26.10%	0.0015	0.0003	37	0.45	186	
Partners CHS (female)		4.49%	0	47,787	47,787	8.0%	3,823	NA	1.0	80	26.10%	0.0058	0.0011	322	3.95	673	
Boyfriend/girlfriend relationship	9.83%		104,667	0	104,667	9.0%	9,420	7.6%	2.0	50	46.80%	0.0015	0.0003	173	2.13	165	10,466,669
Boyfriend/girlfriend relationship		9.81%	0	104,454	104,454	9.0%	9,401	7.6%	2.0	50	46.80%	0.0058	0.0011	642	7.89	615	10,445,374
Discordant couples (pos)	1.75%	1.75%	18,633	18,633	37,267	100.0%	37,267	3.6%	1.0	80	26.10%	0.0037	0.0007	0	0.00	0	
Discordant couples (neg)	1.75%	1.75%	18,633	18,633	37,267	0.0%	-	3.6%	1.0	80	26.10%	0.0037	0.0007	1,708	20.98	4,583	
No risk (no sex/injection in past 12 months)		27.40%	0	291,746	291,746	6.00%	17,505	0.0%	0.0	0	0.00%	0.0058	0.0011	0	0.00	0	
No risk (no sex/injection in past 12 month	26.00%		276,840	0	276,840	6.0%	16,610	0.0%	0.0	0	0.00%	0.0015	0.0003	0	0.00	0	
Very low risk	29.72%	32.91%	316,449	350,373	666,822	8.0%	53,346	3.6%	1.0	80	26.10%	0.0037	0.0007	2,249	27.63	337	
Medical injections	35.80%	34.90%	381,187	371,604	752,791	8.0%	60,223	NA	1.8	1	99.00%	NA	0.004	4	0.05	1	
Blood transfusions	1.00%	1.00%	10,648	10,648	21,295	8.0%	1,704	NA	1.0	1	99.00%	NA	0.9	18	0.22	82	
TOTAL ADULT POPULATION	**100.00**	**100.00**			**1,523,683**	**9.43**	**262,728**						Total incidence	8,139		534	
												Total incidence in **partners** of high-risk individuals					

Appendix 1.5: Revised model for Cross River State, Nigeria

Country:	Nigeria
Adult (15-49) population size:	2,129,536
Adult (15-49) HIV prevalence (%):	8.00

Blue cells: Input necessary
Peach cells: Input optional
Orange cells: Output
Green cells: Need to check data

Transmission per act	
Male -> female	0.0011
Female -> male	0.0003
% men circumcised	98.0%
% reduction in transmission for circumcision	60.0%
STD cofactor	5.3

	Use either method 1 or 2 to determine number with risk behaviour for each group (column F).																
Cross River	Method 1: Percent of population with risk behaviour (%)		Method 2: Population with risk behaviour									*Transmission probability per risky exposure act*					
Adult Risk Behaviour	*Male*	*Female*	*Male*	*Female*	*Total number with risk behaviour*	*Prevalence of HIV (%)*	*Number HIV+*	*Prevalence of STI (%)*	*Number of partners per year*	*Number of acts of exposure per partner per year*	*Percentage of acts protected (%)*	*with STI*	*No STI*	Incidence	% of incidence	Incidence per 100,000	Balance sex act
Injecting Drug Use (IDU)	0.32%	0.27%	3,407	2,875	6,282	3.1%	195	5.5%	4.0	104	79.00%	NA	0.01	147	3.35	2,346	
Partners IDU	0.26%	0.31%	2,768	3,301	6,069	4.3%	261	NA	1.0	80	26.10%	0.0058	0.0011	14	0.31	224	
Brothel based sex workers	0.00%	1.00%	0	10,648	10,648	27.8%	2,960	4.6%	250.0	4	65.50%	0.0058	0.0011	336	7.63	3,151	10,647,680
BBSW Clients	5.00%		53,238	0	53,238	10.3%	5,484	3.3%	50.0	4	65.50%	0.0015	0.0003	300	6.82	564	10,647,680
Partners of BBSW		1.70%	0	18,101	18,101	8.0%	1,448		1.0	80	26.10%	0.0058	0.0011	121	2.75	669	
Non-brothel based sex workers		1.00%	0	10,648	10,648	18.9%	2,012	2.8%	120.0	4	65.50%	0.0058	0.0011	183	4.16	1,719	5,110,886
NBBSW Clients	5.00%		53,238	0	53,238	10.3%	5,484	3.3%	24.0	4	65.50%	0.0015	0.0003	92	2.09	172	5,110,886
Partners of NBBSW		1.70%	0	18,101	18,101	8.0%	1,448		1.0	80	26.10%	0.0058	0.0011	121	2.75	669	
Females transactional sex		8.70%	0	92,635	92,635	3.2%	2,964	3.3%	6.0	20	28.00%	0.0058	0.0011	709	16.12	765	11,116,178
Males transactional sex	4.40%		46,850	0	46,850	7.4%	3,467	3.3%	11	20	28.00%	0.0015	0.0003	70	1.59	149	10,477,319
Partners of clients		1.50%	0	15,929	15,929	8.0%	1,274		1.0	80	26.10%	0.0058	0.0011	77	1.74	480	1,274,314
MSM	0.90%		9,583	0	9,583	2.8%	268	1.9%	8.4	14	56.30%	0.0530	0.0100	139	3.16	1,451	
Female partners of MSM		0.22%	0	2,342	2,342	4.3%	101	NA	1.0	36	22.90%	0.0058	0.0011	2	0.05	87	
Casual heterosexual sex (males)	13.20%		140,549	0	140,549	3.5%	4,919	0.2%	2.0	50	46.80%	0.0015	0.0003	70	1.58	50	14,054,938
Casual heterosexual sex (females)		5.50%	0	58,562	58,562	3.5%	2,050	0.2%	4.8	50	46.80%	0.0058	0.0011	276	6.26	471	14,054,938
Partners CHS (male)	1.87%		19,911	0	19,911	4.3%	856	NA	1.0	80	26.10%	0.0015	0.0003	11	0.25	55	
Partners CHS (female)		4.49%	0	47,787	47,787	4.3%	2,055	NA	1.0	80	26.10%	0.0058	0.0011	103	2.33	215	
Boyfriend/girlfriend relationship	9.83%		104,667	0	104,667	2.1%	2,198	0.2%	1.0	80	46.80%	0.0015	0.0003	16	0.35	15	8,373,336
Boyfriend/girlfriend relationship		9.81%	0	104,454	104,454	1.3%	1,358	0.2%	1.0	80	46.80%	0.0058	0.0011	100	2.27	96	8,373,336
Discordant couples (pos)	1.75%	1.75%	1	18,633	37,267	100.0%	37,267	0.2%	1.0	80	26.10%	0.0036	0.0007	0	0.00	0	
Discordant couples (neg)	1.75%	1.75%	18,633	18,633	37,267	0.0%	-	0.2%	1.0	80	26.10%	0.0036	0.0007	1,496	34.00		
No risk (no sex/injection in past 12 months)		27.40%	0	291,746	291,746	7.90%	23,048	0.2%	0.0	0	0.00%	0.0058	0.0011	0	0.00	0	
No risk (no sex/injection in past 12 month	26.00%		276,840	0	276,840	3.8%	10,520	0.2%	0.0	0	0.00%	0.0015	0.0003	0	0.00	0	
Low-risk	29.72%	32.91%	316,449	350,373	666,822	8.0%	53,346	0.2%	1.0	80	100.00%	0.0036	0.0007	0	0.00	0	
Medical injections	35.80%	34.90%	381,187	371,604	752,791	8.0%	60,223	NA	1.8	1	99.00%	NA	0.004	4	0.09	1	
Blood transfusions	1.00%	1.00%	10,648	10,648	21,295	8.0%	1,704	NA	1.0	1	99.00%	NA	0.9	15	0.34	70	
TOTAL ADULT POPULATION	**100.00**	**100.00**			**1,523,683**	**7.75**	**226,909**						Total incidence	4,399		289	
												Total incidence in **partners** of high-risk individuals					

Appendix 2

Technical Appendix 1.0, contains additional technical data accompanying Research Paper 1.

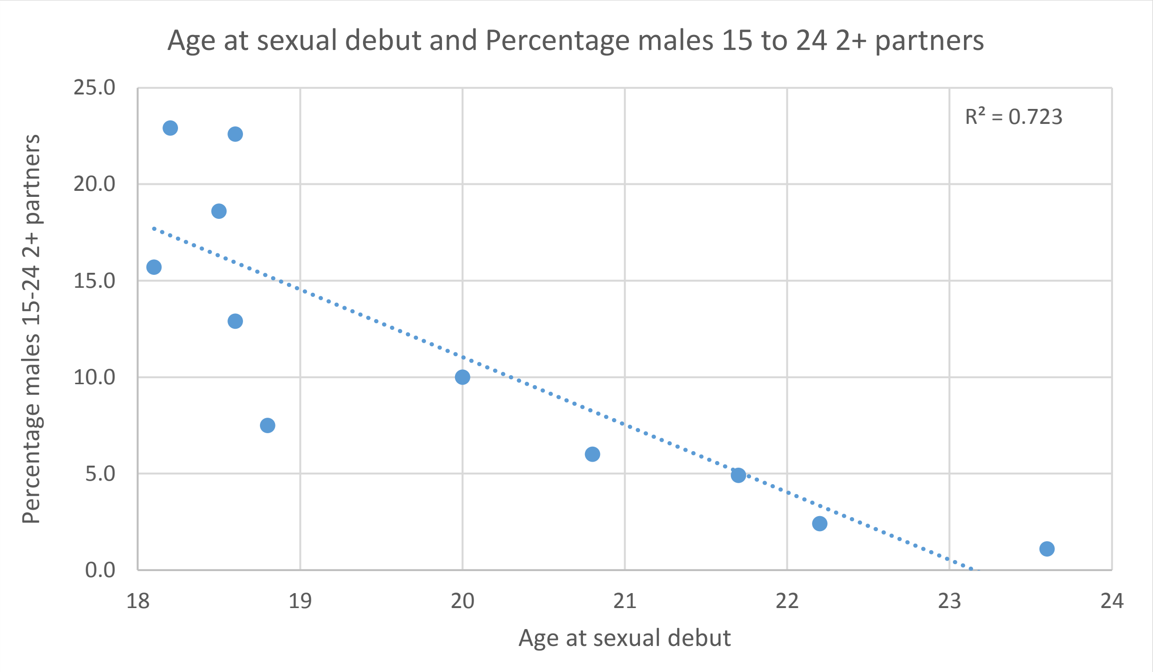
Appendix 2.1

2.1(a) Condom use in population subgroups from DHS surveys 2010-2014

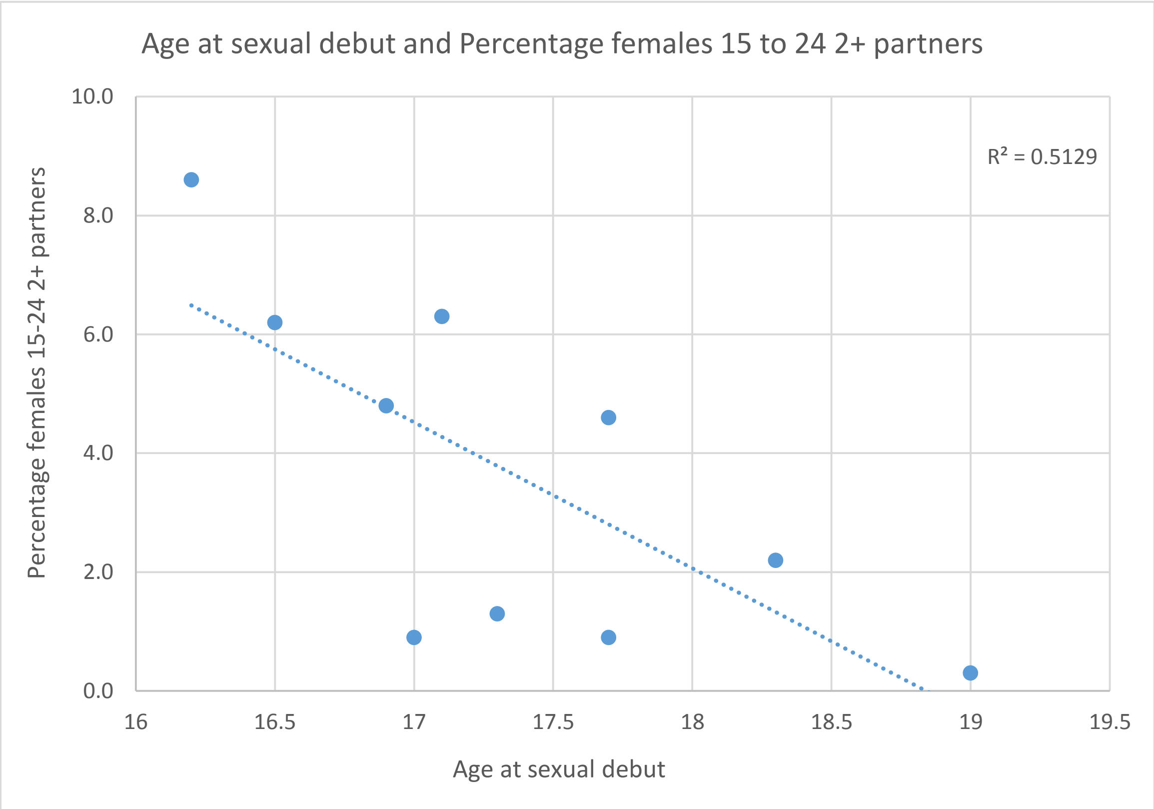
	Females 2+ (%)	Males 2+ (%)	Males Payment (%)
Benin	30.1	19.9	59.9
Burkino Faso	62.3	22.2	32.4
Cameroon	37.3	39.6	53.2
Cote d'Ivoire	29.7	32.9	61.8
Gambia		18.8	
Guinea	32.1	25.4	
Liberia	19.6	23.6	55.9
Mali	9.9*	10.1*	61.2
Niger		22.9[#]	56.8
Nigeria			
Senegal		20.7	
Sierra Leone			
Togo	55.4	23.9	

*Data was heavily biased towards condom reporting from rural population
[#]Data representative of urban populations because actual value was misrepresented by over-sampling rural groups.

2.1(b) Age at sexual debut and association with percentage of males and females reporting 2+ partnerships in population.



Age at sexual debut for males 15-24 and percentage of males aged 15-24 with 2+ partners p=0.001



Age at sexual debut for females 15-24 and percentage of females aged 15-24 with 2+ partners p=0.03

2.1(c) – Literature review Female Sex Worker: Relative population size, condom use, HIV prevalence.

Quantitative and qualitative research studies were searched in Pubmed, Adolec, and Popline, using the following search terms: ‘sex work’, ‘sex worker’, ‘prostitute’, ‘prostitution’, ‘transactional sex’. In addition, when no information was available using these search terms, the term ‘HIV’ was used. The search was limited to the 2010-2013 time period. Abstracts were further examined to determine eligibility for inclusion. In addition, grey literature and reports, such DHS, IBSS, UNGASS, UNAIDS, UNICEF, USAID, World Bank were studied as far as they were accessible.

Benin: population 8 525 574 (UNGASS 2012/2010)

Parameter variable		Source	Study detail	Comment
Consistent condom use FWSs with clients	91·7% last seven days 85·1% last day of work (91,7% among official FSWs, 80,2% among clandestine)	(Programme National de Lutte contre le SIDA et les IST et al., 2012)	1016 FSWs	
	94·6% always during last 7 days	(PSI Research Division, 2011)	773 FSWs (15-29) were interviewed 429 official and 344 clandestine	
HIV prevalence FSWs	20·4%· 25,2% among official FSWs and 17,7% among clan destines	(Programme National de Lutte contre le SIDA et les IST et al., 2012)	1016 FSWs	

Burkina Faso: Population: 14 017 267 (2006)

Parameter variable		Source	Study detail	Comment
Consistent condom use FSWs clients	98·2% last client 94·8% last day 92·8% always	(Bureau d’Appui en Santé Publique’96, 2011)	Sample=1016 FSWS 62% seaters 21% street FSWs, 18% clandestine.	From: l’Enquête bio comportementale auprès des travailleuses de sexe et leurs clients 94% of clandestine FSWs were from particular province Poni
	89·7% last new client 78·3% last regular client	(Konate et al., 2011)	115 professional SWs of the ANRS 1222 Yerelon Cohort at Enrolment	At the base-line

	25·7% 35·9% among professional SWs 23·5% among part-time SWs	(Konate et al., 2011)	658 FSWs (full-time and part-time) of the ANRS 1222 Yerelon Cohort at Enrolment	Mean age 25

Cameroon:

Parameter variable		Source	Study detail	Comment
Consistent condom use	**72·7% last paid sex**	(UNGASS, 2012)		
HIV prevalence				
HIV prevalence FSWs	36·7% 2009	(UNGASS, 2012)		
	36%, the highest in Adamoua region-49.5%; the lowest in Sud region-23.9% The highest prevalence was among 20-29 years old FSWs			

Cote d'Ivore: Population 19 737 800 (2010)

Parameter variable		Source	Study detail	Comment
	92·8% last client	(Conseil National de Lutte Contre le SIDA, 2012)		Enquête CAP PS 2011 dans 12 régions
HIV prevalence FSWs	26·6%	(Vuylsteke et al., 2012)	Cross-sectional survey among 1110 FSWs who attended clinics in 4 regions in 2007 and in 2009	Same study cited in UNGASS report but with prevalence 28·6%

Gambia: population**:** 1 776 000 (2011) World Bank

Parameter variable		Source	Study detail	Comment
Consistent condom use FSWs	96·7% last sex	(National AIDS Secretariat Office of The President, 2012)		

Ghana: population 24 223 430 (census 2010)

Parameter variable		Source	Study detail	Comment
Percentage of FSWs	51,934 (47,786 – 58,920) 0·7% of females aged 15-64	(UNAIDS, 2012a)	National level Mapping	From: IBBSS, 2011 90% of those were roamers
Consistent condom use FSWs clients	92% last client 90·3% among roamers and 95·9% among seaters	(UNAIDS, 2012a)		From: IBBSS, 2011
	79·2% always 74·6% among roamers and 89·9% among seaters	(UNAIDS, 2012a)		From: IBBSS, 2011
	90·2% with clients in last 3 months	(International Organization for Migration (IOM), 2012)	559 FSWs (75% roamers, 25% seaters) mean age 27 in Tema-Paga transport corridor	
HIV prevalence FSWs	25·1%	(UNAIDS, 2012a)		Declined from 34% in 2006

Guinee: population 10 200 000 (UNGASS 2012)

Parameter variable		Source	Study detail	Comment

Consistent condom use FSWs clients	77% last client	(Comite National de Lutte contre le SIDA, 2012)	National survey	
	84·1% during last 12 months	(PSI Research & Metrics, 2010)	National survey among 1009 FSWs	
HIV prevalence				
HIV prevalence FSWs	34·4%	(Comite National de Lutte contre le SIDA, 2012)		From: Enquête nationales auprès des population à Risqué (ESCOMB 2007)
	32·7%	(Comite National de Lutte contre le SIDA, 2012)	In Corridor Boke among 101 tested FSWs	From: Enquête regionale faite sur un échantillon réduit dans trois regions It was 20·7% in the same region in 2007 (among 598 FSWs)

Liberia: population 3 500 000 (Census, 2008)

Parameter variable		Source	Study detail	Comment
Percentage of FSWs	Estimated size 1822 (about 0·2% among 15-49 age)	(UNAIDS, 2012b)	Data collected in 2011	This was a size estimate study in 2011 among MARPs

Mali: population 14 517 176 (UNGASS, 2012, data 2009)

Parameter variable		Source	Study detail	Comment
Consistent condom used FSWs with clients	98·1% last sex	(Haut conseil national de lutte contre le SIDA, 2012)		From: ISBS, 2009
HIV prevalence FSWs	24·2%	(Haut conseil national de lutte contre le SIDA, 2012)		From: ISBS, 2009

Niger: population 14 517 176 (UNGASS, 2012, data 2009)

Parameter variable		Source	Study detail	Comment
Consistent condom used FSWs with clients	94·4% last sex	(Conseil National de lutte contre le SIDA, 2012)		From: Enquête SSG 2011
HIV prevalence FSWs	35·6%	(Conseil National de lutte contre le SIDA, 2012)	N=900	From: Surveillance sentinelle 2009 In different regions from 16,7% to 60,6%

Nigeria

Population: 162,265,000 (UNGASS, 2012)
Note: most data comes from last IBBSS conducted in nine Nigerian states in 2010: Lagos, Kano, Kaduna, Benue, Nasarawa, Edo, Anambra, Cross River, FCT. Study recruited 2, 265 BB-FSWs and 2,194 NBB-FSWs

Parameter variable		Source	Study detail	Comment
Consistent condom use				
Consistent condom use BB-FSWs with client	95·1% (last sex 90·6% (last 30 days)	(Federal Ministry of Health (FMOH), 2010)		
HIV prevalence BB-FSWs	27·4%	(Federal Ministry of Health (FMOH), 2010)		HIV was higher in females with no formal education and in females who reported spending 5+ years in sex work
	29·6%	(Lawan UM et al., 2012)	N=124 FSWs from Kano region, average age 26·4	
HIV prevalence NBB-FSWs	21·1%	(Federal Ministry of Health (FMOH), 2010)		HIV was higher in females with primary education and in females who reported spending 5+ years in sex work
HIV prevalence among transport workers	2·4%	(Federal Ministry of Health (FMOH), 2010)		

HIV prevalence among armed forces	2·5%	(Federal Ministry of Health (FMOH), 2010)		
HIV prevalence among police	2·6%	(Federal Ministry of Health (FMOH), 2010)		

Senegal: population**:** 12 855 153 (2011)

Parameter variable		Source	Study detail	Comment
Consistent condom use FSWs clients	93·7% last client 94·6% last old client among professional SWs 90·7% among clandestine 98·7% new client among professional SWs 95·7% among clandestine	(Conseil national de lutte contre le SIDA and RÉPUBLIQUE du SÉNÉGAL, 2012)	N=703	From: ENCS 2010
HIV prevalence FSWs	18·5% 21·6% among professional SWs 9·9% among clandestine	(Conseil national de lutte contre le SIDA and RÉPUBLIQUE du SÉNÉGAL, 2012)	N=703	It was 19·8% in 2006 23·8% among official sex workers 12·1% among clandestine

Sierra Leone: population 5 600 000

Percentage of FSWs	3·5 % (82,779)	(Kenya P.R et al., 2010)		

Togo: population 6 200 000 (UNGASS, 2012/data 2010) 25% women 15-49 (795,515)

Parameter variable		Source	Study detail	Comment
Percentage of FSWs	5397 (0,7% of 15-49 females)	(Sobela et al., 2009)	Data was collected in 2005 in all Togo regions at SW sites and included both BB and NBB-FSWs	
Consistent condom use BB-FSWs and NBBs	95·3% ever 88% consistently during last day of sex work 79·1% always during the last week	(Programme National de Lutte contre le SIDA et les IST and Direction Nationale de la Santé Publique, 2011)	1106 FSWs	
HIV prevalence BB-FSWs and NBBs	13·1% (21·8 among official FSWs and 10% among clandestines) 28% among 18-24 year olds	(Programme National de Lutte contre le SIDA et les IST and Direction Nationale de la Santé Publique, 2011)	Among 294 official sex workers and 812 clandestine sex workers	

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Appendix 2.2: Figures on Anti-Retroviral treatment for countries across West Africa.

Table 1: Gives figures on the total number of individuals in each country who are receiving ART treatment. Figures for the total population size are estimated from The World Bank. HIV prevalence estimates are calculated by taking (total numbers HIV+/total population)

Countries	Total numbers HIV+	Total number of people receiving ART					World Bank estimates	2010-2014 estimates
		2008	2009	2010	2011	2012	Total population 2009-2013	HIV prevalence
Benin	123881	12078	15401	18230	19930	26035	10,323,474	1.2
Burkina Faso	169348	21103	26448	31543	36248	45910	16,934,839	1.0
Cameroon	956920	59960	76228	89455	105653	122783	22,253,959	4.3
Côte d'Ivoire	751695	51820	72011	75237	82721	110370	20,316,086	3.7
Gambia	29588	770	921	1869	2891	3571	1,849,285	1.6
Ghana	362664	21548	30265	40575	54589	69870	25,904,598	1.4
Guinea	199668	9212	14999	20430	23135	26666	11,745,189	1.7
Guinea-Bissau	90325	1832	2764	3632	5104	6101	1,704,255	5.3
Liberia	47234	2017	2970	4412	5839	5478	4,294,077	1.1
Mali	168318	16475	21100	24778	29237	28751	15,301,650	1.1
Niger	71325	2846	6445	7812	9420	11810	17,831,270	0.4
Nigeria	5902921	238659	302973	359181	432285	491021	173,615,345	3.4
Senegal	70666	9252	12249		12762	14692	14,133,280	0.5
Sierra Leone	91381	1950	3660	5552	8115	8259	6,092,075	1.5
Togo	170424	11211	16710	24635	29045	30311	6,816,982	2.5

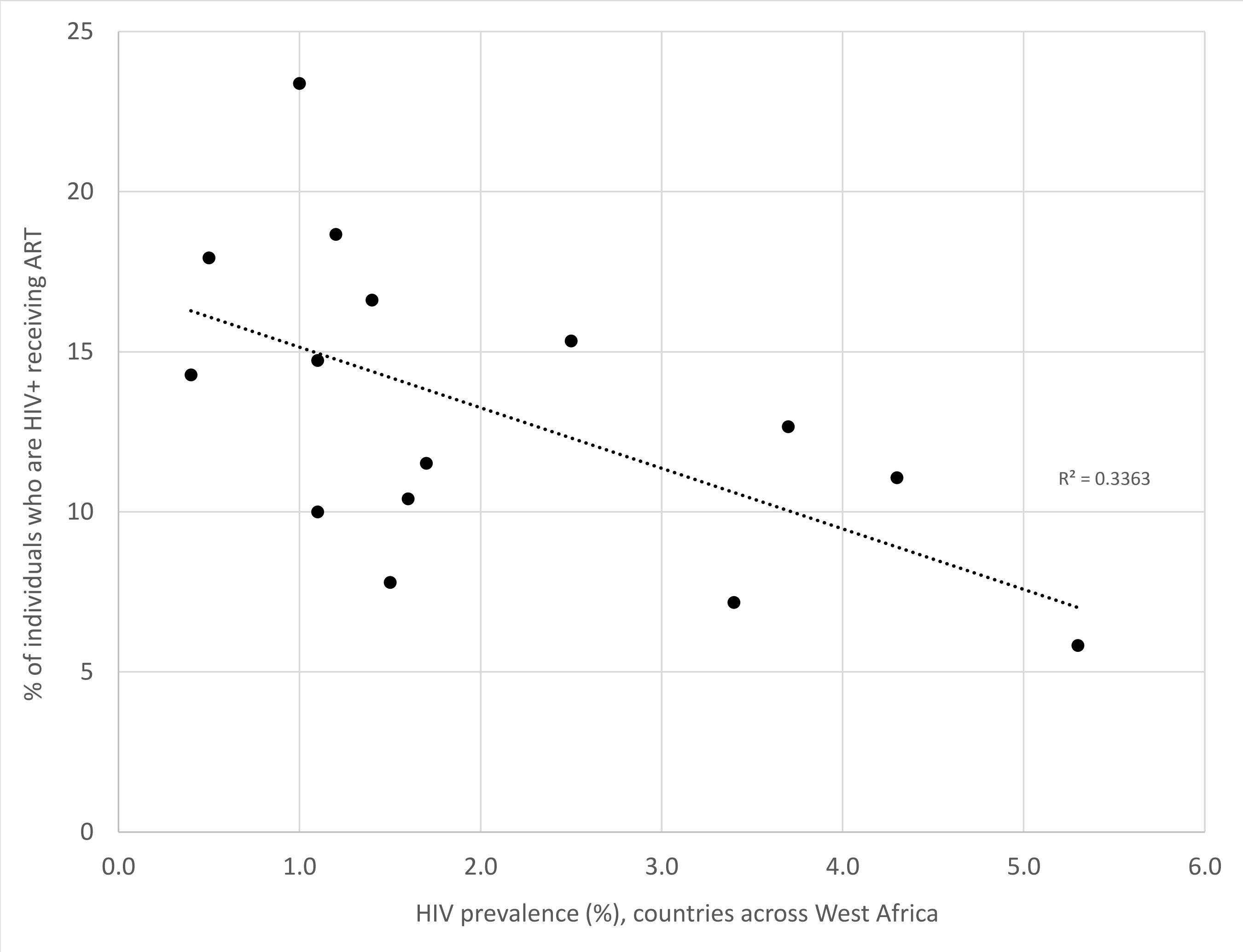
Table 2: Estimates of total population size for those who are HIV+ for countries across West Africa beginning in 2008 and assuming a 3% annual growth rate.

Countries	Population size estimate based on World Bank estimates (3% growth rate)				
	Pop 2008	Pop 2009	Pop 2010	Pop 2011	Pop 2012
Benin	123882	127598	131426	135369	139430
Burkina Faso	174429	179662	185052	190603	196321
Cameroon	985628	1015197	1045653	1077022	1109333
Côte d'Ivoire	774246	797473	821398	846040	871421
Gambia	30476	31391	32332	33302	34301
Ghana	373544	384751	396293	408182	420427
Guinea	205658	211828	218183	224728	231470
Guinea-Bissau	93035	95826	98701	101662	104712
Liberia	48652	50111	51615	53163	54758
Mali	173368	178569	183926	189444	195127
Niger	73465	75669	77939	80277	82685
Nigeria	6080009	6262410	6450282	6643790	6843104
Senegal	72786	74970	77219	79536	81922
Sierra Leone	94123	96946	99855	102850	105936
Togo	175537	180803	186228	191814	197569

Table 3: Estimates for table 3 are calculated using the total number of individuals receiving ART for each respective year, divided by the total number of individuals who are estimated from table 2 and multiplied by 100 to obtain a percentage estimate.

Countries	**Percentage of those HIV positive on treatment**				
	ART 2008	**ART 2009**	**ART 2010**	**ART 2011**	**ART 2012**
Benin	9.7	12.1	13.9	14.7	18.7
Burkina Faso	12.5	14.7	17.0	19.0	23.4
Cameroon	6.3	7.5	8.6	9.8	11.1
Côte d'Ivoire	6.9	9.0	9.2	9.8	12.7
Gambia	2.6	2.9	5.8	8.7	10.4
Ghana	5.9	7.9	10.2	13.4	16.6
Guinea	4.6	7.1	9.4	10.3	11.5
Guinea-Bissau	2.0	2.9	3.7	5.0	5.8
Liberia	4.3	5.9	8.5	11.0	10.0
Mali	9.8	11.8	13.5	15.4	14.7
Niger	4.0	8.5	10.0	11.7	14.3
Nigeria	4.0	4.8	5.6	6.5	7.2
Senegal	13.1	16.3	-	16.0	17.9
Sierra Leone	2.1	3.8	5.6	7.9	7.8
Togo	6.6	9.2	13.2	15.1	15.3

Figure 1: Regression analysis showing relationship between HIV prevalence in different settings and % of individuals receiving ART



Appendix 2.3: Results from the regression analysis showing significant relationships (p<0.05, highlighted in grey) for variables associated with variations in HIV prevalence among different sub-populations.

	Variable	Brothel Based Female Sex Workers^		Men Who Report Payment for Sex								15-24 year old females#				15-24 year old males#				25-29 year old females#				25-29 year old males*	
		HIV prevalence (9)		HIV prevalence (9)		% who report behaviour (11)		% who report behaviour 15-24 (11)		% who report behaviour 25-49 (11)		HIV prevalence		% who report behaviour (10)		HIV prevalence		% who report behaviour (12)		HIV prevalence		% who report behaviour (10)		HIV prevalence	
		R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p		
Brothel Based Female Sex Workers^	HIV prevalence (13)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	% who report behaviour	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	Na	na
Men Who Report Payment for Sex	HIV prevalence (11)	0·28	0·16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	% who report behaviour (8)	0·25	0·20	0·48	0·06	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	% who report behaviour 15-24 (11)	0.48	0.05	-	-	-	-	-	-	-	-														
	% who report behaviour 25-49 (11)	0.77	0.009	-	-	-	-	0.57	0.04	-	-														
15-24 year old females 2+ partners	HIV prevalence (13)	0·33	0·10	0.19	0·17	0·19	0·17	0.52	0.01	0.83	0.005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	% who report behaviour (12)	0·66	0·004	0.15	0·29	0·15	0·29	0.68	0.006	0.64	0.02	0·81	0·003	-	-	-	-	-	-	-	-	-	-	-	-
15-24 year old males 2+ partners	HIV prevalence (13)	0·004	0·86	0·16	0·22	0·16	0·22	0.34	0.06	0.55	0.01	0·47	0·01*	0·21	0·19	-	-	-	-	-	-	-	-	-	-
	% who report behaviour (12)	0·39	0·05	0.29	0.28	0.28	0.09	0.85	0.001	0.61	0.02	0·76	0.001	0·76	0.001	0·53	0·01	-	-	-	-	-	-	-	-
25-49 year old females 2+ partners	HIV prevalence (4)	0.76	0.002	0.21	0.29	0.29	0.09	0.18	0.18	0.27	0.12	0.53	0.01	0.78	0.001	0.02	0.62	0.31	0.05	-	-	-	-	-	-
	% who report behaviour (11)	0·42	0·04	0.002	0·93	0·05	0·54	0.41	0.06	0.51	0.04	0·83	0.001	0·88	0.001	0·28	0·11	0·64	0·002	0.6	0.008	-	-	-	-
25-49 year old males 2+ partners	HIV prevalence (10)	0·61	0·01	0·02	0·74	0·32	0·07	0.30	0.08	0.34	0.08	0·77	0.001	0·83	0·0002	0·18	0·16	0.60	0·003	0.87	0.001	0.72	0.002	-	-
	% who report behaviour (11)	0·78	0·001	0.53	0·06	0·15	0·22	0.33	0.06	0.34	0.08	0·36	0·04	0·77	0.001	0·04	0·48	0·38	0·02	0.60	0.003	0.55	0.009	0.52	0.008

Appendix 3

3.1 Model description

The dynamic deterministic model describes HIV transmission among females and males in a population. The total female population consists of females in the general population (FGP) and two classes of female sex workers (FSWs) which are: brothel based FSWs (FBB) and non-brothel based FSWs (FNB) and females' (2+) with multiple partners (FMP). The total male population consists of males in the general population (MGP) and two groups of clients which are: clients of brothel-based FSWs (CBB) and clients of non-brothel based FSWs (CNB) and males (2+) with multiple partners (MMP). Susceptible individuals (S_i) are recruited at a constant rate $p_i N_{i0}$ where p_i is a constant population growth rate and N_{i0} is the initial population size for $i = \{FGP, FBB, FNB, FMP, MGP, CBB, CNB, MMP\}$.

Upon infection, infected individuals will move into the high-viremia class I_{iV}. Individuals in the I_{iV} class will progress into the low-viremia class (I_i) at a constant rate γ_V. Infected individuals in the I_i category will die of HIV-related illness at a constant rate γ. We assume a natural death rate μ in all classes. The total sexually active population in each class of individuals is given by $N_i = S_i + I_{iV} + I_i$. The forces of infection (λ_i) for susceptible clients, FSWs and general population are as follows:

Forces of infection for the clients (CBB and CNB) and FSWs (FBB, FNB)

$$\begin{cases} \lambda_i = \beta_{fm}(1-\pi)\sum_{\forall i,j,k} C_{ij}^k m_j\left(1-\epsilon f_j\right)\frac{I_{Tj}}{N_j}\text{ , for } i=(CBB, CNB)\text{and } j=\{FGP, FBB, FNB, FMP\} \quad \text{(for clients)} \\ \lambda_i = \beta_{mf}\sum_{\forall i,j,k} C_{ij}^k m_j\left(1-\epsilon f_j\right)\frac{I_{Tj}}{N_j}\text{, for } i=(FBB, FNB)\text{ and } j=\{MGP, CBB, CNB\} \quad \text{(for FSWs)} \\ \text{for } ij=(CBBFBB, CNBFNB, FBBCBB, FNBCNB\ ), k=c, \text{else } k=nc \end{cases}$$

Forces of infection for males 2+ (MMP) and females 2+ (FMP):

$$\begin{cases} \lambda_{MMP} = \beta_{fm} m_{FMP}(1-\pi)C_{MMPFMP}^{nc}(1-\epsilon f_{FMP})\frac{I_{TFMP}}{N_{FMP}} \\ \lambda_{FMP} = \beta_{mf} m_{MMP} C_{FMPMMP}^{nc}(1-\epsilon f_{FMP})\left(\frac{(1-\xi)I_{TMMP}}{N_{MMP}} + \Pi_{CNB}\frac{\xi I_{TCNB}}{N_{CNB}} + \Pi_{CBB}\frac{\xi I_{TCBB}}{N_{CBB}}\right) \\ \Pi_{CNB} = \frac{N_{CNB}}{N_{CBB}+N_{CNB}}, \quad \Pi_{CBB} = \frac{N_{CBB}}{N_{CBB}+N_{CNB}} \end{cases} \tag{2}$$

Forces of infection for the males (MGP) and females (FGP) in the general population

$$\begin{cases} \lambda_{MGP} = \beta_{fm} C^{nc}_{MGPFGP} m_{FGP} (1 - \epsilon f_{FGP})(1-\pi) \left[\frac{\rho_{MGPFBB} I_{TFBB}}{N_{FBB}} + \frac{\rho_{MGPFNB} I_{TFNB}}{N_{FNB}} + \frac{\rho_{MGPFGP} I_{TFGP}}{N_{FGP}}\right] \\ \lambda_{FGP} = \beta_{mf} C^{nc}_{FGPMGP} m_{MGP} (1 - \epsilon f_{FGP}) \left[\frac{\rho_{FGPCBB} I_{TCBB}}{N_{CBB}} + \frac{\rho_{FGPCNB} I_{TCNB}}{N_{CNB}} + \frac{\rho_{FGPMGP} I_{TMGP}}{N_{MGP}}\right] \end{cases} \quad (3)$$

In equations (1)-(3), $I_{Ti} = \eta_V I_{iV} + I_i$ and the parameter $\eta_V > 1$ models the increased HIV transmission in the high-viremia phase(Boily MC et al., 2009). The probability of HIV transmission is denoted by β_l in equations (1)-(3) where β_{fm} and β_{mf} are respectively the probabilities of HIV transmission from infected females to males and infected males to females per sex act. The number of sex acts per each partnership is given by m_i for $i = \{FGP, FBB, FNB, FMP, MGP, CBB, CNB, MMP\}$. The rate of acquiring new sexual partners per unit time are given by C^k_{ij} where $(i,j) = \{FGP, FBB, FNB, FMP, MGP, CBB, CNB, MMP\}$ denotes mixing groups and $k = (c, nc)$ denoted commercial (c) and non-commercial (nc) partnerships. Commercial partnerships are assumed to be within FSWs (FBB and FNB) and their corresponding clients (CBB and CNB) and non-commercial or regular partnerships are assumed to be among sex workers (FBB, FNB, CBB, CNB) of different groups, individuals with multiple partners (FMP,MMP) and the general population (FGP, MGP). Male circumcision and condom use are assumed to result in a reduced force of infection by factors $(1-\pi)$ and $(1-\epsilon f_i)$ respectively, where parameter π is the overall effectiveness of circumcision, ϵ denotes efficacy of condom use, f_i is the consistency of condom use.

Within the model, we assume retirement of FSWs and clients into the respective FGP and MGP at constant rates α_i for $i = \{FBB, FNB, FMP, CBB, CNB, MMP\}$. In addition, we balance the retirement of FSWs and clients but assuming that, FSWs and clients are recruited from the respective FGP and MGP at a rate $\alpha_i(S_i + I_i)$. The recruitment from the infected and susceptible general population is assumed to be proportional to the proportion of infected $\left(\frac{I_i}{I_i+S_i}\right)$ and susceptible $\left(\frac{S_i}{I_i+S_i}\right)$ FSWs.

The parameter $\xi \in (0,1)$ models the mixing of FMP with MMP, CBB and CNB. We assumed the a proportion ξ of the FMP to mix with the CBB and CNB depending on their sizes (i.e Π_{CBB} and Π_{CNB}) and the complementary proportion $(1-\xi)$ to mix with the MMP group. The mixing of FSWs and clients with MGP and FGP respectively is modelled as follows:

$$\begin{cases} \rho_{MGPi} = \frac{p_{mf} N_i}{N_{FGP} + p_{mf}(N_{FBB} + N_{FNB})}, \text{for } i = (FGP, FBB, FNB) \\ \rho_{FGPj} = \frac{p_{mc} N_j}{N_{MGP} + p_{mc}(N_{CBB} + N_{CNB})}, \text{for } j = (MGP, CBB, CNB) \end{cases} \quad (4)$$

The parameters p_{mf} and p_{mc} are the proportion of married FSWs and clients respectively. This mixing formulation is a modified form of that in [2].

We balance the total number of partnerships formed between each group using the general group formula $C_i N_i = C_j N_j$ for $i = \{FGP, FBB, FNB, FMP\}$ and $j = \{MGP, CBB, CNB, MMP\}$. This is consistency condition which states that the number of partnerships formed between males and females in each interacting group must balance [3,4]. We used the balance law to estimate initial population sizes of the male population groups (MGP, CBB, CNB, MMP).

Model description

Individuals enter the model either as members of the general population or as part of a subgroup. Additionally, a percentage of the general population are recruited into individual subgroups. Members of subgroups may remain as such until exiting the population (through death, migration etc.) or re-enter as a member of the general population.

Individuals enter the population as susceptible non-infected individuals and become infected with a force of infection relative to; the type of partnership they form, their rate of change of partners, levels of condom use, duration of sexual activity, HIV prevalence of their partner group, stage of disease (acute versus asymptomatic) of their partner and male circumcision. Once infected, individuals remain in an acute high-viraemia phase for a given time period (when their probability of transmission is higher), before entering into a longer asymptomatic phase. Sexually transmitted infections are not exclusively modelled, instead the transmission probability is adjusted higher to allow for their potential effect both for male to female and female to male transmission. Circumcision is included, and reduces HIV transmission from females to males by 42%(Weiss HA et al., 2000).**Including ART in the model**

In order to model ART use we adjusted HIV related death by assuming that due to increase in ART use, a certain proportion of the infected individuals in the low-viremia stage will have extend life (about 30 years) than those not on ART [5]. In addition we also adjusted the force of infection in each class by assuming that a proportion of those of ART will have reduced HIV transmission [6,7]. In the model analysis we assumed that ART started 20 years from the disease onset.

Model equations

The model assumption results in the following system of generalised differential equations describing HIV transmission dynamics.

Equations for the general population (FGP and MGP)

$$
\begin{cases}
\dfrac{dS_i}{dt} = p_{\,i}N_{i0} + \sum\limits_{\forall j} \alpha_j S_j - \lambda_i S_i - \mu\, S_i - \sum\limits_{\forall i,j} \alpha_j \big(S_j + I_j\big) \dfrac{S_i}{S_i + I_i} \\
\dfrac{dI_{iV}}{dt} = \lambda_i S_i - (\mu + \gamma_V) I_{iV} \\
\dfrac{dI_i}{dt} = \gamma_V I_{iV} + \sum\limits_{\forall j} \alpha_j I_j - (\mu + \gamma) I_i - \sum\limits_{\forall i,j} \alpha_j \big(S_j + I_j\big) \dfrac{I_i}{S_i + I_i} \\
\text{for } i = (FGP, MGP), j = (FBB, FNB, FMP) \text{ if } i = FGP \; or \; j = (CBB, CNB, MMP) \text{ if } i = MGP
\end{cases}
\quad (5)
$$

Equations for FSWs (FBB, FNB) and clients (CBB,CNB), females 2+ (FMP) and males 2+ (MMP)

$$
\begin{cases}
\dfrac{dS_i}{dt} = p_{\,i}N_{i0} + \alpha_i (S_i + I_i) \dfrac{S_j}{S_j + I_j} - \lambda_i S_i - (\mu + \alpha_i) S_i \\
\dfrac{dI_i}{dt} = \lambda_i S_i - (\mu + \gamma_V) I_i \\
\dfrac{dI_i}{dt} = \gamma_V I_{iV} + \alpha_i (S_i + I_i) \dfrac{I_j}{S_j + I_j} - (\mu + \gamma + \alpha_i) I_i \\
i = (FBB, FNB, FMP, CBB, CNB, MMP), j = FGP \;\text{ for } i = (FBB, FNB, FMP) \;\text{ or } j = MGP \text{ otherwise}
\end{cases}
\quad (6)
$$

Model computation method

For input parameters where data were available Latin Hypercube Sampling with uniform distributions were used to generate estimates. Where there was greater uncertainty in parameter values we used triangulation methods to calculate estimates. These were verified post model fitting to check for validity. Below is the underlying process for generating model outputs:

Female Sex Workers and Clients

1. Sample population size estimates and number of partners for both brothel-based and non-brothel based FSWs. We assume on average two sex acts per partner for brothel-based FSWs and four sex acts per partners for non-brothel based FSWs.

2. For clients of both FSW groups, we sample number of partners and assume average number of sex acts with FSWs matches those offered by FSW partners.

By balancing the population sizes of the FSW groups and their number of partners with the number of partners of the clients we independently derive a size estimate for both client groups.

Females 2+ and their Partners – Random mixing model

3. Next we sample a size estimate for the female 2+ group and their total number of partners. We assume 20 sex acts per partner.

4. We next derive a value for ζ, this represents the proportion of sex acts young females engage in with clients of FSWs, with the remaining proportion of partnerships being formed with males 2+.

5. We assume a maximum of two female 2+ partners for males 2+ and from this derive an estimate for their population size.

Females 2+ and their Partners – Proportionate mixing model

The model was coded to allow proportionate mixing, so that partners of individuals are selected with a probability that is proportional to the number of partnerships that they generate.

The General Population

6. General male and female population sizes are derived from DHS surveys for those reporting co-habiting relationships, assuming one partner per individual. We adjust this value to allow for a given percentage of the population who are non-sexually active. The percentage in these groups vary through the duration of the modelling process to allow for continuously changing population dynamics in the other subgroups.

7. Finally, the model accounts for both the percentage of FSWs and male clients who report 'regular' partners. We assume these 'regular' partners to be members of the general population. We use data from reports and the literature to determine both the percentage of clients and FSWs with regular partners and thus create an additional pathway between these groups, as shown in figure 1 above.

8. We assume these individuals have only 'one' regular partner at any given moment.

3.2 Parameter Table

Since the relative size of brothel-based and non-brothel based populations are often estimated only through smaller samples, we used data from an epidemiological mapping report of high-risk subgroups from Nigerian states(National Agency for the Control of AIDS (NACA), 2013), to estimate the potential range for the size of these groups for countries within the West African region. These included both densely populated urban areas such as Abuja in the Federal Capital Territory, where the size of these groups were larger and more rural states, where relative group sizes were smaller in magnitude. Estimates for the size of the groups of "males paying for sex" (clients), young female 2+ and male 2+ groups were extracted from DHS surveys across the region. The remaining sexually active population of males and females are categorised as the general population (assumed to have a single partner) and also estimated from the DHS.

Data on the average and potential range in number of sexual partners and number of sex acts, levels of condom use and duration of time spent in a single subgroup were derived from DHS or available literature. Some inputs (including the size of the client groups and the size of the male 2+ group) were computed from other variables, to ensure that numbers of sexual partnerships balanced across subgroups (e.g. that the numbers of clients that sex workers have balance with the numbers of sex workers that clients report).

Table 1: Biological and behavioural parameter estimates and ranges for countries across the West Africa region

Description	Symbol	Parameter value/range	References and additional details
Biological Parameters			
Probability of HIV transmission	(β_{mf}, β_{fm})	0.006-0.06	(Boily MC et al., 2009)
Multiplicative factor due to increase HIV transmission in the high-viremia phase	γ_V	25	(Boily MC et al., 2009)
Efficacy of condom use	ϵ	80%	(Weller S and Davis K, 2003)
Effectiveness of circumcision	θ	42%	(Weiss HA et al., 2000)
Life expectancy in the population	$1/\mu$	40yrs	(The World Bank, 2014)Life expectancy 55, recruits

			enter model at 15 years of age.
HIV- related death rate	γ	0.125/ yr	
Subgroup Population Sizes			
Relative size of Brothel-based FSWs group	P_{FBB}	0-1.1%	(National Agency for the Control of AIDS (NACA), 2013)
Relative size of Non-brothel based FSWs group	P_{FNB}	0.15-3%	(National Agency for the Control of AIDS (NACA), 2013)
Relative size of Females with 2+ partners group	P_{FTS}	0.1-20%	(Statistics, 2012, Peltzer et al., 2013)
Relative size of group of clients of Brothel-based FSWs	P_{CFBB}	Calculated	
Relative size of group of clients of Non-brothel-based FSWs	P_{NFBB}	Calculated	
Relative size of group of Males 2+ partners group	P_{MTS}	Calculated	
Number of Sexual Partners			
Number of client partners of brothel-based female sex worker.	C_{FBB}^{c}	252-1092/yr (6/week – 26/week)	(Federal Ministry of Health (FMOH), 2010)Assume 10 weeks of non-sexual activity and 2 sex acts per partner.
Number of sex acts client partners of brothel-based female sex workers have with each Brothel-based FSW partner		2	
Number of client partners of non-brothel based FSWs	C_{FNB}^{C}	42-336/yr (8 per week as max, assume 1/wk as lower bound)	(Federal Ministry of Health (FMOH), 2010)Assume 10 weeks of non-sexual activity and 4 sex acts per partner.

Number of sex acts client partners of non-brothel based female sex workers have with each Non-brothel based FSW partner		4	
Number of partners of Females 2+ partners (these include client partners of both brothel-based and non-brothel based FSWs as well as males 2+ partners)	C_{CTS}^{TS}	3-24/yr[1]	(Morhason-Bello et al., 2008) (Barnett JP and Maticka-Tyndale E, 2011, Fawole AO et al., 2011). For lower bound, estimate 3 from DHS, assuming 2+ partners in past 12 months.
Number of sex acts all male partners of females 2+ have with each female 2+ partner and vice versa		20	
Number of brothel based FSWs, clients of brothel-based FSW engage with.	C_{CBB}^{c}	12-48/yr	(Sobela et al., 2009)
Number of females 2+ partners, clients of brothel-based FSW engage with.	C_{CBB}^{TS}	Calculated as part of computational process	
Number of sex acts clients of brothel-based FSW have with females 2+ partners		20	
Percentage of females in the general population who form partnerships with clients of brothel-based FSW clients.	C_{CBB}^{FGP}	Calculated as part of computational process	
Number of non-brothel based FSWs, clients of non-brothel based FSWs engage with.	C_{CNB}^{c}	12-48/yr	(Sobela et al., 2009)
Number of females 2+ partners, clients of non-brothel-based FSWs engage with.	C_{CNB}^{TS}	Calculated	
Number of sex acts clients of brothel-based FSW have with females 2+ partners		20	
Percentage of females in the general population who form partnerships with clients of non-brothel based FSW clients.	C_{CNB}^{FGP}	Calculated	

Average number of partners for males in the general population	C_{MGP}	Set to equal 0.83/yr[2]	
Number of sex acts per year for males in general population		104	
Percentage of males from the general population partnering with each Brothel-based FSWs	C_{FBB}^{MGP}	Calculated	(Federal Ministry of Health (FMOH), 2010)
Percentage of males from the general population partnering with Non-brothel based FSWs	C_{FBB}^{MGP}	Calculated	(Federal Ministry of Health (FMOH), 2010) Based on FSWs reporting percentage who are married or have a regular partner
Average number of partners of females in the general population	C_{FGP}	0.83/yr[2]	DHS multiple countries for females reporting married or co-habiting relationships.
Number of sex acts per year for females in general population		104	
Percentage of females in the general population who form partnerships with clients of Brothel-based FSW clients.	C_{CNB}^{FGP}	Calculated	
Percentage of females in the general population who form partnerships with clients of Non-brothel based FSW clients.	C_{CNB}^{FGP}	Calculated	
Condom Use			
Consistency of condom use among Brothel-based female sex workers	f_{FBB}	41-83% (adjusted for efficacy)	(LISGIS Ministry of Health and Social Welfare National AIDS Control Program, 2008, Division, 2009, Adu-Oppong et al., 2007, Konate et al., 2011)
Consistency of condom use among Non-brothel based female sex workers	f_{FNB}	41-68%	
Consistency of condom use of females with 2+ partners	f_{FTS}	10-39%	From DHS, females 15-24 reporting 2+ partners

Consistency of condom use among females in the general population	f_{FGP}	2%	DHS, % married co-habiting using male condoms as family planning method.
Duration of Time Spent as Member of Subgroup			
Duration of brothel based female sex workers	$1/\alpha_{BB}$	0.5-6 yrs	(Federal Ministry of Health (FMOH), 2010, UNAIDS, 2012)
Duration of non-brothel based female sex workers	$1/\alpha_{NB}$	0.5-6 yrs	(Federal Ministry of Health (FMOH), 2010, UNAIDS, 2012)
Duration of transactional sex based female sex workers	$1/\alpha_{TS}$	1-15 yrs	Assume 15-24 year olds. 10 year period.
Duration of brothel based clients	$1/\varphi_{BB}$	5-10yrs	
Duration of non-brothel based clients	$1/\varphi_{NB}$	5-10yrs	
Duration of males 2+ partners	$1/\varphi_{TS}$	5-20yrs	Assume 15-24 year olds. 10 year period.
Mixing parameter			
Percentage of sex acts of females 2+ with client partners of brothel-based and non-brothel based FSWs	ξ	0-100%	
(Percentage of sex acts of females 2+ with non-client male partners)	$1-\xi$	0-100%	
Prevalence ranges			
Scenario 1	Prevalence in the FGP	0-6%	
	Prevalence in the MGP	0-4%	
	Prevalence in the FBB	15-48%	
	Prevalence in the FNB	10-25%	

The model selects a value from this range and the number of partners are who are clients versus non-clients are determined by the proportionate value ζ (ranging from 0-1). The number of partners from each group is then determined relative to the size of the (male) groups population.

[2]. This is adjusted from 1 partner per individual to allow for 17% of the population (15-49) who are yet to make their sexual debut.

Number of partnerships for FSW groups and their client partners were estimated from in-country reports and the broader literature. For females 2+, we assumed a lower estimate of 3 (assuming more than two partners per year) and an upper bound of 24, from multiple studies and reports. We estimated 2 sex acts per partner for brothel-based FSW and 4 for non-brothel based. For females 2+, we assumed greater longevity in partnerships with 20 sex acts per partner. Number of partners in the general population was assumed to be one per year and adjusted to allow for individuals who were not sexually active (0.83 partners per year). Ranges for consistency of condom use for brothel and non-brothel based FSW with their client partners were extracted from reports. The data for females 2+ and the general population was taken from estimates in the DHS.

Duration of time spent within a subpopulation group, for FSWs and for client partners was taken from reports. Females 2+ were assumed to represent primarily those aged 15-24 and therefore we assumed a 1-10 year duration for this group.

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3.3 Model Verification Method

In order to verify which of the two modelling approaches produced a regression line that most closely matched the data, we generated 1800 model fits for the proportionate method and 1400 for the random method. For each of these we plotted regression lines to compare with the baseline data for West Africa, as shown in figure 1 below.

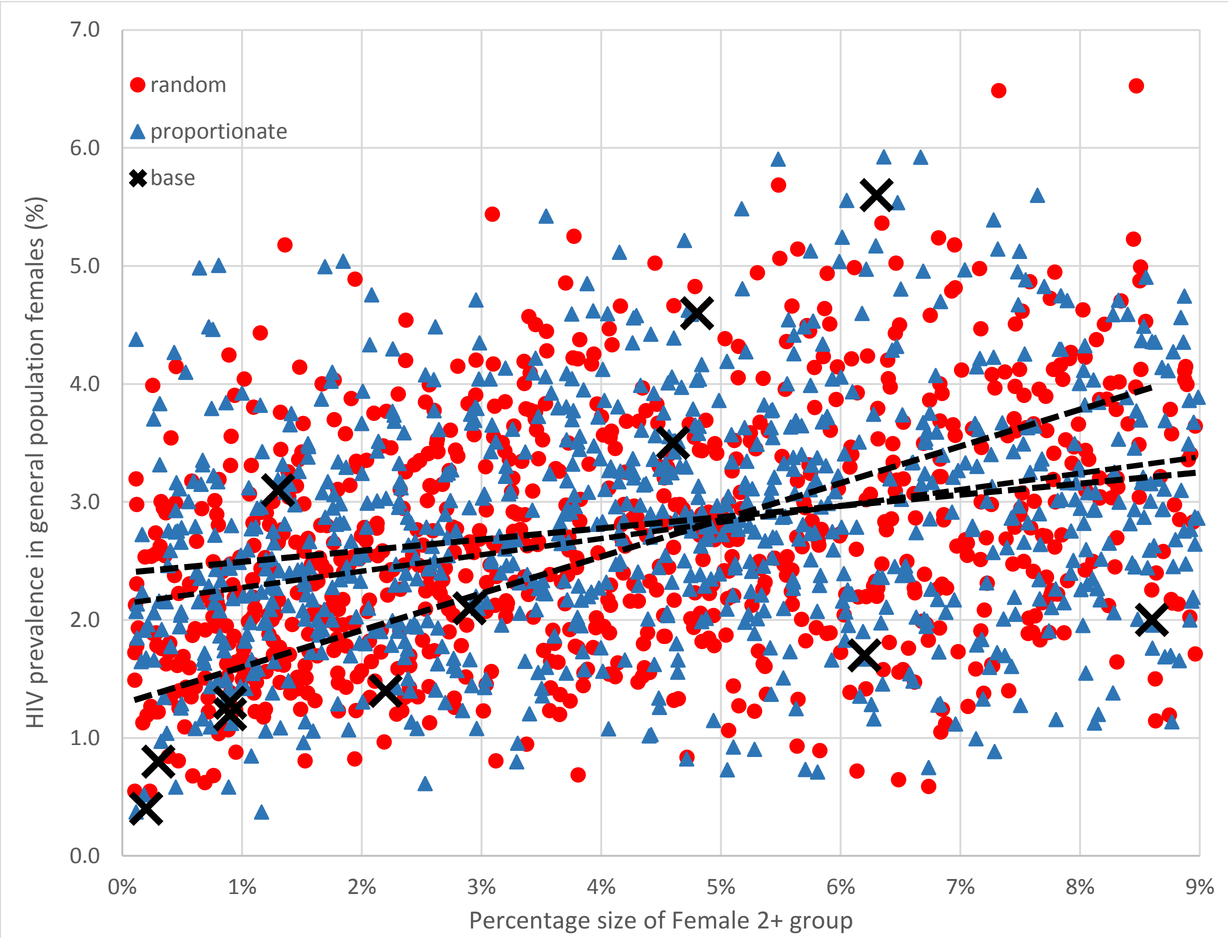

Figure 1: Plot of results from model output exploring the percentage size of the female 2+ group with HIV prevalence in the general female population for the random mixing model and the proportionate mixing model. The baseline data is also shown.

Regression line equations:

Baseline (West Africa data) : $y = 31.184x + 1.2897$. $R^2 = 0.2989$

Proportionate $y = 9.4919x + 2.3963$. $R^2 = 0.056$

Random $y = 13.829x + 2.1364$. $R^2 = 0.116$

To assess which group of fits best represented the baseline data we applied a method of least squares.

Table 1: Results for least squares analysis to assess best fit model for baseline West Africa data

Country	**Female 2+ Size**	**Corresponding HIV prevalence**			**Least Squares Value**	
		Baseline	Proportionate	Random	Proportionate	Random
Benin	2.2	1.4	2.604	2.441	1.448	1.083
Burkino Faso	0.9	1.2	2.481	2.261	1.641	1.125
Cameroon	6.3	5.6	2.990	3.008	6.814	6.720
Cote d'Ivoire	4.8	4.6	2.848	2.800	3.068	3.239
Gambia						
Guinea	2.9	2.1	2.669	2.537	0.324	0.191
Liberia	8.6	2.0	3.206	3.326	1.455	1.757
Mali	0.9	1.3	2.481	2.261	1.395	0.923
Niger	0.2	0.4	2.415	2.164	4.061	3.112
Nigeria	4.6	3.5	2.830	2.773	0.449	0.529
Senegal	0.3	0.8	2.425	2.178	2.639	1.899
Sierra Leone	6.2	1.7	2.980	2.994	1.639	1.674
Togo	1.3	3.1	2.519	2.316	0.338	0.614
					25.272	**22.868**

Results are in bold. The random model produced a marginally lower value for the least squares fitting criteria. We also noted that the value of R^2 (0.116 versus 0.056) gave a better linear approximation.

Appendix 4

Prevalence range	Number of model fits in range	Input parameter	PRCC	p-value
4-5%		P_{FNB}	0.2038	<0.0001
		P_{FTS}	0.1625	0.0002
		P_{FBB}	0.1426	0.001
		β_{mf}	0.1338	0.002
		ξ	0.1062	0.0145
5-6%		P_{FNB}	0.2273	<0.0001
		P_{FBB}	0.1843	<0.0001
		P_{FTS}	0.1587	<0.0001
		ξ	0.1459	<0.0001
		C_{CTS}^{TS}	0.1429	<0.0001
		β_{mf}	0.0907	0.0074
		f_{FNB}	0.0806	0.0174
		$1/\alpha_{BB}$	0.0744	0.0283
6-7%		P_{FNB}	0.1363	<0.0001
		P_{FTS}	0.1166	0.0001
		C_{CTS}^{TS}	0.0858	0.0037
		P_{FBB}	0.0846	0.0042
		β_{mf}	0.0779	0.0085
		f_{FBB}	0.0717	0.0154
		ξ	0.0619	0.0367
		C_{FBB}^{C}	-0.0597	0.0438
7-8%		P_{FTS}	0.1276	<0.0001
		P_{FNB}	0.1256	<0.0001
		β_{mf}	0.1193	<0.0001
		P_{FBB}	0.1073	0.0001
		C_{CTS}^{TS}	0.0781	0.0043
		$1/\alpha_{BB}$	-0.0726	0.0079
		f_{FTS}	-0.0598	0.0288
8-9%	1732	P_{FNB}	0.1112	<0.0001
		P_{FTS}	0.0807	<0.0001
		P_{FBB}	0.0784	<0.0001
		C_{CTS}^{TS}	0.0733	0.0022

		β_{mf}	0.0731	0.0023
9-10%	1385	P_{FTS}	0.1068	0.0001
		P_{FNB}	0.0849	0.002
		β_{mf}	0.0813	0.0031
		C_{CTS}^{TS}	0.0745	0.0068
10-11%%		P_{FNB}	0.1066	0.0003
		P_{FTS}	0.0908	0.0022
		$1/\alpha_{NB}$	-0.0664	0.0252
		β_{mf}	0.0611	0.0397
		P_{FBB}	0.0598	0.0441
11-12%		C_{CTS}^{TS}	0.1303	0.0001
		P_{FTS}	0.1065	0.0015
		C_{FBB}^{C}	-0.0927	0.0057
		β_{mf}	0.0919	0.0061
		f_{FBB}	0.0834	0.0128
		P_{FNB}	0.0787	0.0188
12-13%		P_{FTS}	0.1871	<0.0001
		P_{FNB}	0.1491	0.0001
		C_{CTS}^{TS}	0.1431	0.0003
		β_{mf}	0.1308	0.0009
		f_{FTS}	-0.1254	0.0014
		$1/\alpha_{NB}$	-0.0933	0.0176
		P_{FBB}	0.0898	0.0223
13-15%		P_{FTS}	0.2818	<0.0001
		β_{mf}	0.2474	<0.0001
		C_{CTS}^{TS}	0.2246	<0.0001
		P_{FNB}	0.1659	<0.0001
		ξ	0.1315	0.0002
		f_{FTS}	-0.1259	0.0003

Table 2(a): Results from the Partial Correlation Coefficient sensitivity analysis for females in the general population.

Prevalence range	Number of model fits in range	Input parameter	PRCC	p-value
7-8%	11162	P_{FNB}	0.3646	0.0002
		P_{FBB}	0.3265	0.0003
		C_{CTS}^{TS}	0.2431	0.002
		P_{FTS}	-0.1964	0.0122
		$1/\alpha_{BB}$	0.1859	<.019
8-9%	2225	P_{FBB}	0.1515	<0.0001
		P_{FTS}	0.1139	0.0001
		C_{CTS}^{TS}	0.1173	0.0001
		P_{FNB}	0.1009	0.0005
		f_{FBB}	-0.0952	0.001
		C_{FBB}^{c}	0.0952	0.0011
		$1/\varphi_{BB}$	-0.0739	0.011
		β_{mf}	0.0672	0.0209
9-10%	1935	P_{FBB}	0.1208	<0.0001
		P_{FNB}	0.1169	<0.0001
		P_{FTS}	0.1129	<0.0001
		C_{CTS}^{TS}	0.114	<0.0001
		C_{FNB}^{c}	0.0776	0.0031
		$1/\varphi_{BB}$	-0.0601	0.0221
		β_{fm}	0.0523	0.0465
10-11%	2317	P_{FNB}	0.1037	<0.0001
		C_{CTS}^{TS}	0.0769	0.0021
		P_{FBB}	0.0743	0.0029
		P_{FTS}	0.0692	0.0055
		C_{FNB}^{c}	0.059	0.0182
11-12%	2402	C_{CTS}^{TS}	0.1541	<0.0001
		P_{FNB}	0.1506	<0.0001
		P_{FTS}	0.1445	<0.0001
		C_{FNB}^{c}	0.1152	<0.0001
		P_{FBB}	0.1011	0.0001
		β_{fm}	0.0883	0.0006

		β_{mf}	0.0817	0.0015
12-13%	2282	P_{FTS}	0.1359	<0.0001
		C_{CTS}^{TS}	0.1303	<0.0001
		P_{FBB}	0.1092	0.0002
		P_{FNB}	0.1066	0.0003
		C_{FNB}^{c}	0.0991	0.0007
		β_{mf}	0.0979	0.0008
		C_{CTS}^{TS}	0.1534	<0.0001
		P_{FTS}	0.1279	0.0001
		β_{fm}	0.1129	0.0007
		$1/\varphi_{BB}$	-0.1065	0.0013
		ξ	0.101	0.0023
		f_{FTS}	-0.095	0.0042
		$1/\alpha_{TS}$	-0.0931	0.005
		C_{FNB}^{c}	0.0891	0.0072
		β_{fm}	0.179	<0.0001
		P_{FNB}	0.1262	0.0042
		C_{CTS}^{TS}	0.0895	0.0429
		P_{FTS}	0.0884	0.0455
		P_{FTS}	0.3036	<0.0001
		C_{CTS}^{TS}	0.2904	<0.0001
		f_{FTS}	-0.2111	<0.0001
		P_{FNB}	0.1853	0.0001
		β_{mf}	0.1552	0.0007
		β_{fm}	0.1364	0.003
		P_{FBB}	0.1308	0.0044
		ξ	0.1119	0.015
		$1/\varphi_{NB}$	-0.1056	0.0218
		$1/\alpha_{TS}$	-0.1048	0.0227
		C_{FNB}^{c}	0.1013	0.0277

Table 2(b): Results from the Partial Correlation Coefficient sensitivity analysis for males in the general population.

Appendix 5

5.1 Additional information: Review of behavioural characteristics and HIV prevalence of female sex workers in West Africa

For the ecological review in Research Paper 2 (Chapter 4) it was only necessary to include information on HIV prevalence and to assess levels of reported condom use amongst these groups. Levels of condom use were included to ensure there were not large amounts of variation within the data, which may have resulted in bias in the HIV prevalence in those samples.

Whilst data were available from multiple sources, for the ecological analysis I limited my selection to include only those data sets that specified data collection on brothel-based female sex workers. A large percentage of the surveys reported on 'sex worker' groups but did not specify whether these were solely brothel-based or non-brothel based. Because HIV prevalence tended to be higher in the brothel-based group, including all surveys which may have contained a mixture of HIV prevalence data form different typologies of FSW, may have resulted in prevalence potentially being under-estimated in some settings, since the prevalence in non-brothel based FSWs is generally lower. Additionally, non-brothel based FSWs tend to be heterogeneous, consisting of street-based, home-based and venue based, thus making comparability between these groups difficult. For this reason, for the ecological analysis I used only survey data that was collected from brothel-based FSW groups. The literature review with results included for HIV prevalence and consistency of condom use in the West African settings is shown in Appendix 2.1(c).

However, I included both brothel-based and non-brothel based FSW data estimates for HIV prevalence for the modelling (Chapters 5 and 6), because only a range was required in this instance rather than point estimates for individual countries and the selected data were sufficient to allow for this.

Information on duration of time working in the sex industry (assumed to be continuous work, i.e. not leaving the industry and then returning), number of partners per year and percentage of female sex workers who reported having a non-commercial partner were collated from the review and used for the parameterisation of the models. These estimates are used as model estimates and included in the parameters shown in Chapter 3.3 table 1(a), Appendix 1, 1.3 and Appendix 3 (b) table (1).

Additional information: Review on percentage of young people (15-24) engaging in multiple partnerships.

For the analysis in Chapters 5 and 6, I allowed the size of the adolescent girl group with 2+ partners to vary up to 20%, based on this data. Although when assessing the characteristics of the female 2+ group for the analysis in Chapter 6, I used the highest estimate for a country from the DHS (Liberia) which was 9%.

Table 5.2: Results from the literature review to estimate the percentage of young females and males (15-24) who report different forms of transactional sexual exchange or multiple partnerships.

Country	**Sample size and characteristics**	**Age**	**% likely transactional sex**	**Number of partners reported**	**Sex frequency**	**Year/Ref**
Benin	National Survey of adolescents	15-19			49.2% girls ever had sex 20.2% had sex in the last month	2006(Population Council 2006)
Benin	2,841 not-married students	15-24	10.3% (girls)	31.9% of boys reported multiple partners 10.3% of girls reported multiple partners	61% sexually active	2006(Ministère de la Santé 2006)
Benin	2, 789 not-married working youth	15-24	17.2% (girls)	20.5% of girls have multiple partners 50.2% of boys have multiple partners	67,6% boys; and 64,6% girls had sex ever; 81.3% and 64.1% had sex during last 12 months	2006(Ministère de la Santé 2006)
Benin	2,702 not-married students		7.9% of boys and 7.4% of (20-24) girls reported commercial partner last 12 months	Mean number of commercial partners 1 for boys and 0.2 for girls. Mean number of non-commercial partners: 1.7 for boys and 1 for girls in the last month	75.3% sexually active last 12 months	2012(Ministère de la Santé 2012)
Benin	2,073 not-married working youth	15-24	6.7% of girls 7.4% of boys reported commercial partner last 12 months	Number of partners last month was 1-2. 67.6% of boys and 32.4% of girls had **more than one partner in the last 12 months**	66% sexually active	2012(Ministère de la Santé 2012)

Benin	DHS 2012	15-24		2.2% women and 12.9% men reported **2+ partners in past 12 months**		2012(l'Institut National de la Statistique et de l'Analyse Economique 2012)
Burkina Faso	923 young people national adolescent survey	14-19		1 partner – 57.1% **2+ partners** – 12.9% **past 12 months** among boys 1 partner – 74.1% 2+ partners – 2.8% among girls		2012(Yode and LeGrand 2012)
Burkina Faso	DHS 2010	15-24		**2+ partners** -0.9% among women; 6% among men **past 12 months**		2010(Institut National de la Statistique et de la Démographie (INSD) et ICF International 2012)
Burkina Faso	528 young men and 2577 young women (demographic and health surveys, 2003 data)	15-24		**1+ partners** -among 7% sexually active women **past 12 months**		2009(Stephenson 2009)
Burkina Faso	1474 girls and 593 boys	15-19		**2+ partners** among 6% sexually active women past 12 months 2+ partners among 37% sexually active men **past 12 months**	49% of girls ever had sex, 70% of sexually active had sex in the past 3 months 28% of boys ever had sex, 76% of sexually active had sex in the past 3 months	2004(Guiella G. 2004)

Burkina Faso	National Adolescents Survey	15-19			48.3% of girls ever had sex, 24.5% sexually active in past month	2003(Ouedraogo 2004)
Burkina Faso	1,279 girls and 1,669 boys, national adolescents survey	15-19			22.8% girls and 24.8% boys had sex in the past 12 months	2009(Biddlecom A 2009)
Burkina Faso	3057 a nationally-representative household survey 2004 (of whom 78.4% ever had sex)	12-19		56.8% - 1 partner **2 + partners**- 5% among girls, 24% among boys		2007(Guiella 2007)
Burkina Faso	5,955 a nationally-representative household survey 2004	12-19	35.9% girls (among those who had sex last 12 months)	33.1% of girls who reported transactional sex had **2+ partners past 12 months**	15.6% boys and 12.4% girls had sex during last 12 months	2007(Moore 2007)
Cote d'Ivoire	DHS 2005	15-24		**2+ partners past 12 months** - 6.2% among women, 32.6% among men		2005(Institut National de la Statistique (INS) et Ministère de la Lutte contre le Sida [Côte d'Ivoire] et ORC Macro 2006)
Cote d'Ivoire	412 male and 412 female students	18-30		**2+ partners past 12 months** – 22.1% among women, 33.9% among men		2013(Peltzer, Pengpid et al. 2013)

Cote d'Ivoire	1,262 males and 1,419 never-married females national sample	15-24		**2+ partners past 3 months** – 4.5% among girls and 18.8% among boys	19.3% ,males and 17.3% females did not have sex last 3 months	2005(Babalola S 2005)
Cote d'Ivoire	2360 national sample, data 2005	15-24		**1+ partner last 12 months** 4.5% among women, 19.7% among men		2010(International Group on Analysis of Trends in HIV Prevalence and Behaviours in Young People in Countries most Affected by HIV 2010)
Ghana	DHS 2008	15-24		**2+ partners past 12 months** -1.4% women and 5.9 men		2008(Ghana Statistical Service (GSS) 2009)
Ghana	2180 females and 2225 males in national adolescent survey	12-19	73% among 15-19 girls	Among 15-19 0 partner- 27.6% girls, 34.2% boys **1 partner** - 67.1% girls, 48.7% boys **2 partners** - 5% girls, 12.4% boys **3 partners**- 0.3% girls, 4.1% boys **4 partners** - 0% girls, 0.5% boys **past 12 months**	Ever had sex 30% of females and 16% of males aged 15–19 years and 1–2% of females and males aged 12–14	2006(Awusabo-Asare K 2006)
Ghana	4,430 a nationally-representative household survey 2004	12-19	74.7% girls (among those who had sex last 12 months)	77.6% of girls who reported transactional sex had **2+ partners past 12 months**	5.9% boys and 9.9% girls had sex during last 12 months	2007(Stephenson 2009)

Ghana	1022 young men, 2138 young women (demographic and health surveys, data 2003)	15-24		**1+ partners** -among 4% sexually active women **past 12 months**		2009(Glover EK 2003)
Ghana	704 never-married youth	12-24			35.2% girls had sex last 30 days 24.2% boys had sex last 30 days	2003
Ghana	1345 young men from 3 cities	20-24	16.9%-17.1% had sex with commercial partner last 6 months		56.0%-76.8% had sex last 6 months	2002(Family Health International 2002)
Ghana	1667 young women from 3 cities	18-22	4.6%-10% had sex with commercial partner last 6 months		49.9%-72.8% had sex last 6 months	2002(Family Health International 2002)
Ghana	1,487 in-school youth 2,667 out-of-school youth	15-24			66% had sex in the last 12 months 80% had sex in the last 12 months	2006(Family Health International 2006)
Ghana	1,176 girls and 1,250 boys	15-19			17.4% girls and 10 boys had sex in the last 12 months	2009(Biddlecom A 2009)
Ghana	300 school children (9% ever had sex)	12-19	7.4% 2 students	1 partner -57.0 2 partners-43.0% **past 12 months**	25.9% (n=7) had sex in the past 12 months Out of 2 students who had commercial sex 1 had it once	2009(Adjaloo 2009)

					in the past 30 days and 1 had it twice	
Guinea	DHS 2005	15-24		**2+ partners past 12 months** – 4.1% among women; 33.4% among men		2005(Direction Nationale de la Statistique (DNS) (Guinée) et ORC Macro 2006)
Guinea	National Adolescent Survey 2005	15-19			59.1% ever had sex 26.8% had sex in the last 4 weeks	2005(Population Council 2009)
Guinea	2388 boys and 2108 girls (never married)	15-24	14% girls and 5% boys reported transactional sex 19.2%	0 partners – 17% boys, 4.6% girls 1 partner -52% boys, 71% girls, 2+ partners-31.2% boys, 24.4% girls **last 12 months**	87.2% boys and 86.0% girls ever had sex; 73.1% boys and 79.3% girls had sex last 12 months	2008(Family Health International et STAT VIEW International 2008)
Liberia	DHS 2007	15-24		**2+ partners last 12 months** – 9.5% among women, 22.9% among men		2007(Liberia Institute of Statistics and Geo-Information Services 2007)
Liberia	National Adolescent Survey 2005	15-19			72.8% ever had sex 41.1% had sex last 4 weeks	2005(Population Council 2009)
Liberia	812 students	14-17, mean 16			36% ever had sex 20% were sexually active last 3 months	2012(Atwood KA 2012)

Liberia	820 students	12-19		1 partner last 3 months – 70% boys, 88% girls, 2-3 partners -19% boys, 8% girls, 4+ partners-11% boys and 3% girls	36% ever had sex 18% of boys and 22% of girls had sex in the last three months 79% had sex 1-2 times in three months 21% had sex 3+ times in last 3 months	2012(Kennedy SB 2012)
Mali	National survey	15-19			55.1% ever had sex, 34.6% had sex during last 4 weeks	2006(Population Council 2009)
Mali	531 young people from Bamaco, cross-sectional survey	15-24		**1+ partner in the last six months** 32*% of women and 64% of men	75% of women and 81% of men eve had sex	2009(Boileau C 2009)
Niger	National survey, girls	15-19			60.5% ever had sex, 36.1% had sex during last 4 weeks	2006(Population Council 2009)
Niger	IBBSS 2008	15-24			48.5% of boys and 31.6% of girls ever had sex 57% boys and 59% of girls had sex last 12 months	2008(Coordination Intersectorielle de Lutte Contre les IST/VIH/SIDA 2008)
Niger	Survey young clients of VCT				65% of men and 48% of women ever had sex 61% had sex during last 12 months	2008(Coordination Intersectorielle de Lutte Contre les IST/VIH/SIDA 2008)
Nigeria	536 students	15-29		1+ partner-20%	69.4% ever had sex	2008(Onayade AA 2008)

Nigeria	senior secondary school female adolescents			1+ partner -23%	37.4% ever had sex	2004(Etuk SJ 2004)
Nigeria	896 adolescents	11-25		1+ partner lifetime 66% males and 44% females	34% ever had sex 84.4% had between 1 and 6 intercourses per week	2003(Sunmola AM 2003)
Nigeria	More than 4000 adolescents (programme evaluation)	11-17			30.6-50.7% males and 28.6-37.9 females ever had sex 27.8-65.6% males and 30.5%-46.7% females had sex last three months	2012(Arnold R 2012)
Nigeria	562 female students	15-24			77.6% ever had sex 57.8% had sex past 1 month	2009(Abiodun OM 2009)
Nigeria	716 students	12-24	11.2%	2+ partners – 40%	28.3% ever had sex	2008(Morhason-Bello IO 2008)
Nigeria	583 freshmen students	21 mean age	11% had sex for money	1.8 among men and 1.6 among women -Mean number of sex partners in the last 6 months	36% men and 23% women were sexually active	2008(Olley OB 2008)
Nigeria	368 students		62% of sexually active men reported sex with commercial partner	1+ partner – 48% last six months	63.7% male and 50.3% females had ever had sex 89% were sexually active last 6 months	2008 (data 2005)(Odu OO 2008)
Nigeria	350 out-of-school youth	15-24			75% ever had sex, 79% had sex last 12 months	2009(Adebiyi AO 2009)

Nigeria	818 out-of-street youth	15-24	20.6% of males 12.2% of females reported sex for money 17.4% 2.04	1 partner last 12 months – 43% (64% women and 34% men) 2-3-33% among men and 24 among women 4+ 33% among men and 12% among women	79% ever had sex (83% males, 71% females) 95% sexually active last 12 months	2010 (data 2008)(Owoaje ET 2009)
Nigeria	220 students	Most 20-24	36.5%	1 partner last 2 months –9% 2-3 -20% 4-5-26% 6+-6%	73% ever had sex	2011(Fawole AO. 2011)
Nigeria	628	10-35 Most respondents 16-20		56.1% reported more than 1 partner	43.1% sexually active Almost every day 6.3% Twice in a week 4.1% Monthly 8.4% Sometimes 24.3%	2005 (data 2002)(Mabayoje VO 2005)
Nigeria	1200 students	10-19	8%	Mean number 2-3 69.2% of the males and 32.7% of the females reported multiple partners	24% sexually active	2003(Abdulkarim AA 2003)
Nigeria	1278 sexually experienced never-married males	15-24	2% last 3 months had sex with commercial partner	27.5% reported multiple partners **past 12 months**		2009(Fatusi A 2009)
Nigeria	448 boys and 338 girls (slum dwellers) sexually active unmarried reporting sexual activity in the	15-24		2+ partners in the last 30 days -45% (15-19) men and 50% (20-24) men; 15% (15-19) women and 10% (20-24) women		2008(Adedimeji AA 2008)

	three months before the interview					
Nigeria	365 medical students	Mean age 24	2% had sex with CSW	6% reported multiple partners	38% had ever sex, 28% had sex past 12 months	2010(Daniyam CA 2010)
Nigeria	1008 adolescents			1 partner -43% 2-3 partners-13% 3+ partners -44%	47.4% ever had sex 3.4% - 5+ times 63.2% - 4+ times in the last six months 22.2%- 3+ 11.3% mentioned 1-2 times	2009(Nwankwo BO 2009)
Nigeria, Benin	852 students	10-18		1 partner 20.2% 2 – 10.1% 3+ -2.1%	33.6% sexually active 39.9%-once a week 16.4%-twice a week 20.3% more than 3 times	2006(Wagbatsoma VA 2006)
Nigeria	176 religious males and 165 females	12-35		**1+ partner last 12 months** -28% 1 partner -30%	65% ever had sex 81% had sex last 12 months	2007(Nweneka CV 2007)
Senegal		14-26		1+ partners – 38%	40% sexually active	2005 (data 2004)(Ndiaye P 2005)
Senegal	DHS 2011	15-24	1.8% among men	**2+ partners last 12 months** – 0.3% among women and 2.4% among men		2011(Agence Nationale de la Statistique et de la Démographie (ANSD) [Sénégal] 2012)
Sierra Leone	National survey	15-19			64.8% girls ever had sex 28.8% sexually active last 4 weeks	2008(Population Council 2010)

Sierra Leone	DHS 2008	15-24	1.5% among men	**2+ partners last 12 months** – 4% among women and 10.1% among men		2008(Statistics Sierra Leone (SSL) and ICF Macro)
Togo	800 male and 164 female students	15-29 (93% were 20-29)	6.7% received money 30.9% gave money	1 partner-37.8% 2-23.8% 3-5 -18.6% More than 5 -6.3%	85% ever had sex Mean number of sexual intercourses 31 per year Among 15-19 age group- have sex 1-3 times per month Among 20-29-3-5 times per months	1999(Sallah ED 1999)

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Appendix 6

Additional information on the methods used to revise the Modes of Transmission Model

The Modes of Transmission model has been used extensively to estimate amongst which population risk groups the highest annual fraction of new HIV infections has occurred. It has been included in four journal articles and 20 UNAIDS reports, covering 29 countries(Shubber et al., 2014). Rather than focusing on the broader categorisation of epidemics, the model instead identifies those who are at risk, with the intention to provide better information for implementing polices to prevent disease.

The basis for mathematical modelling is the force of infection equation, which represents the probability (π) that a susceptible individual becomes infected.

It forms the basis for the MoT model that was developed in 2002, by UNAIDS. The model calculates the expected number of new HIV infections over the coming year, based on a description of the current distribution of infections within the population. It uses the current prevalence of infections in a given number of different risk groups, the number of individuals with certain exposures and the rates of those exposures(UNAIDS, 2007).

In this respect the outcome is strongly dependent on the assumptions made and particularly on the size of different population subgroups within the model. Both biological data, including transmission probability estimates (acquired from the literature) as well as HIV prevalence data are required, along with sexual or injecting behaviours in the population.

The model is constructed within an excel spreadsheet and employs a static mathematical equation to generate an estimate of HIV incidence, which is a variation of the standard force of infection equation given above, containing STIs as an additional risk factor and condom use that reduces the probability of transmission:

$$\pi = S\left[1 - \left\{p(B(1-\beta'(1-v))^{\alpha} + (1-B)(1-\beta)^{\alpha(1-v)}) + (1-p)\right\}^{n}\right]$$

Here S represents the number susceptible (in a given risk group), B is the prevalence of STIs (where having an STI increases an individual's chances of infection), β and β' represent the probability of transmission during a single contact in the presence or absence of an STI, v is the proportion of sex acts protected by effective condom use and α, is the number of contacts per partner. In this instance n represents the number of partners.

The NARHS 2007, divides the sexually active population (15-49) as either; martial or co-habiting, boyfriend/girlfriend relationships, casual relationships and commercial relationships.

Boyfriends/girlfriend relationships are defined as non-spousal relationships, which are more stable than casual relationships. Casual relationships are defined as less stable than spousal or boy/girlfriend relationships and may or may not involve transactional exchange of goods.

Based on these findings new behavioural subgroups were added to the model. These are shown below in figure 6.1, which also includes arrows to show the possible direction of transmission of HIV.

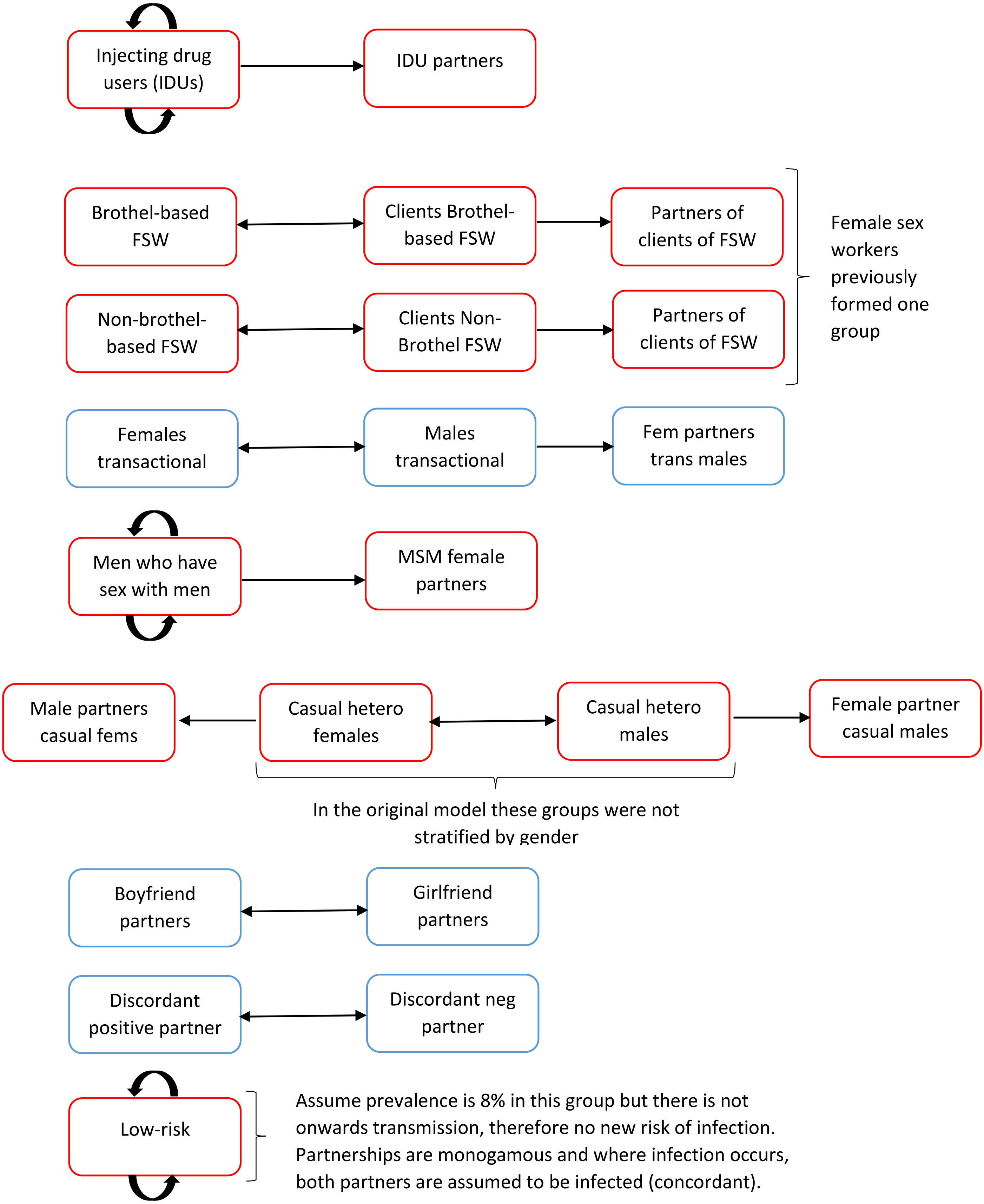


Figure 6.1: show groups from the original MoT model (red boxes) and new behavioural groups that were incorporated into the revised version (blue boxes). Black arrows show the directions of transmission

Appendix 7

The linear regression analysis was carried out using STATA 13·1 (using the command: regress (dependent variable) (independent variable) to obtain the R^2 value and identify which factors or independent variables were associated with the observed variations in HIV prevalence across West Africa.

For the ecological analysis and dynamic modelling chapters (4-6), the approach taken was to compare variations in HIV prevalence at a regional level. For this, the DHS data provided the most consistent and comparable data source for subgroups in the general population, since the surveys are household surveys and are conducted in a similar format between countries.

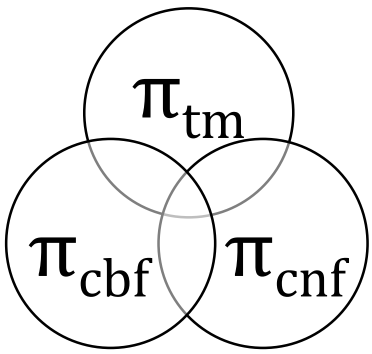
My approach was to use the surveys to identify groups of individuals who are potentially at an increased risk of acquiring HIV, by recognising differences in sexual behaviour amongst the population, which would later help to inform the development and parameterisation of the dynamic mathematical model. The surveys identify individuals on the basis of those who engage in 'higher-risk' sex (sexual intercourse with a non-marital non cohabiting partners) in addition to those with 2 or more partners in the past 12 months and males who have 'paid for sex' in the past 12 months. For the analysis I did not include the 'higher-risk' sex group, because the groups tended to be large and were also likely to represent those who could be in monogamous relationships that were non-marital or non-cohabiting. In HIV population transmission dynamics, these later relationships (assuming neither partner is infected), involve no element of risk. The percentage of individuals who reported 2+ partners and males who 'paid for sex' in the past year were included on the basis that multiple partner numbers may be associated with higher-risk of acquiring HIV.

Appendix 8

Incorporating multiple pathways of risk in the MoT Model

I wished to explore the effect on patterns of incidence if the transactional female group has only 50% of their partnerships with their transactional male partners and 25% of their partnerships with clients of brothel based FSWs and clients of non-brothel based, respectively - such that partnerships are proportionately distributed. The same assumptions were made for the two FSW groups, i.e. 50% of partnerships with main partner groups and 50% distributed between the other male groups. This idea was originally based on evidence from the literature that suggested 50% of client's partners are young females who are not commercial sex workers (Luke N and Kurz KM, 2002). Other additional pathways of risk were identified, for example FSWs and MSM who are also injecting drug users. However, there was not sufficient evidence from the data available in order to parameterise this.

The spreadsheet was adapted to allow for these calculations by incorporating an additional column, "probability of acquiring HIV" from a single partner and a second column that calculated the total risk from all 3 partners for both male and female groups (Appendix 8, table 1). This is more easily visualised using a venn diagram, showing the multiple risk of HIV from different partners:



Where:

π_{tm} is the probability a transactional female has of acquiring HIV from a transactional male

π_{cbf} is the probability a transactional female has of acquiring HIV from a client of a brothel-based FSW

π_{cnf} is the probability a transactional female has of acquiring HIV from a client of a non-brothel based FSW.

Such that;

$$1-(1-\pi_{tm})(1-\pi_{cfb})(1-\pi_{cnb})$$

Is the probability a transactional female has for acquiring HIV.

Results for this analysis are presented below in Table 8.1 and, figures 8a and 8b, which compares the incidence of infections if it assumed female and male groups have one main partner group (figure 1a) versus if there is heterogeneity in mixing patterns, such that sexual partnerships are distributed proportionately (figure 1b). It shows that an additional 2% of total incidence infections occur in transactional females if heterogeneity in mixing patterns is assumed. This analysis provided some initial insights into the concept of multiple risk of acquiring HIV from difference partners or sources.

Cross River Adult Risk Behaviour	Method 1: Percent of population with risk behaviour (%) Male	Female	Define ratio of clients pop %:sex worker pop %	Method 2: Population with risk behaviour Male	Female	Total number with risk behaviour	Prevalence of HIV (%)	Number HIV+	Prevalence of STI (%)	Number of partners per year	Number of acts of exposure per partner per year	Percentage of acts protected (%)	Transmission probability per risky exposure act with STI	No STI	Probability of acquiring HIV	Probability of Acquiring HIV from multiple partner groups	Incidence	% of incidence	Incidence per 100,000	
Injecting Drug Use (IDU)	0.32%	0.27%				6,282	3.1%	195	7.5%	2.0	224.0	79.0%	NA	0.01	0.022501		141	1.94	2,250	
Partners IDU	0.26%	0.31%				6,069	2.7%	164	NA	1.0	80.0	26.1%	0.0058	0.0011			15	0.20	242	
Brothel based sex workers_with BBSW client		1.00%				10,648	27.8%	2,960	12.6%	125.0	4.0	61.1%	0.0058	0.0011	0.020991				0	5,323,840
Brothel based sex workers_with NBBSW client		1.00%				10,648	27.8%	2,960	12.6%	62.5	4.0	61.1%	0.0058	0.0011	0.010573				0	2,661,920
Brothel based sex workers_student partner		1.00%				10,648	27.8%	2,960	12.6%	62.5	4.0	61.1%	0.0058	0.0011	0.007539	0.0386	411	5.65	3,865	2,661,920
BBSW Clients_BBSW	5.00%					53,238	10.4%	5,537	7.6%	25.0	4.0	61.1%	0.0040	0.0007	0.011103				0	5,323,840
BBSW Clients_NBBSW	5.00%		5			53,238	10.4%	5,537	7.6%	6.0	4.0	61.1%	0.0040	0.0007	0.001821				0	1,277,722
BBSW Clients_students	5.00%		1			53,238	10.4%	5,537	7.6%	2.5	20.0	28.0%	0.0040	0.0007	0.000996	0.0139	739	10.15	1,389	2,619,329
Partners of Clients of BBSW		1.70%				18,101	8.0%	1,448	NA	1.0	80.0	26.1%	0.0058	0.0011			139	1.91	769	
Non-brothel based sex workers_with NBBSW client		1.00%				10,648	18.9%	2,012	12.6%	60.0	4.0	61.1%	0.0058	0.0011	0.011405				0	2,555,443
Non-brothel based sex workers_with BBSW client		1.00%				10,648	18.9%	2,012	12.6%	30.0	4.0	61.1%	0.0058	0.0011	0.005723				0	1,277,722
Non-brothel based sex workers_with student partner		1.00%				10,648	18.9%	2,012	12.6%	30.0	4.0	61.1%	0.0058	0.0011	0.004076	0.0211	224	3.08	2,107	1,277,722
NBBSW Clients_NBBSW	5.00%					53,238	10.4%	5,537	7.6%	12.0	4.0	61.1%	0.0040	0.0007	0.003638				0	2,555,443
NBBSW Clients_BBSW	5.00%		5			53,238	10.4%	5,537	7.6%	12.5	4.0	61.1%	0.0040	0.0007	0.005569				0	2,661,920
NBBSW Clients_student	5.00%		1			53,238	10.4%	5,537	7.6%	2.5	20.0	28.0%	0.0040	0.0007	0.000996	0.0102	542	7.44	1,017	2,619,329
Partners of Clients of NBBSW		1.70%				18,101	8.0%	1,448	NA	1.0	80.0	26.1%	0.0058	0.0011			139	1.91	769	
Transactiona females_transactional males		8.20%				87,311	3.2%	2,794	7.6%	3.0	20.0	28.0%	0.0058	0.0011	0.004434				0	5,238,659
Transactiona females_with NBBFSW clients		8.20%				87,311	3.2%	2,794	7.6%	1.5	20.0	28.0%	0.0058	0.0011	0.003119				0	2,619,329
Transactiona females_with BBFSW clients		8.20%				87,311	3.2%	2,794	7.6%	1.5	20.0	28.0%	0.0058	0.0011	0.003119	0.0106	929	12.75	1,063	2,619,329
Male transactional_transactional females	4.40%					46,850	7.4%	3,467	7.6%	5.6	20.0	28.0%	0.0040	0.0007	0.002338				0	5,238,635
Male transactional_NBBFSW	4.40%		4			46,850	7.4%	3,467	7.6%	14.2	4.0	61.1%	0.0040	0.0007	0.006537				0	2,661,920
Male transactional_BBFSW	4.40%		4			46,850	7.4%	3,467	7.6%	6.8	4.0	61.1%	0.0040	0.0007	0.002138	0.0110	514	7.06	1,098	1,277,722
Partners of tranactional males		1.50%				15,929	8.0%	1,274	NA	1.0	80.0	26.1%	0.0058	0.0011			87	1.20	548	1,274,314
MSM	0.90%					9,583	2.8%	268	6.2%	3.0	38.0	56.0%	0.0530	0.0100			142	1.95	1,480	1,092,452
Female partners of MSM		0.22%				2,342	2.7%	63	NA	1.0	80.0	22.9%	0.0058	0.0011			5	0.07	219	187,399
Casual heterosexual sex (males)	13.20%					140,549	3.5%	4,919	7.6%	2.0	50.0	46.8%	0.0040	0.0007			245	3.37	174	14,054,938
Casual heterosexual sex (females)		5.50%	2			58,562	3.5%	2,050	7.6%	4.8	50.0	46.8%	0.0058	0.0011			356	4.89	608	14,054,938
Partners CHS (male)	1.87%					19,911	4.3%	856	NA	1.0	80.0	26.1%	0.0040	0.0007			38	0.52	189	1,609,698
Partners CHS (female)		4.49%				47,787	4.3%	2,055	NA	1.0	80.0	26.1%	0.0058	0.0011			130	1.79	272	3,863,275
Boyfriend/girlfriend relationship (males)	9.83%					104,667	2.1%	2,198	3.6%	1.0	80.0	26.1%	0.0040	0.0007			66	0.90	63	8,373,336
Boyfriend/girlfriend relationship		9.81%				104,475	1.3%	1,358	3.6%	1.0	80.0	26.1%	0.0058	0.0011			155	2.12	148	8,373,336
Discordant couples	1.75%	1.75%				37,267	100.0%	37,267	3.6%	1	80	26.1%	0.0049	0.0009			0	0.00	0	2,981,350
Discordant couples	1.75%	1.75%				37,267	0.0%	-	3.6%	1	80	26.1%	0.0049	0.0009			2,249	30.88	6,034	2,981,350
No risk (no sex in past 12 months)		27.40%				291,746	7.9%	23,048	3.6%	0.0	0.0	0.0%	0.0058	0.0011			0	0.00	0	0
No risk (no sex in past 12 months)	26.00%					276,840	3.8%	10,520	3.6%	0.0	0.0	0.0%	0.0040	0.0007			0	0.00	0	0
Very low-risk	31.47%	35.15%				709,391	0.0%	-	3.6%	1	80	26.1%	0.0049	0.0009			0	0.00	0	56,751,283
Medical injections	35.80%	34.90%				752,791	8.0%	60,223	NA	2	1	99.0%	NA	0.004			3	0.04	0	1,317,384
Blood transfusions	1.00%	1.00%				21,295	8.0%	1,704	NA	1	1	99.0%	NA	0.9			12	0.16	56	21,295
TOTAL ADULT POPULATION	100.00%	100.00%				1,560,950	5.66	173,365						Total incidence			7,281	100.00	466	
														Total incidence in **partners** of high-risk individuals						169,408,091

Table 8: Revised MoT spreadsheet showing revised structure, with additional columns for calculations with additional partner groups

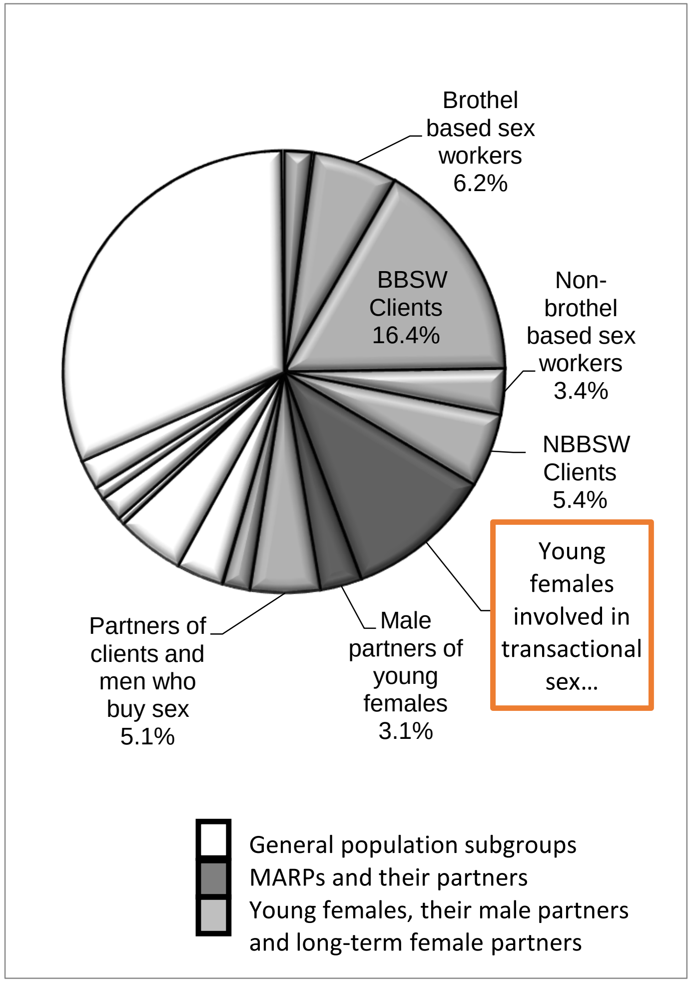


Figure 8(a): Mixing is with main partner groups only.

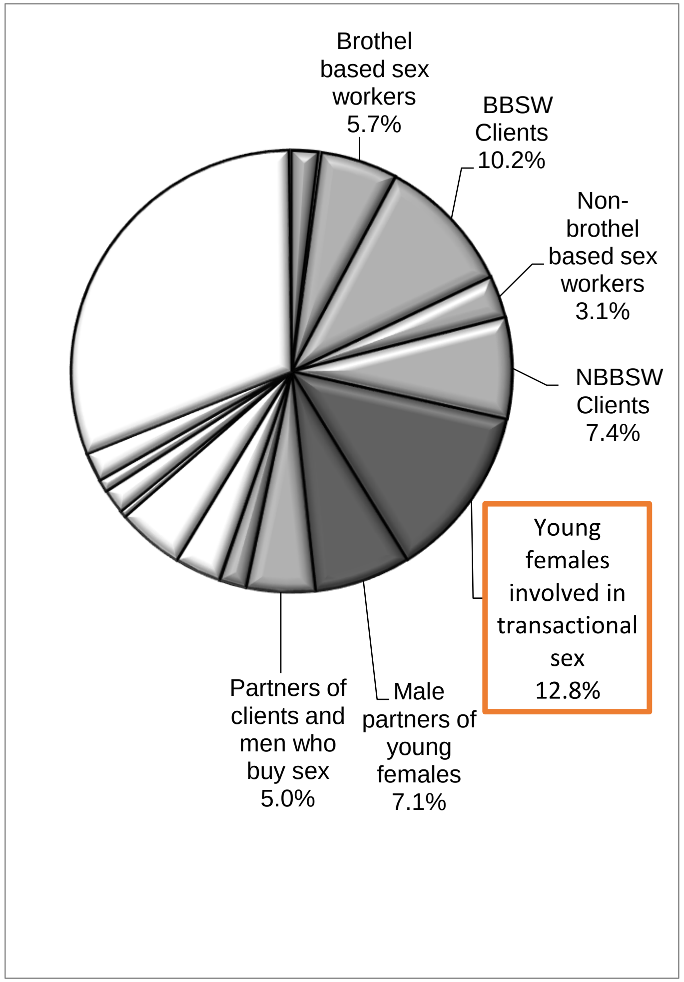


Figure 8(b): Mixing is proportionately distributed; 50% of partnerships with main partner, 25% with other partner groups

Appendix 9

Evidence for the development of the dynamic deterministic compartmental model, based on findings from the earlier results chapter from the thesis chapter

The revised MoT model included a high level of stratification. However, of key importance within the stratification is the ability to identify those individuals who are at highest risk of transmitting and/or acquiring infection.

Evidence from the literature review in Chapter 1, suggests that the groups who are likely to be at the highest risk of infection are the core groups (FSW, MSM and IDUs) (Brunham, 1997, Garnett, 1998) and those subgroups associated with the core groups (Ghani et al., 1997) as well as those engaging in transactional sex, as shown by Jewkers *et al* (Jewkes R et al., 2012).

The revised MoT identifies subgroups associated with core groups as being the sexual partners of IDUs (approximately 0.3% of the respective male and female populations), female partners of MSM, 0.22% of the female population, female partners of clients of FSWs (1.7% of the female population for both client groups, i.e. 3.4% of females) and females engaging in transactional sex (8.7% of the female population).

However, data on the size and behavioural characteristics of IDUs and MSM across the region of West Africa are limited. The original MoT estimates that the size of the subgroups of MSM and IDUs are also relatively small, as is the size of their sexual partner groups. Reports suggest IDUs are likely to have quite low levels of sexual activity (Gorbach et al., 2009) and MSM with female partners are more likely to be “insertive” or ”active” in their sexual role (Phillips et al., 2010), making them at lower risk of acquiring and thus transmitting HIV to their female partners. After careful consideration I decided to omit these groups from the final dynamic model and focus only on heterosexual transmission in West Africa.

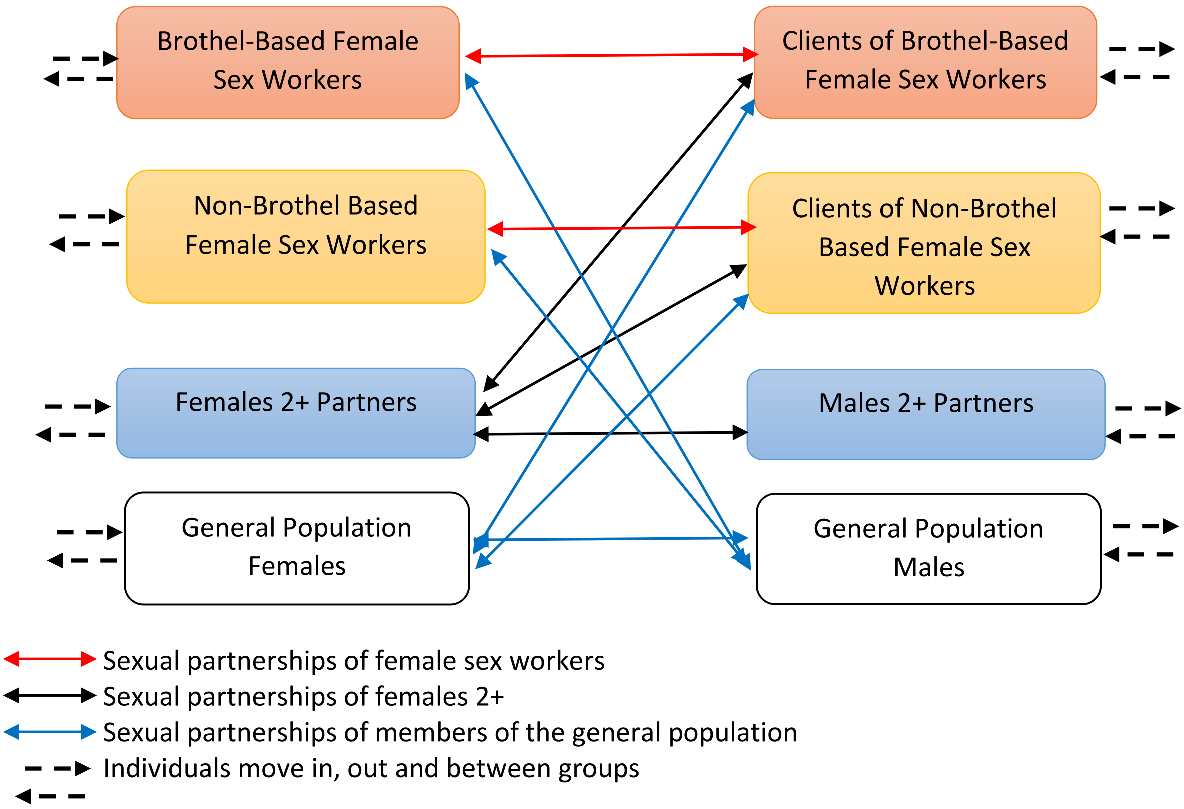
As such, I decided to only include in the dynamic model a group of females with 2+ partners and the long-term partners of clients and FSWs. The female 2+ group is representative of the transactional group from the MoT, but is referred to as female 2+, since this is how these females are identified in the data and because there is not sufficient evidence to suggest their partnerships are exclusively transactional in nature. Inclusion of the female 2+ group was based on several sources of evidence. Firstly, the available data suggests their population size is relatively large (0-9% of the female population from the DHS and as large as 20% as evidenced from the literature), particularly compared to partner groups of MSM (0.22% of the population) and IDUs (0.6% of the population), and therefore this may make them an important subgroup. Secondly the results projected from the MoT show that a high number of incident infections are attributed to this group (16%). Finally, there is evidence to suggest they also form partnerships with clients of FSWs (Luke N and Kurz KM, 2002). I also included in the dynamic model long-term partners of FSWs and clients of FSW, which I assumed to be members of the general population and therefore have the same behavioural characteristics as individuals in this group.

The model structure is shown in figure 9.1. The female 2+ group form partnerships with both clients of FSWs and males 2+ (assumed to have lower HIV prevalence). Structuring the model in this way allows for networks of partnerships that are likely to be associated with a higher-risk of acquiring HIV to be incorporated. Casual and commercial relationships are facilitated by the inclusion of the female 2+ group for females, and the client groups and male 2+ groups that represent casual and commercial partnerships for males. Since the DHS and NARHS data suggest a higher percentage of men engage in casual sex (2+ partners) compared to females, this model structure allows for this by including multiple male groups; male 2+ as well as client groups, to reflect the fact that some partnerships will be transactional, whilst others will not.

In the MoT model I explicitly incorporated partnerships between boyfriends and girlfriends. In the dynamic model, these were included as part of the general population, since they weren't directly associated with any of the higher-risk behavioural groups (i.e. the core groups or transactional sex groups) and therefore are likely to be less relevant for policy. I also omitted discordant partnerships between monogamous partners, since in a dynamic model these arise over time and are likely to be a result of a different source of initial infection. Hence, in this instance I was seeking to understand the source of these infections as opposed to calculating them directly.

The dynamic model samples population sizes and partnership numbers for the three female groups; brothel-based FSWs, non-brothel based FSWs and females 2+. Partnership numbers for the client groups are also sampled (the males 2+ group are assumed to have 2 partners per year). This approach allows for the size of the male client groups to be calculated using a triangulation method, by allowing for one unknown value in the balancing of the equations. This was different than from the approach I took in the MoT model, where I instead used partnerships numbers (as the unknown values) to balance the equations. The rationale for having the population size as the unknown parameter, was based on the fact that it was easier to establish a range for the number of FSW partners, clients have from the data, than it was to accurately estimate the population size of the clients. The size of the male 2+ group was also established in a similar way. In research paper 4 (Chapter 6), I verify the estimates of the male groups again the DHS data to ensure they are plausible. This was a means of model validation.

Figure 9.1: Sexual mixing patterns in the population. Black arrow denote partnership: Sexual partnerships exist between the two FSW groups and their respective client groups and between clients and females with 2+ partners. Younger females 2+ also partner with males 2+. Separate groups of general population males and females form partnerships with one another, with a given proportion also having longer term partnerships with clients (in the case of females) and FSW (in the case of males (to represent the wives of clients and husbands of sex workers, respectively).



Model mixing validation

In order to explore which sexual mixing pattern in the population, best represents that of West Africa, I also tested two alternative sexual mixing patterns in the model. Firstly, we used a standard proportional mixing matrix, whereby sexual partnerships between females 2+, clients and males 2+ were distributed proportionately based on their number of partners. For the second approach we used, what we termed a “random” mixing scenario. Here, we created an additional parameter, ζ, sampled between 0-1 to generate a proportional value. This was set to equal the proportion of partners, females 2+ have who are clients (of either brothel-based or non-brothel based FSW) versus those who are males 2+. For both modelling approaches the method of least square difference was used to minimise the difference between the model projected and the baseline HIV prevalence data from West Africa. The method that gave a smaller difference was a better fit. Details are included in Appendix 3.3.

Appendix 10

Model parameterisation, sensitivity and uncertainty analysis

Below I provide additional details and explanations for the selection of model parameters and the process of model sensitivity analysis for the Modes of Transmission model in Research Paper 1, Chapter 3 and multi-linear regression analysis for the dynamic deterministic compartmental model in Research Papers 3 and 4, Chapters, 5 and 6.

The Modes of Transmission Model

The original MoT model was extracted from a publicly available report (Mbukpa M et al., 2010a) and revised and re-parameterised using newly available data.

Historically FSWs have been identified as an important group to include in HIV transmission models. For the MoT model I divided this group into two different typologies, brothel-based and non-brothel based. The parameterisation of these groups was based on data from the IBBSS 2008, with supporting evidence from the literature.

Evidence from the literature review also supported the inclusion of a group of adolescent females who are involved in non-commercial transactional sex. The NARHS estimated slightly more than 10% of the female population engage in transactional sex (exchange of sex for gifts or favours). I assumed the size of the FSW groups to be similar to that in the original MoT (i.e. 2%, but divided equally between typologies so 1% brothel-based and 1% non-brothel based). Thus I assume around 8% of the female population to engage in non-commercial transactional sex (10% - 2% who are FSWs). Females reporting non-marital partners was approximately 15%, I assumed these to represent all females that engage in either transactional sex or casual sex. As such, those engaging in transactional sex (FSW and non-commercial transactional sex) were discounted from this figure to give an estimate of around 5% for females who have ‘casual’ sex. There were separate estimates in the data for the percentage of males and females in the general population in marital/cohabiting partners and boyfriend/girlfriend relationships. As such I used these estimates directly from the NARHS 2007 data for the model parameterisation. A similar approach was taken to calculate the male groups i.e. non-marital partnerships were assumed to be all men engaging in commercial and casual partnerships of which I discounted those who reported transactional sex and assumed the remaining values to be only those engaging in casual partnerships.

Estimates for female partners of MSM and heterosexual partners of IDUs were extracted from the IBBSS 2008. These were calculated by adding together the casual partners or girlfriends/boyfriends of MSM and IDUs. The total percentage of these were multiplied by the size of the MSM or IDU population to get an estimate for their non-MSM or non-IDU partners i.e. for MSM population size is 0.9% of males and 25% of them report female partners, equating to 0.22% of the female population who are female partners of MSM.

Initial model projections were made for the revised model, with the new structure and revised parameters, and compared with model projections from the original model. An intermediary model was also developed with the revised structure and the original parameterisation.

A model sensitivity analysis was also included as part of the analysis. Latin hypercube sampling, applied using Oracle Crystal Ball Software (Oracle, 2013) was used to generate 10 000 model input combinations. I developed an independent spreadsheet file in Microsoft Excel to carry out the analysis. Screenshots of how this was set up are shown below (Table

10.1-10.3). In short, the sampled input parameters were transferred to the Excel file in tabs corresponding to the subgroups in the population. A separate tab included only the sampled biological parameter estimates. A final tab contained the model calculations for HIV incidence and prevalence.

```
=(B2*(1-C2))*(1-('BBFSWs clients'!C2*('BBFSWs clients'!D2*((1-'Bio params'!H2)^(F2*(1-G2)))+((1-'BBFSWs clients'!D2)*((1-'Bio params'!I2)^(F2*(1-G2)))))+(1-'BBFSWs clients'!C2))^E2)
```

	Brothel based sex workers	Prevalence of HIV (%)	Prevalence of STI (%)	Number of partners per year	Number of acts of exposure per partner per year	Percentage of acts protected (%)	Incidence		Prev*Popsize
1	8,959.94	0.31	0.04	161.47	5.11	0.64	141		2796.492
2	8,741.56	0.21	0.07	151.95	3.51	0.57	181		1834.28
3	12,650.21	0.30	0.03	308.77	4.93	0.60	516		3754.311
4	9,398.12	0.34	0.07	159.27	4.62	0.64	93		3199.141
5	9,783.04	0.23	0.06	362.50	5.43	0.71	799		2253.578
6	10,600.66	0.33	0.04	207.96	3.56	0.70	146		3495.869
7	7,387.27	0.26	0.04	189.53	3.36	0.74	78		1956.895
8	9,807.30	0.23	0.03	279.11	5.84	0.58	753		2234.142
9	12,286.73	0.20	0.07	139.43	3.46	0.72	219		2431.863
10	9,011.96	0.22	0.03	145.65	2.98	0.58	199		1939.535
11	6,698.00	0.32	0.03	129.11	2.63	0.61	95		2145.066
12	14,809.06	0.28	0.02	290.54	5.19	0.57	683		4100.225
13	7,903.39	0.34	0.05	195.05	3.92	0.73	180		2676.337
14	12,464.79	0.20	0.05	256.11	4.79	0.57	498		2484.931
15	9,033.76	0.31	0.05	189.36	2.18	0.72	36		2772.769
16	11,061.75	0.20	0.06	281.32	5.21	0.66	782		2203.913
17	10,754.10	0.34	0.04	320.82	2.37	0.67	163		3617.434
18	6,601.60	0.35	0.06	151.19	4.81	0.68	133		2316.791
19	15,395.25	0.34	0.03	266.29	2.02	0.66	229		5215.359
20	12,080.29	0.21	0.05	325.23	3.68	0.74	345		2537.274
21	11,483.95	0.28	0.02	148.01	4.07	0.62	212		3211.441
22	15,305.19	0.24	0.07	324.95	4.44	0.71	909		3616.534
23	12,637.77	0.20	0.07	359.23	5.74	0.64	512		2469.211
24	15,516.57	0.34	0.05	200.68	5.04	0.72	363		5228.645

Table 10.1: Single tab on spreadsheet with sample of brothel-based FSW sampled parameter inputs. Incidence is calculated by linking this tab (above equation) to data in a separate client tab which enables total infections (incidence) to be calculated.

Population size	IDU trans	MSM trans with STI	MSM trans	STI Discordant trans	Discordant trans	With STI Male ->Female	Male -> female	With STI Female ->male	Female -> male	% men circumcised	% reduction in transmission for circumcision	STD cofactor
2,129,537	0.01	0.25328	0.02	0.00892	0.00057	0.01011	0.0006	0.007723	0.000495	97.0%	74.7%	15.59
2,129,537	0.01	0.06557	0.01	0.00834	0.00102	0.00883	0.0011	0.007847	0.000957	97.6%	48.0%	8.20
2,129,536	0.01	0.23374	0.02	0.00856	0.00061	0.00944	0.0007	0.007687	0.000545	97.8%	71.3%	14.10
2,129,536	0.02	0.09907	0.01	0.00893	0.00071	0.01019	0.0008	0.007667	0.000613	97.3%	67.8%	12.51
2,129,536	0.02	0.29652	0.02	0.01165	0.00085	0.01241	0.0009	0.010882	0.000792	97.6%	57.4%	13.75
2,129,536	0.02	0.01406	0.00	0.00378	0.00060	0.00421	0.0007	0.003352	0.000531	96.9%	72.8%	6.31
2,129,537	0.02	0.16215	0.02	0.00866	0.00094	0.00886	0.0010	0.008457	0.000923	97.5%	50.0%	9.17
2,129,537	0.01	0.09267	0.01	0.00671	0.00071	0.00849	0.0009	0.004937	0.000524	97.9%	72.4%	9.42
2,129,537	0.01	0.12131	0.01	0.01643	0.00098	0.01517	0.0009	0.017685	0.001057	97.1%	42.5%	16.73
2,129,537	0.01	0.07824	0.01	0.01164	0.00088	0.01047	0.0008	0.012806	0.000968	97.4%	47.5%	13.24
2,129,537	0.02	0.35105	0.02	0.01543	0.00085	0.01740	0.0010	0.01346	0.000737	97.7%	60.5%	18.26
2,129,536	0.02	0.02820	0.00	0.01293	0.00108	0.01197	0.0010	0.01388	0.001162	97.1%	36.5%	11.95
2,129,536	0.01	0.40288	0.02	0.01809	0.00104	0.01624	0.0009	0.019943	0.001145	98.0%	37.2%	17.42
2,129,537	0.02	0.30394	0.02	0.01300	0.00090	0.01311	0.0009	0.012891	0.00089	97.2%	52.0%	14.49
2,129,536	0.02	0.03616	0.02	0.00108	0.00054	0.00121	0.0006	0.000946	0.000472	97.2%	75.9%	2.01
2,129,537	0.02	0.35647	0.02	0.01633	0.00098	0.01561	0.0009	0.017046	0.001021	97.0%	44.6%	16.70
2,129,536	0.01	0.04846	0.02	0.00136	0.00062	0.00132	0.0006	0.001394	0.000636	97.5%	66.3%	2.19
2,129,536	0.01	0.36975	0.02	0.01143	0.00075	0.01334	0.0009	0.009512	0.000628	96.8%	67.3%	15.15
2,129,537	0.02	0.20200	0.02	0.00645	0.00074	0.00870	0.0010	0.0042	0.000483	97.6%	74.9%	8.69
2,129,536	0.01	0.07411	0.01	0.00921	0.00092	0.00916	0.0009	0.009256	0.000929	97.5%	49.6%	9.96
2,129,536	0.02	0.24192	0.01	0.01449	0.00081	0.01787	0.0010	0.011106	0.000624	97.3%	67.1%	17.79

Table 10.2: Also included in a separate tab is a spread sheet for sampled biological parameters that is directly linked to the behavioural tabs of individual groups (as in Table 1)

	High risk	IDUs	Brothel based sex work	Non-brothel based sex work	Transactional sex	MSM	Discordant couples	Medium risk risk	General population	Total incidence		HIV prevalence	HIV prevalence
1	2,275	57	574	526	827	291	1,556	96	439	4,365		7%	6.89%
2	3,655	335	1,012	298	1,980	30	1,937	210	951	6,752		8%	7.91%
3	2,726	195	1,114	483	720	214	561	168	344	3,800		7%	7.22%
4	5,012	398	3,243	396	917	57	1,085	152	1,013	7,262		7%	6.74%
5	3,858	120	2,042	292	963	442	678	71	428	5,036		8%	7.61%
6	2,305	13	891	217	1,156	27	984	148	243	3,679		6%	5.81%
7	3,644	373	911	508	1,778	73	1,343	130	829	5,946		7%	6.54%
8	2,331	121	1,300	225	639	46	1,063	49	153	3,597		8%	7.92%
9	2,528	27	1,515	452	455	78	2,456	200	820	6,004		8%	8.17%
10	1,430	252	384	324	419	52	1,571	96	882	3,979		9%	9.49%
11	3,807	433	1,627	255	1,269	223	1,402	91	1,200	6,499		10%	10.11%
12	3,421	204	1,247	603	1,354	13	1,311	113	416	5,261		7%	7.40%
13	3,655	23	1,176	209	1,976	270	604	151	704	5,114		7%	6.88%
14	2,606	25	1,298	214	800	269	2,516	237	827	6,187		9%	8.52%
15	1,529	47	883	173	308	117	286	65	579	2,458		7%	6.78%
16	3,337	227	1,760	730	324	296	861	374	422	4,993		7%	7.19%
17	2,771	114	1,979	147	470	60	1,604	53	539	4,966		9%	8.79%
18	2,343	247	808	581	513	194	1,941	135	840	5,259		10%	10.26%
19	1,800	242	474	345	664	75	901	402	589	3,691		8%	7.68%
20	3,205	42	670	720	1,662	110	2,425	164	1,036	6,830		8%	7.70%
21	4,362	76	3,153	481	523	129	1,550	170	558	6,641		8%	8.42%
22	4,419	162	3,430	330	391	105	802	92	574	5,887		8%	7.76%

Table 10.3: The results from all groups are collated in a final tab to assess number of infections and HIV prevalence in general population

Appendix 11

Additional analysis for Research Paper 4, exploring model projected behavioural characteristics of the Female 2+ for model projections in the presence and absence of male circumcision.

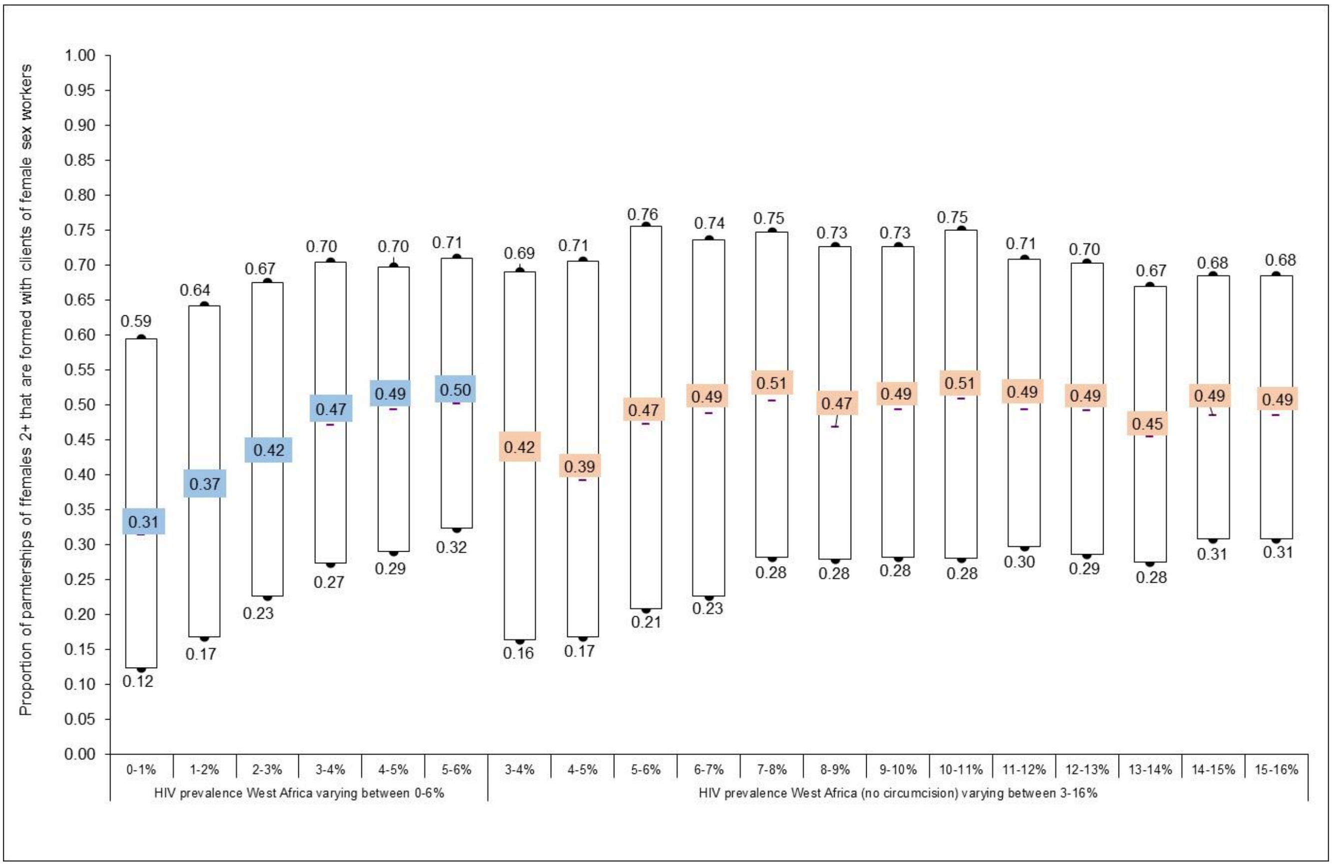


Figure 11.1: Median and Inter-quartile range (IQR) for the proportion of partnerships females 2+ form with client of female sex workers from model projections, for the West Africa region for universal and no male circumcision, for varying HIV prevalence levels in the female general population.

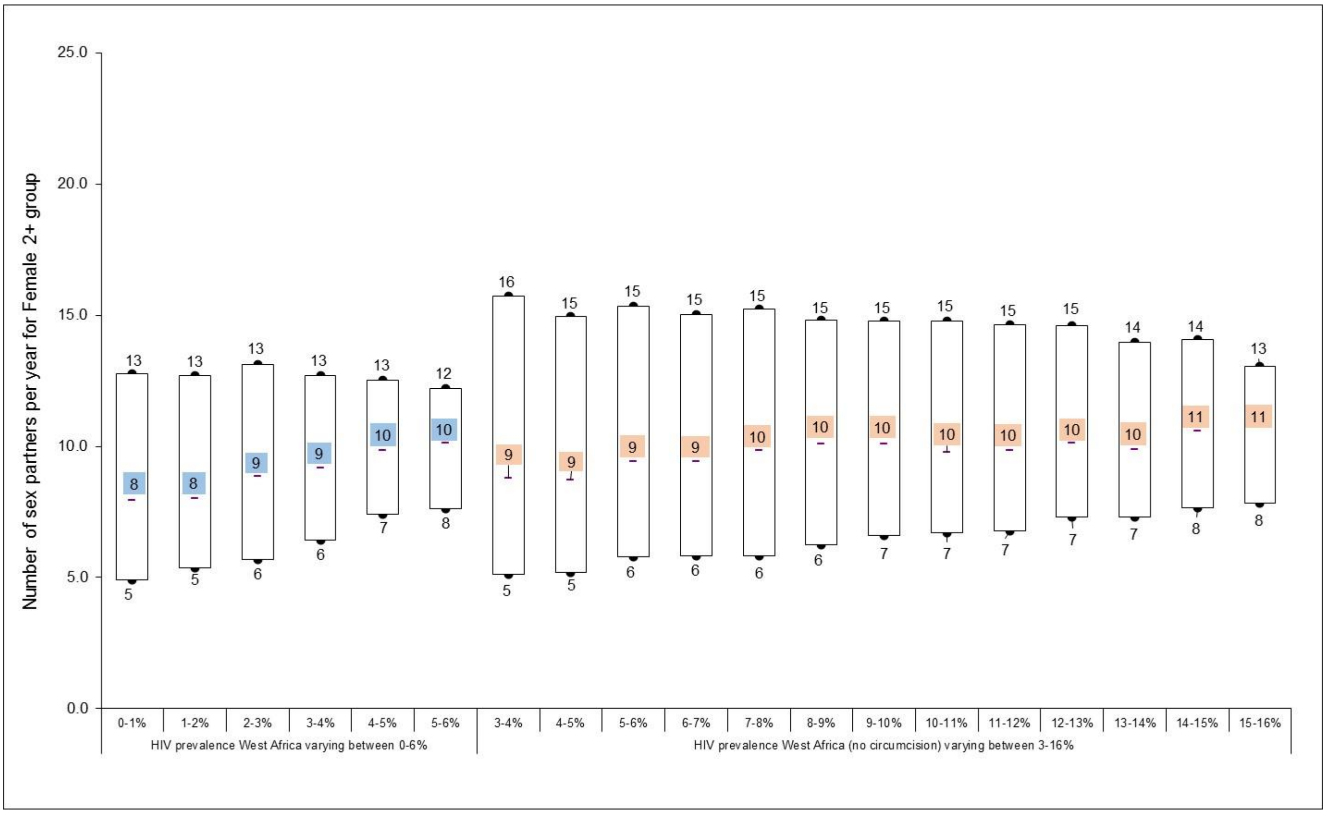


Figure 11.2: Median and Inter-quartile range (IQR) for the number of partners for females 2+ from model projections, for the West Africa region for universal and no male circumcision, for varying HIV prevalence levels in the female general population.

Appendix 12

For the model projections obtained in results Chapters 5 and 6, the model was fit at the endemic phase of the epidemic for the West Africa region. The rationale for this, was primarily based on the availability of HIV prevalence data and sexual behavioural data for the time period 2010 to 2014. By fitting at a point in time in which the HIV epidemic was assumed to have reached equilibrium in the general male and female population, I was able to explore the key determinants of HIV prevalence.

However, whilst the results make it possible to draw conclusions for an epidemic that has reached an endemic phase, it is not possible to have knowledge on the key determinants of the disease at the early stages of the epidemic. However, it is possible to assess the potential characteristics of the HIV epidemic at the earlier stages, by constructing a profile plot of the epidemic as produced by the dynamic model. Figures 12.1a-12.1h below show the projected profile of the epidemic for each of the respective groups that are included in the model.

A key observation, is the more rapid growth of the HIV epidemic in the scenario in which the effect of male circumcision is removed, compared to the West Africa scenario. As expected we also see that the epidemic peaks at higher levels for all population subgroups in the absence of male circumcision. Figure 12.2 and 12.3, compare just the medial HIV level in each of the individual groups with one another, for the scenarios with and without the presence of male circumcision.

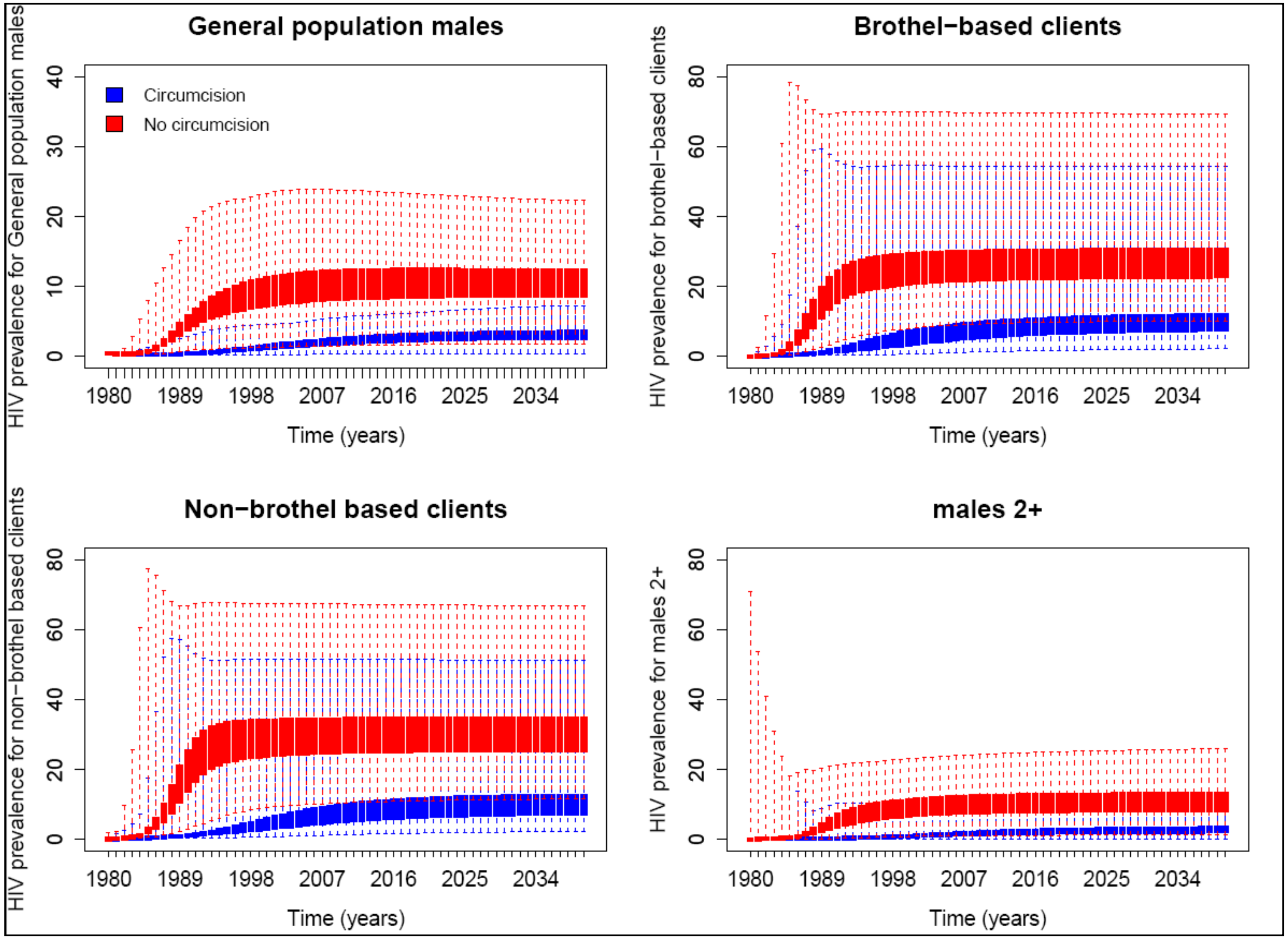


Figure 12a-12d: Epidemic profile for 8187 model fits showing the inter-quartile range and maximum and minimum HIV prevalence estimates for each of the respective male groups in the model, for scenarios in the presence and absence of male circumcision.

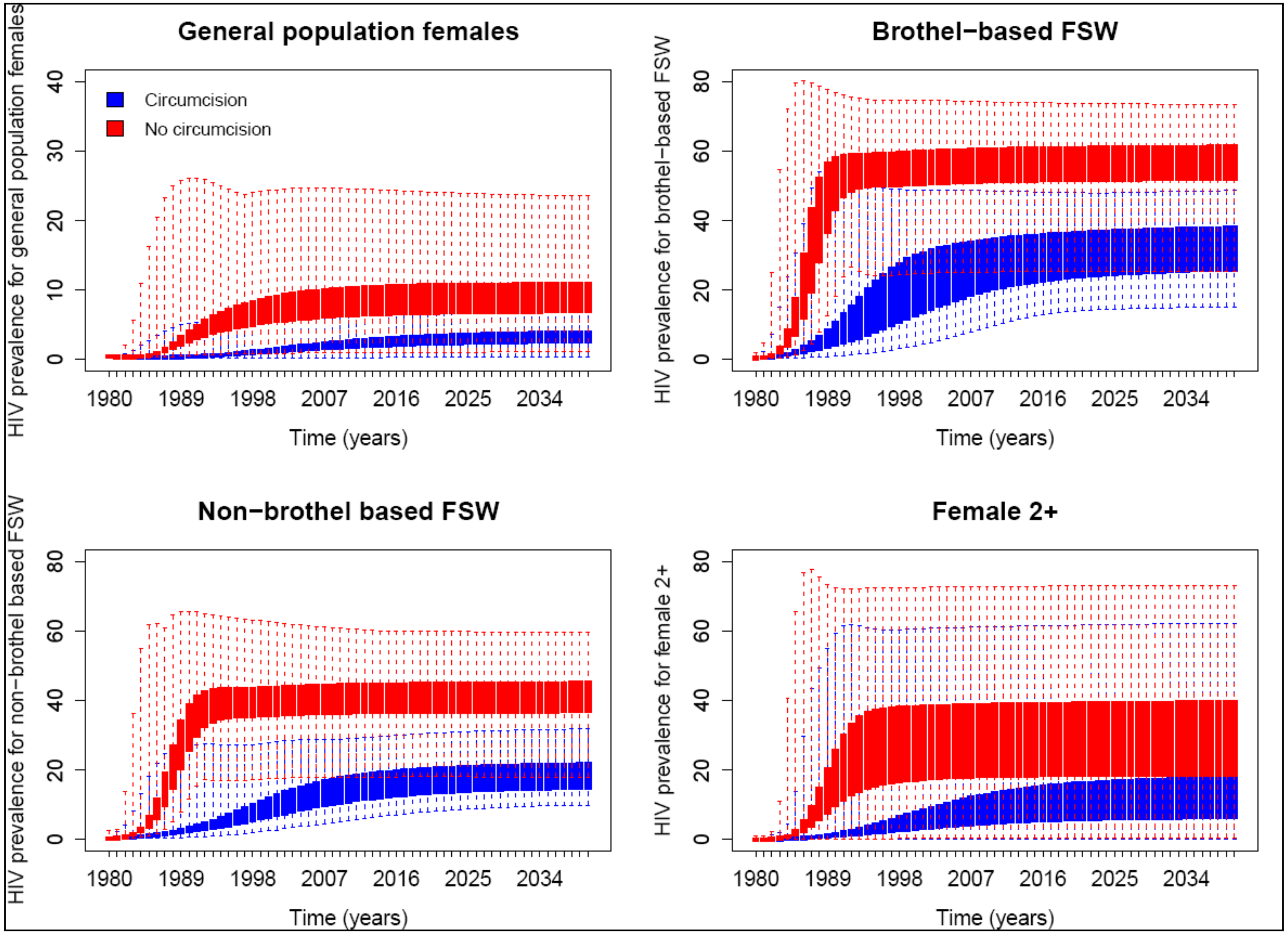


Figure 12e-12h: Epidemic profile for 8187 model fits showing the inter-quartile range and maximum and minimum HIV prevalence estimates for each of the respective male groups in the model, for scenarios in the presence and absence of male circumcision.

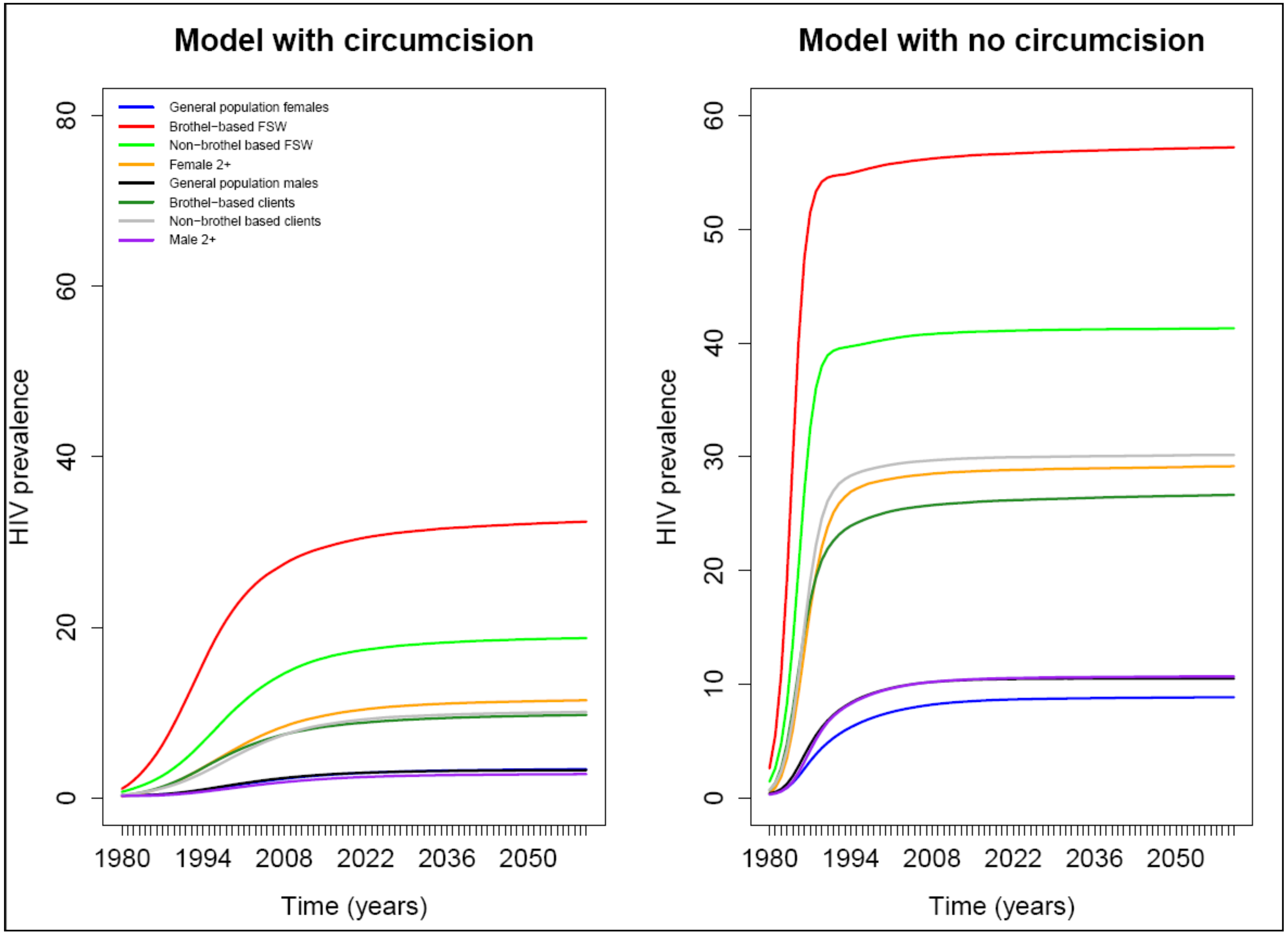


Figure 12.2 and 12.3: Epidemic projections for the median model fit for the scenarios with and without male circumcision for the population subgroups across West Africa

Appendix 13

A full acknowledgement is made to the publishers of this article for the free reuse and inclusion in this thesis: AIDS 13 November 2013 – Volume 27 – Issue 17 – p2679-2689. Wolters Kluwer Health Lippincott Williams & Wilkins.

Can the UNAIDS modes of transmission model be improved?: a comparison of the original and revised model projections using data from a setting in west Africa

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Objective: The UNAIDS modes of transmission model (MoT) is a user-friendly model, developed to predict the distribution of new HIV infections among different subgroups. The model has been used in 29 countries to guide interventions. However, there is the risk that the simplifications inherent in the MoT produce misleading findings. Using input data from Nigeria, we compare projections from the MoT with those from a revised model that incorporates additional heterogeneity.

Methods: We revised the MoT to explicitly incorporate brothel and street-based sexwork, transactional sex, and HIV-discordant couples. Both models were parameterized using behavioural and epidemiological data from Cross River State, Nigeria. Model projections were compared, and the robustness of the revised model projections to different model assumptions, was investigated.

Results: The original MoT predicts 21% of new infections occur in most-at-riskpopulations (MARPs), compared with 45% (40–75%, 95% Crl) once additional heterogeneity and updated parameterization is incorporated. Discordant couples, a subgroup previously not explicitly modelled, are predicted to contribute a third of new HIV infections. In addition, the new findings suggest that women engaging in transactional sex may be an important but previously less recognized risk group, with 16% of infections occurring in this subgroup.

Conclusion: The MoT is an accessible model that can inform intervention priorities. However, the current model may be potentially misleading, with our comparisons in Nigeria suggesting that the model lacks resolution, making it challenging for the user to correctly interpret the nature of the epidemic. Our findings highlight the need for a formal review of the MoT.

AIDS 2013, 27:2623–2635

Keywords: HIV epidemic, mathematical modelling, most-at-risk-populations, Nigeria, UNAIDS

Mathematical modelling has helped increase our understanding of the HIV epidemic and played a key role in decision-making [1–4]. UNAIDS developed a series of stand their current epidemic [5–7]. The Modes of Transmission (MoT) model is one such model. It is a deterministic static compartmental model, used to estimate the distribution of new HIV infections in

Introduction

simple mathematical models, to help countries under-

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different population subgroups based on information about their current HIV prevalence and behavioural patterns. So far, 29 countries have analysed their HIV epidemic using the MoT model [8], with the results being used to help guide interventions [8,9].

The MoT model divides the population into subgroups that represent the percentage of individuals in the population who ascribe to a certain type of behaviour or identity, related to their 'risk' of acquiring HIV. In this instance, 'risk' is dependent on: the degree of sexual contact or injecting drug use activity that is exchanged with their partner group; the HIV prevalence in their partner group; the probabilityof acquiring HIV through a single contact with that partner group and the percentage of sexual or injecting acts which are protected (through condom use or sterile needles). Some individual's have multiple partner groups, but in the MoT, acquisition of HIV is only characterized through the partner group with the highest transmission risk. The HIV transmission pathways were all predefined by the model's authors.

Although this compartmentalization of the population is a standard approach in deterministic modelling, most deterministic models usually take into account multiple exposures, unlike the current MoT. The predefined structure for the MoT may be overly simplistic, especially in settings with important heterogeneities within subgroups. For example, in many settings there are distinct subgroups of sex workers, such as 'brothel-based' and 'street-based', that have different numbers of sexual partners and condom use, and so potentially different HIV risks [10].

Although there are many benefits to having a relatively simple MoT model, there is the risk that the model simplicity and inherent assumptions about patterns of sexual mixing, produces misleading findings [8]. The aggregation may also lead to a masking of key population subgroups that are particularly vulnerable to HIV infection, which should be targeted by HIV programming interventions. There is also a danger of it becoming a 'black box' process [11], in which the findings are taken at face value, without sufficient appreciation of how the underlying assumptions and simplifications may influence the incidence projections obtained.

Given the widespread use of the MoT to inform decision making, the aim of this study was to compare the MoT model projections for Cross River, a Nigerian state with a low-level generalized HIVepidemic of 8%, with a revised MoT model that incorporates additional heterogeneity and updated parameters. An intermediate model, which employs the revised model structure, but retains the original model parameters, is used to illustrate the incremental effect of incorporating additional model complexity, and revising and updating the parameter estimates.

Methods

The modes of transmission model

The model is designed to calculate the number of new HIV infections within a 12-month period among different population subgroups, based on the current distribution of infections in the population. Biological and behavioural surveillance data, supplemented by the broader scientific literature, are used to develop settingspecific model input parameters.

To estimate the risk of infection for a susceptible individual, the model uses an established mathematical equation that estimates the probability of HIVacquisition (appendix C, http://links.lww.com/QAD/A383), if the individual has a given number of sexual partners from a particular (population) subgroup and a specified number of sex acts with those partners [9]. An estimate of the number of incident infections is generated by multiplying the risk of infection by the number of susceptible individuals at risk in a subgroup. In the original MoT model, the total adult population (commonly taken to be 15–49 year olds) is divided into 11 subgroups and disaggregated by sex. HIV transmission probabilities are per act estimates and are based on the published literature [12]. The presence of sexually transmitted infections

(STIs) in the partner group adds a multiplicative effect to an individual's risk of HIV acquisition [13]. The partially protective effect of male circumcision is incorporated [12]. Finally, the model is calibrated, by adjusting the HIV prevalence in certain risk groups to the antenatal care (ANC) prevalence for that particular setting, so the weighted average across all risk groups (men and women) matches the HIV ANC prevalence. The model therefore enables estimates for the total percentage of new infections in different population subgroups to be calculated.

'Original' modes of transmission modelling analysis for Cross River state

An MoT modelling analysis [14], was conducted in 2009 in Cross River state, located in the south of Nigeria with a population of 2.1 million aged 15–49 years. Survey data from 2008 estimates an ANC HIV prevalence of 8%, making Cross River the fifth highest HIV prevalence state in the country [15]. For this study, state level data were used where available, and otherwise data from states in the same geopolitical zone or national-level data were applied. The size of the population was based on the 2008 Demographic Health Survey [16] and 2007 National HIV/AIDS and Reproductive Health Survey Plus (NARHSþ) [17]. The STI prevalence in different population subgroups was based on survey data on the reported presence of unusual genital discharge or genital ulcer in the past 12 months [10,16]. Total numbers of sex acts reported by one population subgroup were not equalized with their partner group. The original MoT indicates that sex acts between clients and FSW should be equal, in this case however this instruction is not followed. This limitation in the MoT may lead to an overestimate of HIV infections for some subgroups and an under-estimate for others. Full details of the methods and data sources used are in Table 1, Appendix D, http://links.lww.com/QAD/A383. The behavioural and biological parameter tables for the model are provided in Appendix E, http://links.lww.com/QAD/A383. The original model was calibrated to ANC prevalence for Cross River state, 8%, for both male and female groups.

Revision of the modes of transmission model for Cross River state

The MoT model was revised to incorporate additional heterogeneity using data from the NARHS 2007þ [17], HIV/AIDS Integrated Biological and Behavioural Surveillance Survey 2007 [10] and wider literature. Figure 1 summarizes the revisions made, showing how some of the original subgroups were divided into smaller subgroups or fed into different subpopulation categories.

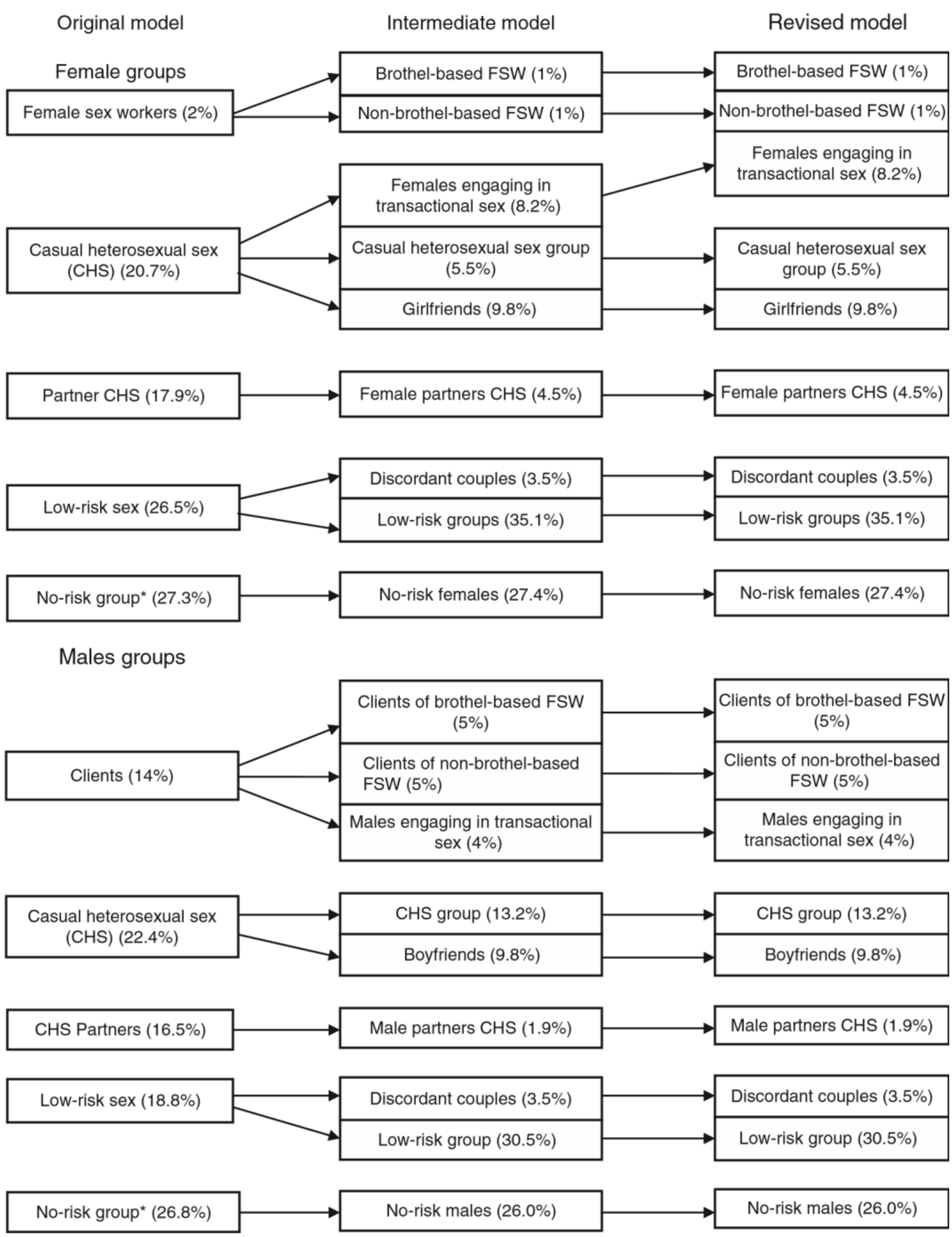


Fig. 1. Schematic overview illustrating the structural changes to the modes of transmission (MoT) model, for the original model, intermediate and revised versions (including revisions to subgroup sizes for each model). No risk individuals are those who report no sexual intercourse or injecting drug use in the past 12 months. The figure does not include MSM, IDUs and any of the partners of the most-at-risk-populations (MARPs) groups, as these were not revised.

Based upon a review of the literature, the revised model included a new group called ‘women involved/engaged in transactional sex’ to represent women ‘who have sex for cash, gifts or favours’ but who would not necessarily identity themselves as ‘sex workers.’ Research from Nigeria indicates that this type of behaviour is prevalent [18–20]. The subgroup is formed from the ‘casual heterosexual sex (CHS)’ group in the original model, although their involvement in the transactional exchange of money for sex and contact with multiple sexual partners place them at higher risk of HIV infection than those in the CHS group. In addition we subdivided the ‘sex worker’ group into ‘brothel-based’ and ‘nonbrothel-based’ FSWs because most surveys in Nigeria distinguish FSWs in this way. We established separate FSW client groups for each.

Revised size estimates for the subgroups from the original model led to an increase in the estimated size of the ‘lowrisk’ population for women from 26.5 to 38.6% and men ‘from 18.8 to 34%, with estimates for ‘partners of those engaged in casual heterosexual sex (partners CHS)’ revised down because the NARHS 2007þ survey suggested the percentage of individuals engaging in ‘CHS’ is lower than in the original model. Individuals who were originally in the ‘partners CHS’subgroup were redistributed to the ‘low-risk’ group in the revised MoT. In the original model, those in the CHS subgroup were defined as individuals who report ‘nonmarital’sex, but in the revised model we reclassified them as individuals who report ‘more than one marital or nonmarital partner’ in a 12-month period [17], as many individuals have nonmarital relationships but do not have multiple partners. For individuals in nonmarital relationships with a single partner, we created additional subgroups called ‘boyfriend’ and ‘girlfriend’ relationships. The number of individuals receiving blood transfusions and medical injections was not revised.

The ‘low-risk’ group was divided into ‘discordant’ partnerships/couples, defined as heterosexual monogamous relationships in which one partner is HIV positive and the other HIV negative. The estimate for the size of this population is based on a previous study [21]. The remaining individuals in this subgroup are considered as being very ‘low-risk’. They represent sexually active individuals in the population who are in stable relationships in which both partners are assumed to be either HIV negative or HIV positive. The prevalence in the ‘low-risk’ group may be adjusted to match the ANC prevalence in the setting, for model calibration purposes, but with no new infections being attributed to this subgroup.

In the revised model, the total number of sex acts offered by a subgroup was balanced between partner groups by adjusting the number of partners (n) in the corresponding subgroup, while assuming the number of contacts per partner (a) was equal between groups. As there is more data available on the number of partners of brothel-based and street-based FSW, we used a triangulation method to calculate the number of partners their client groups have. For the CHS groups, we used the estimate from the original MoTof two partners and 50 sex acts for men, and calculated the number of female CHS partners based on the assumption that they too have 50 sex acts with male partners.

The revised model was calibrated to an 8% HIV prevalence from ANC data and incidence projections were cross-referenced with projections (0.0025 for Nigeria) from the UNAIDS global report [22], which equates to approximately 5000–5500 new infections.

Modes of transmission: intermediate model

An intermediate MoT, with the revised model structure and original parameter estimates was developed. This model contains the revised population estimates for the stratified subgroups from the revised model but maintains the same behavioural and epidemiological estimates as the original model. Table 1(a) compares and summarizes the behavioural parameter estimates across all three models and Table 1(b) the epidemiological parameter estimates. As in the original model, for the intermediate model, balancing of sex act numbers between subgroups was ignored.

The revision to the model structure allows for a comparison of model projections between the original and revised MoT. As the intermediate model uses the revised structure and revised population size estimates it is not possible to draw a direct comparison of the effect of changing the structure because of changes to population sizes and additional risks. However, it does allow for an overview of additional heterogeneity present within individual subgroups. The comparison between the intermediate and revised model is more direct, because only parameter estimates are updated. Therefore, the effects of disaggregating subgroups and including different risk behaviours is shown here.

Categorisation of population subgroups

To assess the distribution of HIV infections in different key population subgroups from an HIV programming perspective, we grouped the population into categories in order to compare the findings from the original versus the revised MoT.

In the original model we classified sex workers, clients, men who have sex with men (MSM) and injecting drug users (IDUs) as 'most-at-risk-populations' (MARPs). In the revised model the MARPs included the brothel-based FSW, non-brothel-based FSW, MSM, IDUs, FSW clients and men and women involved in transactional sex. Subgroups that form partnerships with MARPs were termed 'partners of MARPs', these included female

Table 1. (a) Behavioural parameter estimates for the original, intermediate and revised MoT models.

Population subgroup	*Revised model stratification*	*Percentage of total population*		*Number of partners per year*			*Number of acts of exposure per partner per year*			*Percentage of acts protected* (%)*		
		Male (%)	Female (%)	Original MoT	Intermediate MoT	Revised MoT	Original MoT	Intermediate MoT	Revised MoT	Original MoT	Intermediate MoT	Revised MoT
Injecting drug users (IDUs)		0.32	0.27	2			224			79.0		
Sexual partners of IDUs		0.26	0.31	1			80			26.1		
Female sex workers (FSWs)	Original MoT		2.00	175			4			61.6		
	Brothel-based		1.00		175	250		4	4		61.1	65.5
	Non-brothelbased		1.00		175	120		4	4		61.1	65.5
	Transactional sex (females)		8.70		2	6		50	20		46.8	28.0
Clients of FSWs	Original MoT	14.0		5			20			61.6		
	Brothel-based	5.00			5	50[#]		20	4		61.1	65.5
	Non-brothelbased	5.00			5	24[#]		20	4		61.1	65.5
	Transactional sex (males)	4.40			2	11[#]		50	20		46.8	28.0
(long-term) Female partners of clients	Original MoT		4.76	1			80			26.1		

	Brothel-based clients		1.70									
	Non-brothelbased clients		1.70									
	Transactional sex (males)		1.50									
Men who have sex with men (MSM)		0.9		3			38			56.3		
Female partners of MSM			0.22	1			80			26.1		
Casual heterosexual sex (CHS)	Original MoT	22.4	20.7	2			50			46.8		
	Casual heterosexual sex (males)	13.2				2			50		46.8	46.8
	Casual heterosexual sex (females)		5.50			4.8#						
	Boy/girlfriend relationships (males)	9.83			2	1#		50	80			26.1
	Boy/girlfriend relationships (females)		9.81			1#						
Partners of CHS	Original MoT	16.5	17.9	1			80			26.1		
	Revised MoT	1.87	4.49									
Low-risk heterosexuals	Original MoT	18.8	26.5	1			80			26.1		
	Low-risk	29.7	33.4									
	Discordant couples (positive partners)	1.75	1.75									
	Discordant couples (negative partners)	1.75	1.75									
No risk	Original MoT	26.8	27.3	0			0			-		
	Revised MoT	26.0	27.4									
Medical injections		35.8	34.9	1.8			1			99.0		
Blood transfusions		1.00	1.00	1			1			99.0		

Estimate for number of partners derived by balancing with corresponding partner group

Population subgroup	*Revised model stratification*	*Percentage of total population*		*HIV prevalence*			*STI prevalence*		
		Male (%)	Female (%)	Original MoT	MoTIntermediate	Revised MoT	Original MoT	MoTIntermediate	Revised MoT
Injecting drug users (IDUs)		0.32	0.27	3.1%			7.5%		5.5%
Partners of IDUs		0.26	0.31	8.0%	8.0%	4.3%	NA		
Female sex workers (FSWs)	Original MoT		2.00	23.4%			12.6%		
	Brothel-based		1.00		23.4%	27.8%		12.6%	4.6%
	Non-brothelbased		1.00		23.4%	18.9%		12.6%	2.8%
	Transactional sex (females)		8.70		9.0%	3.2%		7.6%	3.3%
Clients of FSWs	Original MoT	14.0		10.4%			7.6%		
	Brothel-based	5.00			10.4%	10.3%		7.6%	3.3%
	Non-brothelbased	5.00			10.4%	10.3%			
	Transactional sex (males)	4.40			9.0%	7.4%			
(long-term) Female partners of clients	Original MoT		4.76	8.0%			NA		

*Sterile injecting equipment or condoms used

		Brothel-based clients		1.70		
		Non-brothelbased clients		1.70		
		Transactional sex (males)		1.50		

Table 1. (b)

Epidemiological parameter estimates for the original intermediate and revised MoT models.

Men who have sex with men (MSM)		0.9		2.8%			11.0%	11.0%	1.9%
Female partners of MSM			0.22	8.0%	8.0%	4.3%	NA		
Casual heterosexual sex (CHS)	Original MoT	22.4	20.7	9.0%			7.6%		
	Casual heterosexual sex (males)	13.2			9.0%	3.5%		7.6%	0.2%
	Casual heterosexual sex (females)		4.50		9.0%	3.5%		7.6%	0.2%
	Boy/girlfriend relationships (males)	9.83			9.0%	2.1%		7.6%	0.2%
	Boy/girlfriend relationships (females)		9.81		9.0%	1.3%		7.6%	0.2%
Partners of CHS	Original MoT	16.5	17.9	8.0%	8.0%	4.3%	NA		
	Revised MoT	1.87	4.49		8.0%	4.3%			
Low-risk heterosexuals	Original MoT	18.8	26.5	8.0%			3.6%	3.6%	0.2%
	Low-risk	29.7	33.4		8.0%	8.0%			
	Discordant couples (positive partners)	1.75	1.75		100%	100%			
	Discordant couples (negative partners)	1.75	1.75		0%	0%			
No risk	Original MoT	26.8	27.3	6.0%	6.0%	7.9%	0%		
	Revised MoT	26.0	27.4		6.0%	3.8%			
Medical injections		35.8	34.9	8.0%			NA		
Blood transfusions		1.00	1.00	8.0%			NA		

Comparison of behavioural (Table 1a) and epidemiological (Table 1b) parameter estimates and population sizes for original MoT, intermediate MoT and revised MoT. For instances in which model revisions were made, the table represents the three model estimates as respective column headings. Population size estimates are depicted in blue, with original model estimates (no stratification) as the top row shaded in lighter blue. Figures in white boxes, are those in which no stratification within the subgroup was made between the original, intermediate and revised models and for which parameter estimates are also unchanged. Light grey squares represent those parameter estimates from the original model, which are conserved in the intermediate and revised models, despite additional stratifications being applied to certain subgroups. Finally, dark grey squares correspond to revised parameter estimates, established through the stratification of subgroups in the intermediate and revised models.

partners of MSM, sexual partners of IDUs and regular female partners of FSW clients in the original model. For the revised model, regular female partners of men involved in transactional sex were additionally included in this category. Subgroups not directly connected through sexual or injecting contact with high or medium-risk groups were categorized as 'general population' groups. In the original and revised model, these included the lowrisk group, the CHS subgroup and partners of CHS subgroup. In the revised model, the 'boyfriend' and 'girlfriend' subgroups were also included as 'general population' groups. Finally, discordant couples, who are not explicitly recognized in the original model were assigned their own category in the revised MoT to assess the importance of this group for HIV programming purposes.

Evaluation of parameter estimates and methods for sensitivity analysis

In order to assess the robustness of model projections a detailed sensitivity analysis was conducted, for all parameter estimates. Latin Hypercube Sampling was used to generate 10000 random parameter sets using uniform distributions for all parameters. For the majority of behavioural and epidemiological parameters estimated from surveys within the Nigerian setting (either state level or geopolitical zone) 95% CI from the survey data were used as uncertainty bounds. For parameter estimates obtained through alternative data sources or from the wider literature, we sampled each parameter relatively 50% to reflect the higher levels of uncertainty. Parameter sets were included if the HIV prevalence projection fell within the 95% CI uncertainty range for the ANC estimate, obtained through the 2008 sentinel surveillance survey which collected HIV data from 300 women in Cross River. Additional sampling details for all parameter estimates are provided below in Table 2.

Table 2. Description of sampling methods used for the modes of transmission revised model sensitivity analysis, including data sources and rationale.

Parameter	Method of sampling uncertainty
Population sizes	Population size estimates were sourced from the National HIV/AIDS and Reproductive Health Survey Plus (NARHSþ) surveys for general population subgroups. Details on high-risk group population estimates and additional calculations are contained in appendix D, http://links.lww.com/QAD/A383, with most of these estimatesconservedfromtheoriginalmodel.Owingtothehighlevelsofuncertaintyinthesizeofthepopulation estimates we sampled each parameter relatively 50%.
HIV prevalence	For all HIV prevalence values estimated from survey data for Cross River state or regional estimates from NARHSþ 2007, 95% confidence interval (CI) intervals were generated and applied in the sensitivity analysis. These included all risk-groups with the exception of women engaging in transactional sex and their partners, clients of brothel-basedandnon-brothel-basedfemalesexworkers(FSW)andtheirregularfemalepartners.Becauseofthe greater level of uncertainty in these estimated values each parameter was varied 50% relative to its original value.
STI prevalence	Allestimatesweregeneratedfromsurveydataforwhich95%CIwereavailable.Forgeneralpopulationgroups,the estimate was taken from the 2003 sentinel survey for individuals tested for syphilis. From this, 95% CI were derived based on the sample size for the south-south geopolitical zone. Sexually transmitted infection (STI) prevalence estimates for high-risk groups and clients were generated from the Integrated Biological and Behavioural Surveillance Survey (IBBSS) 2010 for reported genital ulcer/sores. This estimate was selected because no serological data were available and as it was considered that genital ulcers/sores present as more visible forms of STIs and are more likely to reflect the presence of syphilis. 95% CI were generated from the data to reflect the uncertainty in these estimates.
Number of partners and number of sex acts with individual partners per year	To allow for the uncertainty in the number of partners and number of sex acts with each partner for individual subgroups, all parameter estimates were varied 50%. This was to reflect the uncertainty in these estimates and the fact that some estimates were generated through triangulation methods based on population size estimates, whereas others were based on assumptions from the original MoT model.
Condom usage	EstimatesforcondomuseforclientsofbrotheI-basedandnon-brothel-basedFSWcomefromtheDHSformenwho report ‘payment for sex’. The same value was assumed for brothel-based and non-brothel-based FSW, as FSW in the Integrated biological and behavioural surveillance survey (IBBSS) survey report 100% condom use and this estimate was deemed to be unrealistic. Estimates for condom use in men who have sex with men (MSM) and sterile needle use for injecting drug users (IDUs) are taken from the IBBSS 2007 and all other subgroup estimates were generated using appropriate estimates from the NARHS 2007þ, taking 95% CI on each occasion to generate uncertainty ranges for data sampling.

Results

Comparisons of the original and revised modes of transmission model projections

Figure 2(a)–(c) show the projected overall distribution of HIV infections produced by the original, intermediate and revised MoT models respectively. Results from the original model show 73% of infections occur in general population subgroups, compared with 21% in MARPs. HIV prevalence in the population is estimated to be 8% and the rate of HIV infection in the 15–49 population, 0.005 per year (500 infections per 100 000 population).

Following revisions to the MoT model structure through the introduction of additional subgroups, model projections are modified. The new ‘discordant couples’ group, are projected to account for 21% of all infections. The percentage of infections distributed amongst MARPs remains similar to the original model, partly as a result of maintaining the same parameter estimates. The percentage of infections in the general population subgroups is still significant, with 50% of infections occurring within this category. The overall population HIV prevalence for this model is 9.4%, 1.4% higher than the ANC HIV prevalence, with an HIV incidence rate of 0.0059 per year. The higher prevalence and incidence is largely due to infections being attributed to the ‘low-risk’ group, because of their large population size, despite the stratification of discordant partnerships away from this group.

Figure 2(c), shows the revised MoT model, including all parameter updates. The projected distribution of incident HIV infections is significantly different, with approximately 45% of infections nowoccurring amongst MARPs. In the revised model individuals in the low-risk group are assumed not at risk from transmitting or acquiring HIV. This lowered the number of infections in

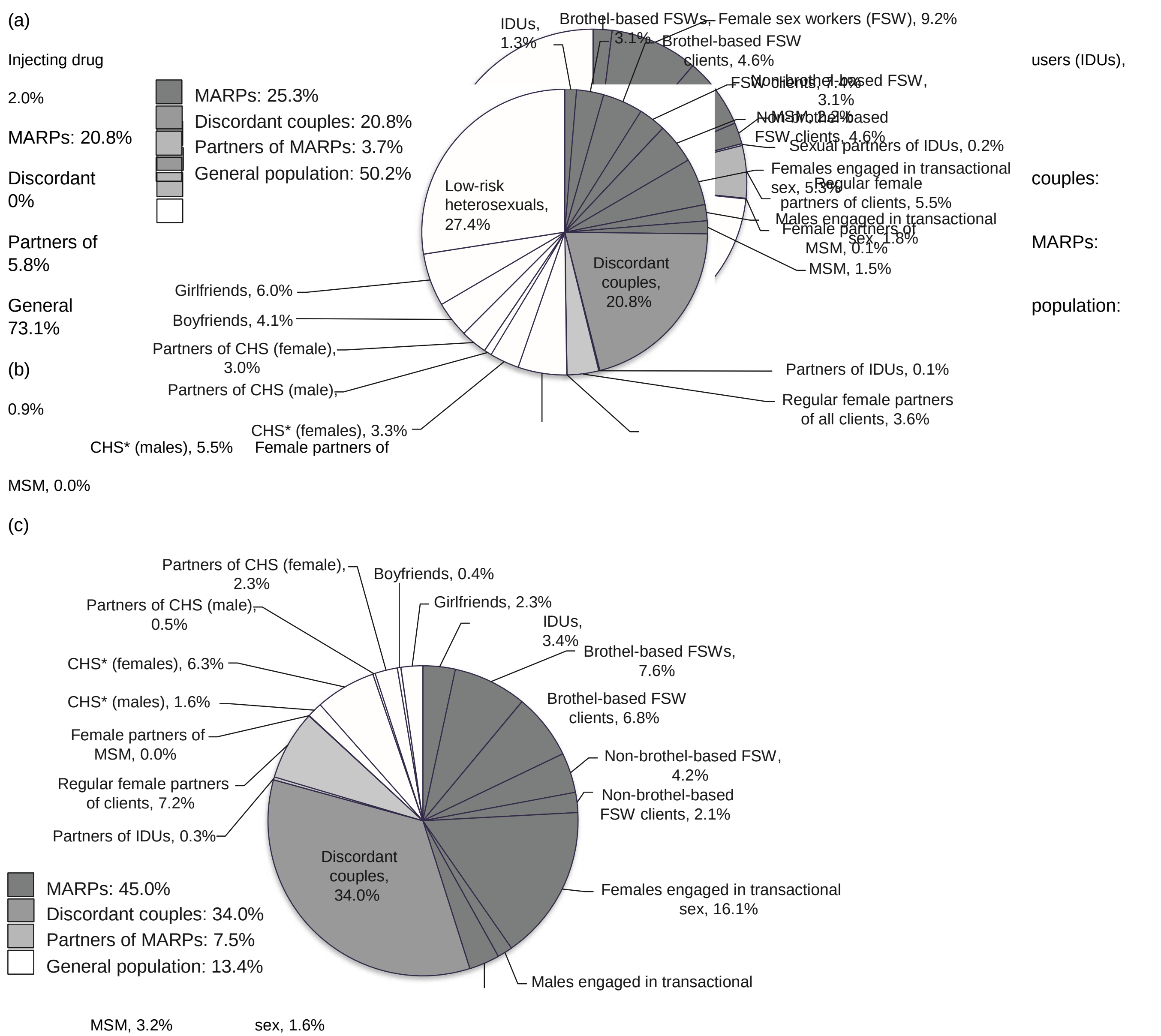


Fig. 2. Comparison using the three different modes of transmission (MoT) models for the projected distribution of new HIV infections in the population. (a) shows results from the original MoT model, (b) displays results from the intermediate MoT model and (c) illustrates modelling projections for the revised MoT model. CHS, casual heterosexual sex.

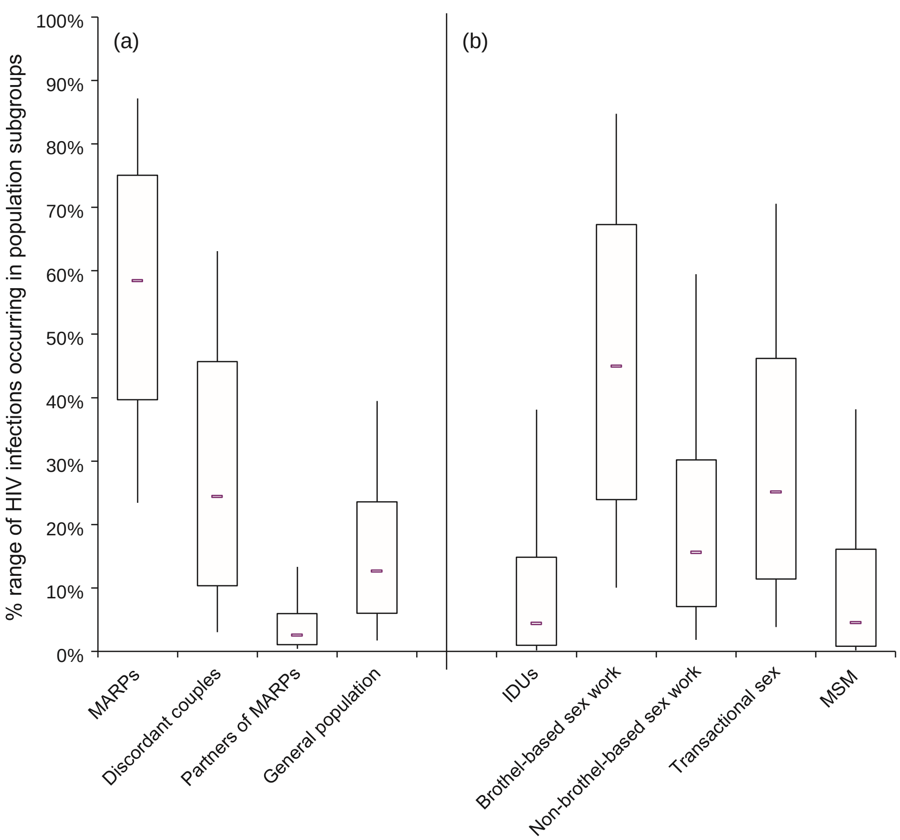
the population, resulting in a proportional redistribution to other subgroups, with discordant couples now accounting for 34% of infections instead of 21% in the intermediate model. The stratification and reparameterization of individuals involved in transactional sex, from the CHS group, is also important. We see that 23% of infections in the original MoT originate from casual heterosexual sex, whereas for the revised model the CHS and transactional sex groups combined contribute 25% of infections (with 16% arising from women engaging in transactional sex). The HIV prevalence for this scenario is 7.8% and the HIV incidence rate is 0.0031 per year.

Model sensitivity analysis

Figure 3 shows the distribution of infections amongst different subgroups as produced in the sensitivity analysis. In the revised MoT model, 18% of the sexually active 15–49 years old population were part of a MARP subgroup. Model projections suggest these groups contribute 40–75% (95% CrI) of incident HIV infections. This is in contrast to those in the general population subgroups which account for 6–24% (95% CrI) of new infections but make up 78% of the sexually active population. Interestingly, discordant couples, who constitute around 3.5% of the population, may contribute 10–46% (95% Crl) of total infections.

We also analysed the number of infections amongst each female sex worker (FSW) group with their respective client groups to explore the percentage of infections derived from each type of sex work, including transactional sex. Our sensitivity analysis suggests that brothelbased sex work (FSW and clients) contributes the most infections (24–67%, 95% Crl) amongst MARPs, likely to be as a result of high numbers of partners and moderate condom usage (65%). In addition, a high percentage of infections (11–46%, 95% Crl) also occur amongst those involved in transactional sex. In contrast, although still significant, fewer infections occur as a result of non-brothel-based sex work (7–30%, 95% Crl), IDUs (1–15%, 95% Crl) and MSM (1–16%, 95% Crl).

Results from the original modelling analysis in Cross River state concluded that the HIV epidemic generalized in nature, with the highest percentage of infections occurring through heterosexual sex amongst persons in the general population and that the majority of infections can only be curbed by targeting interventions towards general population subgroups [14].



Following model revisions to

incorporate additional population subgroups, the conclusions about the distribution of new infections have changed substantially. The explicit inclusion of discordant couples into the model helps illustrate the burden of new infections that are likely to occur in these individuals. The incorporation of updated parameter estimates into the fully revised model, produces an epidemic profile with a significantly higher percentage of infections in MARPs, compared with the original modelling analysis. This more plausible scenario is due largely to the removal of the implicit assumption that all low-risk individuals have some risk of acquiring HIV, which results in high numbers of new infections occurring in the 'low-risk' group.

The results from the sensitivity analysis indicate that infections generated through brothel-based sex work in both FSWand their clients may be an important source of infections in this setting. However, with a high incidence of infections amongst this group, it is important to obtain better estimates of the size of the brothel-based FSW population. In the absence of more comprehensive mapping data, it is difficult to ascertain how accurate these projections are, as a smaller population may considerably lower this estimate. However, evidence from the modelling shows that continued surveillance and intervention programmes are essential for maintaining high rates of condom use and education amongst brothel-based FSW and their clients.

Transactional sex is also indicated to be an important source of new HIV infections, previously not included in the original MoT. Despite being well documented in the literature [23–27], until now mathematical models have rarely differentiated this as distinct from casual sex. However, identifying women engaging in transactional sex may be challenging because, while one-off sex acts may take place within this context, quite commonly it may be the principal motivation for on-going relationships with primary or secondary partners.

There are also challenges in identifying discordant couples. Discordant couples are often identified through ANC testing for women; however, this strategy relies on the attendance and willingness of the male partner to also test.

The high percentage of infections occurring in discordant partnerships illustrates the importance of identifying these individuals and providing effective prevention options – including condoms, early ART treatment and possibly pre-exposure prophylaxis treatment. The source of infection in a discordant couple also needs to be considered. Various studies indicate [10,28] the duration of time that women spend selling sex may be short, and similarly, it may well be that girls only engage in transactional sex for a limited duration of time, before getting married. Therefore, it is possible that many of the infections within discordant partnerships arise from infections acquired from previous partnerships [29].

Our results highlight both the challenge and importance of appropriately parameterizing the MoT model to a particular setting. The introduction of greater model complexity provides a more comprehensive and realistic insight into which population subgroups are most vulnerable to HIV infection. The original MoT report for the state suggested focusing on primarily the general public groups, while also continuing to target high-risk groups such as FSWs [30]. For Cross-River State, our findings suggest most new HIV infections will occur among MARPs, and so effective prevention strategies need to be delivered to these groups as a priority. However, there is a requirement for sufficient data to be available before using the revised model. As demonstrated by the intermediate MoTanalysis, unless more due care is taken in model parameterization, the user is likely to generate misleading results. In addition the results of the analysis should be used as a guide rather than a platform on which to inform policy, as cost-analyses and epidemiological reviews of the setting must also be taken into consideration.

The UNAIDS MoTremains an accessible and potentially a useful model that can inform intervention priorities in different settings. However, our findings suggest that the current model may produce misleading findings, especially in concentrated or low-level generalized HIV epidemic settings, such as Cross River. Our analyses for Nigeria illustrate that the current model may underestimate the importance of different vulnerable groups, including girls involved in transactional sex and will be most significant for less generalized HIV epidemic settings, although further research to explore this question for other settings is needed. Nevertheless, our findings point to the need for UNAIDS to formally review and revise the MoT model.

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N.B.: Contributed and resourced key data estimates for parameterization of model. Provided insight into story line, assisted in writing of all sections of article and reviewed final draft of article.

H.: Advised on storyline of article and provided insightsinto key messages. Reviewed multiple drafts including final draft of article.

O.: Advised and provided data sources for parameter-ization of model and provided key insights into the context of the setting to allow model structure development. Reviewed and provided feedback on final draft of article.

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Conflicts of interest

There are no conflicts of interest.

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Appendix 14

Factors Associated with Variations in Population HIV Prevalence across West Africa: Findings from an Ecological Analysis

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RESEARCH ARTICLE

Abstract

Background

Population HIV prevalence across West Africa varies substantially. We assess the national epidemiological and behavioural factors associated with this.

Methods

National, urban and rural data on HIV prevalence, the percentage of younger (15–24) and older (25–49) women and men reporting multiple (2+) partners in the past year, HIV prevalence among female sex workers (FSWs), men who have bought sex in the past year (clients), and ART coverage, were compiled for 13 countries. An Ecological analysis using linear regression assessed which factors are associated with national variations in population female and male HIV prevalence, and with each other.

Findings

National population HIV prevalence varies between 0 4–2 9% for men and 0 4–5.6% for women. ART coverage ranges from 6–23%. National variations in HIV prevalence are not shown to be associated with variations in HIV prevalence among FSWs or clients. Instead they are associated with variations in the percentage of younger and older males and females reporting multiple partners. HIV prevalence is weakly negatively associated with ART coverage, implying it is not increased survival that is the cause of variations in HIV prevalence. FSWs and younger female HIV prevalence are associated with client population sizes, especially older men. Younger female HIV prevalence is strongly associated with older male and female HIV prevalence.

Interpretation

In West Africa, population HIV prevalence is not significantly higher in countries with high FSW HIV prevalence. Our analysis suggests, higher prevalence occurs where more men buy sex, and where a higher percentage of younger women, and older men and women

Competing Interests: The authors have declared that no competing interests exist.

have multiple partnerships. If a sexual network between clients and young females exists, clients may potentially bridge infection to younger females. HIV prevention should focus both on commercial sex and transmission between clients and younger females with multiple partners.

Background: HIV in West Africa

In Sub-Saharan Africa, an estimated 23 5 million people are infected with HIV [1]. Whilst in West Africa HIV prevalence levels tend to be lower, Nigeria with a population of 178 million has an HIV prevalence of 3.1% and is the country with the second highest number of individuals infected globally. HIV prevalence in other countries in the region ranges from 0.5–4% [2].

There is substantial variation in population HIV prevalence within and between countries, with the almost universal practice of male circumcision in the region likely to be playing a central role in limiting the scale of the epidemic [3]. However, there are also substantial differences in the levels of infection between West African countries, with Nigeria, Cote d'Ivoire and Cameroon having estimated female population HIV prevalence levels ranging from 4–7%, compared to 0.5–2% more generally across the region [4].

Throughout West Africa, HIV remains largely concentrated in the most vulnerable populations [5], with transmission between female sex workers (FSWs) and their male clients thought to have a central influence on the scale of the epidemic [6,7]. Although population HIV prevalence remains relatively low [8], infection levels among brothel-based FSWs are far higher, ranging from 16% to 37% [9,10]. In such 'concentrated' HIV epidemic settings, prevention programming is focused on FSWs and their male clients [10,11], with the latter conceived as the main 'bridging group' through which HIV spreads to the general population [12,13].

However, such a simple programmatic focus may fail to respond to the complexity of sexual networks. Evidence suggests that a diverse group of women may exchange sex for money or resources, ranging from more formal commercial sex work that tends to be targeted by HIV programmes, through to informal transactional exchange, which may be more hidden [14–16]. Similarly, men who pay or provide resources for sex are a heterogeneous group [17,18]. As well as men who purchase sex from FSWs, men may provide money and/or resources to other long term and/or occasional sexual partners [19,20]. Multiple sexual partnerships are an important risk factor for HIV infection, if condoms are not used consistently [17,21]. Therefore, it is important to gain a clearer understanding of the relative epidemiological importance of commercial sex, versus the less visible dynamic of casual sex, which may or may not have a transactional element.

This paper presents the findings from an ecological analysis that explored whether the variations in population HIV prevalence observed across West Africa are associated with variations in the extent of formal commercial sex work, and/or the degree to which women and men of different ages report having multiple sexual partnerships in the past year. As the provision of anti-retroviral therapy (ARV) will also increase life expectancy (and so could potentially contribute to higher HIV prevalence levels), we similarly explore whether the variations in HIV prevalence may be associated with variations in national ARV coverage levels.

Methods

A review of demographic health surveys (DHS) was used to compile recent epidemiological and behavioural data on patterns of sexual behaviour and levels of HIV infection for 2010– 2014 amongst members of the general population. Most data were available from 13 West African countries. No DHS data were available for Ghana or Guinea Bissau and therefore these countries were excluded from analyses. A 2013 preliminary report for Gambia was available but contained only data on sexual behaviour and no HIV prevalence data. Data on brothelbased FSWs, were sourced from publications published after 2010 from regional sites within country settings. We included data on brothel-based FSWs only, since this group was easier to identify and categorise from the literature (S1 File).

For each country we extracted the most recent national estimates of the population prevalence of HIV among men and women nationally, and in urban and rural areas. Where available, we also extracted population data on the percentage of younger (15–24) and older (25– 49) males and females reporting 2 or more (2+) partners in the past year (non-sexually active individuals were also included in the estimate), and the percentage of men reporting ‘paying for sex’ in the past year (assumed to be clients of FSWs). HIV prevalence among each subgroup was also compiled. In addition we collected data on condom use. Reported levels of condom use were relatively similar across countries for partnerships between key subgroups (S2 File) and FSW (also S1 File) and were therefore not considered within our analysis.

Estimates of the number of individuals receiving ART treatment (15–49) and the percentage of the population, 15 years or above who were HIV positive, were used to calculate the percentage of HIV infected people receiving ART treatment (S3 File). Population size estimates were sourced from the World Bank database [22], allowing for a 3% population growth rate (the average across West Africa).

Using this data a series of linear regression analyses were conducted in STATA 13 1 to identify which factors or independent variables were associated with the observed variations in HIV prevalence across West Africa. For this, a systematic approach was adopted where we explored whether factors hypothesised as being associated with population HIV prevalence (dependent variable), were significant. The independent variables included HIV prevalence in FSW and in clients, assuming that these factors may be independently associated with higher prevalence levels seen in the general population. We also assessed whether the percentage of younger and older males and females reporting 2+ partners in the past year, were significantly associated with higher HIV prevalence levels in the general population. The rationale for this being, that if there are more individuals with 2+ partners and they are at higher risk of acquiring HIV, then overall more infections will occur in the population, leading to higher levels of HIV prevalence.

In addition we explored whether HIV prevalence in younger and older females and males was associated with HIV prevalence in general population groups (of males and females). Here we wished to assess whether patterns of HIV observed in the younger age groups was correlated with general population prevalence, to understand patterns of infection and when infections are likely to occur. Finally, we analysed data on mean age at first sex to assess whether this variable was associated with the percentage of young males and females reporting 2+ partners.

Next we conducted regression analyses to explore patterns of association between different population subgroups. Our main objective for this was to explore whether the concept that HIV is predominantly transmitted along a pathway from FSWs, to clients to the general population is supported by empirical data. Firstly, we assessed whether HIV prevalence in FSWs and clients, treated as independent variables, was associated with HIV prevalence in subgroups of younger and older males and females with 2+ partners (dependent variables), i.e. does higher prevalence in these core groups directly impact on HIV prevalence in other high-risk subgroups. Next we assessed whether the percentage of clients in the population and younger and older males and females with 2+ partners were independently associated with HIV prevalence levels in FSWs, clients and younger and older males and females in the general population, i.e. are larger risk populations associated with higher prevalence levels in all groups.

Finally, we assessed the previous round of DHS data sets from 2003–2009 for countries across West Africa, to assess whether sexual behavioural patterns that pre-date the analysis have a delayed impact on HIV prevalence in the later surveys.

Results

There is substantial variation in population HIV prevalence across the region for men (0.4–

2.9%) and women (0 4–5.6%) respectively. Fig 1 shows how Cameroon, Cote d'Ivoire and Nigeria have the highest prevalence levels (4–5.6%) in general population females. For the remainder of countries, HIV prevalence tends to range from 0.4–2%. HIV prevalence is often higher in females than males and as expected, HIV prevalence is far higher among FSWs (15.9–36.7%).

Fig 2(A) shows the percentage of males reporting payment for sex (clients) in the past year and compares the older males with the younger male group. We see that overall, levels tend to be low across countries (0.4% - 4.8%) with similar levels of younger and older males reporting payment being generally relative to one another in each country.

Fig 2(B) compares the percentage of younger and older males who report 2+ partners in the past year. With the exception of Liberia and Nigeria, a higher percentage of older males consistently report 2+ partners in the past 12 months (p = 0.002). For the male group the age of sexual debut ranges from 18.1–23.6 years with a negative correlation (p = 0.001) between age at first sex and percentage of young males reporting 2+ partners (S4 File). This may account for the lower percentage of younger males reporting 2+ partners in those countries.

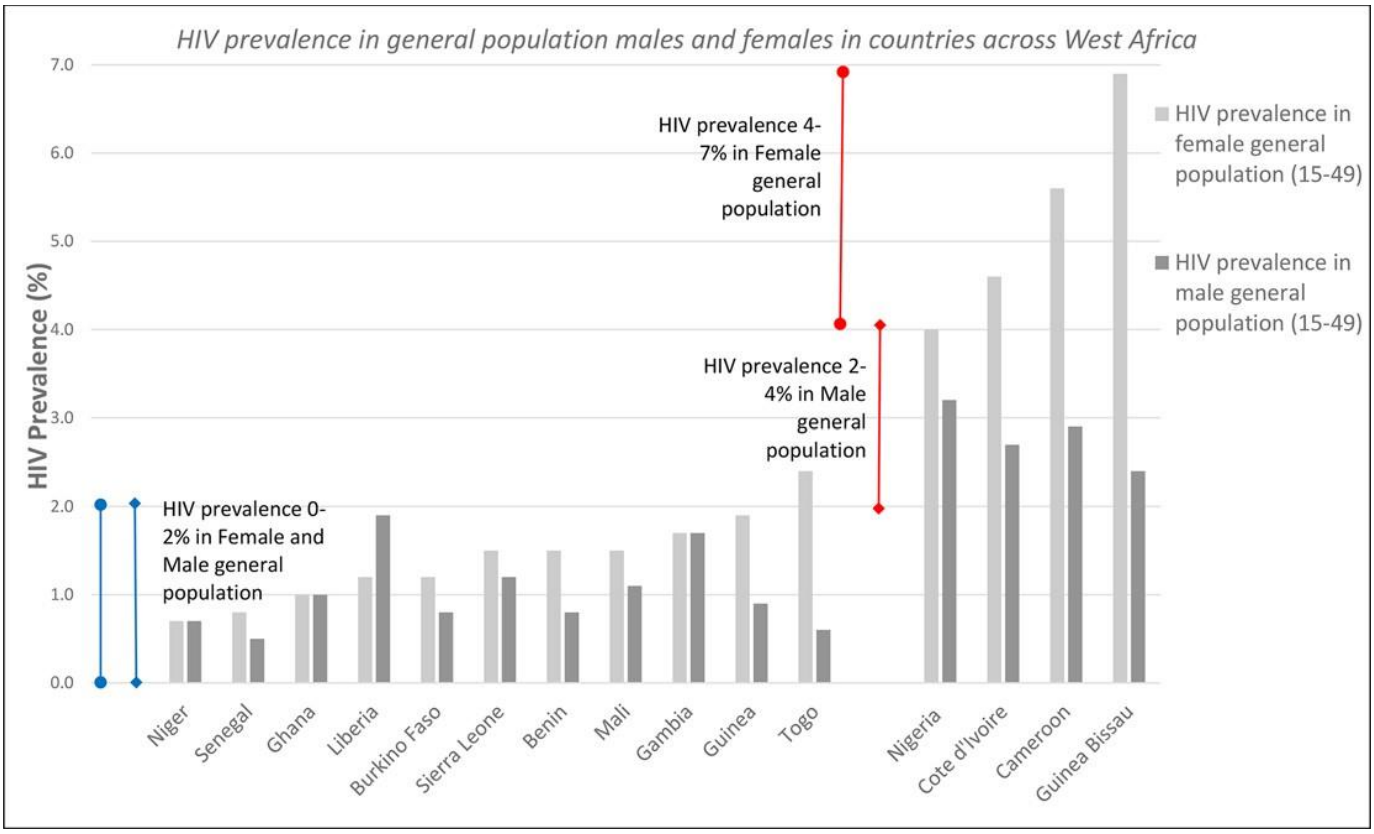

Fig 1. HIV prevalence data taken from DHS and UNGASS reports in West African settings from 2010–2014.

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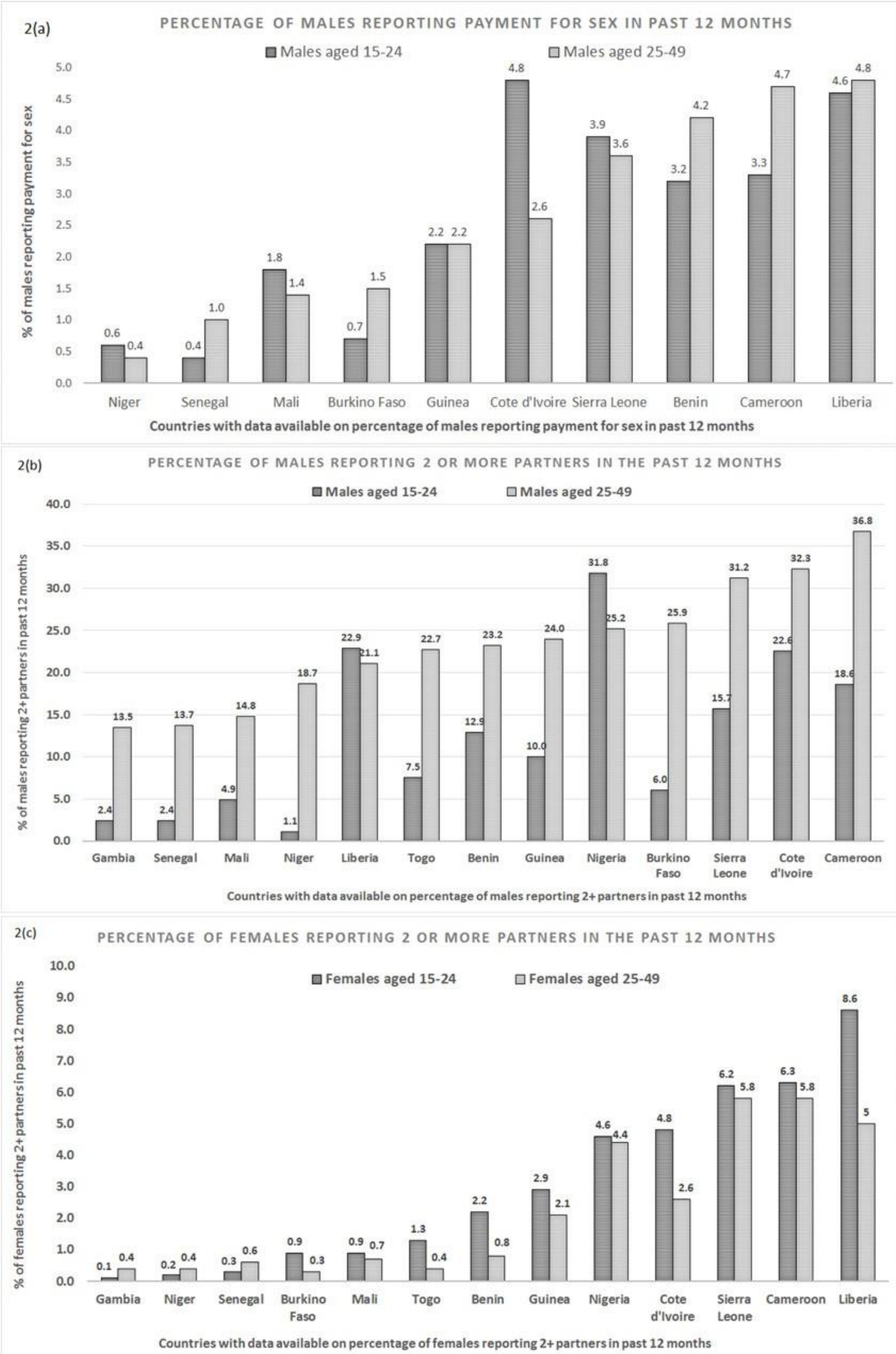

Fig 2. Fig 2(a): DHS Data from 10 West African countries, stratified by 15–24 and 25–49 year old males. Presented in ascending order of 25–49 year old males reporting payment for sex in the past 12 months, by country (2010–2014), data not available for Nigeria, Gambia and Togo. Fig 2(b): DHS data from 13 West African countries, stratified by age. Presented in ascending order of 25–49 year old males reporting 2 or more partners, by country. Fig 2(c): DHS data from 13 West African countries, stratified by age. Listed in ascending order of 15–24 year old females reporting 2+ partners in the past year, by country.

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A similar country pattern is seen amongst females (Fig 2(C)). However, for females the reverse pattern is seen, with a higher percentage of the younger group reporting 2+ partners compared to the older females. For younger females, age at first sex ranges from 15.9–19 years and is also negatively associated (Niger is removed as an outlier) with having 2+ partners ($p = 0.03$) (S4 File).

Exploring the potential influence of variations in ART coverage and national HIV prevalence

From the available ART data there is an increase in coverage of ART from 2008–2012. In 2008 Burkina Faso had the highest coverage rate with approximately 12.5% of HIV positive individuals receiving treatment and Niger the lowest rate at 2.1%. The mean coverage across countries was 6.7%. By 2012 the mean coverage had risen to 13.5%, ranging from 7.2%-23.4%. The results from the regression analysis (S3 File) indicate a weak negative relationship between HIV prevalence and the percentage of individuals on ART. This suggests that levels of ART treatment within countries are unlikely to be responsible for differences in HIV prevalence levels.

Associations between HIV prevalence among different-subgroups and male and female national, urban and rural HIV prevalence

Table 1 shows results from the linear regression analyses (p-values and R^2) that assessed whether variations in national, urban and rural population HIV prevalence are associated with variations in the HIV prevalence or size of different subgroups. Significant associations ($p<0$ 05) are shown in bold.

The findings show that brothel-based FSW HIV prevalence is not strongly associated with the HIV prevalence in any other population group. This is also true for the HIV prevalence in male clients. However, there is a significant association between the size of the client groups (in particular the younger group) and HIV prevalence in males at the urban and national levels.

As expected HIV prevalence among younger and older females and older males is significantly correlated with urban, rural and national HIV prevalence. However, there was only a very weak correlation between HIV prevalence among younger males and female HIV prevalence at a rural, urban or national level, and with only weak (ranging from $p = 0.03$ for rural males to $p = 0.07$ for urban males and at a national level) associations with male HIV prevalence levels.

Next, we considered the potential influence on variations in national, urban and rural HIV prevalence of the size of younger and older males and females reporting 2+ partners or buying sex (for men) in the past 12 months. For females, when all countries were included in the regression, the percentage of both younger and older females having 2+ partners was only significantly associated with urban male HIV prevalence. However, when the two outliers, Liberia and Sierra Leone, were removed from the analyses, the percentage of younger and older females reporting 2+ partners was significantly positively ($p<0.005$) associated with variations in national, urban, and rural HIV prevalence among males and females. For males, regression analysis for those including and excluding Liberia and Sierra Leone, gave similar results,

Table 1. Results from linear regression analysis. Associations between population subgroup HIV prevalence and relative population size, and levels of HIV infection in the general population (the number of countries included is shown in parenthesis).

	Variable (n = number of countries included in regression analysis)	Females						Males					
		Urban HIV prevalence		Rural HIV prevalence		National HIV prevalence		Urban HIV prevalence		Rural HIV prevalence		National HIV prevalence	
		R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p
Brothel based FSWs	HIV prevalence (10)	0.39	0.08	0.31	0.11	0.44	0.06	0.31	0.11	0.25	0.17	0.34	0.10
Brothel based FSWs	% with risk behaviour	na	na	na	na	na	na	na	na	na	na	na	na
Males reporting payment for sex in past year	HIV prevalence 15–49 (10)	0.001	0.95	0.06	0.53	0.001	0.95	0.001	0.94	0.05	0.57	0.003	0.88
Males reporting payment for sex in past year	% with risk behaviour aged 15–49	0.31	0.1	0.27	0.31	0.37	0.06	0.64	0.005	0.23	0.16	0.54	0.02
Males reporting payment for sex in past year	% with risk behaviour aged 15–24	-0.34	0.08	0.22	0.17	0.38	0.05	0.79	0.0005	0.28	0.12	0.58	0.01
Males reporting payment for sex in past year	% with risk behaviour aged 25–49	0.24	0.16	0.26	0.13	0.31	0.09	0.46	0.03	0.12	0.23	0.43	0.04
15–24 year old females	HIV prevalence (12)	0.44	0.01	0.76	0.0002	0.68	0.0001	0.85	0.0001	0.85	0.0001	0.87	0.0001
25–49 year old females	HIV prevalence (12)	0.93	0.0001	0.82	0.0001	0.97	0.0001	0.61	0.003	0.65	0.001	0.78	0.0001
15–24 year old males	HIV prevalence (12)	0.01	0.79	0.25	0.10	0.08	0.36	0.30	0.07	0.40	0.03	0.30	0.07
25–49 year old males	HIV prevalence (12)	0.79	0.0001	0.87	0.0001	0.95	0.0001	0.84	0.0001	0.83	0.0001	0.96	0.0001
15–24 year old females 2+ partners in past 12 months	% with risk behaviour (12)	0.21	0.12	0.22	0.13	0.30	0.06	0.49	0.01	0.18	0.16	0.44	0.019
25–49 year old females 2+ partners in past 12 months	% with risk behaviour (10)	0.64	0.005	0.88	0.0001	0.85	0.0002	0.76	0.001	0.78	0.0008	0.86	0.0001

15–24 year old males 2+ partners in past 12 months	% with risk behaviour (12)	0.23	0.11	0.46	0.02	0.43	0.02	0.80	0.0001	0.57	0.0047	0.74	0.003
25–49 year old males 2+ partners in past 12 months	% with risk behaviour (10)	0.31	0.09	0.70	0.003	0.56	0.01	0.83	0.0003	0.83	0.0003	0.82	0.0003

Data in bold for p<0.05. * Subgroup population size data for Liberia and Sierra Leone were both significant outliers in the regression analysis for females 15–24 and 25–49 with 2 or more partners in the past 12 months. We therefore performed a second round of analyses for the 2+ partner groups where these were excluded, to compare results across both the male and female subgroups with 2+ partners.

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showing that the percentage of both younger and older males reporting 2+ partners were significantly associated with HIV prevalence among all population groups.

Given the strong associations between population HIV prevalence and the size of the subgroups reporting 2+ partners in the past 12 months, we explored which factors were associated with variations in HIV prevalence among the different sub-populations considered. Tables 2 and 3 summarise these results. Table 2 shows the relationships between HIV prevalence in

Table 2. Results from regression analysis showing level of association (p-values) from the linear regression analysis for associations between levels of HIV prevalence in different subgroups.

Table 2 HIV Prevalence

(n = number of countries included in regression analysis)	Brothel Based Female Sex Workers	Men Who Report Payment for Sex (15–49)	15–24 year old females	15–24 year old males	25–49 year old females	25–49 year old males
Brothel Based Female Sex Workers (10)	-	-	-	-	-	-
Men Who Report Payment for Sex (15–49) (10)	0.16	-	-	-	-	-
15–24 year old females (12)	0.10	0.17	-	-	-	-
15–24 year old males (12)	0.86	0.22	0.01*	-	-	-
25–49 year old females (12)	0.002	0.29	0.01	0.62	-	-
25–49 year old males (12)	0.01	0.32	0.001	0.16	0.001	

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different groups. Firstly, there are no significant associations between the HIV prevalence in male clients (15–49) nor younger males and other population groups. FSW HIV prevalence is correlated with HIV prevalence among both older males and females, but not with any other groups. Finally, there is strong evidence for an association between HIV prevalence in young females (despite a lack of association in their young male counter-parts) and both groups of older males and females. As expected HIV prevalence in older males and females is correlated.

Table 3 explores the association between HIV prevalence in different sub-groups and their behaviour. The HIV prevalence in young females and in FSWs are associated with the size of both the younger and older group of male clients, and with the size of both younger and older groups of males and females who report 2+ partners in the past year. Yet, we see little evidence for an association with HIV prevalence in male clients or in the younger males reporting 2 + partners and the size of other population subgroups.

Exploring significant relationships between the sizes of population subgroups, we observe a strong association between the size of the older group of male clients and HIV prevalence among (i) FSWs, (ii) younger males and younger females. For the young male client group, there is only an association with HIV prevalence in FSWs and younger females reporting 2 +partners.

Table 3. Results from regression analysis showing the level of association (p-values) from the linear regression analysis between the size of different subgroups in the population and HIV prevalence amongst the subgroups. Significant relationships (p<0.05) are in bold text.

Table 3 HIV Prevalence

(n = number of countries included in regression analysis)	Brothel Based Female Sex Workers	Men Who Report Payment for Sex (15–49)	15–24 year old females	15–24 year old males	25–49 year old females	25–49 year old males
Men Who Report Payment for Sex (15–49) (10)	0.2	0.06	0.17	0.22	0.09	0.07
Men Who Report Payment for Sex (15–24) (10)	0.05	-	0.01	0.06	0.18	0.08
Men Who Report Payment for Sex (25–49) (10)	0.009	-	0.005	0.01	0.12	0.08
15–24 year old females 2 + partners (10)	0.004	0.29	0.003	0.19	0.001	<0.001
15–24 year old males 2+ partners (10)	0.05	0.28	0.001	0.01	0.05	0.003
25–49 year old females 2 + partners (10)	0.04	0.93	0.001	0.11	0.008	0.002
25–49 year old males 2+ partners (10)	0.001	0.06	0.04	0.48	0.003	0.008

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Assessing evidence for a time lag in HIV prevalence as a result of earlier high-risk sexual behaviour

Because of the apparent time lag in high-risk behaviours impacting on HIV prevalence at a later date, we also reviewed the data from earlier DHS surveys from 2003 to 2009. We compared this with the data used in the analysis from 2010 to 2014. Due to revisions in the questionnaire, several of the earlier questionnaires did not include questions on 2+ partnerships. Despite this, two key observations are evident from the six country studies that could be compared. Firstly, HIV prevalence across this period tended to remain fairly constant in countries with lower prevalence levels, with the exception of Liberia where prevalence fell from 1.8% to 1.2% in general population females. For the countries where HIV prevalence is higher, Cameroon and Cote d'Ivoire, prevalence also declined from 6.8% to 5.6% and 6.4% to 4.6%, respectively. For the five countries with data available on 2+ partners in both rounds, either a decline in this behaviour or no change was also observed. In Liberia, the percentage of young females reporting 2+ partners declined from 9.5% to 8.6% and in Cote d'Ivoire from 6.2% to 4.8%. For the remaining countries (Benin, Guinea and Sierra Leonne) there was no reported change in behaviour. Here, we see that declines in HIV prevalence seem to mirror changes in high-risk behaviours, amongst the female 2+ group. However, there is no clear indicator of a delay in behaviour leading to a reduction in HIV prevalence, since both variables appear to decline concurrently.

Discussion

This study has sought to identify which ecological variables are associated with the 6–10 fold variation in population HIV prevalence across West Africa–a region where male circumcision is widespread.

Our analysis has several main limitations. The first is the ecological nature of the analysis, as we compare patterns of association using aggregated national data coming from multiple sources. In practise the multiple data sources are unlikely to be a major limitation, as most of the behavioural and HIV data used came from national DHS surveys, with some comparability internally and between countries. For each country we used the most recent data available, and the 4 year timespan will only have influenced our findings if HIV prevalence levels and/or patterns of population sexual behaviour changed substantially over this time. This is difficult to assess in the absence of data. However, given the ecological nature of this analysis, the findings should be seen as hypothesis generating, rather than providing strong evidence of causality.

Secondly, reporting bias is likely to have influenced our estimates of the size of different sub-populations. Questions on sexual behaviour—including on men's purchasing of sex or the numbers of sexual partners–are highly sensitive, and prone to under-reporting, especially among women [23]. For this reason, our values will be under-estimates [21]. If there is no substantial differences in the degree of under-reporting between countries, the findings may nevertheless reflect true variations between countries. If there is also varying degrees of underreporting between countries, we cannot rule out this hidden confounder. However, such misclassification is likely to weaken associations found in regression analyses, and so if anything, will lead to null findings. Given this, we expect that significant associations are meaningful, but caution against over-interpreting the lack of associations seen.

More broadly, the forms of analysis that we could conduct were limited by available data. There is multiple heterogeneity in patterns of sexual behaviour between countries. We were limited to using variables extracted from national DHS and other data sets. In particular, some variables (such as the size of the female sex worker population) was only available for a limited number of countries considered; HIV prevalence data on males reporting payment for sex was not disaggregated by age; we were not able to assess the degree to which men's reporting of purchasing sex related primarily to engagement in commercial sex, or other forms of sexual exchange; the degree to which young girls have sex with men with a history of multiple partners, consider whether sex worker and/or client migration may be important; or explore the influence of other factors, such as male sex work and injecting drug use.

Despite these limitations, we found several strong associations. Variations in population HIV prevalence across West Africa are strongly associated with variations in the extent that males and females in the general population report 2+ partners in a 12 month period. Stratification (into 15–24 and 25–49 year olds) by age and further analysis of these subgroups reporting 2+ partners in the past year reveals that HIV prevalence in younger females and female sex workers is strongly associated with the size of both male and female populations reporting 2 + partners in the past year. However, data on brothel-based FSWs within countries was collected mostly within specific locations or districts, often using different sampling criteria and parameters, so we must caution over-interpretation for this set of results.

Additionally we see that the percentage of males in the population reporting payment for sex (in the past 12 months), especially amongst the older males is associated with HIV prevalence in younger males and females as well as FSWs.

From the earlier rounds of DHS data we did not observe any clear evidence for a time lag in sexual behaviour, impacting on

HIV prevalence. A reason for this is that it is likely that behaviour changes involving multiple partners, increases in condom use and other preventative methods may pre-date these surveys and as such, here we observe the impact of these. Historical data suggests the HIV epidemic in West Africa peaked around 1999–2000 in most countries [24], although in the absence of reliable early data it is difficult to verify this behaviour change.

The findings have implications for the way in which epidemiologists understand the determinants of HIV epidemics. Fig 3(A) visually depicts the dominant epidemiological theory of HIV transmission in heterosexual concentrated epidemics [25,26]. Epidemiological models and HIV programmes are often constructed on the assumption that HIV is transmitted from FSWs to men who purchase sex (clients), with the multiple encounters of a large group of men with a small 'core' of sex workers providing a context in which rapid HIV transmission may occur (the core group theory) [27]. In turn, HIV then passes from these male clients to their steady or casual female partners in the general population, with clients being an important 'bridging population' for HIV transmission [26].

Fig 3(B) shows a revised theory, emerging from this analysis. This is similar to 3(a), but also highlights that sexual activity between higher risk men (such as clients) and young girls may provide an important additional bridge of infection into the general population. In this revised theory, the proportion of adolescent females with multiple partnerships who have sex with high-risk men are at higher risk of HIV infection than other young females. Onward transmission may subsequently occur if girls also partner with lower risk men or re-infect higher-risk partners, either casually, or as they enter more stable partnerships. In this way, the higher HIV levels among these young women then leads to higher infection rates in all men. Over time also, adolescent females age into the general population, and so influence population HIV prevalence, especially if this group is large and survival is high.

In this revised theory, the size of the HIV epidemic is dependent on the extent that 'men pay for sex and/or have multiple partners', the extent that young girls have multiple

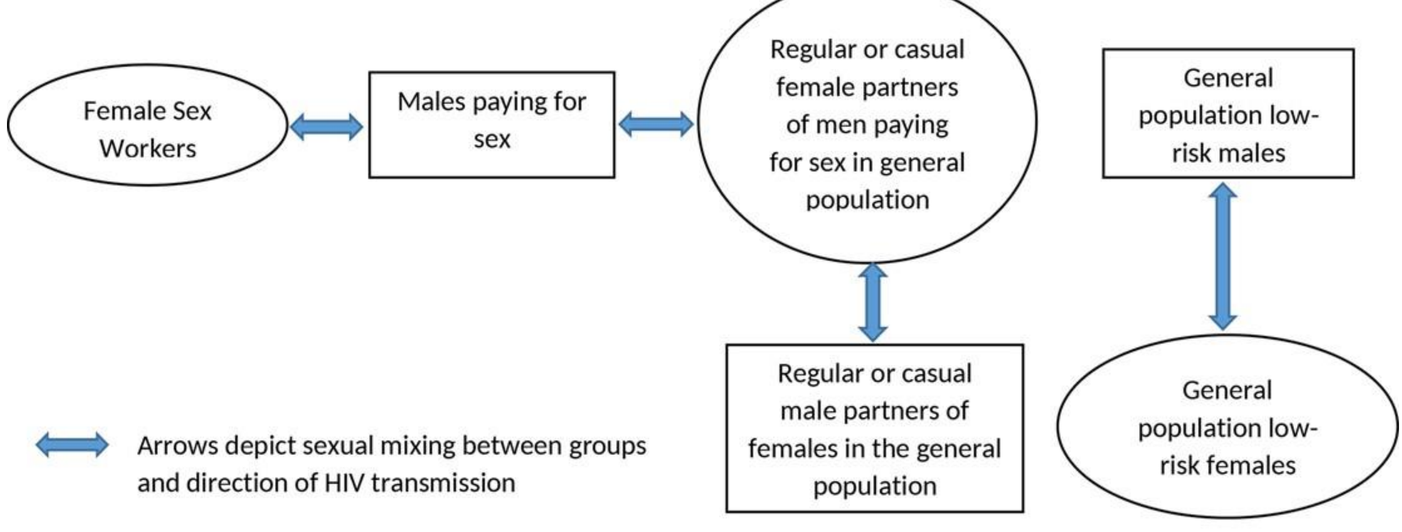

Figure 3a

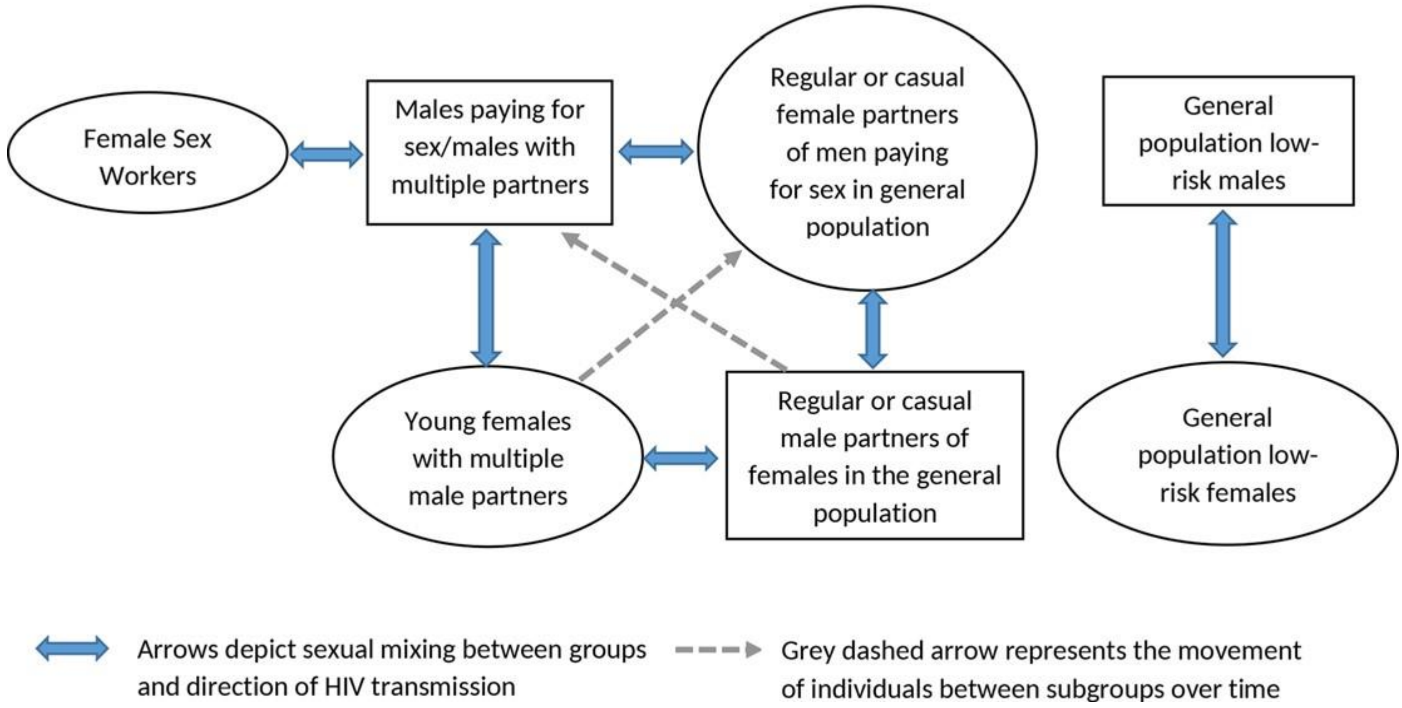

Fig 3. Fig 3(a): Conceptual pathway of heterosexual HIV transmission from female sex workers to the general population in West Africa and Fig 3 (b) Revised conceptual framework of HIV spread through sexual networks of individuals within the population.

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partnerships, and the levels of ‘connectivity’ of these groups. Populations with large proportions of young females having multiple partners and large proportions of males reporting payment for sex or multiple partners would tend to have higher levels of HIV prevalence. It may also explain why there is a greater disparity between male and female HIV prevalence in countries with higher HIV prevalence levels, because of the higher incidence rate in young females.

Conversely, in countries where HIV epidemics remain at lower levels and are more concentrated, it may be that the proportion of young females with multiple partners is not large enough or not ‘connected’ enough to higher risk men, to have a large contribution to the HIV epidemic. This may be the case for Liberia and Sierra Leone. For example, Liberia the only country in the analysis where male HIV population prevalence is greater than in females, suggesting possibly a different dynamic in the transmission pathway for HIV. We are currently conducting epidemiological modelling to explore these issue further.

Conclusion

The observed variation in population HIV prevalence across West Africa is strongly associated with national variations in the extent that men buy sex and individuals have multiple partners. The results from the regression analysis appear to show a linear trend between the percentage of individuals who report 2+ partners and HIV in the general male and female population. Interestingly, however, it is only the HIV prevalence in younger females and among brothel-based female sex workers that is associated with both multiple partnerships (2+ partners) in the population and males reporting payment for sex. This may highlight an important link between these population groups. Females with 2+ partners may form a critical bridge between high-risk men and the general population, that helps sustain larger HIV epidemics. In these countries prevention should focus both on commercial sex and adolescent girls with multiple partners.

The findings illustrate the importance of continually monitoring the distribution of HIV infection, and patterns of sexual behaviour, and the need to use this information to inform the efficient use of HIV prevention resources.

The results also support dominant epidemiological thinking about the important role of commercial sex to the HIV epidemic in West Africa, as highlighted in a recent modelling study [28]. There is substantial programmatic experience with the provision of HIV prevention to sex workers and their clients, and multiple examples of where such programming has had marked impacts on the HIV epidemic [29,30]. It is important that such programmes are sustained and expanded, and that opportunities to achieve greater impacts, for example, through the additional provision of ART based prevention technologies, are explored.

Our findings also highlight that sexual activity between high-risk men and young girls is an important additional route through which HIV infection may spread to the general population. This poses major challenges for HIV programmes, as girls with multiple partners who may be involved in transactional exchanges (both monetary and material) but who do not identify themselves as sex workers, can be difficult to identify and reach. A number of potentially promising intervention models for adolescents are starting to emerge in other African regions. This includes the Zomba trial in Malawi, that showed an impact on HIV by providing cash transfers to keep girls in school [31] interventions that provide information about the risks of 'risky male' partners [32], and interventions which aim to socially and economically empower women [33]. There is an urgent need for interventions to address HIV risk among adolescent girls and their sexual partners in the West African context, especially, where multiple partnerships are more commonly reported. With recent studies showing a lack of association between age disparate relationships between older males and younger females [34], it is important to understand the mechanisms through which young females become infected in such high numbers.

Supporting Information

S1 File. (a) Condom use in population subgroups from DHS surveys 2010–2014.
(b) Age at sexual debut and association with percentage of males and females reporting
2+ partnerships in population. (c) Literature review Female Sex Worker: Relative population size, condom use, HIV prevalence. Quantitative and qualitative research studies were searched in Pubmed, Adolec, and Popline, using the following search terms: 'sex work', 'sex worker', 'prostitute', 'prostitution', 'transactional sex'. In addition, when no information was available using these search terms, the term 'HIV' was used. The search was limited to the

2010–2013 time period. Abstracts were further examined to determine eligibility for inclusion. In addition, grey literature and reports, such DHS, IBSS, UNGASS, UNAIDS, UNICEF, USAID, World Bank were studied as far as they were accessible.

(PDF)

S2 File. Figures on Anti-Retroviral treatment for countries across West Africa.
(PDF)

S3 File. Results from the regression analysis showing significant relationships (p<0.05, highlighted in grey) for variables associated with variations in HIV prevalence among different sub-populations. (PDF)

S4 File. Age at sexual debut and association with percentage of males and females reporting 2+ partnerships in population. (PDF)

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Author Contributions

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Appendix 15

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