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**MENTAL DISORDER, SEXUAL RISK BEHAVIOUR,  
SEXUAL VIOLENCE AND HIV IN UGANDA**

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## **ABSTRACT**

### **Aim**

The overall aim of this thesis was to investigate the association between mental disorder and risk of sexual HIV transmission in a low-income country with a generalized HIV epidemic. Specific objectives were to investigate in Uganda, (1) the association between common mental disorder and sexual risk behaviour, (2) how severe mental disorder could influence sexual risk behaviour, (3) the prevalence of HIV in persons with severe mental disorder, and (4) the association of severe mental disorder with sexual risk behaviour and sexual violence exposure.

### **Methods**

(1) Population-based household survey of 646 Ugandans. Depression, psychological distress and alcohol use were assessed, and questions asked about sexual risk behaviour. (2) Facility-based qualitative semi-structured interview study of 20 Ugandans, exploring sexual risk behaviour and violence exposure. (3) Facility-based study of HIV prevalence among 602 persons with severe mental disorder. (4) Facility-based study of prevalence of sexual risk behaviour and sexual violence among 602 persons with severe mental disorder, with nationally representative comparison data.

### **Results**

(1) Depression, psychological distress and alcohol use were all associated with sexual risk behaviour, with stronger associations found in women than in men. (2) Severe mental disorder can influence sexual risks by contributing to casual sex during episodes, to rape by non-partners, to exploitation by partners, to non-monogamy in partners, and to sexual inactivity. (3) HIV prevalence was higher in women with severe mental disorder than in women in the general population, but no similar difference was found in men. (4) Severe mental disorder was associated with sexual risk behaviour in women, but not men. In women, severe mental disorder was associated with exposure to sexual violence by a non-partner. The above associations were not confounded by basic socio-demographic variables.

### **Conclusions**

Mental disorder is associated with risk of sexual HIV transmission in a low-income country with a generalized HIV epidemic. Associations were found across levels of mental disorder severity and in relationship to several indicators of sexual risk. Stronger associations were found in women. By design we were not able to show that mental disorder preceded the development of sexual risk behaviour, or first sexual violence exposure. However, qualitative and quantitative findings were consistent. Our findings suggest that women with mental disorder in Uganda may be at higher risk of HIV, and at higher risk of sexual violence, than women in the general population.

## LIST OF PUBLICATIONS

- I. **Lundberg P**, Rukundo G, Ashaba S, Thorson A, Allebeck P, Östergren PO, Cantor-Graae E. Poor mental health and sexual risk behaviours in Uganda: a cross-sectional population-based study. *BMC Public Health*. 2011 Feb 21; 11: 125.
- II. **Lundberg P**, Johansson E, Okello E, Allebeck P, Thorson A. Sexual risk behaviours and sexual abuse in persons with severe mental illness in Uganda: a qualitative study. *PLoS One*. 2012; 7(1): e29748.
- III. **Lundberg P**, Nakasujja N, Musisi S, Thorson AE, Cantor-Graae E, Allebeck P. HIV prevalence in persons with severe mental illness in Uganda: a cross-sectional hospital-based study. *Int J Ment Health Syst*. 2013 Jul 17; 7(1): 20.
- IV. **Lundberg P**, Nakasujja N, Musisi S, Thorson A, Cantor-Graae E, Allebeck P. Severe mental illness, sexual risk behaviour, violence and HIV: Clinical survey and national data from Uganda. *Submitted*.

These publications will be referred to as Paper I to IV.

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## LIST OF ABBREVIATIONS

|         |  |
|---------|--|
| AIDS    | Acquired immunodeficiency syndrome             |
| CMD     | Common mental disorder                         |
| DALY    | Disability adjusted life-year                  |
| DHS     | Demographic and health survey                  |
| EU      | European Union                                 |
| GDP     | Gross domestic product                         |
| HAND    | HIV associated neurocognitive disorders        |
| HIV     | Human immunodeficiency virus                   |
| HSCL-25 | Hopkins symptoms checklist 25-items version    |
| MDG     | Millennium development goal                    |
| PITC    | Provider initiated HIV testing and counselling |
| PL      | Patric Lundberg                                |
| SMI     | Severe mental illness                          |
| SMD     | Severe mental disorder                         |
| STD     | Sexually transmitted disease                   |
| UDHS    | Uganda demographic and health survey           |
| USD     | United States dollar                           |
| VCT     | Voluntary counselling and testing              |
| WHO     | World Health Organization                      |

## **1 INTRODUCTION**

Mental disorder is a major cause of disease burden globally. Moreover, the global burden is increasing, mainly due to demographic changes in low- and middle-income countries.

Mental disorder has consequences beyond the experience of psychiatric symptoms. Thus, mental disorder can lead to medication side-effects, contribute to unhealthy lifestyle, hinder education, lead to unemployment, and influences marital opportunities and outcomes. Further, mental disorder is also associated with poor access to physical health care, and in fact, with poorer quality of received health care. Finally, mental disorder can lead to stigma, social exclusion and discrimination.

The combined effect of all aspects of mental disorder on physical health can be devastating. Persons with severe mental disorder in high-income countries have 10 to 20 years shorter life expectancy than persons without mental disorder, mainly due to excess mortality from physical diseases.

Recent studies from middle- and low-income settings suggest that physical health and survival of persons in this group may be particularly poor in such settings. This finding may not be unexpected, however, given that most persons with mental disorder go untreated in resource-poor settings. Furthermore, programmes for social protection of marginalised persons are often weak, or absent. Thus, it is important to investigate physical health and disease in persons with mental disorder in middle- and low-income settings.

HIV is the leading cause of morbidity and mortality in southern and eastern Africa. While in high-income countries mental disorder is associated with HIV risk behaviour, much less is known about this association in sub-Saharan Africa. Nevertheless, in sub-Saharan African countries where HIV is prevalent, HIV could potentially be a major cause of morbidity and mortality in persons with mental disorder. Further, in these settings, mental disorders that are common could hypothetically influence overall population HIV transmission dynamics.

The aim of this thesis was to address this knowledge gap, using Uganda as an example of a low-income setting with a generalized HIV epidemic. In the first study, we investigated the association between common mental disorders and sexual risk behaviour in the general population. In the subsequent studies, we focused on sexual risk behaviour, sexual violence and HIV in the group suffering worst consequences of their mental disorder, i.e. persons with severe mental disorder.

## 2 BACKGROUND

### 2.1 MENTAL DISORDER

#### *Global burden*

Mental disorders are present globally[1,2,3,4,5], with expressions, explanations, and help-seeking responses influenced by factors in the local contexts[6]. Mental disorder (including substance use) caused 7.4% of the global disease burden in 2010[7]. The same year, mental disorder caused 22.9% of all years lived with disability, and was indeed the leading contributor of years lived with disability[7]. The global burden of mental disorder is increasing. Between 1990 and 2010 the proportion of all disease burden attributable to mental disorder increased from 5.4% to 7.4%. This increase was mainly driven by demographic changes in low- and middle income countries, with population growth and changing age structure[7].

#### *Treatment*

The resources available for treating persons with mental disorder dramatically vary according to level of economic development. In low- and middle income settings, resources are often extremely limited. For example, in 2011, the psychiatrist per population ratio was 0.5 per million persons in low-income countries, compared to 86 per million persons in high-income countries[8]. Consequently, a wide treatment gap exists for mental disorders in resource-poor settings. It has been estimated that in low- and middle-income countries, three in ten of persons with schizophrenia, and one in ten with bipolar affective disorder or major depression, receive treatment[9,10]. In low-income countries specifically, only one in ten of persons with schizophrenia was estimated to receive treatment. Corresponding treatment prevalence for physical non-communicable diseases is considerably higher[9].

#### *Common versus severe mental disorder*

Mental disorders are sometimes categorized into common mental disorders (CMD) and severe mental illnesses (SMI), or severe mental disorders (SMD)[11]. In the papers included in this thesis, the term severe mental *illness* was used, but in this thesis summary, for ease of reading, the terms common and severe mental *disorder* will be used. CMD corresponds to depressive and anxiety conditions that are common in the general population and often not treated in specialised care, while SMD broadly corresponds to psychotic conditions often requiring specialised care[11]. Exact definitions vary; duration and disability criteria are sometimes added to a diagnosis criteria[12,13]. For the purpose of this thesis, CMD is defined as anxiety and depression without psychotic symptoms, and SMD is defined as any primary psychotic disorder, including schizophrenia, bipolar affective disorder and major depression with psychotic symptoms.

#### *Consequences*

The previous assumption that the prognosis and consequences of mental disorder are less severe in resource-poor settings, is being increasingly questioned[14]. In fact, an alarming picture is starting to emerge with regard to the severe consequences of mental disorder in



many low- and middle-income settings[15]. Stigmatization, discrimination, and human rights abuse of persons with mental disorder seem to be equally, if not more, common and devastating, in many resource-poor settings[16]. Persons with mental disorder are denied civil and political rights, and are discriminated against regarding opportunities for education, employment, marriage, and other societal participation[17]. Persons with mental disorder also suffer disproportionate exploitation, abuse and violence, globally[17].

Mental disorder can also lead to physical illness[18]. In high-income countries, persons with severe mental disorder have higher morbidity[18,19] and mortality[20,21,22] from physical health conditions than the general population. In low- and middle-income settings, the evidence is scarce, but recent studies suggest that excess mortality in this group may be particularly elevated in such settings[23,24]. Thus, factors potentially contributing to excess mortality in persons with mental disorder in resource-poor settings merit further attention.

## **2.2 HIV**

### *Global burden*

HIV/AIDS caused 3.3% of all global disease burden, and was ranked as the fifth global cause of disability adjusted life years (DALYs) in 2010[25]. In southern and eastern sub-Saharan Africa, HIV was ranked as the leading cause of DALYs that year. The global HIV prevalence among adults is stable at 0.8% since about ten years[26]. The region most heavily affected by HIV is sub-Saharan Africa with an overall HIV prevalence at 4.7%, followed by the Caribbean at 1.0%, and Eastern Europe/Central Asia at 0.7%[26]. The countries with the highest HIV prevalence in the world are Swaziland 26.5%, Lesotho 23.1%, Botswana 23.0%, and South Africa 17.9%[26].

An estimated 35.3 million persons lived with HIV in 2012, globally, representing an increase from 30.0 million in 2001[26]. This increase is driven by a reduction in the number of AIDS related deaths (1.9 to 1.6 million), and occurs despite a concurrent reduction in new HIV infections (3.4 to 2.3 million)[26]. The global HIV incidence probably peaked in 1997[27]. The causes of the global decrease in HIV incidence are not fully understood[26], but decreased HIV risk behaviour in sub-Saharan Africa provides one possible explanation[28,29].

### *Treatment*

Large efforts are being made to scale up antiretroviral treatment for persons living with HIV globally[30]. Indeed, the decrease in AIDS related mortality mentioned above is driven by this anti-retroviral treatment roll-out in sub-Saharan Africa. Over ten years, the number of persons receiving antiretroviral treatment in sub-Saharan Africa has increased from 50000 in 2002 to 7.5 million in 2012[30]. In 2012, an estimated 68% of persons in this region eligible for treatment according to the 2010 WHO guidelines, indeed received treatment[26].

### *Concentrated versus generalized epidemics*

The dynamics of population HIV transmission differ between concentrated and generalized epidemics. Concentrated epidemics are defined as having HIV prevalence in the general population below 1%, but above 5% in at least one population sub-group[31]. In concentrated epidemics, most HIV transmission takes place in such population sub-groups at higher risk of HIV. Typical sub-groups at higher risk of HIV are men who have sex with men, persons who inject drugs, and sex workers[26]. In generalized epidemics, however, the prevalence in the general population is 1% or more, and heterosexual transmission in the general population is responsible for most population HIV transmission[31].

### *Risk factors at many levels*

The probability of sexual acquisition of HIV for a susceptible individual in a community depends on individual-level determinants such as (1) the frequency of sexual acts with an HIV-infected partner, (2) the transmission risk when having sex with an infected person, and (3) the time in the community[32]. Many HIV prevention interventions have therefore focused on changing individuals' personal choices, aiming at reduction of relevant HIV risk behaviours (e.g. number of sexual partners, condom use)[33]. However, there is now recognition that many persons are not able to make informed and voluntary decisions about their sexual behaviour, and a broader focus in HIV prevention is necessary, including also structural factors[33]. Gender inequality is an example of a structural factor, leading to lack of decision-making power about sex for women in intimate relationships. One global expression of gender inequality is intimate partner violence against women[34], and indeed, intimate partner violence, including sexual violence, has been identified as a risk factor for HIV in women[35,36]. The pathways by which intimate partner violence might influence HIV risk are however not clear, but increased transmission probability due to forced intercourse may not necessarily be the sole mechanism. Intimate partner violence may also be a marker for how decisions about sex are taken within marriage[35,36]. For example, women in violent relationships may not be able to influence the frequency or circumstances of safe sexual intercourse, or question partner non-monogamy.

### *Consequences*

Access and adherence to antiretroviral treatment determine the long term consequences and survival of persons with HIV. Thus, in resource-poor settings, HIV is still a fatal condition for many[26]. In addition to the physical consequences, persons living with HIV are stigmatized and discriminated against globally[37]. Further, persons in population sub-groups at higher risk of HIV (e.g. men who have sex with men, sex workers) are also stigmatized and discriminated against, irrespective of HIV status, simply because they are members of these groups. HIV-related stigma is associated with decreased uptake of, and adherence to, HIV prevention and care[37].

## 2.3 MENTAL DISORDER AND HIV

### *Comorbidity*

Comorbidity between mental disorder and HIV can have serious consequences. Mental disorder can influence antiretroviral treatment adherence[38,39] leading to worsened prognosis and decreased survival[40]. In addition, comorbidity confers the risk of double stigma and a potentially exacerbated process of discrimination and social exclusion[41].

HIV can cause secondary mental disorder through its direct effects on the brain[42,43]. The presence of the virus contributes to local inflammation, neuro-degeneration and neuronal death[44]. Brain damage causes cognitive and motor disturbances of varying degrees, with the most severe manifestation being HIV-associated dementia, often referred to as HIV-associated neurocognitive disorders (HAND)[42,43]. HIV may also cause depression, mania and psychosis, in the absence of HAND[42,43]. For depression, biological[45], psychological and social mechanisms may all be relevant.

Mental disorder can in turn contribute to risk of HIV. Common mental disorder could influence HIV risk through mechanisms acting on multiple levels, e.g. cognitive (inflexible adjustment to risky circumstances), psychological (decreased self-efficacy for protective behaviour), behavioural (substance use), and interpersonal or social (association with high-risk peers)[46]. The association between depression severity and HIV risk could potentially have the form of an inverted U curve, with the strongest association for moderated depressive symptoms[47]. Severe mental disorder could contribute to sexual risk behaviour due to e.g. cognitive problems (inflexible adjustment to risk), negative symptoms (poor inter-personal skills), positive symptoms (poor reality testing), psychological mechanisms (internalized stigma), behavioural factors (substance use), and interpersonal and social consequences of the mental disorder (high-risk partners, homelessness)[48,49]. In this thesis, the focus is on mental disorder as a potential risk factor for HIV, in order to inform HIV prevention.

### *Common mental disorder and HIV in concentrated epidemics*

Studies in concentrated epidemic settings provide strong support for the notion that mental disorder can contribute to risk behaviour for HIV. Several longitudinal studies in youth in the United States have shown associations between common mental disorders at baseline, and sexual risk behaviour at follow-up[50,51,52,53]. Associations have also been found in cross-sectional studies in similar settings[54,55].

In addition, Devries et al, in a review of longitudinal studies, found associations between baseline common mental disorder and incident intimate partner violence victimization, including sexual violence[56].

It is uncertain however whether in concentrated epidemics the increased risk behaviour associated with common mental disorder indeed translates into increased HIV incidence. Of two longitudinal studies in high-risk groups, one found no association, while the other found an association with moderate depressive symptoms[57,58]. Associations have however been found in cross-sectional studies; Ciesla et al reviewed ten studies, mainly including participants from high-income setting with concentrated epidemics, and found double depression rates in HIV-infected persons[59]; this was interpreted as an indication that HIV

causes depression. Two studies in the United States reported depression rates five times those in the general population[60,61]. In cross-sectional studies in China and India, no clear association was found between common mental disorder and HIV status[62,63,64].

#### *Severe mental disorder and HIV in concentrated epidemics*

Studies suggest that also severe mental disorder is associated with risk behaviour for HIV in concentrated epidemic settings. However, longitudinal studies investigating this are lacking. Meade and Sikkema reviewed cross-sectional studies on sexual risk behaviour in persons with severe mental disorder[48]. Of 52 studies, all but one were from high-income countries with concentrated epidemics (85% from United States), and one from India. The authors found that overall, sexual activity was lower in persons with severe mental disorder than in the general population, but that nevertheless, sexual risk behaviour was more common than in the general population, in several studies. Of note, HIV risk behaviours indicating membership in, or contact with, population sub-groups at higher risk of HIV, such as injecting drug use, sex with same-sex partner (for men), and trading sex for money or goods, were commonly reported[48]. These conclusions were similar to those made in an earlier review of studies from the United States, by Carey et al[49]. With regard to specific diagnoses, schizophrenia has been associated with less sexual activity[48,65], while differences in HIV risk behaviours have generally not been demonstrated between psychiatric diagnoses[48]. Recent studies however suggest that persons with bipolar affective disorder may have particularly risky sexual behaviours[66,67].

Severe mental disorder in women has been associated with past year sexual violence in the United States[68,69,70]. It has been suggested that intimate partner violence, specifically, is more common, but evidence is scarce[71]. Studies from middle- and low-income settings on this topic are also few: In Egypt[72] and India[73] lifetime prevalence of sexual violence in women with severe mental disorder was 30% and 19%, respectively, but control groups were not used.

One longitudinal study investigated the association between severe mental disorder and HIV[74]. This study from the United States suggested that in the absence of substance use, severe mental disorder was not positively associated with HIV infection. Indeed, persons with schizophrenia without substance use had a lower risk of HIV infection than persons without these problems[74]. Himelhoch performed a controlled cross-sectional study, also in United States, and reported a double HIV prevalence in persons with severe mental disorder versus controls, after adjustment for socio-demographic variables[75]. In addition, a large number of uncontrolled prevalence studies, mainly from the United States, have suggested disproportionate HIV burden in this group[61,76,77,78,79,80,81,82,83].

#### *Common mental disorder and HIV in generalized epidemics*

An increasing number of studies suggest that also in generalized epidemics, common mental disorder is associated with HIV risk behaviour. However, results are not entirely consistent. The strongest evidence is provided by a longitudinal study of volunteers in South Africa, showing associations between depressive symptoms and transactional sex in women, and non-condom use in men[84]. Results from cross-sectional studies in middle-income countries have been mixed, however. In Botswana, depression was associated with multiple sexual partners in men and women, and with paying for sex in men, in a population-based study[85].

In South Africa, one study in women showed null findings[86], another study using a sex-mixed sample found associations with *increased* condom use[87], and a third found associations with unprotected sex in women, but not men[88]. In low-income settings, cross-sectional studies have shown associations between depression and unprotected sex in HIV-infected persons of both sexes in Kenya[89], with multiple partners in male, but not female, university students in Ivory Coast[90], and with sex with commercial sex workers in male military personnel in Rwanda[91]. Several recent cross-sectional studies from Uganda have also shown associations in adults in war-affected areas (Kinyanda et al[92]), in university students (Agardh et al[93]), and in HIV-infected persons (Musisi et al[94]).

The above longitudinal South African study found that depressive symptoms also predicted intimate partner violence victimization in women[84], and similar associations have also been reported in cross-sectional studies[87,88].

Longitudinal studies investigating the association between common mental disorder and HIV in generalized epidemics are lacking. Associations have however been found in cross-sectional studies in Rwanda and Uganda[95,96], but no association was found in a cross-sectional study in pregnant women in South Africa[97]. In addition, studies in Uganda without control groups have reported high or very high depression prevalence in persons living with HIV[98,99,100].

#### *Severe mental disorder and HIV in generalized epidemics*

Studies on the association between severe mental disorder and HIV risk in generalized HIV epidemics are few. Longitudinal studies investigating the association between severe mental disorder and sexual risk behaviour in generalized epidemic settings are lacking. Three cross-sectional studies have compared sexual risk behaviours in persons with severe mental disorder to those in controls, and in two of these no prevalence difference was found[101,102]. In the third study, more sexual risk behaviour were found in women with severe mental disorder, but not men[103]. Other sub-Saharan African studies on this topic have not used a control group[101,102,104,105,106,107].

A recent cross-sectional study from Ethiopia found that lifetime prevalence of forced sexual intercourse (perpetrator not specified) was more common in persons with severe mental disorder than in controls[108]. Results in that study were not stratified by sex.

Longitudinal studies on the association between severe mental disorder and HIV in a generalized epidemic are lacking. Cross-sectional studies do exist, but results diverge. Of three prevalence studies in South Africa[109,110,111], one reported a higher prevalence than in the general population[109]. One study in Zimbabwe reported prevalence similar to that in the general population[112]. In Uganda, HIV prevalence among persons with severe mental disorder was twice that in the general population, but that study targeted first-time psychiatric admissions only[105].

#### *Implications for further research*

In summary, the literature from concentrated HIV epidemics suggests that *common* mental disorder predicts sexual risk behaviour and exposure to sexual violence. Common mental disorder is also associated with prevalent HIV infection, but the association with incident HIV infection is uncertain. The literature from concentrated epidemics also suggests that *severe*

mental disorder is associated with sexual risk behaviour, with exposure to sexual violence, and with prevalent HIV infection. One longitudinal study did not suggest that severe mental disorder predicts incident HIV infection[74].

In this thesis the focus is on low-income settings with generalized epidemics. However, findings pertaining to concentrated epidemics may not be applicable to generalized epidemics, for several reasons: (1) The majority of studies from concentrated epidemics have been performed in high-income settings, while most generalized HIV epidemics are low- or middle-income countries. Societal level of economic development may influence the consequences of mental disorder. (2) Potentially mediating determinants of sexual risk behaviour may differ between contexts[113]. (3) The extent to which specific behaviours predict HIV differs between concentrated and generalized epidemics.

At the time when the work with this thesis started, literature from generalized HIV epidemics on the association between common mental disorder and HIV risk was virtually non-existent. However, our review shows an increasing literature suggesting that common mental disorder is associated with sexual risk behaviour also in generalized epidemic settings. Studies on common mental disorder as a predictor of HIV incidence in generalized epidemics are however lacking.

Several knowledge gaps exist, however, with regards to the association between severe mental disorder, sexual risk behaviour, sexual violence and HIV, in generalized epidemics. Specifically, no study has investigated the association between severe mental disorder and sexual risk behaviour, separately for men and women, while controlling for basic demographic variables. Further, data regarding the association between severe mental disorder and sexual violence is very limited. Finally, studies on HIV prevalence in persons with severe mental disorder in generalized epidemics do not permit an overall conclusion with regards to a potential disproportionate burden of HIV in this group.

Given differences in symptom profiles and severity between common and severe mental disorder, and their associated differential social consequences, common and severe mental disorder may well have different associations with sexual risk behaviour and HIV incidence. Thus, further study is needed of sexual risk behaviour and HIV risk in persons with severe mental disorder in generalized HIV epidemic settings.

## 2.4 UGANDA

Uganda is a low-income country with a generalized HIV epidemic.

### *Demographics*

Uganda has a projected population of 35.4 million for 2013[114]. The annual population growth is 3.4% (Sub-Saharan Africa 2.7%, EU 0.2%)[115]. The fertility rate is extremely high, at 6.1 born children per woman (Sub-Saharan Africa 5.2)[115]. The proportion of the population under 15 years is 50.1%[114]. Most Ugandans (85%) live in rural areas. The overall population density is nevertheless high at 190 persons per square kilometre[114]. The Ugandan population includes a variety of ethnic groups. In the last census (2002), the largest groups were Baganda, Banyankole and Basoga. These groups are all Bantu and culturally and linguistically related. The capital of Uganda is Kampala.

### *Development indicators*

Uganda is ranked as number 161 out of 186 countries in terms of human development[116]. The country had a GDP per capita at 1188 USD in 2011 (purchasing power parity, 2005 international dollars)[116]. The proportion of the population below the international poverty line at 1.25 USD per day (purchasing power parity, 2005 international dollars) was 38% in 2009[116]. The Gini coefficient was 44 in 2009, indicating economic inequality at the same level as China: 42, but more equal than South Africa: 63[116]. The mean number of years of schooling in adults is low at 4.7[116]. The adult literacy rate for both sexes is 73%[116], for women 61%[114].

### *Health and health system*

Overall health indicators in Uganda are poor. Under-five mortality rate was 69 deaths per 1000 live births in 2012 (Sub-Sahara Africa 98, Developed regions 6). This indicator has however improved substantially from 147 in 2000[117]. The maternal mortality ratio remains high at 438 deaths per 100000 live births, and has shown less improvement, from 505 in 2001[118]. Life expectancy at birth is 50 years[118].

The health system in Uganda has been decentralized, with health facilities ranging from national referral hospitals, through regional referral hospitals, district general hospitals, down to health centres at four levels. The lowest level is the Village Health Team, without a physical structure, performing community sensitization, mobilization, and linking to higher level health centres. The implementation of this system is however incomplete. In 2013, 55% of all villages had trained Village Health Teams[119].

## 2.5 MENTAL DISORDER IN UGANDA

### *Occurrence*

Both common and severe mental disorder are present in Uganda (see for example Orley & Wing[120], Abbo et al[121], Nakimuli-Mpungu et al[122] and Muhwezi et al[123]). Population-based studies on depression prevalence have generally reported high estimates (approximately 20%)[124,125] with large variations across districts. Extremely high rates have been reported from war-affected areas in northern Uganda (approximately 40%)[126,127]. Prevalence estimates have however been obtained using screening instruments, not clinical interviews, and true rates may thus be lower. Population-based prevalence data on severe mental disorder is however scarce. Two studies reported high levels of psychosis-like experiences and psychotic symptoms in the general population, but caseness for psychotic disorder was not ascertained[128,129]. In one study using random household sampling in western Uganda, heads of households were asked to identify family members with mental illness, and a 12 months prevalence of mental illness of 31% was thus obtained[130]. Based on reported features of family members' mental illnesses, many persons probably had severe mental disorder, but the validity of this measure is nevertheless uncertain[130]. The incidence of both common and severe mental disorder in Uganda is unknown.

### *Cultural explanatory models*

Cultural explanatory models influence the social consequences of, and help-seeking for, mental illness. Cultural explanatory models for mental illness have been investigated in the Baganda and Basoga ethnic groups[131,132,133]. Specific local terms exist that correspond to specific mental disorders. Among the Baganda, major depression without psychotic symptoms was understood as a consequence of challenging life events or social problems, and as an illness of thinking too much, but often not as a disease to be treated by western medicine[132,133]. In contrast, major depression with psychotic symptoms was attributed to problems in the relationship with dead ancestors, e.g. due to breaking taboos or neglecting rituals, or as a 'clan' illness (i.e. familial illness)[132]. Cultural explanatory models of schizophrenia were investigated in the Basoga, and this condition was understood as the most severe mental illness, and was attributed to problems with ancestors, or to witchcraft[131]. Bipolar disorder was considered less severe, and was mainly attributed to physical disease[131].

### *Help-seeking and response*

Care of the sick person is often performed by women, such as a mother, sister or grandmother[134]. As mentioned above, help-seeking for mental illness is influenced by the causal attribution of the condition. Persons with depression without psychotic features commonly seek help for somatic complaints[123,132]. Major depression with psychotic symptoms and schizophrenia may both require performing rituals, and/or seeking assistance from traditional healers[131]. Help for bipolar affective disorder may be sought from traditional healers, or from formal medical care. If the condition does not improve, the causal attribution may change, and help is often sought from several sources[132]. The mentally ill person may however also be kept hidden in order to avoid family stigma. Indeed, when heads



of households in one Ugandan district were interviewed about how they managed the mental illness in a family member, more than half reported isolation as the response[130]. Methods of isolation involved tying the sufferer to a tree and locking the person inside a house. That study was performed in 2002[130]. If the person's behaviour becomes aggressive or otherwise difficult to handle, this can trigger help-seeking at psychiatric services[132].

### *Mental health services*

Of the total health expenditure in Uganda 4% was spent on mental health in 2005[135]. However, 55% of this budget was directed towards one hospital, Butabika National Referral Mental Hospital in Kampala. There are currently 30 Ugandan psychiatrists, mainly concentrated to Kampala and to university teaching hospitals in Gulu (northern Uganda) and Mbarara (western Uganda). Most mental health care is provided by psychiatric clinical officers, psychiatric nurses or non-psychiatric health staff. The Health Sector Strategic Plan specifies that a Minimum Package of Care, consisting of the most cost-effective and prioritized health care interventions, should be delivered to all Ugandans[136]. Mental health is included in this package, aiming at integration of mental health care into primary health care. Policy allows prescription by nurses and general health workers. Clinical management guidelines include a chapter on mental health for reference. Psychotropic medicines are free and centrally procured and distributed. However, a recent assessment showed major shortcomings in implementation of this package[135]. Of higher level health centres, less than one in five had treatment protocols for mental disorders, and less than half had at least one psychotropic medicine of each therapeutic category (antidepressant, antipsychotic, mood stabilizer, anxiolytic, and antiepileptic). Among lower level health centres, only one in five had treatment protocols, and only one in five also had essential medicines[135]. The vast majority of persons with mental disorder in Uganda do not receive adequate psychiatric treatment.

### *Consequences*

Negative consequences of mental disorder in Uganda are many. While common mental disorder does not generally carry stigma in Uganda, severe mental disorder is massively stigmatized. Cultural explanatory models suggest that mental illness is a consequence of wrongdoing (cultural, ancestral, religious), and the persons themselves may thus feel shame and guilt[133,137]. Further, family members, themselves under the risk of being stigmatized, may blame and further stigmatize the mentally ill person[133]. As noted above, some families hide the mentally ill[133]. Distancing and rejection by families and partners also occurs[133,137]. The larger community, in turn, often sees the persons as incapable, a figure of ridicule, as dangerous, or as contagious[133]. Institutional stigma can cause loss of employment, exclusion from schools, universities, politics and often marriage[133,137]. Going for mental health treatment is thus often secretive. Severe mental disorder contributes to poverty due to loss of income, and given treatment-related costs. The often decreased social support leads to less resilience to cope with poverty[133,134,137]. Poverty, in turn, hinders access to treatment, thus causing a cycle of illness, stigma and further poverty[133,137].

## 2.6 HIV IN UGANDA

### *Occurrence*

Uganda has a generalized HIV epidemic. The latest HIV prevalence estimate for adults 18-49 years in Uganda is 7.3%[138]. A recent estimate of HIV incidence in adults is 0.67 per 100 person-years[139]. In 2008, an estimated 35% of all HIV transmission occurred within currently monogamous stable relationships, while 37% occurred in persons currently connected to wider sexual networks[140]. Population sub-groups at high risk of HIV exist, but account for a small proportion of total HIV incidence (e.g. sex workers 9%, persons who inject drugs and men who have sex with men <1%)[140]. Mother-to-child transmission accounted for 18% of all HIV transmission[140]. Demographic sub-groups having high HIV prevalence in the general population (ages 15-49 years) are: women, persons above 30 years, urban dwellers, and persons ever married (especially widowed/separated/divorced)[138]. Low education is associated with higher HIV prevalence in men, but not women. Wealth is associated with higher HIV prevalence in women, but not men[138].

### *HIV testing and care*

In 2011, an estimated 57% of all Ugandan adults had ever been HIV-tested and had received the result[138]. The two main HIV-testing circumstances in Uganda are voluntary counselling and testing (VCT), where persons actively seek the service, and provider-initiated HIV-testing and counselling (PITC), where health providers offer HIV-testing as part of routine care[141]. Acceptability of PITC is very high, with one study in referral hospitals reporting a 98% acceptance rate[142]. Most, but not all, patients accepting PITC do understand that they can opt-out[143]. The coverage of lifesaving antiretroviral treatment is being rapidly scaled-up in Uganda, and is provided for free by government hospitals and health centres. The proportion of persons eligible for treatment (based on 2010 WHO guidelines) that are estimated to receive treatment has increased from 37% in 2009, to 64% in 2012[115]. Many HIV-infected persons are however not retained in care, due to transport costs, fear of disclosure, staff shortages, waiting times, and fear of side effects[144,145]. Media campaigns and civil society work to decrease HIV stigma, but HIV remains stigmatized in Uganda[138,146].

### *Prevention*

In the national HIV prevention strategy, reducing sexual HIV transmission is the main priority[147]. The following sexual risk behaviours are specifically targeted: age under 18 sexual debut, casual sex, multiple partnerships, cross-generational sex, and transactional sex. Other methods are: scale-up biomedical interventions (HIV testing, prevention of mother-to-child transmission, male circumcision, antiretroviral treatment, condom use, blood safety), structural change (gender inequality, gender-based violence, HIV stigma and discrimination, orphan school attendance, childhood marriage), and strengthened HIV information systems. The national strategy focuses on the general population, but also mentions sub-groups in need of tailored preventive services: sex workers, fisher-folk, uniformed personnel, truck-drivers. However, adults with mental disorder are not mentioned as a high-risk group in this document[147].

## 2.7 SEXUAL RISK BEHAVIOR IN UGANDA

### *Occurrence*

Men in Uganda, similar to men in other settings[148], report a greater mean number of sexual partners than do women (7.4 vs 2.1[138]). The mean number of sexual partners in men and women should however be equal in a closed population[148]. Social desirability bias might provide one explanation for this discrepancy. Alternatively, if some women have very large number of partners (e.g. sex workers), and if these women are missed in population surveys, that could also account for the inconsistency[148].

The proportion of persons reporting more than one sexual partner during past year is also much higher in men than in women (19% vs 3%[138]). Traditional cultural norms in Uganda often condone, or expect, extramarital sexual relationships in men, but not women[149], while current HIV preventive messages condemn such behaviour[150]. Situations exist however when it may be acceptable for married women to have extramarital sex, e.g. if the man fails to provide for the woman and the children[149]. Thus, social desirability bias could contribute also to these figures. Approximately 16% of Ugandan married men are in polygynous unions[138]. Condom use is rare, with only about 15% of men and women with two or more partners during past year reporting condom use at last occasion of sexual intercourse. Men generally have a greater say over condom use in stable relationships[151].

### *Determinants*

In men, older *age* is strongly associated with having multiple partners[138]. *Being married* is also a strong correlate of having multiple partners in men. However, both single and married women generally do not report multiple partners[138]. No simple relationship seems to exist between *wealth/poverty* and HIV risk in sub-Saharan Africa[152]. For example, the influence of having an income on sexual decision-making depends on cultural context, also within Uganda[153]. Thus, as noted, poor women in Uganda may have sex for money in order to cover basic needs[149,154]. Women may also have sex to meet less pressing 'wants'[155]. At the same time, however, women with access to cash income may attract male partners, since such women do not need much financial support[156]. In Ugandan men, given expectations of the provider role, poverty may hinder or delay marriage[150]. Conversely, wealth may permit a man to have concurrent sexual partners[150]. In a national survey, wealth was weakly associated with having multiple partners in both men and women[138]. *Education* increases women's ability to negotiate sex (e.g. refuse to have sex within marriage[153]), but was not associated with having multiple partners in either men or women in a national sample[138]. *Urban residence* increases the range of potential partners available, offers anonymity, and may also be a proxy for past or current mobility, potentially causing periods of absence between spouses contributing to sexual risk behaviour[157]. Urban women but not men reported more often multiple sexual partners in a national survey[138].

## 2.8 SEXUAL VIOLENCE IN UGANDA

The first experience of sex for women in Uganda is commonly not consensual: In Rakai district, 14% of women 15-19 years reported forced first intercourse. Women with early sexual debut reported more often forced sexual debut[158].

### *Violence by partner*

Most sexual violence occurs within marriage, and together with other forms of violence. In a national survey[159], violence by an intimate partner (including sexual violence), ever and during past year, was reported by 51% and 35%, respectively, of ever-married women. Sexual violence was reported by 31% and 20%, respectively. Elevated rates of sexual violence have been reported also in other studies[160,161]. Violence within marriage is widely practiced and often accepted. In the survey above, women were asked whether a man was justified in beating his wife in any of five situations: if she burns the food, if she argues with him, if she goes out without telling him, if she neglects the children, and if she refuses to have sexual intercourse with him. The view that at least one of these situations justified beating was endorsed by 60% of all women. That beating was justified if the woman left home without telling the man was endorsed by 40% of all women. That beating was justified if the woman refused to have sex was endorsed by 22% of all women[159].

Within marriage, men generally have more decision-making power than women over whether to have sex, although this power is not absolute[153]. In one study, 94% of married women felt they could deny sex when menstruating, 61% when being tired or not in the mood, and 56% if the husband had sex outside marriage[153]. Control over *income* can improve decision-making power for women within marriage, but this may depend on the context (e.g. the size of bridewealth payment)[153]. Market-women with cash income felt empowered to leave relationships, but within relationships could only refuse sex 'on isolated occasions'[156]. These women said that refusal could 'trigger verbal insults, withdrawal of financial support, beatings or rape'. *Urban residence* and *education* are associated with better negotiating power for women within marriage[153].

### *Violence by non-partner*

Outside marriage, women may have the possibility to refuse sex for many reasons[162]. In unmarried adolescents in Masaka, girls were expected to refuse sex when a boy first proposed[163]. In the same district, adolescent women could acceptably leave sexual relationships and move between partners[155]. Sexual violence by non-partners does nevertheless occur. In a national survey, of women 15-49 years, 28% reported sexual violence ever (all perpetrators). Of these, a substantial proportion of perpetrators were not partners: Family/relative/in-laws (7%), friend/friend of family (8%), stranger (14%), and teacher/police/soldier/other (3.7%). In the Masaka study, victims of non-partner rape felt this as being unacceptable and indeed a crime, but did not report or seek help due to fear of bringing shame to the family[162].

### **3 AIM AND RESEARCH QUESTIONS**

#### **3.1 AIM**

The aim of this thesis was to investigate the association between mental disorder and sexual risk of HIV transmission, in a low-income country with a generalized HIV epidemic.

#### **3.2 RESEARCH QUESTIONS**

The specific research questions were:

1. Is common mental disorder associated with sexual risk behaviour in Uganda?
2. How can severe mental disorder influence sexual risk behaviour in Uganda?
3. How prevalent is HIV in persons with severe mental disorder in Uganda?
4. Is severe mental disorder associated with sexual risk behaviour and sexual violence exposure in Uganda?

## 4 METHODS

### 4.1 OVERVIEW OF STUDIES

| Study                        | 1  | 2  | 3  | 4  |
|------------------------------|--|--|--|--|
| <b>Research question</b>     | Is CMD associated with sexual risk behaviours?             | How can SMD influence sexual risk behaviour?                 | How prevalent is HIV in persons with SMD?                    | Is SMD associated with sexual risk behaviour and sexual violence exposure?               |
| <b>Study design</b>          | Cross-sectional population-based study                     | Facility-based qualitative interview study                   | Cross-sectional facility-based study                         | Cross-sectional facility-based study with population-based comparison data               |
| <b>Sampling method</b>       | Purposive with random element                              | Purposive  | Consecutive  | Consecutive<br>Random  |
| <b>Population</b>            | 646 men and women 18-30 years                              | 20 men and women 18-49 years                                 | 602 men and women 18-49 years                                | 602 + 9211 men and women 18-49 years   |
| <b>Mental disorder</b>       | Depressive and anxiety symptoms                            | Major depression, schizophrenia, bipolar affective disorder. | Major depression, schizophrenia, bipolar affective disorder. | Major depression, schizophrenia, bipolar affective disorder.                             |
| <b>Sexual risk indicator</b> | Sexual risk behaviour                                      | Categories of sexual risk                                    | HIV status   | Sexual risk behaviour<br>Sexual violence exposure  |
| <b>Analysis</b>              | Logistic regression<br>Adjustment for multi-stage sampling | Manifest content analysis                                    | Logistic regression<br>Age standardisation                   | Log-binomial and logistic regression<br>Weighting<br>Adjustment for multi-stage sampling |

Table 1. Overview of studies.

## 4.2 STUDY SITES

Studies were performed in Mbarara district (Study 1) and Kampala district (Study 2-4).

Mbarara district is mainly rural, but has one semi-urban town, Mbarara, the district capital, with a projected population of 83 700 persons for 2011[164]. Mbarara district is dominated by the Ankole ethnic group. The predominant economic activity is subsistence farming. The district capital is a transport hub, with banks, shops, dairy plants, a university, and a regional referral hospital which also serves as a teaching hospital.

Kampala district is entirely urban, and is also a city. Kampala is Uganda's capital with a projected population of 1 723 300 persons for 2012[164]. Kampala is dominated by the Ganda ethnic group, but is more culturally and ethnically mixed than the rest of Uganda. Kampala is a relatively metropolitan city. It has universities, banks, shopping malls, and a significant international community. It also has a large number of hospitals, of which two are national referral facilities: Mulago hospital for somatic illness, and Butabika hospital for psychiatric illness.

Butabika hospital is situated in the outskirts of Kampala. The catchment area covers all of Uganda. However, it also functions as a general psychiatric hospital for persons with psychiatric problems in Kampala. Thus, patients residing in Kampala are over-represented. Butabika has 450 beds. It has two admission wards, two convalescent wards, one somatic ward, and one forensic psychiatric ward. The hospital is generally fully occupied. Ward rounds are held approximately twice a week with psychiatrists. Psychiatric clinical officers make treatment and discharge decisions on the other days. Men and women are admitted to separate wards. Food, medicine, and treatment are all provided for free. The hospital also has a psychiatric outpatient department, a dental outpatients unit, and a general medical outpatients department. There is also an HIV outpatient department. In addition, the hospital has three specialized units: a drug and alcohol unit, a child and adolescent unit, and a psycho-trauma unit.

In Kampala district in 2011, the HIV prevalence in persons aged 15-49 was 4.1% in men, and 9.5% in women[138]. In south-western statistical region, to which Mbarara district belongs, HIV prevalence was 6.6% in men and 9.0% in women[138] in the same age group, for the same year.

### **4.3 STUDY 1**

#### **Study design**

Cross-sectional population-based study of the association between common mental disorder and sexual risk behaviour, in nine divisions/sub-counties in Kampala and Mbarara districts.

#### **Purposive population-based sample**

Data was collected from September 2004 to June 2005. A modified three-stage cluster sampling method was used. First, three sub-counties/divisions were purposively selected in each of Kampala, Mbarara town, and Mbarara district. Then seven villages/neighbourhoods were purposively selected in each sub-county/division. These two steps used purposive sampling in order to obtain a wide range in level of urbanicity and economic development. The third sampling step comprised a random element, with ten participants selected in each village/neighbourhood. We used a random walk procedure, since we did not have a sampling frame at the time of the study[165]. From a central location in each selected village/neighbourhood, a walk was performed in a random direction. Every third household encountered was visited, until ten interviews had been conducted. All persons aged 18-30 years, present at home, and residing in study areas, were interviewed. Persons suffering from severe mental or physical illness, or heavily influenced by alcohol or drugs, were excluded. The proportion of eligible persons in selected households who were at home at the time of the visit was estimated at 90-95%. The proportion of those at home who accepted to participate was estimated at >95%.

#### **Exposure**

Three measures of poor mental health were used: depression, psychological distress, and heavy-episodic alcohol drinking. The Hopkins Symptoms Checklist (HSCL-25) was used to assess depression and psychological distress[166]. This instrument consists of 25 questions assessing symptoms of anxiety (10 items) and depression (15 items) during the past week. The response to each item is graded from 1 (i.e. not at all) to 4 (i.e. extremely). The HSCL-25 was chosen since it has been widely used in different cultural contexts, and given that its depression section has been validated among the Baganda[126,167]. Thus, probable depression was measured by applying a cut-off score for screening of major depression among the Baganda, to depression items of the HSCL-25[126]. Similar to the previous study[126] we reasoned that given the cultural relatedness between the Baganda and the Banyankore (the other ethnic group under study) the same cut-off score could be used also among the Banyankore. Psychological distress was measured using both depression and anxiety items of the HSCL-25, and calculating an average item score. Psychological distress was categorised based on quartiles. We took the following measures to obtain cross-cultural equivalence[168] of the HSCL-25: Forward and backward translation was followed by discussions and modifications in two bilingual teams including the first or second authors, and Ugandan clinical psychologists, aiming at semantic equivalence. We showed case-vignettes of depressed persons (with HSCL-25 symptoms) to a small convenience sample of lay Ugandans, in order to explore whether the condition was recognized; results indicated content equivalence. We had



interviewers read and explain questions and Likert scale options in order to obtain technical equivalence. Further, as mentioned previously, we noted that (other translations of) the depression sub-scale of the HSCL-25 had been validated against structured clinical interviews[126], and local illness constructs[167], suggesting criterion validity. The distribution of HSCL-25 total scores, i.e. psychological distress, in men and women is shown in Figure 1 below. Heavy-episodic drinking refers to risky single-occasion drinking[169], and was measured as the number of times ‘drunk on alcohol’ per week (0 vs. 1 or more).

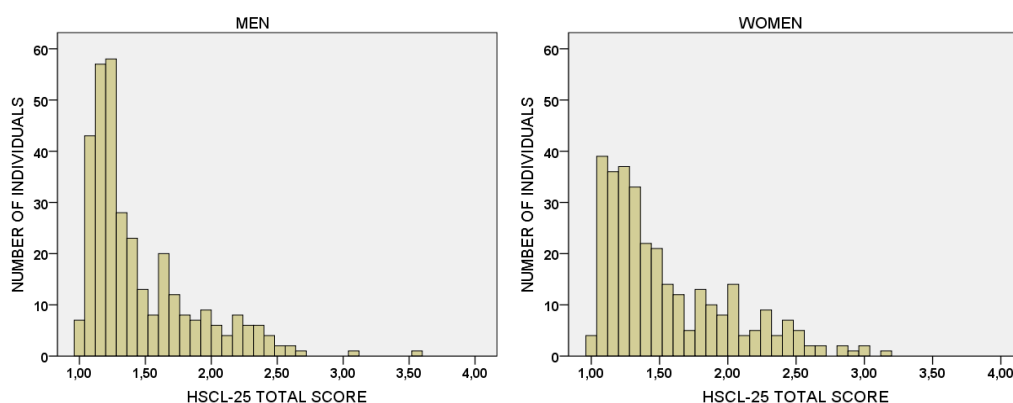


Figure 1. Description of exposure. Distribution of HSCL-25 total scores in men and women.

## Outcome

Three indicators of sexual risk behaviour were used: Number of lifetime sexual partners indicates accumulated HIV risk[170], and current HIV risk[171,172]. Number of current sexual partners indicates current HIV risk[173], and was categorized in order to target concurrent sexual relationships (0-1 vs. 2+), i.e. possible membership of a wider sexual network[174]. Condom use was based on a question about ‘condom use when having sex’, with response alternatives being always, sometimes, or never. Condom use was dichotomized as always (consistent) vs. sometimes/never (inconsistent), since consistent, but not inconsistent use, is protective against HIV[175].

## Covariates

We selected for adjustment a set of variables that were deemed plausible confounders: age, place of residence, education, and marital status.

## Statistical analysis

Analyses were stratified by sex, based on the literature[52,84]. Logistic regression analysis was used to investigate the association between each exposure variable and outcome, while adjusting for covariates. Adjustment for design effect due to cluster sampling was performed, but results only marginally changed, and unadjusted results are therefore shown in Paper I.

## **4.4 STUDY 2**

### **Study design**

Qualitative facility-based interview study of sexual risk behaviours and sexual violence, in patients at Butabika and Mulago hospital inpatients and outpatients departments.

### **Purposive hospital-based sample**

Data was collected from November 2009 to January 2010. Participants were recruited from psychiatric outpatients departments and from convalescent inpatients wards using purposive sampling, in order to obtain variability in terms of sex, diagnosis, in- or outpatient status, and HIV status. Clinicians referred potential participants from the patients attending their services to the research interviewers, based on information from research assistants about the type of participant desired. Inclusion criteria were: age 18-49 years, diagnosis of schizophrenia, bipolar affective disorder or major depression, and mental capacity to give informed consent. We required that inpatients had been cleared for discharge. Participation rate among persons approached by the research interviewers was 77%.

### **Qualitative data**

Data was collected using a semi-structured interview guide with open-ended questions covering participants' living situation, the mental illness, previous sexual experiences, and HIV. Interviewers were Ugandan sex-matched clinical psychologists. Interview languages were English or Luganda. Interviews were audio recorded, translated, and transcribed verbatim into English. Discussions were held after each interview, with interview content and quality discussed. Modifications to the interview guide were made when indicated. Field notes were made throughout the fieldwork. Structured questions were used to collect data on socio-demographic characteristics and HIV status. Psychiatric diagnoses were extracted from patient charts.

### **Qualitative data analysis**

Preliminary data analysis started during field-work. After field-work, transcripts were read several times. Case-summaries were developed for data overview. Data was analysed using manifest content analysis[176]. Meaning units (e.g. sentences) were labelled using descriptive codes, identical codes were merged, and final codes were aggregated into categories. Names of categories were inductively derived from the data. The NVIVO 9 software was used. All co-investigators read a selection of transcripts, with a consensus decision taken on the final list of categories.

## 4.5 STUDY 3

### Study design

Cross-sectional facility-based study of HIV prevalence in patients consecutively discharged from psychiatric wards at Butabika hospital.

### Consecutive facility-based sample

Study 3 and Study 4 were based on the same data collection for psychiatric patients. Data pertaining to psychiatric patients was collected from February to April 2010. A minimum sample size of 500 was found necessary based on requirements for Study 4. All consecutive patients discharged from the two psychiatric admission wards during the study period were screened for eligibility. Inclusion criteria were: age 18-49 years, diagnosis of schizophrenia, bipolar affective disorder, major depression, and other non-substance-use-related psychosis, knowledge of English or Luganda, and mental capacity to give informed consent. Participation rate (and HIV testing rate) among persons approached was 96%. Figure 2 shows the distribution of age of self-reported mental illness onset in participants included in the study.

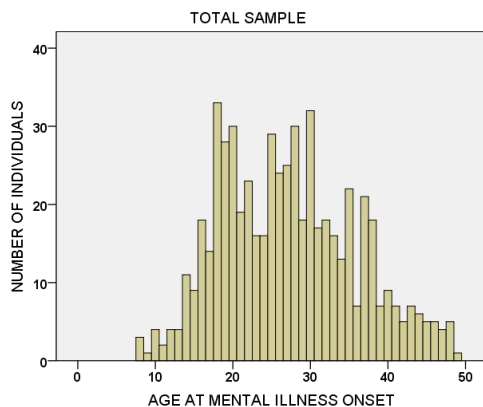


Figure 2. Description of the sample. Self-reported age of mental illness onset.

### Outcome

The outcome was participants' HIV status. Blood sampling was performed in the same session as the interview. Pre-test counselling was given by the research assistant as part of the informed consent procedure. Laboratory procedures were performed in the hospital laboratory. We used an HIV testing algorithm widely used in Uganda: First, the rapid test Determine HIV-1/2 was used. If negative, the participant was diagnosed HIV negative. If positive, a second rapid test was performed, HIV 1/2 Stat-Pak Dipstick. If both tests were positive, the participant was diagnosed HIV positive. If results were discordant a third rapid test was used, Uni-Gold Recombigen, with result of this last test used to determine the diagnosis. Participants having a previous positive HIV test result in their patient file were not tested again. Post-test counselling was given the same day by the research assistant, or later for some participants who declined to wait. Participants testing HIV positive were referred for care and treatment following standard clinical procedures in the hospital.

## **Exposure**

We investigated the following variables as potential predictors of HIV: sex, age, place of residence, marital status, education, occupation, income, psychiatric diagnosis, and history of previous psychiatric admission. Psychiatric diagnoses were extracted from clinical charts and categorized into three broad categories: bipolar affective disorder, non-affective psychosis, and major depression.

## **Covariates**

Age and sex were a priori included as covariates.

## **Statistical analysis**

Logistic regression was used to explore associations between exposure and outcome variables, while adjusting for covariates. Interaction between each variable and sex was investigated. Since no interaction with sex was found, analyses were not stratified by sex. Age-adjusted HIV prevalence was calculated using the age distribution of the general population as standard population[138]. Sensitivity analyses were performed to investigate the potential influence of selection bias due to inclusion of persons having severe mental disorder secondary to HIV.

## **4.6 STUDY 4**

### **Study design**

Cross-sectional facility-based study of sexual risk behaviour and sexual violence exposure in patients at Butabika hospital inpatient departments. Comparison with data from a nationally representative sample.

### **Consecutive facility-based sample**

See Study 3.

### **Random population-based sample**

Data pertaining to persons in the general population was obtained from the 2011 Uganda Demographic and Health Survey[159] (UDHS). The UDHS data was collected from June to December 2011. In the UDHS, a two stage random sampling method was used. In the first stage, 404 clusters were randomly selected from all over Uganda. In the second stage, thirty households were selected per cluster. Women aged 15-49 years, residents, or who slept in the households the night before the survey, were eligible. In every third household, men aged 15-54 years, residents, or who slept in the households the night before the survey, were also eligible. We restricted the UDHS sample to persons aged 18-49 years for comparability. Participation rate among eligible persons identified in the selected households in the entire UDHS sample was 89% in men and 94% in women[159].

### **Exposure**

Severe mental disorder (yes vs no) was the main exposure variable. All persons included in the facility-based sample were considered to have severe mental disorder, while all persons in the general population were considered not to have severe mental disorder. Data on actual mental disorder was not available in the UDHS. In further analyses only pertaining to persons with severe mental disorder, sexual risk behaviour and sexual violence exposure (see below for operationalization) were also treated as exposure variables.

### **Outcome**

The study focused on sexual risk behaviour and sexual violence exposure (against women) during the past twelve months, as main outcome variables. The choice of outcome variables was partly determined by the availability of comparable data between study samples. We derived two sexual risk behaviour variables indicating progressively greater HIV risk: multiple partners during past twelve months, and multiple partners and no condom use during last sex during past twelve months. Multiple partners denote two or more sexual partners, and is a risk factor for HIV in Uganda[172,173,177]. We also derived two sexual violence variables: sexual violence by a marital or cohabiting partner during past twelve months, and sexual violence by another person than a marital or cohabiting partner during past 12 months. Data on sexual violence was collected using the WHO Violence Against Women Instrument[178] in

the psychiatric sample, and the Demographic and Health Survey Domestic Violence Module in the UDHS sample[159]. The exact wording of sexual violence questions differed slightly between studies and is described in Paper IV, page 7. In analyses among persons with severe mental disorder only, HIV status was also treated as an outcome measure; see Study 3 for information about this measure.

### **Covariates**

Age, place of residence, and education were a priori included as covariates in analyses of the association between severe mental disorder and sexual risk behaviour/violence. We did not adjust for marital status since this variable may unlikely cause severe mental disorder, and given that marital status could in fact be on a causal pathway from severe mental disorder to sexual risk behaviour/violence. The same reasoning applied to occupation and income, since these variables indicate current socio-economic position. Education, however, indicates childhood socio-economic position, and was considered a potential confounder since social adversity during upbringing may contribute to psychosis risk[179]. In analyses pertaining to the association between sexual risk behaviour/violence and HIV status, among persons with severe mental disorder, age, place of residence, education, occupation, and marital status were included as covariates.

### **Statistical analysis**

Analyses were stratified by sex, based on previous studies[103]. Log-binomial regression was used to calculate prevalence ratios, while adjusting for covariates. Analyses pertaining to the UDHS sample were adjusted for design effect due to the cluster sampling used. Adjusted results are shown in Paper IV. Estimates for the UDHS sample were weighted using the survey weights provided in the UDHS data file, in order to obtain national representativeness. Logistic regression was used to calculate adjusted odds ratios for analyses within the sample of persons with severe mental disorder.

## **4.7 STUDY PROCEDURES**

Study instruments were translated, back-translated, modified, and pilot-tested, with PL supervising these activities in all studies. Data was collected by Ugandan research assistants. Research assistants were university students (Study 1), clinical psychologists (Study 2), psychiatric nurses (Study 3-4), and psychiatric clinical officers (Study 3-4). Training of research assistants focused on technical and ethical issues pertinent to interviews about sensitive topics. Training and data collection was supervised by Ugandan psychiatrists Dr Godfrey Rukundo and Dr Schola Ashaba (Study 1), by PL and Ugandan medical anthropologist Dr Elialilia Okello (Study 2), and by PL and Ugandan psychiatrist Dr Noeline Nakasujja (Study 3-4). Data collection in Study 1 was followed by PL through phone conversations with Dr Godfrey Rukundo and Dr Schola Ashaba. Interviewers and respondents were not sex-matched in Study 1, but were sex-matched in Study 2-4. All interviews were conducted in privacy.

In the UDHS (Study 4), translated instruments were pre-tested in seven districts. 146 field workers were recruited and trained. Training included interviewing techniques, field procedures, questionnaire review, mock interviews and role plays. Team supervisors and

editors received further training. Interviewers were sex-matched. Interviews in the UDHS were conducted in privacy[159].

#### 4.8 ETHICAL CONSIDERATIONS

Study procedures were approved by the Institutional Ethical Review Committee at Mbarara University (Study 1) and by the Makerere University Research and Ethics Committee (Study 2-4). Below is a discussion of risks and benefits associated with study participation. Table 2 shows risks (-) and benefits (+) and their relationship to the four principles of bio-ethics: Autonomy, non-maleficence, beneficence, justice[180].

| Principle       | Study 1                    | Study 2                                    | Study 3   | Study 4                                    |
|-----------------|----------------------------|--|---|--|
| Autonomy        |                            | Mental incapacity (-)                      | Mental incapacity (-)                             | Mental incapacity (-)                      |
| Non-maleficence | Psychological distress (-) | Psychological distress (-)                 | Psychological distress<br>Social consequences (-) | Psychological distress (-)                 |
| Beneficence     | Referral for care (+)      | HIV prevention<br>Psychosocial support (+) | Referral for care (+)                             | HIV prevention<br>Psychosocial support (+) |
| Justice         |                            | Research benefits<br>vulnerable group (+)  | Research benefits<br>vulnerable group (+)         | Research benefits<br>vulnerable group (+)  |

Table 2. Risks and benefits in sub-studies, and their relationship to bioethics principles.

##### *Mental capacity to give informed consent*

In Study 2-4, the clinician in charge and the research assistant independently assessed participants' mental capacity to give informed consent. Clinicians made overall clinical judgments. Research assistants used the following criteria: (1) Capacity to understand the information about the study, (2) capacity to express a choice based on this information, (3) insight about having a mental health problem, and (4) capacity to participate in a focused discussion. All participants had been cleared for discharge at the time of the informed consent procedure.

### *Informed consent procedures*

Consent forms in all studies included information that participation was voluntary, that participants had the right to withdraw at any time, that the information collected was confidential, and that participation would not influence the right to future medical care. Consent forms were given to, or read to, all participants. All participants gave written or oral consent. Oral consent was accepted given the high illiteracy rate in the study populations.

### *Psychosocial support*

In Study 2, research assistants (clinical psychologists) provided psychological or other counselling after the interview, when deemed indicated. In Study 3-4, research assistants (mental health workers) linked participants to the psycho-trauma centre at Butabika hospital, when deemed indicated. Prior to commencement of Study 3-4 an arrangement had been made with this centre, and a psychiatric nurse was thus available for psychological and psycho-social support throughout the study period.

### *Referral*

In Study 1, at least one psychiatrist was present during all field-work. If any participant showed signs of severe mental disorder, the participant was excluded from the study, and was referred to an adequate health facility.

In Study 3, HIV-testing was performed. HIV-testing in psychiatric settings has been recommended in other contexts[181,182]. Provider-initiated HIV-testing and counselling[141] was being implemented in Butabika hospital at the time of the study, with all patients in theory being offered an HIV-test. However, due to lack of resources, implementation was not complete. In this context, we performed our study where we, by design, made sure that all consenting participants received an HIV-test. Participants testing HIV positive were referred for care and treatment following standard clinical procedures in the hospital.

### *Monetary compensation*

Participants in Study 1 received a bar of soap, and participants in Study 2-4 received 5000 Ugandan Shillings (2.5 US dollars), as compensation for their time.



## 5 RESULTS

### 5.1 STUDY 1

Depression was associated with having a greater number of lifetime sexual partners in women, but not in men. Depression was also associated with having concurrent sexual partners in women, but not in men. However, depression was not associated with inconsistent condom use in either men or women. Results pertaining to depression were not confounded by age, place of residence, education, or marital status (Paper I, Table 2).

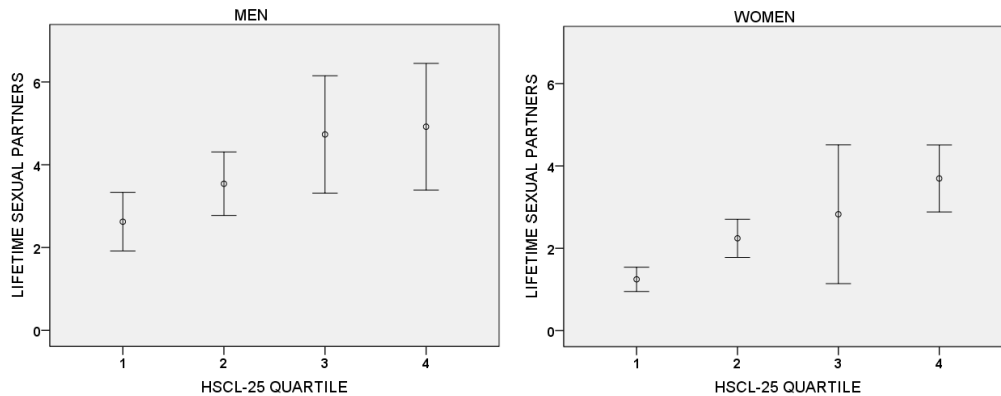


Figure 3. Mean number of lifetime sexual partners with 95% confidence intervals, according to level of psychological distress (HSCL-25 total score quartile).

Psychological distress was associated with a greater number of lifetime sexual partners in both men and women, see Figure 3 above. Psychological distress was not associated with having concurrent sexual partners in men or women. Psychological distress was associated with inconsistent condom use in men, but not in women. Results pertaining to psychological distress were not confounded by age, place of residence, education, or marital status (Paper I, Table 3).

Alcohol use was associated with a greater number of lifetime sexual partners in both men and women. Moreover, alcohol use was associated with having concurrent sexual partners in both men and women. Alcohol use was not associated with inconsistent condom use in men or women. Results pertaining to alcohol used were not confounded by age, place of residence, education, or marital status (Paper I, Table 4).

We performed sensitivity analyses investigating how the decision to use sex-specific HSCL-25 total quartile cut-off scores might have influenced results. Logistic regression analyses were performed anew using cut-off scores common to men and women. Results of these analyses were similar to those presented above.

## 5.2 STUDY 2

Analysis of interview transcripts generated five content categories: casual sex during illness episodes, rape by non-partners, exploitation by partners, non-monogamous partners, and sexual inactivity (Paper II, Table 3). Data variability was greater in women than in men. Women's accounts contributed data to all content categories, while men's accounts contributed data to only two categories, i.e. non-monogamous partners and sexual inactivity.

Psychiatric symptoms were described as a contributing cause of casual sex by some participants. Several women with bipolar disorder described how increased sexual drive, abnormal impulsivity, and self-destructiveness had contributed to casual sex during illness episodes.

Experiences of rape by a non-partner were reported by several women. Five women had been raped after the mental illness started, and at least three of these women had been raped when acutely ill. Rapes had occurred when women were alone at home, when walking alone outside, or when homeless and sleeping in the street.

*“// For me, when I slept on the street I was raped again. // I reached a point where these street men stole all my clothes. // When night came one of them took advantage of me. He was a boda-boda man [motorcycle taxi rider].”*

Women described sexual exploitation by partners. Unmarried women without own income and with poor support from family were dependent on partners, and were not able to leave abusive relationships. One woman became sexually exploited by the clinician treating her mental illness, when the participant's family no longer paid for the psychiatric medication.

*“Sometimes our parents are the ones who put us in such temptations. Because when the man said that he was going to treat me, they should have stopped him and said NO [tapping table], we are going to give you money. But they said thank you musawo [clinician]. Now, doesn't that mean that you have fully given away your daughter? Yes, you have given away your daughter. Do you think that that man can treat me without anything?”*

Some participants suggested that their mental illness caused relationship instability, and made partners have other partners. Psychiatric symptoms such as agitation caused conflict during illness episodes, contributing to marital disruption. Stigmatizing attitudes from family members pushed partners to look for an alternative partner, free of mental illness. In addition, participants suggested that absence from home due to hospital admission caused opportunity and motivation for extramarital sex in partners.

Finally, mental illness contributed to sexual inactivity. Psychiatric symptoms such as irritability, social withdrawal, and loss of energy decreased some participants' interest in sexual activity. However, other participants desired to have sex, but were unable to find a partner. Participants described how being seen as 'mad' or 'mental' made it difficult to attract potential partners. In addition, participants described loss of income due to mental illness as a cause of sexual isolation:

*"Surely for me at my age I would desire to get children, but ever since I got this illness my life has changed. You know, ladies cannot come to you after knowing that you're a mental patient. That's why I have spent seven years without having sex. // You know, women love men who have money. Now, like me, how do I go to church requesting to marry someone when I don't even have enough money to support myself? It is so hard."*

### 5.3 STUDY 3

HIV prevalence in the total sample was 11.3% (95% CI 8.8-13.8). HIV prevalence in men was 7.3% (95% CI 4.1-10.5), i.e. similar to the prevalence reported for men in the general population: 6.1% (95% CI 5.5-6.7)[138]. HIV prevalence in women was 14.3% (95% CI 10.6-18.0), i.e. higher than the prevalence reported for women in the general population: 8.3% (95% CI 7.6-9.1)[138]. Standardization of HIV prevalence for age did not have a major influence on this pattern (Paper III, Table 3).

Within the sample of persons with severe mental disorder, women were more often HIV infected than men, after adjustment for age. Further, older patients were more often HIV infected than younger patients, after adjustment for sex. Place of residence, marital status, income, education, occupation, psychiatric diagnosis and history of psychiatric admission were not associated with HIV infection, after adjustment for sex and age. These associations did not differ between men and women (Paper III, Table 2).

In HIV positive persons with severe mental disorder, the year of mental disorder onset came before the year of HIV diagnosis in 41 participants (15 men, 26 women). The year of mental disorder onset was the same as the year of HIV diagnosis in 15 participants (3 men, 12 women). The year of mental disorder onset came after the year of HIV diagnosis in 11 participants (1 man, 10 women). Figure 2 shows the year of self-reported mental illness onset in all participants, and the year of HIV diagnosis in HIV positive participants.

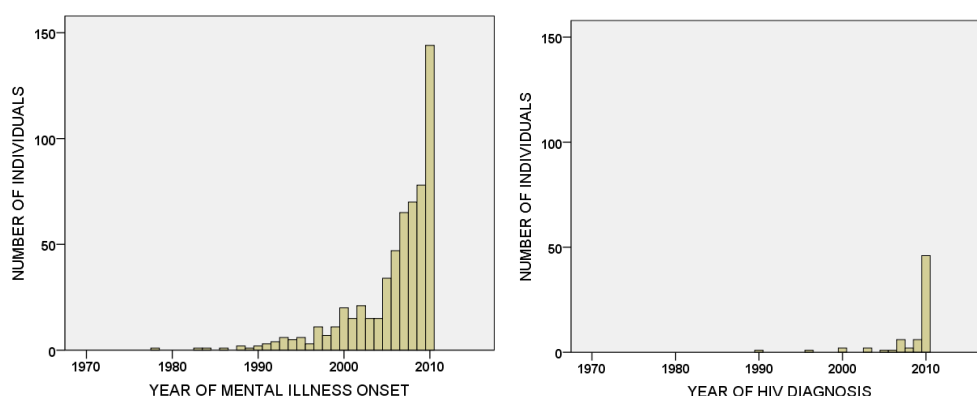


Figure 4. Year of mental illness onset and of HIV diagnosis (in those HIV positive).

Sensitivity analyses were performed in order to explore the extent of selection bias due to inclusion of persons with severe mental disorder secondary to HIV. HIV prevalence in a restricted sample excluding persons with severe mental disorder secondary to HIV (n=588) was: 9.2% (95% CI 6.9-11.5) overall, 7.0% (95% CI 3.9-10.1) in men, and 10.9% (95% CI 7.5-14.3) in women.

## 5.4 STUDY 4

The prevalence of sexual risk behaviour was higher in women with severe mental disorder, than in women in the general population. The prevalence of sexual risk behaviour was similar in men with severe mental disorder, and in men in the general population. These results were not confounded by age, place of residence or education (Paper IV, Table 3).

Persons with severe mental disorder were less sexually active than persons in the general population. However, among those sexually active, the prevalence of sexual risk behaviour was higher in persons with severe mental disorder than in persons in the general population, in both men and women: Prevalence of multiple partners; severe mental disorder: 42.9% in men and 8.2% in women, general population: 25.8% in men and 2.1% in women.

The prevalence of sexual violence by partner was similar in women with severe mental disorder, and in women in the general population. The prevalence of sexual violence by non-partner was higher in women with severe mental disorder than in women in the general population. These results were not confounded by age, place of residence, or education (Paper IV, Table 3).

In men with severe mental disorder, multiple partners was not associated with HIV infection, while multiple partners and no condom use was associated with HIV infection. In women with severe mental disorder, no association was found between sexual risk behaviour and HIV infection, or between sexual violence and HIV infection. These results were not confounded by age, place of residence, education, occupation or marital status (Paper IV, Table 4).

Sensitivity analyses suggested that for stricter definitions of sexual risk behaviours (i.e. 3+, 4+, 5+ partners past twelve months), both men and women with severe mental disorder had higher prevalence than men and women in the general population.

Sensitivity analyses also suggested that selection bias due to inclusion of persons with severe mental disorder secondary to HIV (in turn secondary to sexual risk behaviour) was not a plausible explanation for the differences in sexual risk behaviour found between persons with severe mental disorder and persons in the general population.

## 6 DISCUSSION

Our findings suggest that mental disorder is associated with risk of sexual transmission of HIV in a generalized HIV epidemic. Associations were present across different levels of mental disorder severity, and in relationship to several indicators of sexual risk. There was a clear sex-difference in results, with stronger associations found in women than in men. In addition, women with severe mental disorder were at higher risk of sexual violence than women without severe mental disorder.

### 6.1 MAIN FINDINGS

Common mental disorder in the general population was associated with sexual risk behaviour, with stronger associations in women. Most previous studies in countries with generalized epidemics (but not all[85]) have been performed in selected populations (volunteers[84], university students[93], HIV service users[94]) or high-risk areas (war-affected[92], bars[88]). The current findings thus contribute information about this association in a sample from the general population in Uganda.

Moreover, we found that severe mental disorder requiring hospital admission was also associated with sexual risk behaviour in women, but not men. These findings contribute to previous studies from generalized HIV epidemic settings[101,102,103,104,105,106,107] by the use of a large consecutive sample, and a general population comparison group. Further, in contrast to previous studies, we showed that differences relative to the general population were not due to confounding by socio-demographic variables. Qualitative data in patients with severe mental disorder suggested possible explanatory mechanisms for this association. Thus, severe mental disorder might contribute to sexual health risks through casual sex during illness episodes, rape by non-partners, sexual exploitation by partners, non-monogamous partners, but could also contribute to sexual inactivity. Moreover, our qualitative and quantitative studies suggested that women with severe mental disorder were more often victims of sexual violence by a non-partner, than women in the general population. These findings extend recent quantitative results from Ethiopia by suggesting that the excess risk of sexual violence experienced by women with severe mental disorder may be due to sexual violence perpetrated by non-partners specifically, not by partners[108].

Finally, HIV testing in persons with severe mental disorder showed results consistent with the above patterns. Thus, HIV prevalence in women with severe mental disorder was higher than in women in the general population, but again, no difference was found in men. Previous studies in psychiatric populations in generalized HIV epidemics have suggested that HIV prevalence may be similar to that in the general population[109,110,111,112]. Our findings however, consistent with one previous study from Uganda[105], suggest that this is not the case for Ugandan women.

## 6.2 MECHANISMS UNDERLYING THE ASSOCIATIONS

Potential mechanisms underlying the associations between mental disorder and sexual risk behaviour for HIV are discussed below.

### *Mental disorder causes sexual risk behaviour*

Several plausible mechanisms have been suggested for how common mental disorder could increase sexual risk behaviour[46,47]. For example, depressive symptoms could increase sexual risk behaviour through cognitive, psychological, behavioural (e.g. substance use), and inter-personal (e.g. selection of risky peer groups) mechanisms[46]. The finding that common mental disorder was associated with non-condom use in men but not women, might provide support for a causal interpretation, since men have a greater say over condom use in Uganda[151], and a causal association would therefore be stronger in men. In addition, similar associations were found in a longitudinal study in South Africa, suggesting that mental disorder might have preceded sexual risk behaviour also in our study[84]. Moreover, the finding that both common and severe mental disorder were associated with multiple partners in women but not men has contextual validity; having multiple partners is generally outside cultural norms for women, but men[149,150], and associations between psychopathology and multiple partners (of both directions) might therefore be expected in women, but not men. The South African study did not report such associations, but definitions of multiple partners differed[84]. Longitudinal studies from other contexts have also shown that common mental disorder predicts risk behaviour[50,51,52,53,84], although negative findings do exist[183].

Plausible mechanisms exist also for severe mental disorder causing sexual risk behaviour[48]. For example, cognitive and negative symptoms can hinder planning and execution of safe sexual behaviours, manic symptoms can cause risky pleasure-seeking activities, and psychosis can impair risk perception. In addition, severe mental disorder can have negative socio-economic consequences[184], potentially influencing sexual risk taking[48]. The finding that severe mental disorder was associated with sexual violence by non-partner might also provide a possible mechanism, since some women may not be able to clearly differentiate between consensual and non-consensual sex. Our qualitative findings demonstrated the relevance of these, and other, mechanisms in Uganda. As noted earlier, there is a lack of longitudinal studies on severe mental disorder as a predictor of sexual risk behaviour in the published literature.

### *Sexual risk behaviour causes mental disorder*

Sexual risk behaviour could also contribute to mental disorder. This seems plausible especially for common mental disorder. For example, sexual risk behaviour may involve frequent relationship disruptions causing emotional distress, and could also cause anxiety due to perceived HIV risk. Further, depressive symptoms could develop due to actual sexually transmitted disease[185] including HIV infection[59,186]. Longitudinal studies have provided support also for sexual risk behaviour as a risk factor for common mental disorder[183,185,187], but negative results again exist[188].

Whether sexual risk behaviour causes severe mental disorder may be more uncertain; plausible mechanisms seem fewer. Mediation by Syphilis or HIV infection is however possible, since these conditions can cause severe mental disorder[42,43,189]. However, the prevalence

of Syphilis is low in Uganda (1.8%)[138]. Further, no sex-difference in Syphilis prevalence is present in the Ugandan general population[138], while associations between mental disorder and sexual risk behaviour were only found in women. Concerning HIV, sensitivity analyses suggested that mediation by HIV was not a plausible explanation. Thus, reverse causation mediated by Syphilis or HIV seems unlikely. Longitudinal studies investigating whether sexual risk behaviour predicts severe mental disorder are lacking.

#### *Other explanations of the association*

Mental disorder and sexual risk behaviour could also be linked through a common cause. Some possible common causes have been treated as confounders in analyses, to the extent information has been available, e.g. age, urbanicity of place of residence, and education (as a proxy for childhood socio-economic position), but others were not controlled for and might contribute to associations found, e.g. current socio-economic position (in Study 1).

In summary, several explanations are possible for the associations found between mental disorder and sexual risk behaviour. For the association between common mental disorders and sexual risk behaviour, a bi-directional association is likely. Regarding severe mental disorder, however, the main direction of association arguably goes from severe mental disorder to sexual risk behaviour. These conclusions, of course, pre-suppose that associations were not due to bias or confounding. Methodological limitations will be discussed later.

The fact that associations between mental disorder and sexual risk behaviour could be bi-directional, however, adds to the gravity of the topic. Bi-directional associations could cause vicious circles, resulting in persisting or recurring mental health problems, and aggravated or prolonged sexual risk behaviours.



### 6.3 INTERMEDIARY DETERMINANTS OF HIV RISK

Psychiatric symptoms can directly influence sexual risk behaviour, as already discussed, and our findings suggest that this might indeed have been the case, especially for manic symptoms. This finding is consistent with previous studies [66,67]. However, other factors than psychiatric symptoms also seemed to be involved. In this section, such factors hypothetically mediating the influence of mental disorder on HIV risk will be discussed. These factors are referred to as 'intermediary determinants', in order to comply with the terminology used by the WHO Commission on Social Determinants of Health[190].

Alcohol use is one factor that could mediate the association between mental disorder and sexual risk behaviour[191], although the current findings did not suggest this. Another factor is socio-economic downward drift due to mental disorder, such as unemployment and loss of income[184]. Lack of income could potentially increase the number of sexual partners in women, due to transactional sex[149,154], but also hinder sexual relationship forming, particularly in men. Psychological aspects of living with mental disorder could also influence sexual decisions. Thus, internalized devaluing judgments about self with feelings that options regarding sexual relationships are limited, could contribute to risky sexual decisions in order to obtain intimacy[192,193].

Social support from family members is often decreased in persons with severe mental disorder, due to family members experiencing, or trying to avoid, family stigma[133,137]. For women without own income, poor social support could contribute to transactional sexual relationships, as indicated by our qualitative findings. In addition, the combination of poor social support and lack of income might cause marked relationship inequality, due to economic dependence on the partner[154]. Thus, hypothetically, women with mental disorder could more often live in unequal relationships than other women, decreasing women's influence over sexual decision-making (e.g. condoms), and therefore increasing sexual risk[194]. Women in unequal relationships may also feel forced to accept that partners' have other partners, hypothetically resulting in disproportionate occurrence of partner non-monogamy, and HIV risk. Similarly, lack of alternative sources of support could hinder women from leaving violent sexual relationships[154]. Intimate partner violence may be more common in persons with mental disorder than in the general population[195], although the current data did not suggest such an association. Non-partner sexual violence against women with mental disorder could contribute to HIV risk, especially if occurring repeatedly.

Health system related factors could contribute to HIV risk. Persons with mental disorder receive poorer quality of health care for physical conditions than persons without mental disorder in other settings[196], and this could be the case also in Uganda (e.g. for genital ulcer disease contributing to HIV risk). With regards to mental health services, the incomplete coverage of such services in Uganda most probably have consequences on HIV risk, since inadequately controlled psychiatric symptoms can directly contribute sexual risk behaviour, but also, indirectly contribute to HIV risk, through some of the mechanisms discussed above.

## 6.4 STRUCTURAL DETERMINANTS OF HIV RISK

What factors might act upstream of those in the previous section? This question will be discussed below, with the discussion informed by the WHO Commission for Social Determinants of Health conceptual framework[190]. This conceptual framework suggests that an individual's position in social hierarchies (i.e. structural determinants, e.g. socio-economic position, gender) determines access to economic resources, prestige and power. Access to these resources influences intermediary factors, such as psychological mechanisms, health behaviour, material circumstances, social relationships, and access to health care, in turn having impact on health outcomes (as discussed in the previous section).

Although the above framework does not explicitly include stigma as a structural determinant of health, Hatzenbuehler et al[41] recently suggested that stigma may contribute to population health inequalities, and stigma could well be included in the framework alongside other dimensions of the social hierarchy. Our findings suggest that at least three structural determinants indirectly influenced sexual risk behaviour, violence exposure and HIV risk in our study participants, namely, mental illness stigma, gender inequality, and poverty.

Stigma was described by Goffman as a situation of being disqualified from full social acceptance[197]. The concept of stigma was further developed by Link and Phelan who described a social process comprising the following components: labelling of differences, separation (them vs. us), stereotyping, discrimination[198]. A pre-existing power differential is needed for stigmatization to take place[198].

Stigma can be present on multiple levels, intra-personal, inter-personal, and structural[198]. Our findings show that this is the case also in Uganda. Persons with mental disorder expressed devaluating judgments about self (intra-personal), described exploitative and abusive relationships (inter-personal), and described discrimination in the work-place (structural). Further, the neglect of mental health services and the long-standing absence of an updated mental health legislation[135] may illustrate stigma (structural) on the highest societal and policy levels.

Based on Hatzenbuehler et al[41], and given our findings, the interpretation that stigma indirectly contributed to sexual risk behaviour, sexual violence exposure, and HIV risk seems plausible. Of note however, our findings indicate that mental illness stigma increased sexual risk for women, but not to the same extent for men. This observation is consistent with the concept of intersectionality, suggesting that when axes of inequality (e.g. stigma, gender) interact in one person, effects can be non-additive [192,199].

Gender refers to a social construct regarding culture-bound conventions, roles, and behaviours[200]. Gendered social vulnerability of women is one suggested explanation of the generally higher HIV prevalence rates in women than in men in sub-Saharan Africa[201]. In Uganda, gender inequality contributes to women's sexual vulnerability to HIV due to relative cultural acceptance of male extramarital sex[149,150], male dominance in decision-making over sex within marriage[151], and violence from men to women within marriage[159,160,161].

Our findings suggest that mental illness stigma exacerbated this existing sexual vulnerability in women, in line with the concept of intersectionality[199]. For example, some women experienced how mental illness stigma led to devaluing attitudes from partners, and described how this resulted in sexual exploitation, and to the partner being non-monogamous. Thus, women with mental disorder seemed to have *even less* influence over decision-making about sex in intimate relationships, than other women. Further, women with mental disorder seemed to experience *even more* sexual violence (by non-partners) than other women, hypothetically due to interplay between societal norms condoning gender-based violence and perceived impunity by rape perpetrators due to women being stigmatised.

In contrast, although men in our study did complain over stigma, it was not clear that this stigma increased their sexual risk of HIV. Mental disorder interferes with the male gender role (i.e. be a bread-winner), indeed leading to stigma[202,203]. For many men this however results in sexual isolation, thus decreasing sexual risk behaviour. Nevertheless, it remains possible that some men with mental disorder do engage in risk behaviours, potentially to compensate for experienced social and sexual isolation.

Poverty has also been suggested to be a structural driver of the sub-Saharan African HIV epidemics[204], although aspects of both poverty and wealth could probably contribute to HIV transmission[152]. Societal economic inequality is another suggested structural factor of importance[205]. In Uganda, the association between poverty/wealth and HIV risk is only partly understood, but at least in some contexts, access to and power over cash income are associated with decreased sexual risk behaviour in Ugandan women[153]. Further, as mentioned, poverty can contribute to transactional sexual relationships[149,154].

Stigma and poverty can influence each other leading to a downward spiral of social exclusion[137,184,206]. Many persons with severe mental disorder, and especially women, did not have a current income in our study. We did not investigate in detail the interplay between mental disorder and poverty in shaping sexual risk, but data nevertheless suggested that when present in the same person, mental illness stigma, gender disadvantage and poverty may reinforce each other and create situations of high sexual vulnerability and elevated HIV risk.

## 6.5 RELEVANCE FOR DEVELOPMENT AND HUMAN RIGHTS

The WHO Report on Mental Health and Development states that persons with mental disorder should be targeted as a vulnerable group in development programmes[17]. Our findings provide support for this notion, in a sub-Saharan African setting.

Our findings are in line with the view that targeting mental health is relevant to achieving the Millennium Development Goals (MDG)[207,208]. Thus, the findings suggest that mental health considerations should be part of HIV preventive efforts in generalized epidemics in order to achieve MDG 6, i.e. combat HIV/AIDS. The findings also suggest that a focus on sexual exploitation and violence of women with severe mental disorder should be included in efforts to achieve MDG 3, i.e. promote gender equality.

Findings regarding sexual exploitation and violence against women with severe mental disorder indicate ongoing violations of these women's human rights. Of note, the right to freedom from exploitation, violence and abuse is specifically spelled out in the United Nations Convention on the Rights of Persons with Disabilities[209].

The current findings are of relevance to other settings with scarce mental health services, limited programmes for social protection, and marked gender inequality, and especially, for such settings that also have a generalized HIV epidemic. Thus, our findings are of relevance to many other low- and middle-income countries in sub-Saharan Africa.

## 6.6 METHODOLOGICAL CONSIDERATIONS

### *Selection bias in population-based study*

The household sampling method used in Study 1 confers the potential of two types of selection bias. First, persons who were not at home at the time of the visit were not followed-up, and if such non-responders were different in terms of mental health *and* sexual risk behaviour, spurious associations would result. The proportion of all eligible persons who were not at home was estimated at 5-10%. Descriptive data on non-responders was not collected. Second, the random walk procedure used in the final sampling step could potentially induce bias. In random walks, households close to village/neighbourhood centres are more likely to be selected than those in the periphery[165]. In Mbarara district, village centres are generally places of greater economic and social exchange than the village periphery. Potentially, residents of village centres therefore have more sexual contacts than residents in the village periphery, but this is speculative. However, place of residence within villages would also have to be associated with mental health, in order to cause spurious associations.

### *Selection bias in facility-based study*

Selection was probably implicated in Study 2-4, although one can only speculate about its nature. Patients admitted to Butabika hospital may be selected for clinical severity, since Butabika is a national referral hospital, but other types of selection could also be involved. Geographical distance from Kampala is an obvious barrier to access, since transport can be costly. Thus, economic resources facilitate admission for persons residing in distant areas. However, economic resources may also enhance access and adherence to maintenance treatment in the area of residence, and could thus instead prevent admission. In addition, health beliefs can influence help-seeking, and might also hypothetically be associated with sexual risk behaviour.

In Study 3, HIV prevalence might be inflated due to inclusion of persons having severe mental disorder secondary to HIV. We performed sensitivity analyses, but the predictive value of the definition of secondary severe mental disorder is unknown. However, some aspects of the findings nevertheless suggest that the excess HIV prevalence found in persons with mental disorder was *not* due to selection bias. First, excess prevalence was only found in women, and it is not clear why HIV-related psychiatric disorders would preferentially affect women. Studies in high-income countries with low HIV prevalence have generally reported a high male-to-female ratio for this diagnosis, while a Ugandan study reported a ratio below one[122]. These differences might simply reflect sex ratios in HIV prevalence in the settings involved. Second, the fact that also young women with severe mental disorder had more HIV than young women without, could suggest that selection bias is not the sole explanation. Rates of HIV transmission during childhood/early adolescence are low in Uganda, and the HIV prevalence in our young participants therefore likely reflect either (1) recent HIV infection, or (2) perinatal HIV infection. Since mania and psychosis generally develop late in HIV/AIDS disease progression, infection during late adolescence unlikely causes secondary severe mental disorder just a few years later. Further, the youngest participants were born 1992, and antiretroviral therapy was introduced to scale in Uganda more than ten years later. Some Ugandans perinatally HIV-infected at that time have indeed reached their twenties[210], but the population proportion of this group is probably small[211].

### *Measurement of mental disorder*

HSCL-25 is a symptom rating scale which can also be used for screening purposes. Thus, our measure of depression in Study 1 is a measure of possible, not definitive, major depression. Nevertheless, several factors suggest that HSCL-25 was a valid measure of depressive psychopathology in Study 1: (1) Construct validity was indicated by a brief pre-study (in Mbarara district only) where lay Ugandans recognized HSCL-25 symptoms in case-vignettes, as signs of a condition that was common, distressing, and that may lead to several types of response: addressing underlying social problem, seeking counselling from friends/relatives, going to church to pray, going to traditional healer, seeking formal care. Further, expected associations were found between known predictors of poor mental health, and HSCL-25-scores (see our previous article[129]). In addition, the Chronbach's alpha was high, indicating the existence of a whole underlying construct. Finally, the distribution of HSCL-25 scores was similar to the distribution of depression scores in other populations[212]. (2) Criterion validity was not established, but has been previously confirmed for other translations of the same instrument in Uganda[167,213].

The validity of psychiatric diagnoses in Study 2-4 is questionable. Diagnoses in Butabika hospital are often made based on very limited information, and often by non-psychiatrists. This possible misclassification likely contributed to null-findings in Study 3. However, virtually all patients admitted to Butabika hospital are psychotic at admission, and most participants included in Study 3-4 therefore fulfilled inclusion criteria.

### *Measurement of sexual risk behaviour*

Rates of sexual risk behaviour in Study 1 and 4 might be inaccurate due to reporting bias[214,215]. Given socio-cultural norms in Uganda[149,150], social desirability bias likely yields overestimates of the number of sexual partners in men, but underestimates in women, similar to other sub-Saharan African settings[216]. The observation of no association between behavioural and biological data in women with severe mental disorder in Study 4 might arguably suggest low validity of these women's reports, but other explanations are possible, since data were cross-sectional. Recall bias could also influence accuracy of reporting, and in theory this could be an important problem in persons with severe mental disorder. However, studies in other settings suggest satisfactory reliability of sexual risk behaviour reports in this group[217,218].

The question about condom use in Study 1 was general and did not have a specific time frame. Questions about usual behaviour may be particularly prone to elicit normative responses, potentially influencing validity of this measure[219]. Further, the predictive power of condom use on HIV risk likely increases if condom use is stratified by other risk behaviours, e.g. number of sexual partners, and this was not done in Study 1. In Study 4, however, one outcome measure was multiple partners and no condom use at last sex.

### *Measurement of sexual violence*

Measurement of gender-based violence is sensitive to methods and context of data collection[220]. In Study 4, prevalence estimates in women with severe mental disorder were compared to those in a different survey in the general population. Therefore, non-differential misclassification is possible. First, the instruments used in these studies were not identical. The DHS Module was developed from an early draft of the WHO instrument[221], and questions regarding sexual violence by a partner were broadly similar. Questions regarding sexual violence by non-partner however differed, with the WHO instrument asking about whether the woman had been 'forced to have sex or to perform a sexual act', but the DHS instrument asking about having been 'physically forced [...] to have sexual intercourse'. The latter formulation is narrower, potentially leading to lower rates in the UDHS. Second, the context of the interviews differed. Psychiatric patients were interviewed inside Butabika hospital by mental health workers known by patients, while participants in the UDHS were interviewed at home by anonymous field-workers. These differences might have caused greater disclosure of sensitive information in the UDHS, but the opposite bias is also possible.

A more general issue in Study 4 is how the cultural understanding of what constitutes sexual violence might influence rates obtained. This could be a particularly important issue for reporting of sexual violence within marriage, where men generally have more decision-making power over sex, and where many Ugandan women feel physical violence is justified if the woman does not fulfil her marital duties. In Rakai, young women felt that it is the 'married woman's duty to unconditionally satisfy her male partner's sexual desires'[162]. These women stated that forced sex within marriage could not be deemed rape, and indeed questioned whether sex within marriage could at all be 'done against the woman's will'. These statements represent the views of only a few Ugandan women, but it is nevertheless plausible that rates of sexual violence by partners are underestimates. Of note however, reporting of sexual violence might differ between women with mental disorder and women without. Based on our qualitative findings in Study 2, women with mental disorder might be less likely to object against abusive behaviour from partners. The lack of difference in rates of sexual violence exposure by partner between women with mental disorder and women without mental disorder could thus hypothetically be due to such differential reporting.

### *Confounding*

The associations found could potentially be due to confounding by factors not measured, or not fully adjusted for. Wealth is (weakly) associated with sexual risk behaviour in the Ugandan general population[159] and might also be associated with mental health in Study 1. Intimate partner violence against women could cause both poor mental health[84] and risk behaviour[222] and also confound associations in Study 1. In Study 4 we did not adjust for childhood abuse. Childhood abuse increases risk of psychosis[223], and is associated with adult sexual risk behaviours[224] and sexual violence[225], and is thus a possible confounder.

### *Data quality in semi-structured interviews*

We attempted to obtain rich data on sensitive topics by working with interviewers who were sex-matched Ugandan clinical psychologists, used to communicating with persons with severe mental disorder, and wearing civil clothes. This strategy was at least partly successful; we did obtain very sensitive information from several participants. Data quality was however variable. Some interviews were poor in information, especially for persons with schizophrenia, but also for some other participants. Possibly the gap in socio-economic status between interviewers and interviewees might have discouraged disclosure in some cases. This notion was suggested by interviewers during de-briefing. The interview context (treatment setting) and the semi-structured interview guide used might also have decreased rapport between interviewer and interviewee.

### *Rigour in qualitative analysis*

In order to enhance credibility of findings, data disconfirming previous and emerging theories were noted and also actively sought. For example, we sought data disconfirming the emerging hypothesis that mental disorder did *not* increase sexual risk behaviour in men. However, we failed to find such disconfirming evidence. A larger sample of men, and more effective sampling strategies (e.g. screening for sexual risk behaviour prior to inclusion) might have been needed to obtain information-rich cases also among men, within the duration of the study period. Analyst triangulation was used, also to enhance credibility. First, during data collection, two authors read interview transcripts and agreed on preliminary (mainly inductive) categories. Second, after data collection and during formal analysis, three authors were directly involved in content category forming. Generally, agreement in interpretation was high between analysts. Finally, frequency counts were included in the manuscript to show the extent to which categories were based on data.



## 7 CONCLUSIONS

We aimed to investigate whether mental disorder was associated with sexual risk of HIV transmission in a low-income country with a generalized HIV epidemic. Our studies suggest that such an association exists. The association was stronger and more consistent in women than in men.

In women, both common and severe mental disorders were associated with sexual risk behaviour. Severe mental disorder was also associated with exposure to sexual violence by a non-partner, and with prevalent HIV-infection.

In men, common mental disorder, but not severe mental disorder, was associated with sexual risk behaviour. No association was found between severe mental disorder and prevalent HIV infection.

The associations found were not due to confounding by basic socio-demographic variables. By design we were not able to show that mental disorder preceded the development of sexual risk behaviour, or first sexual violence exposure. However, qualitative and quantitative findings were consistent.

Our findings suggest that women with mental disorder in Uganda may be at higher risk of HIV, and at higher risk of sexual violence, than women in the general population.

These results are likely transferable to other resource-poor settings with low mental health treatment coverage, high level of gender inequality, and widespread HIV transmission in the general population.

## 8 IMPLICATIONS

### *Research*

Longitudinal studies should further explore the potential impact of common mental disorders on population level HIV transmission. Integrating brief mental health measurements into ordinary data collection rounds in population-based HIV cohorts is one feasible strategy.

Longitudinal studies are needed to investigate HIV incidence also in persons with severe mental disorder. Ideally, studies should be population-based, but facility-based cohort would also provide important information.

Community-based research should identify interventions reducing negative medical, social and economic consequences of severe mental disorder. Community-based rehabilitation provides one possible alternative.

### *Policy and practice*

Provider-initiated HIV testing and counselling should be fully implemented in psychiatric wards, with due consideration to psychiatric patients' mental capacity to give informed consent.

Assessment of sexual violence experiences should be part of routine clinical history taking. Support structures should be established for violence victims.

Policy makers and HIV prevention practitioners should consider focusing on women with severe mental disorder as a group at high risk of HIV infection.

Urgent action is warranted to protect women with severe mental disorder against sexual exploitation and violence. Action is needed at multiple levels, including policy making and protective legislation.

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