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HIV TRENDS, RISK BEHAVIOURS, SOCIAL STRUCTURAL BARRIERS AND RETENTION IN HIV CARE AMONG KEY POPULATIONS IN NEPAL AND THE ASIA- PACIFIC REGION

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HIV Trends, Risk Behaviours, Social Structural Barriers and Retention in HIV Care among Key Populations in Nepal and the Asia-Pacific Region

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HIV TRENDS, RISK BEHAVIOURS, SOCIAL STRUCTURAL BARRIERS AND RETENTION IN HIV CARE AMONG KEY POPULATIONS IN NEPAL AND THE ASIA-PACIFIC REGION

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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“Our greatest glory is not in never falling, but in rising every time we fall.”
Confucius

ABSTRACT

Background: The HIV epidemic in the Asia-Pacific region is characterised by a number of concentrated, and in some geographical areas, growing epidemics, particularly among key populations [men who have sex with men (MSM), transgender (TG), female sex workers (FSW), and people who inject drugs (PWID)]. Some countries in the region have been particularly successful in reducing the incidence rate, but other countries in the region have experienced opposite scenarios. The coverage of antiretroviral treatment (ART) is still low in the region, ranging between 6-42%. Key populations in many Asia-Pacific countries also frequently suffer from discrimination and marginalisation, and their behaviours, often classified as illegal, further increase their already high vulnerability to HIV infection. HIV continues to spread predominantly through sexual transmission and can be linked to sexual risk behaviours, such as inconsistent condom use. More than 90% of all new HIV infections among young people in the Asia-Pacific region occur among young key populations belonging to either the MSM, TG, FSW or PWID group. The aim of this study was to understand HIV trends, social structural barriers, risk behaviours and retention in HIV care among key populations in 7 countries of the Asia-Pacific region, with a special focus on Nepal.

Methods: This project utilised two main data sources: (a) baseline data from a prospective longitudinal study of community access to HIV treatment, care and support services (CAT-S) that involved 59 sites in 7 countries (Bangladesh, Indonesia, Lao People's Democratic Republic, Nepal, Pakistan, Philippines, Vietnam). Between 1 October 2012 and 31 May 2013, a total of 7 843 people living with HIV (PLHIV) aged 18-50 years were recruited in CAT-S. (b) Nationwide surveillance survey data collected from key populations (PWID, MSM, TG, FSW, male labour migrants) across Nepal for over a decade. A total of 7 505 young (aged 16-24 years) key populations were recruited using two-stage cluster and respondent driven sampling from four epidemic zones over a 12-year period, 2001–2012.

Results: We found a high prevalence of inconsistent condom use among PLHIV in the seven study countries: overall 40%, but varying from 17% in Lao People's Democratic Republic to 60% in the Philippines, did not practice safe sex. This was associated with belonging to a key population (drug users, FSW or a refugee sub-population), poor HIV-treatment literacy and not receiving ART (Paper I). A high proportion of PLHIV (40-51%) presented late for HIV care, which delayed linkage to care. However, once PLHIV enrolled in care, retention in the various steps of the HIV care cascade including adherence to ART was satisfactory (Paper II). Findings based on surveillance survey data suggest that adverse micro-level social structural factors such as reduced condom-negotiation skills, economic vulnerability, inadequate social support, and experience of abuse, contribute to enhance the risk environment associated with unprotected sex among FSW in Nepal (Paper III). Our analyses also indicate that the presence of two or more adverse conditions in the physical, social, or economic environment of FSW, interacted to increase the risk of unprotected sex among Nepalese FSW (Paper III). However, the trend analysis suggests a sharp and consistent decline in HIV prevalence over the past decade in different epidemic zones among young key populations in Nepal, most likely due to a parallel increase in safe needle and syringe use and increased condom use (Paper IV).

Conclusions: Non-use of condoms and late presentation for HIV care is still highly prevalent among PLHIV in the seven study countries. Different adverse conditions, so-called micro-level social structural factors such as physical factors (client refusal to pay after having sex), social factors (poor social support and poor condom negotiation skills) and economic level factors (unprotected sex to make more money) levels are associated with increased odds of HIV-related risk behaviours among Nepalese FSW. HIV prevalence and risk behaviours have declined among young key populations in Nepal, but to maintain this downward trend, the focus should be on addressing the burden of negative social structural factors (unprotected sex to boost income and poor social support).

Keywords: Condom use behaviour, HIV infections/ prevention, antiretroviral therapy (ART), HIV care cascade, syndemic, key populations, Nepal, Asia-Pacific region

LIST OF SCIENTIFIC PAPERS

I. **Keshab Deuba**, Verena Kohlbrenner, Sushil Koirala, Anna Mia Ekström. Condom use behaviour among people living with HIV: A 7-country community-based participatory research in the Asia-Pacific region.

(Submitted).

II. Sushil Koirala, **Keshab Deuba**, Oranuch Nampaisan, Gaetano Marrone, Anna Mia Ekström. Facilitators and Barriers for Retention in HIV Care between Testing and Treatment in Asia - a Study in Bangladesh, Indonesia, Lao, Nepal, Pakistan, Philippines and Vietnam.

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III. **Keshab Deuba**, Sarah Anderson, Anna Mia Ekström, Satish Raj Pandey, Rachana Shrestha, Deepak Kumar Karki, Gaetano Marrone. Micro-level social and structural factors act synergistically to increase HIV risk among Nepalese female sex workers.

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IV. **Keshab Deuba**, Anna Mia Ekström, Göran Tomson, Rachana Shrestha and Gaetano Marrone. HIV decline associated with changes in risk behaviours among young key populations in Nepal: analysis of population-based HIV prevalence surveys between 2001 and 2012.

Int J STD AIDS. 2016 Oct 31. pii: 0956462416678303.

The papers will be referred to in the text by their Roman numerals.

TABLE OF CONTENTS

List of abbreviations.....	4
1 BACKGROUND	5
1.1 The HIV epidemic in the Asia-Pacific region	5
1.2 The HIV epidemic in the Study countries	5
1.2.1 Burden of HIV among young key populations.....	10
1.2.2 Burden of social and structural risk factors among key populations.....	12
1.2.3 Prevalence of unprotected sex among PLHIV and key populations	14
1.2.4 The importance of retention in HIV care.....	17
1.3 Health system response to HIV in the study countries	20
1.3.1 Interventions targeting key populations in the region.....	23
1.4 Key population surveillance methods for this thesis	24
1.5 Rationale for this thesis.....	25
2 AIM AND OBJECTIVES.....	27
2.1 Conceptual framework for study.....	28
3 MATERIALS AND METHODS	30
3.1 Theoretical framework to study retention in HIV care and syndemic effects of structural factors.....	30
3.2 Study design	31
3.3 Study setting	33
3.4 Study population, data management, and data analysis	33
3.5 Ethical aspects of the studies	38
3.6 My role in the field work, data collection, analysis and writing.....	40
4 RESULTS	41
4.1 Prevalence of inconsistent condom use and the associated factors among PLHIV (PAPER I).....	41
4.2 Factors affecting retention in HIV care between HIV testing and treatment initiation (PAPER II)	42
4.3 Prevalence of HIV and the syndemic effects of micro-level social structural factors of risk behaviors (Paper III).....	47
4.4 Trends in HIV prevalence and risk behaviors among young key populations in Nepal (PAPER IV).....	48
5 DISCUSSION.....	51
5.1 Methodological considerations	54
6 CONCLUSIONS	58
7 PROGRAMMATIC AND POLICY IMPLICATIONS	59
8 ACKNOWLEDGEMENTS	60
9 REFERENCES	61

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
ARV	Antiretrovirals
ART	Antiretroviral Therapy
CBPR	Community Based Participatory Research
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immunodeficiency Virus
HTC	HIV Testing and Counselling Services
KTM valley	Kathmandu Valley
Lao PDR	Lao People's Democratic Republic
FSW	Female Sex Workers
GSEM	Generalized Structural Equation Modeling
MSM	Men who have sex with men
PWID	People Who Inject Drugs
PLHIV	People Living with HIV
RDS	Respondent Driven Sampling
RERI	Relative Excess Risk due to Interaction
STI	Sexually Transmitted Infection
TasP	Treatment as Prevention
T 2.0	Treatment 2.0
TG	Transgender
UNAIDS	Joint United Nations Program on HIV/AIDS
USD	United States Dollar
VIF	Variance Inflation Factor

1 BACKGROUND

1.1 THE HIV EPIDEMIC IN THE ASIA-PACIFIC REGION

The contribution of HIV/AIDS to years of life lost globally has been decreasing over time (i.e. ranked fourth in 2005 to seventh in 2015) (1). Similarly, the global burden of HIV/AIDS estimated as age-standardised disability-adjusted life years also declined by more than 40%, from 2005 to 2015 (2). An estimated 36.7 million people were living with HIV (PLHIV) globally in 2015, 14% of those live in the Asia-Pacific region (3). Almost all countries in the Asia-Pacific region are experiencing concentrated HIV epidemics, defined as a HIV prevalence of less than 1% in the general population, but more than 5% in at least one key population (4, 5). The identified key populations at highest risk of HIV in the region are people who inject drugs (PWID), men who have sex with men (MSM), transgender (TG) people and female sex workers (FSW) (4). In this region, the epidemic among key populations is especially concentrated in urban cities (Figure 1) (4), with some exception in local areas within countries that are experiencing a more generalised spread (6). One example of this is a remote province of Papua in Indonesia, with a generalised epidemic and a 2.4% HIV prevalence among the general population aged 15-49 years (6, 7). Another example is that new HIV infections are rapidly increasing among MSM in the Philippines where MSM account for 85% of all new infections acquired through sexual transmission, due to a lack of targeted health services for this group in the country (8, 9). In 2015, Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that 5.1 million PLHIV in the region, of which 12% were aged 15-24 years (10). In the same year, an estimated 300 000 new HIV infections and 180 000 AIDS-related deaths occurred in the region (10). Through partnerships with national ministries of health and international collaboration, the countries in the Asia-Pacific region have overall successfully managed to reduce the number of new HIV infections by 31% between 2000 and 2014 (4). However, this preventive achievement has not been consistent, either between or within countries in the region (4). Regarding HIV treatment, all countries in the region are rapidly expanding access antiretroviral (ARV) treatment services, but the regional coverage of antiretroviral combination therapy (ART) in is lower (41% in 2015) than the global average (46%) (3, 4).

1.2 THE HIV EPIDEMIC IN THE STUDY COUNTRIES

Two of the papers included in this thesis focus on seven countries in the Asia-Pacific region: Bangladesh, Indonesia, Lao People's Democratic Republic (PDR), Nepal, Pakistan, the Philippines and Vietnam. In November 2010 a concept called Treatment 2.0 (T 2.0) (11)

was launched by the WHO and the UNAIDS to promote a simplification of a model of HIV care, in order to achieve the ambitious target of reaching 15 million people on ART by the year 2015. T 2.0 identified community mobilisation as one of five key areas (optimising drug regimens; advancing point-of-care; reducing cost; adapting health service delivery systems; community mobilisation) that help to reach and engage key populations (11). In February 2010, the gathering of 11 National PLHIV Networks from the Asia-Pacific region in Bangkok recognised a necessity to monitor, document and share information related to access and barriers to HIV treatment among PLHIV in the region. The Asia Pacific Network of People Living with HIV/AIDS (APN+) lead its national networks to establish a platform, the so-called 'Monitoring Treatment Access', to document, monitor and advocate issues related to treatment access for PLHIV in the Asia-Pacific region. This platform initially focused on seven countries, namely: Bangladesh, Indonesia, Lao PDR, Nepal, Pakistan, Philippines, and Vietnam. One of the co-authors (Sushil Koirala) of Paper I and II has been involved from the beginning, in establishing the 'Monitoring Treatment Access' platform in the region.

Table 1 summarises the key indicators related to population, government type and major health indicators in the study countries (Table 1). The study countries demonstrate substantial diversity in terms of the size of the population (from 7 million in Lao PDR to 258 million in Indonesia), the type of government (communist vs. parliamtiary republic), literacy rate (from 58% in Pakistan to 96% in the Philippines), and mortality outcomes such as the mortality rate among mothers and their infants: from 54 maternal deaths in Vietnam to 258 maternal deaths in Nepal per 100 000 live births, and from 18 infants deaths in Vietnam to 51 infants deaths in Lao PDR per 1 000 live births (Table 1). However, all the study countries fall under the lower middle-income country category (i.e. a gross national income per capita between \$1,026 and \$4,035) except Nepal, which is categorised as a low-income economy (i.e. a gross national income per capita of \$1,025 or less) (Table 1). Nonetheless, Nepal has been among the most successful countries when it comes to tackling the HIV epidemic in the region.

Table 1. Study countries population size, government type, income level, and major health indicators in 2015 (12).

Country	Total population (in millions)	Government type	Income level	Life expectancy (in years)	Maternal mortality rate (deaths/100,000 live births)	Infant mortality rate (deaths/1,000 live births)	Literacy (male/female)
Bangladesh	156	Parliamentary republic	Lower middle income	73.2	176	32.9	61.5% (65/ 59)
Lao PDR	7	Communist state	Lower middle income	64.3	197	51.4	80% (87/ 73)
Indonesia	258	Presidential republic	Lower middle income	72.7	126	23.5	94% (96/ 92)
Pakistan	201	Federal parliamentary	Lower middle income	67.7	178	53.9	58% (70/ 46)
Philippines	100	Presidential republic	Lower middle income	69.2	114	21.9	96% (96/ 97)
Vietnam	95	Communist state	Lower middle income	73.4	54	17.8	95% (96/ 93)
Nepal	29	Federal parliamentary	Low income	70.7	258	28.9	64% (76/ 53)

In 2016, six countries (China, India, Indonesia, Myanmar, Thailand, and Vietnam) of the Asia-Pacific region accounted for more than 90% of the estimated number of PLHIV in the region (3). New HIV infections declined over time in Bangladesh, Lao PDR, Nepal and Vietnam (Table 2). Nepal and Vietnam stand out as positive examples in many ways related to national response to HIV prevention and treatment. In Nepal, new HIV infections fell by 87% between 2001 and 2012 (Table 2). However, other study countries experienced an opposite scenario, such as an 8-fold increase in HIV incidence in Pakistan, an almost 3-fold in Indonesia and more than double the HIV incidence in the Philippines between 2001 and 2012 (4). Similarly, AIDS-related deaths declined or stabilised in Nepal and Vietnam, both with relatively high access to ARV treatment but multiplied in other nations with very poor ART coverage such as Indonesia and Pakistan (with a 4 vs 3.5 fold increase in AIDS-deaths respectively) (4). The rapid expansion of HIV treatment centres in Nepal increased the coverage of ART from 18% to 31% in just three years between 2012 and 2015. Currently, there are 67 ART centres across in 59 districts (out of a total of 75 districts) of Nepal. In March 2017, the country adopted and began to implement a Test and Treat strategy throughout the country, meaning that all who test positive for HIV should be initiated on ART immediately, regardless of immune status (measured as CD4 count) (11). Nepal also expanded the prevention of mother to child transmission services beyond the birthing centre in order to move towards elimination of vertical transmission of HIV from a mother living with HIV to her child. Since the inception of the HIV epidemic, Nepal has been unique in comparison to other countries regarding the involvement of key populations in the formulation of both policy, and the design and implementation of HIV prevention programs (13). However, other countries such as the Philippines have only recently started to implement targeted intervention among key populations such as MSM and the involvement of MSM in service delivery is at the infancy stage (8). Vietnam managed to reduce new HIV infections in key populations and stabilise death rates among PLHIV with multiple effective responses, such as rapid expansion of HIV testing and counselling services, a targeted 'Test and Treat' strategy i.e. the initiation of HIV treatment immediately after HIV diagnosis among PWID (11) and integration of HIV services into primary health care (14). In Vietnam, ART services are delivered through 364 HIV outpatient clinics. The integration of HIV services into primary health centres at sub-district level has drastically reduced the time between CD4 testing and the provision of results from 109 days to same day notification which has improved timely linkage to HIV care (14). Vietnam prioritises the expansion of such efforts in areas where the burden of HIV is high. Incarcerated PWID who are living with HIV also received ART through health services in prison, nearby ART centres

or through their family members or friends (15). The ART coverage is also higher in Vietnam in comparison to other study countries (Table 2).

There are a plenty of local and regional differences also within countries, but a common feature is the concentration of HIV in key populations across all the study countries. For example, the HIV prevalence is very high among key populations in certain areas such as in Faisalabad in Pakistan where an estimated 50% of PWID are living with HIV and 15% of TG people were living with HIV in the Larkana of Pakistan in 2011 (Figure 1) (16). A similar level of burden HIV was observed among PWID in Jakarta (56%), and FSW in Jayawijaya (25%) of Indonesia in 2013 (16). However, the prevalence of HIV is lower in Nepal (ranges from 5% to 8% among PWID in different areas) in comparison to the other study countries (Figure 1). Nepal was the first country in Asia to implement a harm reduction program with a focus on needle exchange already from the beginning of the epidemic in 1991 (13). Outreach workers from community organisations play a crucial role in implementing the needle exchange program in Nepal. Members of community organisations are not only active in the implementation of interventions, but also responsible for putting pressure on the government and donors to prioritise and implement comprehensive HIV preventions services. The HIV prevention and treatment responses are heavily dependent on donor support, which ranges from 58% in Indonesia to over 90% of the total cost in Nepal (84% in Bangladesh, 93% in Lao PDR, 64% in Pakistan, 60% in the Philippines and 68% in Vietnam) (16). Some study countries are experiencing a very low coverage of ART, much lower than in most African countries for example, e.g. only 6-9% of PLHIV have access to ART in Pakistan and Indonesia (Table 2).

In addition to free ARV treatment, some study countries also provide health insurance programs that covers costs for PLHIV who seek general health services. Four countries (Indonesia, Vietnam, Philippines and Lao PDR) provide ARV drugs and CD4 cell count tests free of charge, and have social protection programs such as the Asuransi Kesehatan untuk Keluarga Miskin–Askeskin in Indonesia; the Community-Based Health Insurance in Lao PDR; the PhilHealth in Philippines; and the Vietnamese Social Security Social Health Insurance Program in Vietnam. These programs provide healthcare and other services i.e. monthly cash allowance for daily necessities and common drug provision for PLHIV. However, studies conducted in Indonesia, Lao PDR and Vietnam found that PLHIV still often experience a catastrophic financial burden while seeking HIV/AIDS-related health services that are not covered by social protection programs, such as viral load tests, hospital

admission fees or diagnosis and treatment of concurrent diseases (6, 17, 18). Loopholes also exist in available social protection programs, for example, Indonesian PLHIV who are not yet eligible for ART due to high CD4 cell count, need to pay for HIV care (6). The coverage of social protection programs is also limited because of health system barriers, such as lengthy administrative processes (to obtain an identification card and certificate of poverty), unclear procedures, and lack awareness of available social protection services among PLHIV (18-20). Insurance that covers health care among PLHIV does not exist in Nepal and Bangladesh. In Pakistan, PLHIV can enrol in a health insurance program, but there is no available information about coverage or its impact on accessing health care among PLHIV.

Table 2. Estimated number of PLHIV, ART coverage, new HIV infections and AIDS-related deaths in study countries (4, 16)

Country	Estimated number of PLHIV*	ART coverage*	Trends in new HIV infections**	Trends in AIDS-related deaths**
Bangladesh	9600	16%	< 1100 individuals in total	< 1000 individuals
Lao PDR	11000	36%	< 1000 individuals in total	< 500 individuals
Indonesia	690,000	9%	Increased > 2.6-fold	Increased 4-fold
Pakistan	100,000	6%	Increased 8-fold	Increased 3.5-fold
Philippines	42,000	27%	Increased by 100%	< 1000 individuals
Vietnam	260,000	42%	Declining	Stable
Nepal	39000	31%	Declined by > 80%	< 1500 individuals

*Until the end of 2015 defined as the number PLHIV currently on ART divided by total estimated PLHIV in the country; ** Between 2001-2012.

1.2.1 Burden of HIV among young key populations

In HIV literature, young people are defined as individuals aged 10-24 years (21), but my studies focused on late adolescence (15-19 years) and young adulthood (20-24 years). Their developmental stage (experience of complex physical, psychological, emotional and social changes) put them in a unique position, often resulting in increased risk-taking associated with an increased risk of HIV infection. These behaviours, both sexual risk-taking and experimentation with drugs, are due to multiple factors, varying between individuals but also

typical for many young people, such as peer pressure, the curiosity of new things and a feeling of being immortal (21, 22). Young people belonging to key populations are even more vulnerable to the risk behaviours mentioned above because of social rejection of them as a group (such as transgender) and because many of their behaviours are highly stigmatised in society. Discrimination and violence in combination with power imbalances in sexual relationships, developmental immaturity and alienation from family and friends, makes young people even more vulnerable to risk behaviours related to HIV-infection (22). Young people aged 15-24 years account for 12.4% of the estimated total PLHIV in the region (10), and young key populations constitute more than 90% of all new HIV infections among young people in the Asia-Pacific region (23). Different surveys found that most of the key populations in the region engage in HIV-related risk behaviours already at a very young age (Table 3) and they are therefore at high risk of getting infected with HIV early in life and while being more sexually active (4, 24, 25).

Table 3. Age of initiation of HIV-related risk behaviours among young key populations in the selected study countries (24)

Country	Mean age in years of sexual debut	Median age at initiation of drug use	Mean age of sex work initiation
Bangladesh	16 (PWID), 14 (FSW), 13 (MSM), 13 (TG)	-	12 years (FSW)
Pakistan	22 (FSW)	-	-
Philippines	16 (PWID)*, 16 (MSM)	19 years (PWID)	-
Vietnam	18 (MSM)	-	-
Indonesia	0-19% of were < 15 (FSW)	-	-
Nepal	20% FSW are 10-14, Kathmandu 19% FSW are 12-14, Pokhara Valley	9% PWID 20–24 years 53% PWID 15–19 years	20 years (Male sex worker)

*Median age

Previous comprehensive assessments of the HIV prevalence among young people in countries experiencing generalised epidemics, primarily in Sub-Saharan Africa, have found that the prevalence of HIV has declined or at least stabilised in this group over time (26). However, the burden of HIV among young key populations has not been analysed as systematically in countries in the Asia-Pacific region that have experienced more concentrated epidemics (24). The analysis of trends in HIV prevalence at the national level may also mask the differences in the burden of HIV between different geographic areas within countries (27, 28). The wide knowledge gap in many countries about the burden of HIV among young key populations and their behaviours has also been highlighted in the 2014 World Health Organization (WHO) report, by the Interagency Working Group on four

Young Key Populations (MSM, TG, FSW and PWID) (29). Filling the knowledge gap related to the burden of HIV, risk behaviours and the effectiveness of interventions targeting young people should be an urgent priority to reduce their vulnerability to HIV in the Asia-Pacific countries (22, 24, 29).

1.2.2 Burden of social and structural risk factors among key populations

Key populations in many countries in the Asia-Pacific region not only experience stigma, discrimination based on their behaviours (e.g. anal intercourse, injecting drugs) or occupation (sex work), but also suffer from state punitive laws that criminalise their behaviours (injecting drug use), (see Table 4 for further details) (23). This double burden forces key populations into hiding, making them even more marginalised, and in turn, increasing their vulnerability to HIV. Vietnam and Lao PDR have punitive laws that penalise sex workers for being involved in sex work or solicitation (Table 4), and these countries also have compulsory detention centres for PWID and impose the death penalty for drug-related offences (4). Pakistan and Bangladesh criminalise same-sex sexual activities (4). Indonesia has mandatory detention centres for PWID and the death penalty for drug-related crimes (4). The Philippines does not only have punitive laws against sex work and solicitation, but the recent inhumane approach of president-elect Rodrigo Duterte in dealing with drug-related issues is not only affecting harm reduction programs negatively, such as needle-and-syringe exchange programmes, but has so far also resulted in the death of around 7 000 people since the abusive war on drugs started in June 2016 (30, 31).

Evidence suggests that sex workers and MSM/TG experience inexplicably high burdens of physical and sexual violence that affect their self-efficacy to negotiate condom use (32, 33). The situation becomes worse in contexts where sex work is criminalised by penal laws (34, 35). There are also protective laws and policies against discrimination and violence in many of the study countries (34, 36). However, typically for some Asian countries, there is a lack of enforcement of law and order that in turn exacerbates the experience of discrimination and violence among key populations (34). Violence against sex workers by security personnel (police/ military) is frequently reported in Bangladesh, Nepal and the Philippines (34). In Indonesia, the Philippines and Vietnam police often harass sex workers when they confiscate condoms from them (34). Nepalese law allows police to criminalise the clients, not the sex workers, but sex workers were charged with creating a nuisance in a public place (34). Some countries in the region allow sex workers to work in specific areas under government requirements and the government regulates some system of the sex industry,

even in countries where sex work is criminalised. Examples are the *affidavit* system (a document made by public notary specifying that woman is an adult and wants to involve in sex work with her will) in Bangladesh and *Lokalisasi* (a government-registered brothel complex) in Indonesia (34). Sex work is criminalised in the Philippines, but the government recognises the existence of the sex industry and has a law that requires the compulsory testing of sexually transmitted infections (STIs) among the staff of entertainment industries, such as massage parlours. The law in Indonesia requires some key populations (sex workers) to undergo regular testing of HIV and other STIs, but mandatory and coerced testing is also reported from Vietnam (34).

For example, the constitution of Nepal explicitly highlights the protection of sexual and gender minorities from discrimination, violence, and abuse (37). However, the experience of violence, social rejection and discrimination by society and service providers (health workers) is not at all uncommon among MSM/TG in Nepal (38). Another common example of the lack of protective law enforcement, is in relation to FSW. There are no specific laws that penalise sex work in Nepal, but different studies still suggest that the police frequently harass and detain FSW and TG who are involved in sex work, or who are working as peer educators (23, 34, 38, 39).

Evidence also suggests that the risk behaviours among PWID are influenced by the interaction between individual level and structural factors that operate in their environment, both at the micro (i.e. immediate space, setting, and groups) and macro level (i.e. broad social structural characteristics: physical, social, economic, and policy-related) (40). Recently, studies conducted among MSM/TG in the USA and Vietnam found that different factors (such as experience of depression, violence, sexual stigma, homelessness, substance abuse victimisation related to TG identity and incarceration) act synergistically (so-called *syndemic effects*) to increase the risk of unprotected sex and HIV infection among them (41-43). Sex workers not only experience disproportionately high burdens of HIV in concentrated epidemics, but they are also more likely to experience violence, rejection and economic insecurity (32). However, assessments of the role of such adverse factors that work at the different level of environment and its synergistic effects on unprotected sex among sex workers are very limited (44).

Table 4. Situation of punitive laws related to sex work, drug use and male-male sex in the study countries (4)

Country	Acts and behaviours criminalised by national law				
	Male-male sex	Sex work	Soliciting for sex	Compulsory detention centres for PWID	Death penalty for drug-related offence
Bangladesh	Yes	No	Yes	No	Yes
Lao PDR	No	Yes	Yes	Yes	Yes
Indonesia	No	No	No	Yes	Yes
Pakistan	Yes	Yes	Yes	No	Yes
Philippines	No	Yes	Yes	No	No
Vietnam	No	Yes	Yes	Yes	Yes
Nepal	No	No	Yes	No	No

1.2.3 Prevalence of unprotected sex among PLHIV and key populations

Protected sex (condom use) among PLHIV is important because it not only prevents sexual transmission of HIV but also prevents transmission of drug-resistant HIV strains or re-infection with a new more virulent HIV strain (45). Globally, around 46% of all estimated PLHIV are unaware of their HIV status (46), and the situation is similar or worse across the Asia-Pacific region. For example, in Indonesia and Bangladesh, only 26% and 36% respectively, of all estimated PLHIV are aware of their HIV status (16). Sexual transmission and non-use or inconsistent use of condoms among MSM/TG and sex workers is the main cause of infection in the region (4). In Nepal, 85% of all new HIV infections can be attributed to sexual transmission, oral, vaginal or anal intercourse (47). The unsafe work environment of sex workers, such as changes of venue for selling sex, and varying policing policies for sex workers, undermine their accessibility to condoms.

Meta-analysis findings suggest that factors such as the HIV positive status of partner, poor knowledge of HIV and belief that use of condoms decreases the pleasure for male partners, lower the likelihood of condom use among PLHIV (48). Some have argued that the use of ART and the fact that more people are becoming aware that ART prevents transmission of HIV, “treatment as prevention” (TasP), also increases the risk of unprotected sex among PLHIV (49). The TasP concept is based on the evidence that PLHIV who adhere to ART and

have no detectable viral load are at least 96% less likely to transmit the virus to their HIV-negative partners (50). A meta-analytic review of 25 studies found no association between receiving ART and inconsistent condom use (31), but it did show that the risk of unprotected sex increased among those PLHIV who believed that receiving ART or having an undetectable viral load protects against transmission of the virus (51). However, importantly, this meta-analysis did not include more than one study from the Asia-Pacific region (Australia) (31). A 2013 UNAIDS assessment of the HIV epidemic in the Asia-Pacific region found that the major route of transmission is through unprotected sex, among both the general public and key populations (FSW, MSM, TG and sex workers), while the second most common contributor to HIV incidence is unsafe use or sharing of unsterile needles and syringes among PWID, especially in certain epidemic zones (Figure 1) (4). The 2015 UNAIDS estimate suggests that new HIV infections increased by 20% in thirty countries globally including, among others, Indonesia, Pakistan and Philippines (52). The identification of factors that influence unprotected sexual intercourse versus promote consistent condom use among key populations including PLHIV is essential in order to plan and implement effective preventive interventions (48). However, these factors have not previously been systematically assessed among key populations and PLHIV in the Asia-Pacific region.

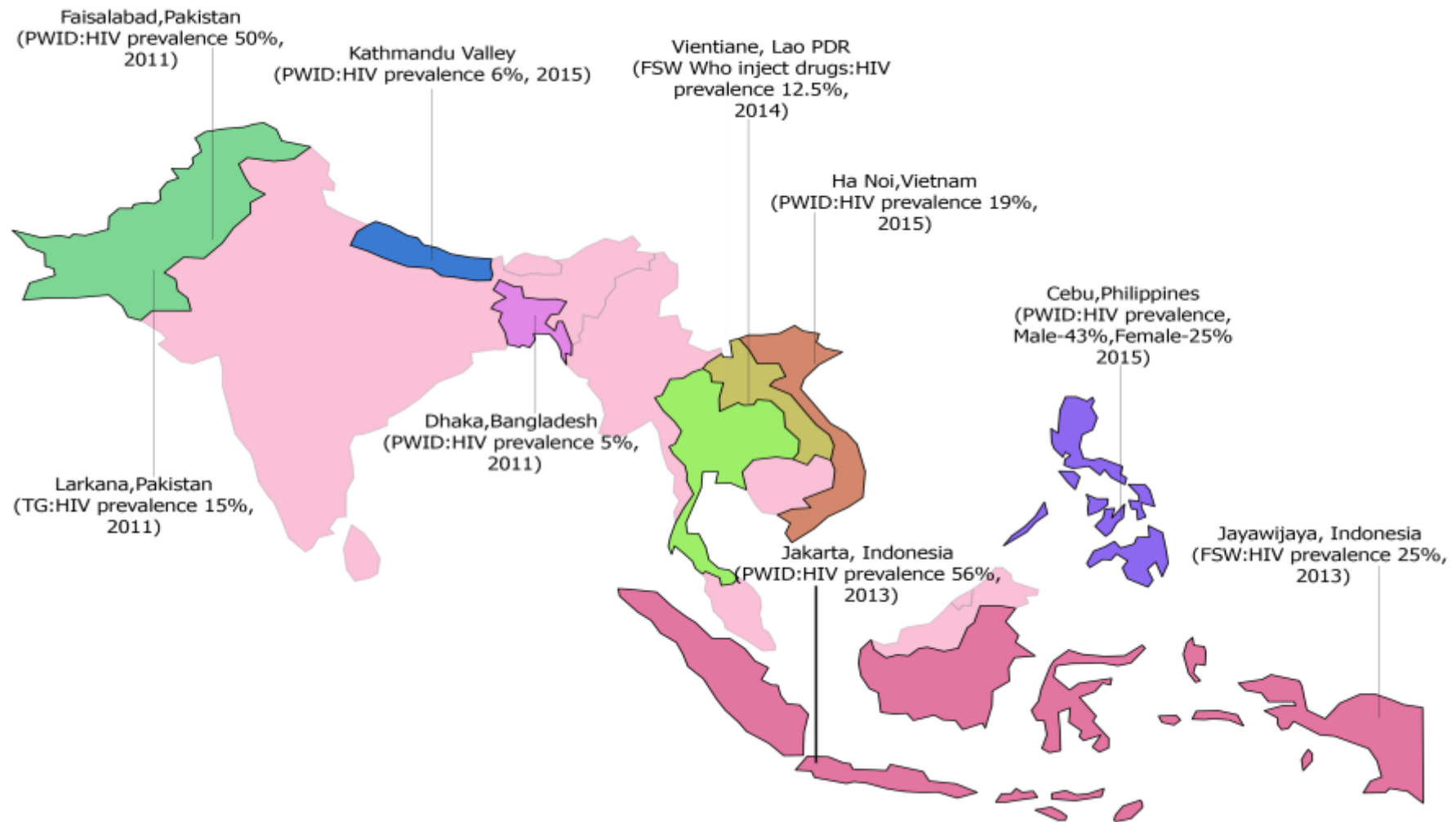


Figure 1. HIV prevalence among people who inject drugs and female sex workers in selected areas and cities in the study countries

1.2.4 The importance of retention in HIV care

The relatively recent evidence of TasP (i.e. the very strong protective effect of ART regarding the prevention of HIV transmission from an HIV- positive partner adhering to daily ART mentioned above), has given hope that it is possible to end the AIDS epidemic by 2030 (50). Traditionally, the eligibility for HIV treatment among PLHIV is guided by the CD4 cell thresholds. However, the evidence from different studies (HIV Prevention Trials Network 052 Trial, the Strategic Timing of Antiretroviral Treatment Study) (50, 53) clearly suggest that the benefits of early initiation of ART (immediately after diagnosis) is far better in terms of both health and prevention benefits of ART, than delaying treatment for any reason. The initiation of HIV treatment immediately after diagnosis is called the ‘Test and Treat’ strategy (11).

National strategic plans for the countries of the Asia-Pacific region have aligned with UNAIDS’ so-called “fast track strategy” towards achieving the “90-90-90 target” by 2020 and “95-95-95 target” by 2030 (54). The 90-90-90 target, means that 90% of PLHIV should know their HIV status, 90% of PLHIV who know their HIV status should receive HIV treatment, and 90% of PLHIV on ART should be virally suppressed i.e. have undetectable viral load and thereby be at minimal risk of transmitting HIV as well as of symptomatic HIV (54, 55). If the world managed to reach the 95-95-95 target in 2030, it would mean the end the AIDS epidemic as a global public health threat. Regarding figures, this would mean that the number of new HIV infections would be 89% lower, and the number of AIDS-related deaths would be 81% lower compared to 2010 (54). An improved coverage of ART among PLHIV would result in a total number of below 97 000 new HIV infections in the Asia-Pacific region (54). However, if the ART coverage remains at the 2013 level, then new infections would be expected to reach 480 000 by 2030 which is even higher than the current level of 300 000 new infections in 2015 (54).

Treatment of HIV is usually assessed by and divided into the following critical steps for treatment success, the so-called “HIV care (or treatment) cascade”: proportion of PLHIV should know their HIV status, proportion who present in health care on time (i.e. with a CD4 at higher level of 350-500 cells/ μ l or with no AIDS-defining illnesses), proportion linked to care on time (for CD4 test and other health-related assessment) and proportion that initiates ART if eligible (if test and treat strategy adopted in the country then they should immediately start ART) and fully adhere to ART to achieve viral load suppression (54) (Figure 2).

To what extent these different steps within the HIV care cascade are reached will heavily influence the success or failure of the 90-90-90 targets. Countries in the region assessed the achievement of the 90-90-90 targets by combining modeled data with cumulative routine program data (47). Estimating the number of PLHIV living in each country requires many sources of information for entry into existing HIV models (56), including mapping the number of key populations at risk in the country, collecting surveillance data on HIV prevalence and risk behaviours among key populations, measuring access to ART and coverage of prevention of mother to child transmission service related information and other inputs (56). Some of the countries in the region lack such information because valid estimates require surveillance survey data of at least three time points, or because there are no valid or updated estimates of the number of key populations in the country, and /or because they lack accurate data on AIDS deaths, etc.) (57). This information gap obviously increases the uncertainty of estimated numbers in these countries and in the region as a whole. For example, Nepal conducted the latest mapping to estimate the number of key populations only in 2016 and before that, country was using 2010 mapping data as an input for national HIV estimates for over 5 years.

Similarly, cumulative routine program data also suffers from several limitations, such as duplications of cases, aggregate level data since the inception of the epidemic and so on. Figure 2 shows the different steps of HIV care cascade among PLHIV in Nepal (Figure 2). The first bar represents the estimated number of PLHIV as modelled using the UNAIDS' developed Spectrum/ AIDS epidemic model, while other values were extracted from routine national program data of country (56). Current data sources do not, give a completely clear picture of various countries' progress towards the 90-90-90 target due to inherent uncertainty limitations of the estimated number of PLHIV and aggregated routine program data as mentioned above (58). Hence, the identification of facilitators and barriers for each individual step in the HIV care cascade is essential in order to modify and improve existing programs and for planning new even more effective interventions.

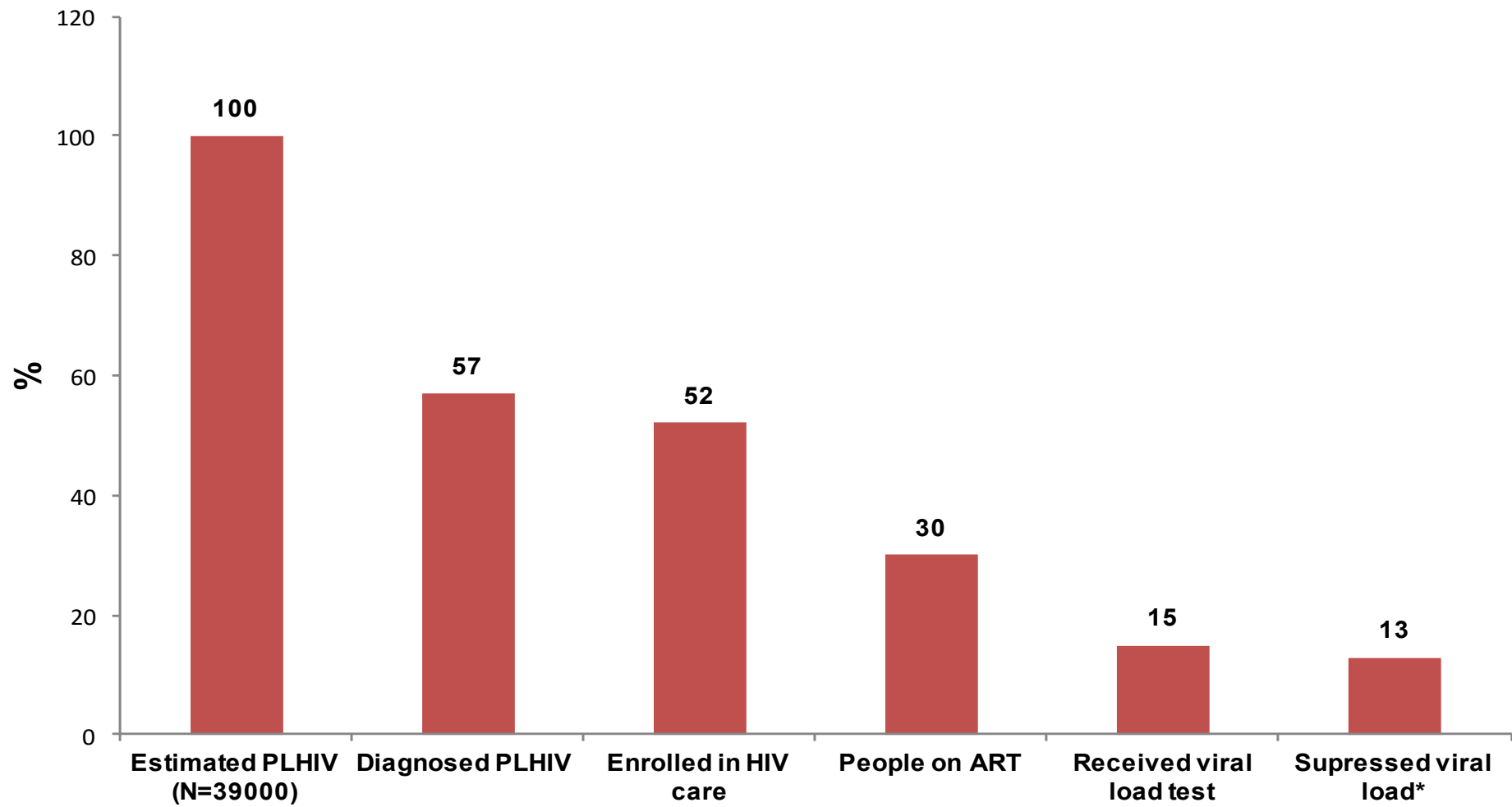


Figure 2. The 2015 HIV care cascade in Nepal (16). *Number of people on ART who received a viral load test in the past year and have viral load <1000 copies/mL

1.3 HEALTH SYSTEM RESPONSE TO HIV IN THE STUDY COUNTRIES

Several achievements have been made in the last two-three decades in the region, related to economic and health status such as improved life expectancy, declining fertility, improved social capital and increasing income (Table 1) (59). However, such achievements are neither consistent between countries nor within countries. A wide variation in the availability of opportunities and services by location (nation-wide vs. rural- urban) in many countries of the region increases the inequities between populations with regards to health risks, health-seeking behaviour, accessibility to services and health outcomes. For example, Singapore managed to deliver well-resourced medical services within reach of all citizens, whereas inequity in access to healthcare between rich and poor, and between urban and rural areas is common in Indonesia (59, 60). Studies found that wealthy Indonesians living in urban areas were seven times more likely to access health services from both public and private health facilities than Indonesians in the poorest income groups (60). The entrenched poverty and gender inequality in many countries of the region has also resulted in one-fifth of all deaths being due to infectious diseases despite the on-going global transition from communicable to non-communicable burdens of disease (59).

Health systems are comprised of many components, with the primary aim to promote, restore, and maintain health. The 2007 WHO framework, so-called '*Everybody's business: strengthening health systems to improve health outcomes*', identified six building blocks of a health system: health service delivery, human resource, health information system, medical products and technology, health financing, leadership and governance (59). The central concept of that framework is that the health system should be understood in totality, and that just focusing on one block will not be sufficient to achieve high-quality health care.

Some groups (women and children, especially girls) within the region are more disadvantaged than others both in terms economic and health status (59). The poor status of women in different aspects of life such as literacy level, nutritional status, access to health care and decision-making power regarding contraceptive use and family size, results in persistently high maternal and child mortality rates in some countries of the region (Table 1). Male child preference has led to selective abortion of female fetuses, because of the belief that a son is the better provider in patriarchal societies, regarding both religious and economic aspects (59, 61). Thus, in many patriarchal societies, female children are still being deprived of education, which ultimately affects both women's employment opportunities and their health status (61). In 2015, all study countries exhibited low Gender Inequality Index

rankings (62). The Gender Inequality Index measures gender inequalities in three aspects of human development—reproductive health (measured by maternal mortality ratio and adolescent birth rates), empowerment (measured by proportion of parliamentary seats occupied by females and the proportion of adults with at least some secondary education) and economic status, (female/male labour market participation rates). The lower down on the list of 159 ranked countries, the worse the inequality and although rankings vary significantly between the study countries, from 71 in Vietnam to 130 in Pakistan, 119 in Bangladesh and 106 in Nepal none of them does well(62).

The guiding principles behind all the health systems in the Asia-Pacific region come from the 1978 Alma-Ata declaration on Primary Health Care (63). In the Declaration of Alma-Ata, primary health care was defined as: “.....essential health care on practical, scientifically sound and socially acceptable methods, and technology made universally accessible to individuals and families in the community through their full participation, and at a cost that the community or country could afford to maintain at every stage of their development, in the spirit of self-reliance and self-determination. (63).”

In reality, the health system is fragmented in many countries of the region resulting in ineffective delivery of health services. Poor access and low quality of health services result in low uptake and coverage even of basic health services in many Asian-Pacific countries. The reasons for poor access and low quality of health services are summarised in Figure 3 (Figure 3). An attempt has been made by governments to improve health service delivery in partnership with the private sector, but the public-private partnership is not regulated by effective laws, in turn resulting in the region having the world’s highest reliance on out-of-pocket expenditure to finance health care system (59). The governments in the region contribute the larger portion of the health workforce, but the distribution of health personnel is skewed and mainly concentrated in the major cities. In many low-income countries of the region, the current health management information systems do not generate valid and useful indicators at the disaggregated level required in order to enable decision-makers to evaluate existing efforts and to support an evidence-informed response. Thus, the available health system information is rarely used in designing policy and implementing interventions. The laboratory services are often under-resourced and fragmented. In Nepal for example, only one viral load-testing machine for ARV treatment assessment is available outside of the capital city. Government spending on health services is highly inadequate, resulting in a challenge to provide even basic health services, and HIV-related programs are therefore largely dependent on and supported by international donors (59).

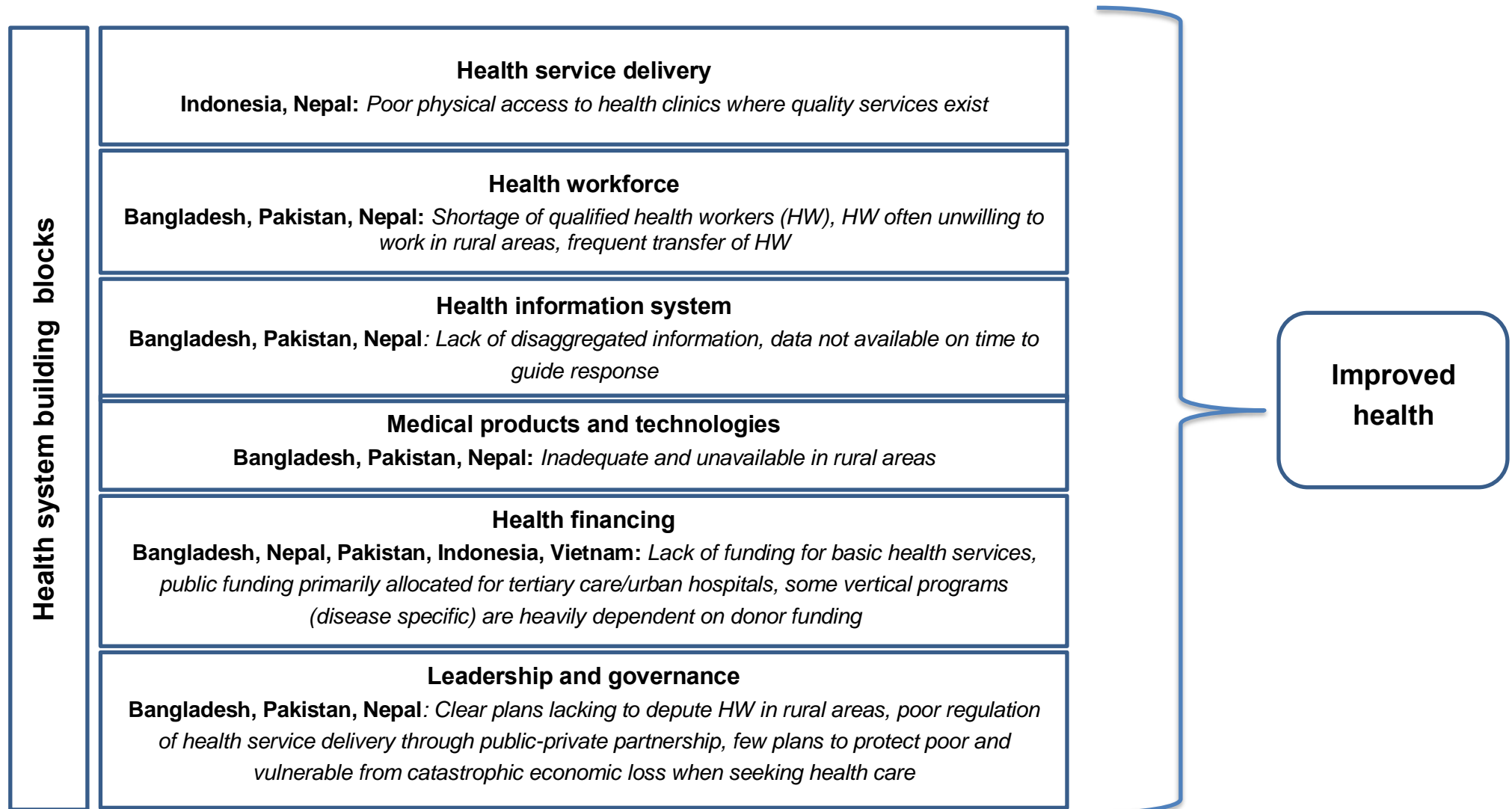


Figure 3. Challenges unique to six building blocks of the health system in the Asia-Pacific region (59, 60).

1.3.1 Interventions targeting key populations in the region

Behavioural interventions targeting key populations often include peer-driven education interventions and HIV testing and counselling services (HTC), both of which are widely implemented in both formal and informal settings in the Asia-Pacific region (64). In peer education interventions, individuals (peer educators) are selected from key populations and trained to increase their awareness on HIV/AIDS and other STIs and to encourage behavioural change among other key population members (65). The peer interventions are usually implemented through peer educators in informal settings (public meeting places such as parks, bus stops, temple areas and injecting hot spots such as under bridges and jungle areas) or through drop-in centres in more formal settings such as outpatient clinics. Peer educators also usually distribute necessary supplies such as condoms, lubricants and syringes, often paid for by the government, or by donors via community organisations lead by various key populations. Peer educators often also receive salary support from such community organisations.

The second intervention, HTC, consists of pre-test counselling, post-test counselling and informing clients about their HIV status following the HIV test. In pre-test and post-test counselling, the counsellors assess the clients' risk behaviour, prepare clients for their HIV test result and teach coping and risk reduction strategies, as well as recommend further care and support if necessary. Both interventions are effective in influencing different intermediate outcomes such as increasing knowledge of HIV risk reduction strategies, beliefs, attitudes and behaviours, which in turn is thought to promote clients to take up safer and healthier behaviours that affect health outcomes (HIV infection) in the long run (64, 66).

Seventeen countries of the Asia-Pacific region, with an estimated 3.15 million PWID, make up a 1 in 4 population of PWID out of the global total (67). The majority of the governments in the region understand the importance of harm reduction packages to prevent the sharing of injecting equipment, rates of drug use and HIV infections among PWID (35, 68). However, until 2014, only 17 countries in Asia implemented needle and syringe exchange programs, and only 15 countries implemented opioid substitution therapy (67), although 3-5 million are estimated to be PWID in the whole region, 16% of them living with HIV (69). The evidence, therefore, shows that the adoption and implementation of harm reduction is slow and challenging in many Asian countries (68). Due to poor coverage of harm reduction services (for example, the number of syringes per person injecting drugs distributed in one year ranges from only 10 in Indonesia to 214 in Bangladesh) and other existing barriers, such as policy inconsistency between different ministries, negative opinions with regards to harm reduction

among health care managers and medical staff, negative attitudes towards PWID in general, lack of knowledge about addiction treatment etc., all means the sharing of unsafe needle and syringes among PWID remains a big problem in the region (35, 69, 70). So far, only four countries of the Asia-Pacific region are able to reach the recommended standard coverage of more than 200 needles/syringes provided per PWID per year (67). Most of the countries in the region adopt a blanket approach in implementing interventions without considering the needs and demands of different age groups, often because the needs and demands are insufficiently known.

Existing harm reduction programs mainly focus on needle and syringe exchange programs and drug addiction treatment, primarily opioid substitution therapy i.e. oral methadone and buprenorphine distribution as replacement drugs to opioid/heroin dependency (71) These programs are largely funded by foreign donors (as much 81% of the total harm reduction activities in the region) such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and other bilateral partners (46). Also, many programs lag behind the rapidly changing drug scene in the region, where the use of methamphetamine is increasing over the use of heroin, but the harm reduction programs focus solely on injecting drug use among PWID (35). Despite the strong international evidence-base in favor of harm reduction (69), for example, the Vietnamese government required long efforts of piloting and more evidence generation (46). As of June 2015, there were 32 000 clients receiving methadone maintenance therapy through 162 clinics in 44 provinces (46), estimated to make up only 12% of the total PWID population in Vietnam (72). Nepal is also implementing opioid substitution therapy through 14 sites in eight districts, but the retention rate is dismal, at less than 3% (47). Different factors may contribute to poor retention in opioid substitution therapy among PWID Nepal, such as no takeaway doses being provided meaning that the patient needs to go to the clinic to pick up his or her dose every day. Pakistan is also finally implementing a needle exchange program, but with limited coverage and poor access to opioid substitution therapy for PWID, it is still in its infancy (73).

1.4 KEY POPULATION SURVEILLANCE METHODS FOR THIS THESIS

Random sampling of key populations was not feasible in this study because of the unavailability of a sampling frame. Key populations are hidden in society and difficult to recruit, mainly due to the stigma and discrimination associated with their behaviours (74). A unique sampling technique, the so-called respondent driven sampling (RDS) technique has

been designed to recruit hard to reach populations without a sampling frame. In the Asia-Pacific region RDS has therefore been used to recruit key populations (75, 76), oftentimes by using networks of study participants for recruitment with the help of their peers who practice the same behaviour. The recruitment process is controlled in a number of ways, such as a fixed number of peers that can be recruited by one participant. The strength of RDS is that it manages to produce selection probabilities of study participants, which enhances its credibility as a probability sampling technique. The selection probability is based on the personal network size of study participants, which is measured by assessing the number of people in the network of study participants who also fulfil the inclusion criteria of the study. Evidence suggests that RDS produces statistically proven unbiased population estimates when all the criteria are fulfilled (77, 78). One disadvantage of this sampling technique is that RDS sometimes only is able to reach a subset of the study population in some contexts (76). or the estimate is biased if the study participants only recruit those peers who have characteristics related to the outcome of interest, such as referring only MSM with known HIV positive status (78).

1.5 RATIONALE FOR THIS THESIS

The well-established evidence regarding the effectiveness of ART both in reducing secondary HIV transmission, so-called ‘Treatment as prevention’, as well as its strong health benefits has given hope to ending AIDS as a public health threat. However, to achieve this ambitious target, the risk behaviours that contribute to HIV transmission need to be addressed, and the achievement of a high level of retention in HIV care among PLHIV is crucial. The identification of facilitators and barriers of PLHIV in different steps of the HIV care cascade is essential in order to modify existing interventions or to plan a new ones. At present, there is a knowledge gap in the study countries, in understanding the factors affecting for example inconsistent condom use and retention in HIV care among PLHIV

Evidence from high-income countries suggests that the risk behaviours among key populations are influenced by the interaction between different factors that operate on the micro versus macro levels of their environment. Those factors also act synergistically (so-called *syndemic* effects) to increase the risk of unprotected sex and HIV infection in these groups. However, such associations have not earlier been assessed among FSW in low-income countries despite the fact that experience of violence, social rejection and economic insecurity is very common among them. This thesis aimed to contribute to filling the

knowledge gaps related to factors affecting inconsistent condom use and retention in HIV care among PLHIV in 7 countries, including the burden of HIV prevalence, risk behaviours among young key populations and synergistic effects of structural factors among FSW in Nepal.

Despite the significant proportion of key populations in the Asia-Pacific region engaging in risk behaviours at a young age, the burden of HIV among young key populations has not been systematically analysed in the Asia-Pacific region, and Nepal is not an exception. The analysis of trends in HIV prevalence at the national level may also mask the differences in the burden of HIV between different geographic areas within countries. Filling the knowledge gap related to the burden of HIV, risk behaviours and the effectiveness of interventions targeting young key populations by local epidemic zones is an urgent priority to reduce their vulnerability to HIV.

2 AIM AND OBJECTIVES

General Aim

To assess the HIV trends, risk behaviours, social structural barriers and retention in HIV care among key populations in seven countries (Bangladesh, Indonesia, Lao PDR, Nepal, Pakistan, Philippines and Vietnam) of the Asia-Pacific region and in Nepal in particular.

Specific Objectives

1. To examine the prevalence of inconsistent condom use and associated risk factors among people living with HIV in seven countries located in the Asia-Pacific region (Paper I).
2. To assess factors affecting retention in HIV care at the most crucial steps in the HIV treatment cascade for people living with HIV in seven countries in the Asia-Pacific region (Paper II).
3. To assess the prevalence of HIV and the syndemic effects of micro-level social structural factors of unprotected sex among female sex workers in Nepal (Paper III).
4. To determine any change in HIV prevalence and risk behaviours, socio-demographics and comprehensive HIV/AIDS knowledge over the last decade (2001-2012) among young key populations aged 16-24 years in Nepal (Paper IV).

2.1 CONCEPTUAL FRAMEWORK FOR STUDY

Figure 4 shows how availability, accessibility and utilisation of different interventions influences risk behaviours and HIV incidence. The performance of the health system also affects the retention of PLHIV in HIV care, in turn ultimately affecting the HIV burden (HIV prevalence) and health status (morbidity and mortality) of PLHIV. Health system responsiveness, either in a positive or negative way, is a yardstick of its performance. For example, how health systems meet the needs of people's expectations is one of the measures of its performance. Individual level and structural factors act synergistically (so called syndemic effects: the idea that two or more adverse conditions interact interdependently to heighten the burden of disease in a population) to influence the outcome and impact either in the positive or negative way.

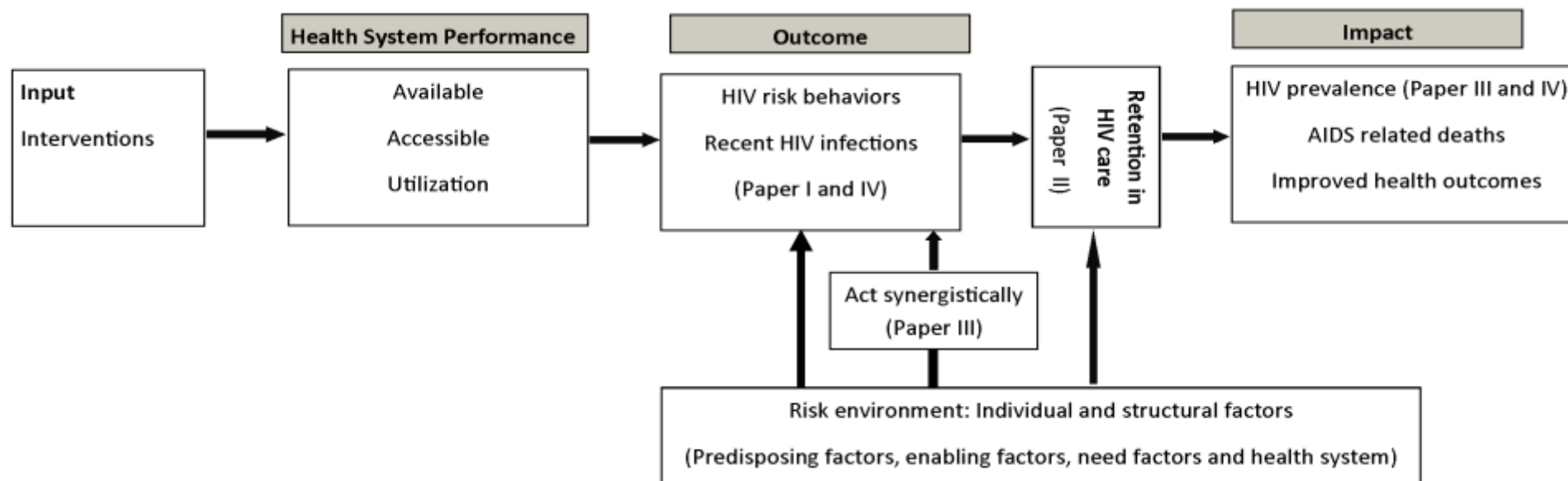


Figure 4. Conceptual framework for factors affecting risk behaviours, HIV prevalence and retention in care among key populations and PLHIV. Adapted from Funnell (79); Rhodes (40); Singer (80)

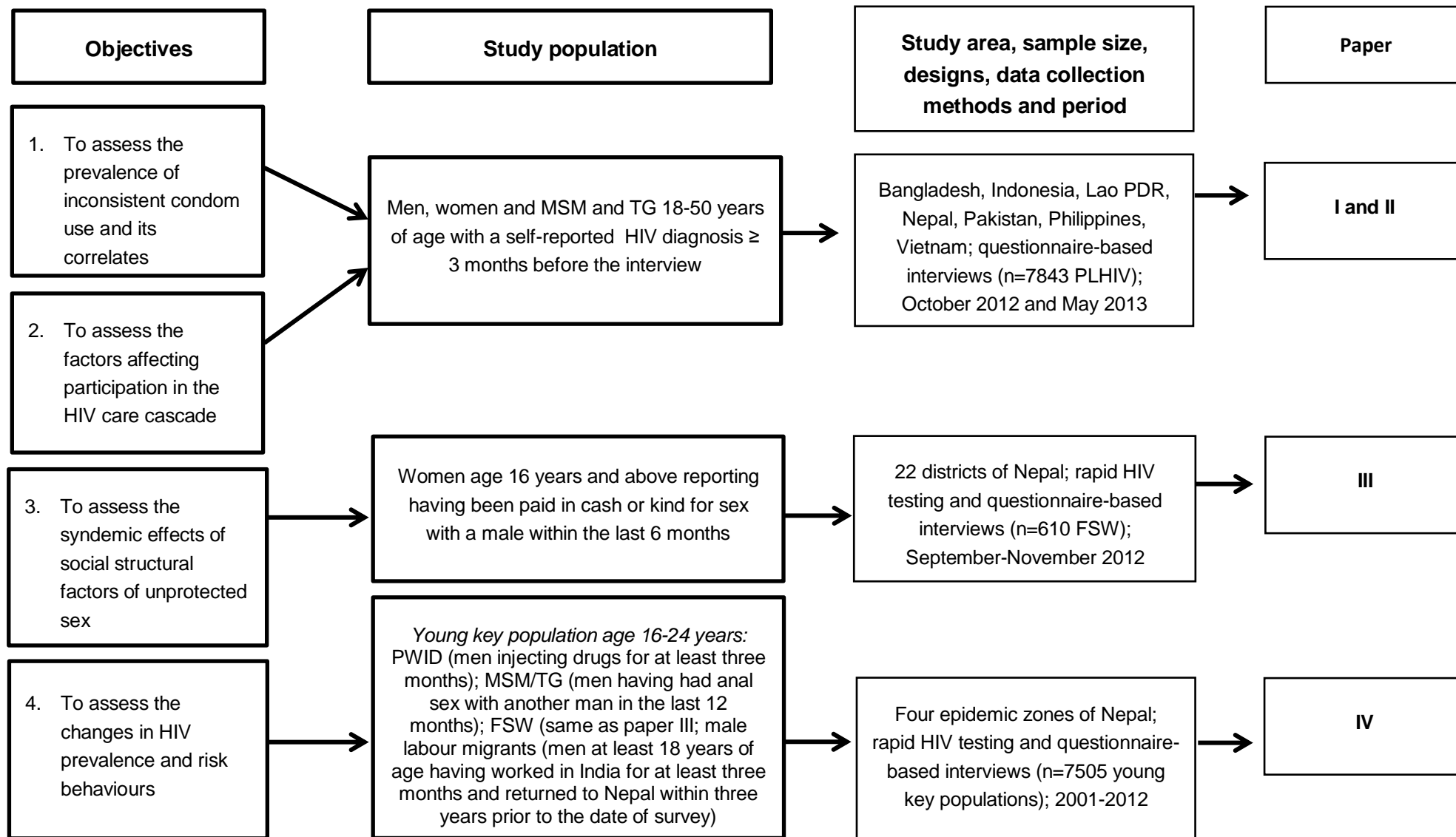


Figure 5. Summary of objectives, study population, study design, study area and data collection methods

3 MATERIALS AND METHODS

3.1 THEORETICAL FRAMEWORK TO STUDY RETENTION IN HIV CARE AND SYNDEMIC EFFECTS OF STRUCTURAL FACTORS

Barriers and facilitators of retention in HIV care between HIV testing and ART initiation were assessed based on a theoretical framework of access to health care developed by Anderson (81). Based on this theory, we further identified different populations and health system factors that could influence access to care and retention in care for PLHIV (the HIV care cascade) (50). **Population level determinants** have earlier been categorised as *predisposing, enabling and need determinants* (81). **Predisposing individual level** factors include socio-demographics (age, sex, marital status, family size), social factors (education, occupation, and ethnicity) and beliefs (knowledge of health and health services) (81). **Enabling factors** facilitate or hinder individuals' access to and participation in care such as insurance, income and cost of health care (81). **Need factors** were categorised as the *perceived need of care* defined as an individual's perception of one's health status and the need for care, and *evaluated need* where health workers more objective quantification of an individual's need for care (81). **Health system factors** involve resources (human resources, availability of medical equipment, infrastructure) and organisational factors (interoperability of resources and system in the delivery of care) (81). Based on Anderson's theory of access to health care, Paper II defined population and health system factors that facilitate or hinder PLHIV from HIV testing, linkage to HIV care, engagement in care and ART initiation.

A synergistic effect of micro-level social structural factors on unprotected sex among FSW was assessed based on the 'risk environment' and '**syndemic theory**' proposed by Rhodes (40) and Singer (80) respectively. A risk environment framework suggests that the behaviours of key populations are determined by the interactions between individual and social structural factors (i.e. physical, social, economic, and policy-related) that operate at the *micro* (immediate setting) and **macro** level (broad social structural characteristics). *Social structural factors* are defined as barriers and facilitators at different levels such as economic, social and policy-related that influence the ability of an individual's HIV prevention behaviour (82). Syndemic theory, a recently gained momentum for a new pathway for global health research (83), studies the synergistic effects of two or more epidemics or adverse conditions that increase the burden of disease in a population (80). Based on the risk environment concept developed by Tim Rhodes and syndemic theory developed by Meril Singer, Paper III assesses the syndemic effects of micro-level structural factors that operate at

a physical, social and economic level to increase the likelihood of unprotected sex among FSW in Nepal (Paper III).

3.2 STUDY DESIGN

This research project utilised two main data sources:

For Paper I and II: For paper I and II, baseline data from a prospective longitudinal study of community access to HIV treatment, care and support services (CAT-S), which used a community-based participatory research (CBPR) approach (84) that involved 59 sites in 7 countries (Bangladesh, Indonesia, Lao PDR, Nepal, Pakistan, Philippines, Vietnam) between October 2012 and May 2013 in the Asia-Pacific region (Figure 6). CAT-S is one of the key pillars of Monitoring Access to Treatment in Asia (MATA) -a tool to document, monitor, and advocate issues related to access to treatment, care and support for PLHIV over the long term (85). The CAT-S collected data through face-to-face interviews, regarding wide range of variables (sociodemographics, HIV diagnosis and healthcare, health seeking behaviour/access to general health care and associated cost, access to social support, stigma and discrimination, general health and HIV risk behaviours, access to reproductive health and family planning service, tuberculosis and hepatitis C virus infection, HIV treatment literacy, access to information technology, ART initiation and adherence, side effects of ART and relationship with health workers). The CAT-S study was funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) Round 10 regional grants.

For Paper III and IV: A National level surveillance survey, called the integrated biological and behavioural surveillance (IBBS) survey data was used to answer the objectives of Papers III and IV. The IBBS survey is a serial cross-sectional survey that has collected data among key populations (PWID, MSM/TG, FSW, male labour migrants) across Nepal since 1999. IBBS surveys have since then been conducted at regular intervals (every 2-3 years) among key populations from 16 years of age and above in different HIV epidemic zones of Nepal (please see below and also Figure 7).

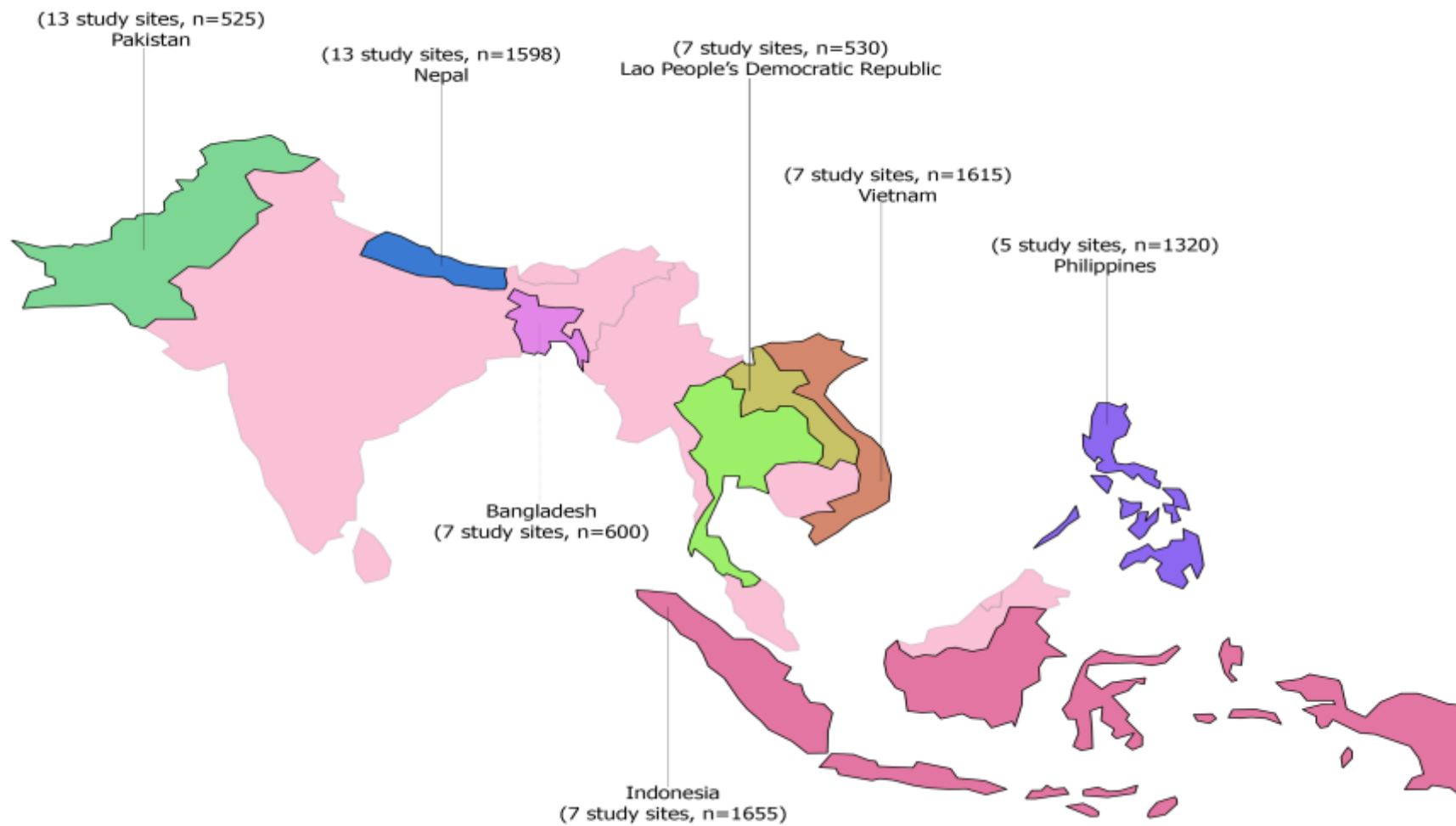


Figure 6. Sample sizes and sites in the study countries of Papers I and II.

3.3 STUDY SETTING

Details of the study countries, number of study sites and sample sizes related to Papers I and II are shown on the map in Figure 6 (Figure 6). Details of IBBS survey by epidemic zones are shown on the map in Figure 7 (Figure 7). Nepal is divided into different epidemic zones based on the burden of HIV, risk behaviours and mobility patterns in the area. The HIV epidemic in some Nepalese regions is driven by unsafe needle sharing and unsafe anal sexual intercourse, whereas it in the other local regions is driven more by labour migrants being clients of sex workers when working abroad (86). The IBBS survey was conducted in such areas targeting specific key populations in each area.

3.4 STUDY POPULATION, DATA MANAGEMENT, AND DATA ANALYSIS

For Papers I and II, individuals (men, women and MSM/TG) aged 18-50 years, who self-reported to having been diagnosed with HIV at least three months before the date of interview, were recruited. We used both targeted sampling and facility-based sampling. A modified targeted snowball sampling technique (77) that helped us understand the existence of different subgroups in a particular setting, was used to recruit study participants from identified geographical areas. *Snowball sampling* is effective for recruiting hidden populations, but increases the risk of oversampling easily available study participants and may also be too much influenced by the characteristics of the initial study recruits also called ‘seeds’ (77). We therefore used *modified targeted snowball sampling*, assumed to be more effective and valid for recruiting hidden marginalised populations. We call it modified snowball sampling because we followed two key steps before identifying ‘seeds’ that could facilitate the enrolment of study participants. In the first step, we identified areas within each of the seven countries where we could enrol study participants by using national and local networks of PLHIV. Most key populations are involved in smaller or larger networks of people who have similar behaviours and characteristics. Contact persons for the various networks also helped us to identify different key populations (sex workers, MSM and transgender and PWID living with HIV) in each study area. In the second step, we also performed a review of the secondary literature to estimate a possible number of PLHIV in the country study areas. Thereafter, we selected ‘seeds’ in each of these study areas to enroll study participants. Facility-based sampling techniques were used to recruit study participants from different institutions (health centers/hospitals, self-help groups, outreach/drop-in centers and different treatment, rehabilitation centers).

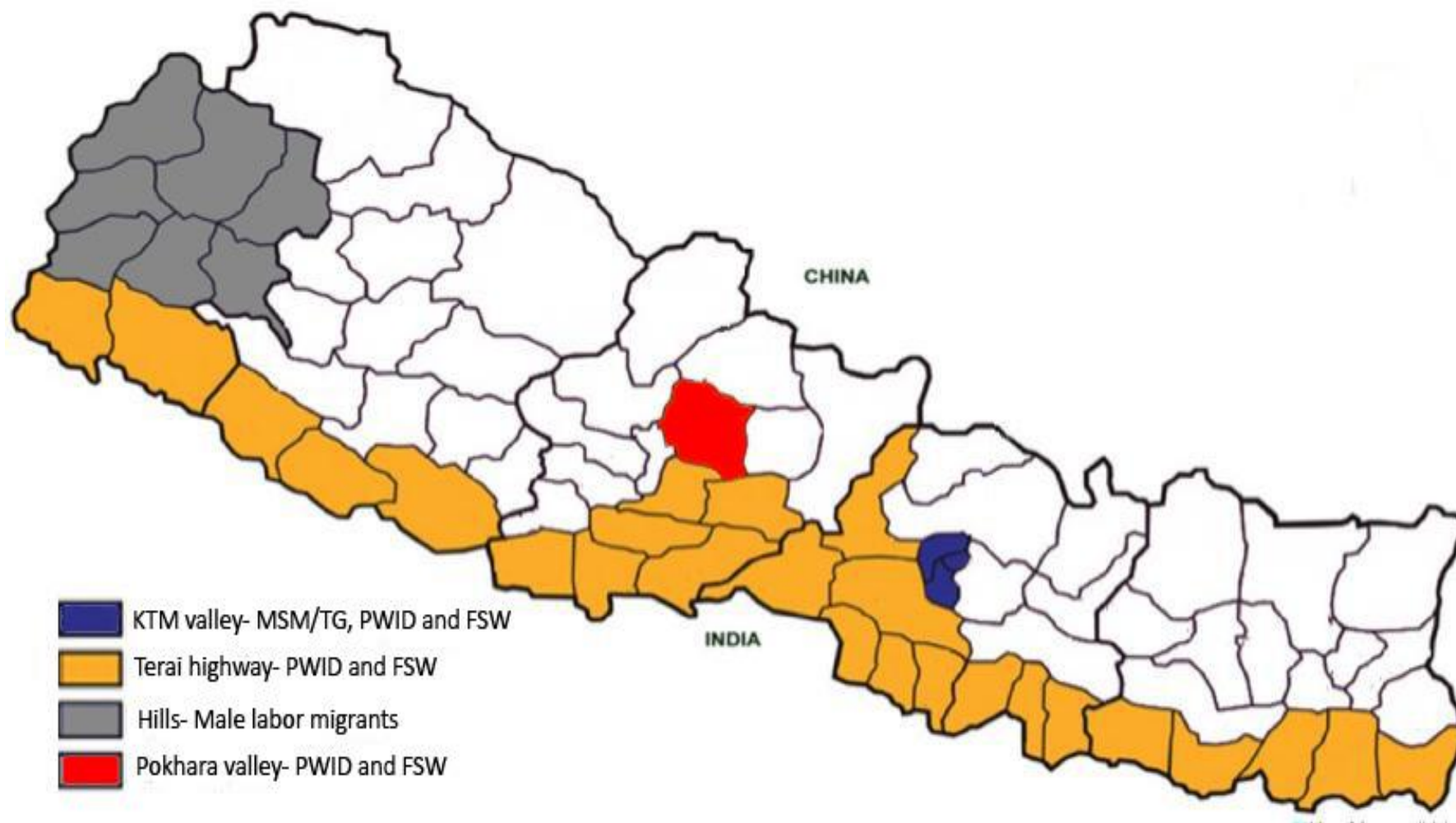


Figure 7. IBBS survey population by epidemic zone in Nepal (Papers III and IV).

KTM valley: Kathmandu valley; MSM/TG: Men who have sex with men/transgender; PWID: people who inject drugs; FSW: Female sex workers.

An Electronic Data Capture system (iDataFax) was used to submit data to the Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS) located at Mahidol University. Upon receipt of the data, a data officer at the Asia Pacific Network of People Living with HIV/AIDS (APN+) was responsible for a visual review of the data for missing values and query other inconsistencies in country specific data.

All the data analysed using the RDS Analyst version 0.42 and STATA version 13.1 software (Stata Corporation, College Station, TX).

For Paper I, various independent variables were analysed to answer the objectives of Paper I. Age, sex, education, occupation, income, living area, nongovernmental organization or community-based organization membership, and belonging to a key population (MSM, TG, PWID, refugee, migrant workers or sex workers) at high risk of becoming infected with HIV were recorded as demographic characteristics. Factors having an established or theoretical association with condom use behavior were taken into consideration: social support, stigma and discrimination, general and reproductive health, HIV diagnosis, and HIV treatment and related literacy.

Measures on stigma and discrimination included physical assault and housing instability in the past twelve months, amongst others. To assess general and reproductive health, self-rated health, illicit drug use (“Have you ever used any illicit drugs?”; the response was categorized as “never used drugs” vs. “current drug user” vs. “former drug user”), and alcohol consumption (categorized as “never drinkers” vs. “former drinkers” vs. “current drinkers”) were recorded. Furthermore, participants were asked if they had children and/or if they had a desire to have children in the future. Time since the HIV diagnosis, in years and place of the HIV diagnosis, were recorded as measures related to the HIV diagnosis. Measures on HIV treatment included current enrollment in ART and related so called treatment literacy, which was assessed by asking participants to rate HIV-related statements (e.g. “Condoms are not needed if both sexual partners are HIV-positive.”) as either true or false. Participants who had had sex with a regular partner in the past six months were further asked to indicate their partner’s HIV status, whether they had ever disclosed their HIV status to their partner, and whether they had sexual intercourse with someone other than their regular partner in the past six months. Condom availability (“Can you get a condom when you need it?”) was recorded and categorised into “always or mostly”, “sometimes”, and “never”.

For Paper I, logistic regression was used to examine the association between independent variables and the outcome defined as inconsistent condom use. *Svy: logistic* of STATA

software was used to fit the statistical model, taking into account the complex survey data (in our case multilevel cluster design with seven countries and 59 sites). Logistic regression analysis was done to assess factors associated with condom use behaviour with a regular partner and with a casual partner. The variance inflation factors (VIF) indicated no problematic multi-collinearity (all VIF-values ≤ 1.51). All statistical tests were based on a significance level of a p-value ≤ 0.05 and confidence intervals (CI) were set at 95% confidence level.

The outcome variables of Paper II were *HIV testing, linkage to care, engagement in care, initiation of ART and ART adherence*. HIV testing was assessed as a late presentation for HIV care (yes vs. no), which was defined as PLHIV presenting with CD4 cell count <200 cells/ μ l at the time of the first diagnosis of their HIV infection. *Linkage to care* was dichotomized as ‘*timely meeting with health workers for HIV care*’ (attending an appointment within 30 days of an HIV diagnosis) and *timely CD4 testing* (having had one or more documented CD4 tests within three months of an HIV diagnosis). *Engaged in care* was assessed as PLHIV who had at least one HIV medical care visit in the last 12 months. *Initiation of ART* was assessed as PLHIV who were eligible to take ART and also actually did receive ART. *ART adherence* over the past month was assessed by visual analog scale (VAS): “*We would like to get your best guess about how much of your anti-HIV medication you have managed to take in the last month?*” and asking the interviewee to estimate their adherence proportion (visual analog scale from 0% to 100% in 10% intervals; 0% meaning that the respondent has not taken any medication, and 100% meaning that s/he has taken every single dose) of their prescribed ART in the last month. ART adherence was later dichotomized into $\leq 90\%$: poor vs. $>90\%$: good adherence.

For Paper II, statistically significant associations between independent variables (population and health system factors) and the retention in HIV care between HIV testing and ART initiation were computed using a generalised structural equation model (GSEM), using the ‘Bernoulli-Logit function’. GSEM also allowed us to address the complex sample survey design in the analysis. Svy: gsem of STATA was used to fit the statistical model for complex survey data.

For Paper II, the different independent variables that are related to population level and health system factors are analysed as independent variables (Table 5).

For Paper III and IV, the inclusion criteria for IBBS survey participants were defined as follows: PWID (men at least 16 years of age and self-reported as injecting drugs for at least

three months); MSM/TG (men at least 16 years of age and self-reported having had anal sex with another man in the last 12 months); FSW (women aged 16 years or above reporting having been paid in cash or kind for sex with a male within the last 6 months); and male labor migrants (men at least 18 years of age having worked in India for at least 3 months and returned to Nepal within three years prior to the date of survey).

Table 2. Independent variables of Paper II

Factors	Variables
<u>Population characteristics</u>	
Predisposing factors	Demographics: Age, risk groups and marital status.
	Social structure: Education, occupation, substance use (alcohol and injecting drug use), disclose HIV status to anyone except spouse, a close family member and doctor, discrimination, violence and housing instability.
	Beliefs: HIV treatment literacy (measured by 25 true/false items) and perceived confidentiality of the medical records relating to HIV status in the clinic/hospital PLHIV are visiting.
Enabling factors	Income enrolled in any kind of health insurance program, cost to reach ART centre, distance to the ART centre, duration of ART started, ART side effects and social support (Multidimensional Scale of Perceived Social Support).
Need factors	Perceived health status, the reason for HIV testing, use of the internet to find the HIV-related information, ever diagnosed with tuberculosis (TB) after becoming HIV positive (TB/HIV co-infection), and HIV/ hepatitis C virus (HCV) co-infection.
Health system	
Resources/organisation	Received home-based care services, relationship with health workers (Patient Reactions Assessment (87), health care professional ever told other people about HIV status without consent, and place of HIV diagnosis (government hospital, private hospital, HIV voluntary and counselling centre (VCT) in a hospital, VCT centre in non-governmental organization).

For Paper III, the outcome variables were HIV prevalence and unprotected sex (“The last time you had sex with your client, did he use a condom?”). A composite index was created based on micro-level physical (client refuse to pay money after having sex), social (poor

social support and condom negotiation skills) and economic factors (unprotected sex to make more money). The index ranges from 0 to 5, where five means sex workers experienced all the five adverse conditions. In the analysis, the results based on the logit model were converted to the predictive margins and average marginal effects of syndemic conditions on unprotected sex. The CI was set at 95%, and the significance level was set at 0.05 in the final model. To identify the additive interaction estimate, the relative excess risk due to interaction (RERI) for binary exposures was used. A RERI over 0 indicates a synergistic effect of micro-level social structural factors on unprotected sex. The RERI was 1.97 (95% CI -13.7 to 17.6), suggesting a positive synergistic effect of micro-level social structural factors on unprotected sex.

For Paper IV, changes in HIV prevalence, risk behaviours, socio-demographics and comprehensive HIV/AIDS knowledge was assessed. Comprehensive HIV/AIDS knowledge was defined as a correct answer to all the following five questions: 1) condoms can be used to prevent HIV transmission; 2) HIV can be prevented by limiting sex to one faithful uninfected partner; 3) a person can get HIV from mosquito bites; 4) a person can get HIV by sharing a meal with someone infected and 5) a healthy-looking person can have HIV. RDS-related data were presented and analysed as per the guidelines of the ‘Strengthening the Reporting of Observational Studies in Epidemiology for Respondent Driven Sampling Studies’. Moreover, information related to RDS seeds, waves, coupons and sample recruitment homophily of the survey population was collected. All the RDS-related estimates were adjusted to represent the structure of the study population, which is based on information regarding who recruited whom, and the relative size of the respondent’s network using the Volz-Heckathorn estimator (RDS II). A Chi-square test for trend and for two-stage cluster sampling data, and a likelihood ratio test for RDS data, were used to test for trend in proportion. One-way analysis of variance or the Kruskal–Wallis test was used to compare changes in mean or median of continuous variables. All statistical tests were based on a significance level of a p-value \leq 0.05.

3.5 ETHICAL ASPECTS OF THE STUDIES

The protocol for Papers I and II was approved by the responsible research council in each country (Bangladesh: Bangladesh Medical Research Council, Number: BMRC/NREC/2010-

2013/1016; Indonesia: Atmajaya University, Number: 949/III/LPPM-PM.10.01/11/2012; Lao PDR: National Ethics Committee for Health Research at the Department of Hygiene and Diseases Control, Ministry of Health, Number: 63NECHR; Nepal: Nepal Health Research Council, Number: 478; Pakistan: National Institution Bridge Consultants Foundation, Karachi; Philippines: Department of Health Research Ethics Committee (DREC), Number: DREC201207; Vietnam: Ha Noi School of Public Health, Number: 128/2012/YTCC-HD3. MOU was signed between Asia Pacific Network of People Living with HIV (data owner) and PhD student to use data for this study. The participation in the CAT-S was voluntary, and participants were made aware of the study objectives and study processes at the beginning of the interview. Those who were willing to give voluntarily written informed consent (thumbprint was obtained from those who were not able to sign) were recruited for the CAT-S. Monetary incentives were provided to study participants (5 USD in Lao, Indonesia, Nepal and Vietnam and 10 USD in Bangladesh, Pakistan and Philippines) for participation in the study. Support was sought from the local law-enforcing agencies to enrol study participants from the two Pakistani provinces [Khyber Pakhtoonkhwa bordering with Afghanistan (study sites- Peshawar and Swabi) and Baluchistan bordering with Iran and Afghanistan (Study sites- Quetta and Turbat)].

The IBBS survey protocol for Papers III and IV was approved by Nepal Health Research Council. Permission was sought to utilise data from National Centre for AIDS and STD Control, a government body based in Kathmandu (Ref. no: 069/070/496). The key populations who participated in the survey were informed that their involvement in the study was entirely voluntary (oral witnessed consent) and that they were free to withdraw at any time. They were assured that if they did decide to withdraw, this decision would not affect the services that they were offered as part of participation. A consent form regarding the nature of the study and confidentiality of their answers was read to them.

All IBBS survey participants received pre- and post-test counselling on HIV and STIs, a physical examination, and treatment for any STI symptoms, as well as vitamins, condoms, and transportation reimbursement (2 USD). Key populations who tested HIV-positive were informed about the availability of free HIV-related treatment, care, and support services. Participants received an incentive of approximately 5 USD (which is around 17% of the average weekly income of FSW) for participating in the IBBS survey.

3.6 MY ROLE IN THE FIELD WORK, DATA COLLECTION, ANALYSIS AND WRITING

I have analysed the raw data from Phase I of the community access to HIV treatment, care and support services (CAT-S) implemented in 7 countries. I was directly involved in conducting CAT-S Phase II study design workshop and building consensus to finalise variables, methods and field implementation plan. I also guided representatives of community organisations in their development proposals for ethical approval in each of the seven study countries. To achieve the outcomes of the research project, I have worked closely with the main officials of Asia Pacific Network of People Living with HIV/AIDS (APN+) based in Bangkok and National Centre for AIDS and STD (sexually transmitted disease) Control based in Nepal. To be more specific, my role was to contribute to the development of study tools, train data collectors, develop data analysis plan, analyse phase I data of CAT-S, contribute in draft report writing and sharing it with key stakeholders (for a Paper I, II, III). I have also initiated the signing of a memorandum of understanding (MOU) between HIV/AIDS group of KI (led by Prof. Anna Mia Ekström) and the Asia Pacific Network of People Living with HIV/AIDS with the aim of utilisation of CAT-S data for scientific publication.

Since 2012 I have been directly involved in managing overall IBBS surveys, targeting key populations in different epidemic zones in Nepal. My role in relation to the thesis work was to finalise the survey tools, provided training to field workers, quality assurance, data management, analysis and dissemination of survey findings between 2013 and 2014. I was one of the key team members to update the survey tools of Phase II in 2015 to incorporate key issues faced by key populations that may have an affect on their behaviours.

4 RESULTS

This section summarises the main findings of Papers I-IV.

4.1 PREVALENCE OF INCONSISTENT CONDOM USE AND THE ASSOCIATED FACTORS AMONG PLHIV (PAPER I)

Paper I contributes to the understanding of the outcome phase (risk behaviours- inconsistent condom use) of the conceptual framework (Figure 4). In Paper I, we found a very high prevalence of risk behaviour, measured as inconsistent condom use in the past six months among PLHIV with different partners (regular partner 43.3% vs. casual partner 46.2%). Inconsistent condom use with various partners varied between countries where PLHIV from Lao PDR reported the lowest practice, whereas PLHIV from the Philippines reported the highest inconsistent condom use.

Female participants were more likely to report inconsistent condom use with regular partners (marginally significant-adjusted odds ratio (AOR): 1.55; 95% CI: 0.91-2.62, $p = 0.088$) and casual partners (AOR: 1.71; 95% CI: 1.08-2.70, $p = 0.029$). The likelihood of inconsistent condom use was lower among PLHIV living in rural areas (AOR: 0.60; 95% CI: 0.42-0.86, $p = 0.014$) or small towns (AOR: 0.69; 95% CI: 0.53-0.93, $p = 0.021$), as compared to those living in urban areas. FSW were more likely to report inconsistent condom use with regular partners (spouse or partner in a relationship with the interviewee for at least three months) (AOR: 1.57; 95% CI: 1.21-2.05, $p = 0.006$). The likelihood of inconsistent condom use with regular (AOR: 2.74; 95% CI: 1.70-4.44, $p = 0.002$) and casual partners (as any other sexual partner) (AOR: 5.15; 95% CI: 2.09-12.66, $p = 0.003$) was higher among refugees than PLHIV not belonging to any of these key populations. Being employed (AOR: 0.56; 95% CI: 0.29-1.04, $p = 0.062$) and diagnosed with HIV through an HTC centre of a non-governmental organization (AOR: 0.63; 95% CI: 0.51-0.77, $p = 0.001$) lowered the likelihood of inconsistent condom use with casual partners. HIV treatment-related literacy (i.e. being aware that condoms are still needed even if both sexual partners are HIV-positive) also lowered the likelihood of inconsistent condom use with both regular (AOR: 0.52; 95% CI: 0.45-0.62, $p < 0.001$) and casual partners (AOR: 0.76; 95% CI: 0.65-0.89, $p = 0.006$).

Partner status also significantly affected the likelihood of inconsistent condom use: having a partner who was HIV positive (AOR: 3.03; 95% CI: 1.91-4.80, $p = 0.001$) or not knowing partner's HIV status (AOR: 2.76; 95% CI: 1.69-4.51, $p = 0.002$) increased the likelihood of inconsistent condom use, compared to knowing that the partner was HIV negative. PLHIV who were not on ART or not aware of ART (AOR: 1.40; 95% CI: 1.09-1.81, $p = 0.017$), who experienced physical assault (AOR: 1.57; 95% CI: 1.24-1.99, $p = 0.003$) or who currently

were using drugs (AOR: 1.90; 95% CI: 1.08-3.36, $p = 0.033$), had a higher likelihood of inconsistent condom use with a causal partner.

4.2 FACTORS AFFECTING RETENTION IN HIV CARE BETWEEN HIV TESTING AND TREATMENT INITIATION (PAPER II)

Paper II contributes to our understanding of the outcome phase (retention in HIV care) of the conceptual framework (Figure 4). Paper II analysed the effects of different factors (predisposing, enabling, need and health system) retention in care between HIV testing and ART initiation among PLHIV. The study findings suggest that 40% of PLHIV in our study presented late for HIV care, with a large variation between countries, from 17% in Pakistan to 65% in Lao PDR. Similarly, timely CD4 testing varied from 31% in Nepal to 65% in Indonesia. Small variations were observed between countries in other steps of the HIV care cascade (engagement in care and ART initiation). Below are the findings related to different steps of retention in HIV care.

HIV testing: PLHIV is presenting with CD4 cell count less than 200 cells/ μ l at time HIV diagnosis.

Different factors increase the likelihood of presenting late for HIV care such as those who identified as transgender, living area (rural and small town), current/past alcohol user and public health centre as a place of HIV diagnosis. Details are shown in figure 8 (Figure 8).

Timely linkage to HIV care: timely appointment with health workers for HIV care and/ or having a timely CD4 test performed.

Factors such as perceived poor health status or not being sure if records are kept confidential at the clinic/hospital they were visiting, lowered the likelihood of timely appointment with a health worker. Similarly current and past injecting drug use behaviours, going overseas for work, and preparation for marriage as a reason for HIV testing, also lowered the likelihood of timely CD4 assessment. Details are shown in Figures 8 and 9 (Figures 8 and 9).

Engaged in HIV care: PLHIV who had at least one HIV-related medical visit in the last 12 months.

Different characteristics such as young age ≤ 24 years, being a prisoner, having no formal education, and lacking a health insurance lowered the likelihood of engaging in HIV care. Similarly, current injecting drug use behaviour also decreased the likelihood of engaging in HIV care but was only marginally significant (Figure 9).

ART Initiation: PLHIV eligible for ART who also started ART

Factors such as good HIV treatment literacy (Condoms are not needed if both sexual partners are HIV-positive) and being diagnosed with tuberculosis after HIV infection, increased the likelihood of initiating ART. On the contrary, being young (16-24 years) and living with HIV, being a FSW and a lack of health insurance significantly lowered the chance of initiating ART (Figure 10).

ART adherence: adherence over the past month was assessed by visual analog scale. Visual analog scale from 0% to 100% in 10% intervals; 0% meaning that the respondent has not taken any medication) and dichotomized into $\leq 90\%$: poor vs. $>90\%$: good adherence.

PLHIV from Bangladesh reported the highest level of adherence to ART ($> 95\%$), while participants from the Lao PDR (69.7%) and Vietnam (70%) had the lowest level of adherence to ART. Factors such as young age and being a current alcohol user (yes vs. no) increased the likelihood of poor ART adherence. On the contrary, a good relationship with a health worker (assessed using patient communication index) lowered the likelihood of poor ART adherence. The patient communication index (87) assesses the satisfaction level of PLHIV regarding the communication they have with their health workers about HIV infection and ART treatment (Figure 10).

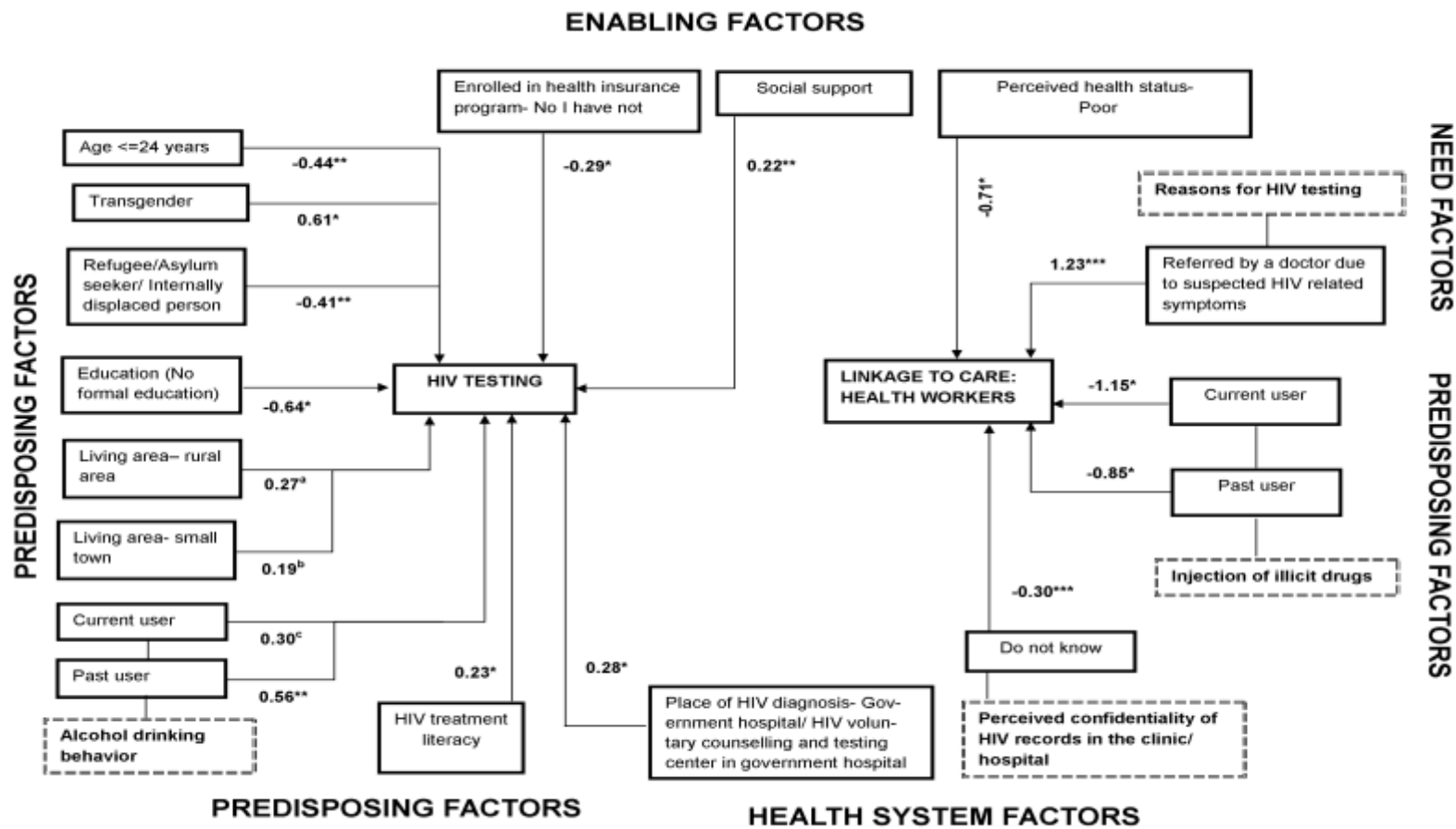


Figure 8. Factors associated with late presentation for HIV care and linkage to care (health workers) among people living with HIV in seven countries of the Asia-Pacific region. Coefficients of factors of late presentation for HIV care and linkage to care based on generalized structural equation model (GSEM) * $p \leq .05$; ** $p < .01$; *** $p < .001$; ^a $p = 0.083$; ^b $p = 0.073$; ^c $p = 0.084$.

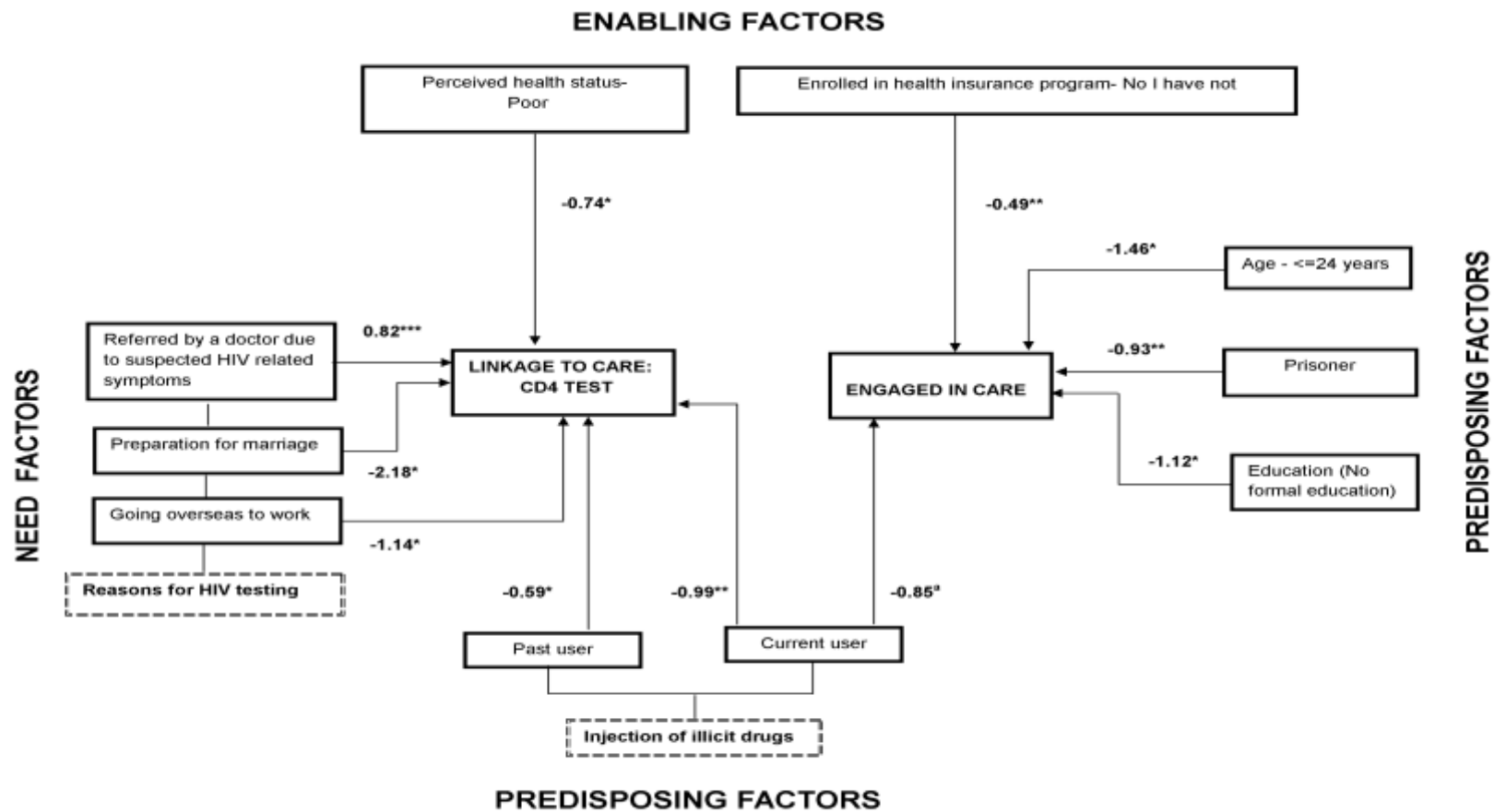


Figure 9. Factors associated with linkage to care (CD4 test) and engagement in care among people living with HIV in seven countries of the Asia-Pacific region. Coefficients of factors of engagement in care, retention in care and poor ART adherence, based on generalised structural equation model (GSEM). * $p \leq .05$; ** $p < .01$; ^a $p = .075$.

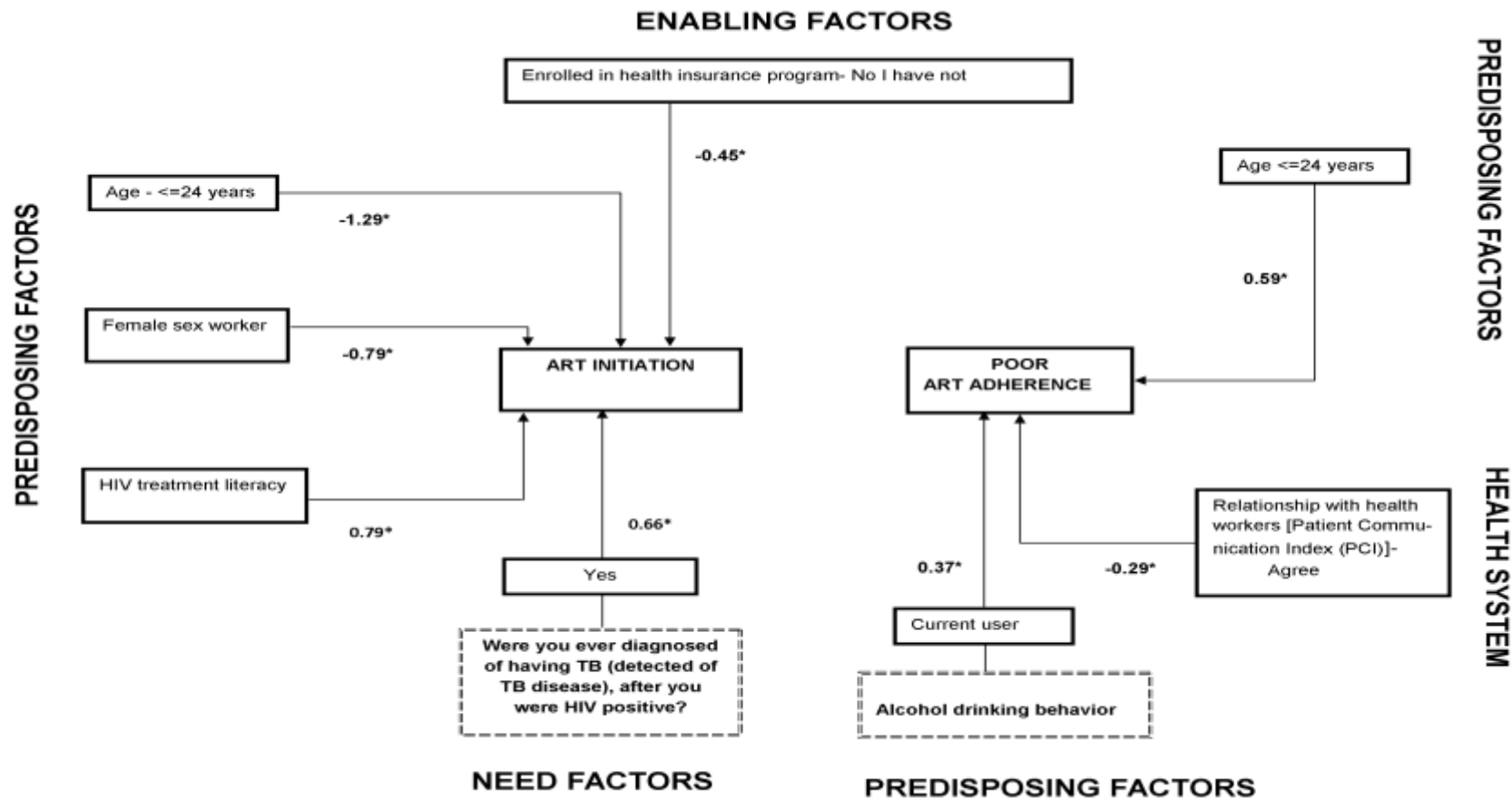


Figure 10. Factors associated with ART initiation and poor ART adherence among people living with HIV in seven countries of the Asia-Pacific region. ¥ coefficients of factors of engagement in care, retention in care and poor ART adherence, based on generalized structural equation model (GSEM). * $p \leq .05$; ** $p < .01$.

4.3 PREVALENCE OF HIV AND THE SYNDemic EFFECTS OF MICRO-LEVEL SOCIAL STRUCTURAL FACTORS OF RISK BEHAVIORS (PAPER III)

Paper III contributes to understanding the synergistic effects of social structural factors on the outcome phase (risk behaviors) of the conceptual framework (Figure 4). Paper III also assessed the prevalence of HIV among FSW in 22 highway districts of Nepal that share an open border with India (Figure 7).

The HIV prevalence among FSW was 1%. FSW experiencing one adverse syndemic condition were 12% more likely to practice unprotected sex with the client than those with no condition. The risk of unprotected sex (“The last time you had sex with your client, did he use a condom?”- ‘yes vs. no’) increased with experience of additional adverse conditions (for example poor social support, poor condom negotiation skills). Details are shown in Table 5 (Table 5).

Table 5. Average marginal effects of syndemic conditions on unprotected sex among female sex workers in Nepal, 2012.

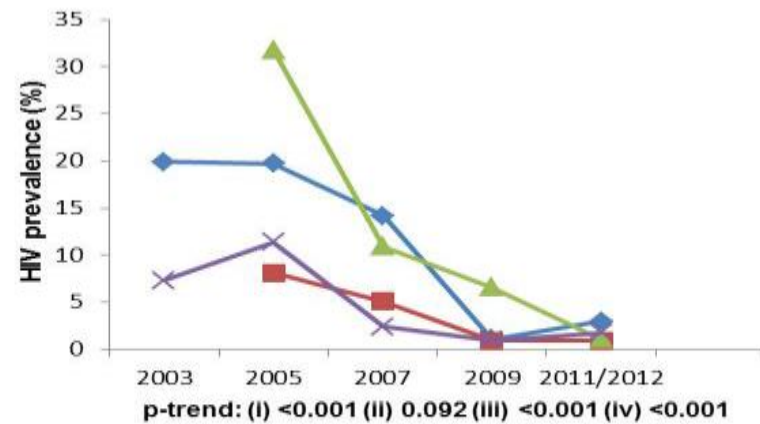
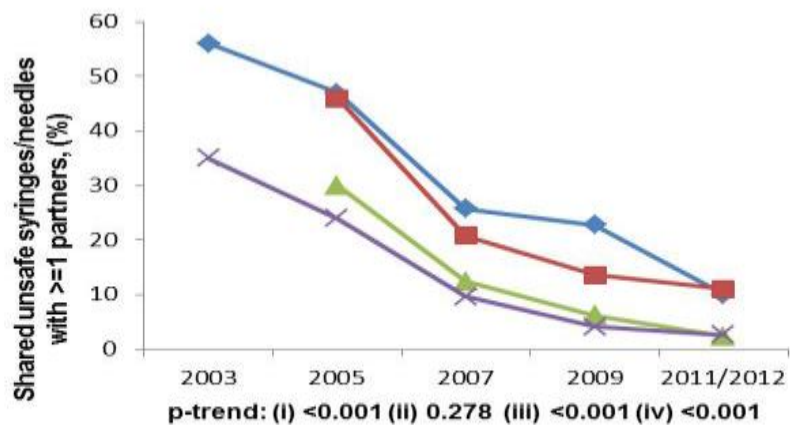
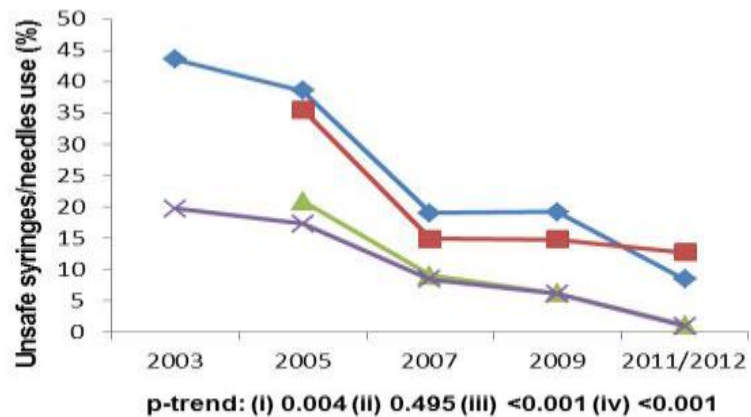
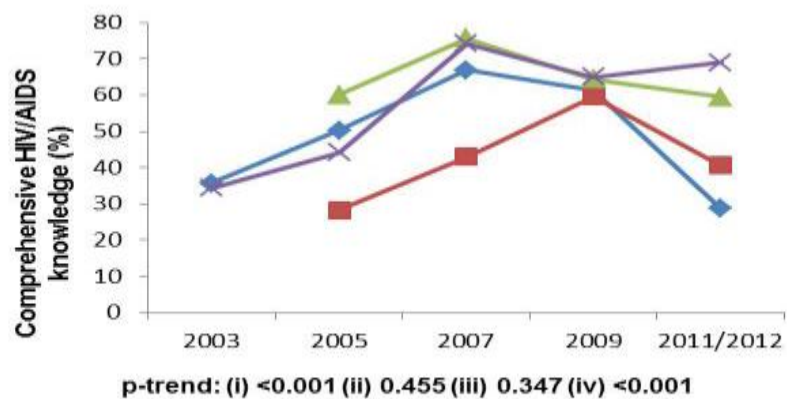
Syndemic conditions	Average marginal effects on unprotected sex	95% confidence interval		p-value
1	.12	.04	.21	0.005
2	.19	.09	.29	0.000
3 and above	.38	.25	.52	0.000

Other covariates included in logit model- age, education, income, place of solicitation, the length of time working as a sex worker and days per week working as a sex worker.

4.4 TRENDS IN HIV PREVALENCE AND RISK BEHAVIORS AMONG YOUNG KEY POPULATIONS IN NEPAL (PAPER IV)

Paper IV contributes to understanding the synergistic effects of social structural factors on the outcome (risk behaviours) and impact (HIV prevalence) phase of the conceptual framework (Figure 4). Paper IV analysed the trends in HIV prevalence, risk behaviors (non-use of condoms, needle/syringe sharing) and other individual-level factors related to sociodemographics, comprehensive HIV/AIDS knowledge and other risk factors among young key populations aged 16-24 years (PWID, MSM/TG, FSW and male labour migrants) over a 12 year period (2001-2012 in Nepal). To better characterise the epidemic, we analysed trends in HIV prevalence and risk behaviours by local epidemic zones (Figure 7). The HIV epidemic zones in Nepal are the Valley (capital city-Kathmandu Valley, major tourist area-Pokhara Valley), the Hills (West to Farwest) and the Terai Highway (districts which share an open border with India). The burden of HIV is not consistent throughout the country, so the local HIV epidemic zones have been identified in Nepal based on the size and distribution of key population at risk, mobility links and HIV-related risk behaviours.

Paper IV found a sharp decline in HIV prevalence and risk behaviours among young key populations (PWID and MSM/TG) in the different epidemic zones of Nepal (Figure 11 and Table 6). Similarly, the decline in HIV prevalence was also consistent with improved condom use among young FSW (Table 6). Though the prevalence of HIV was low throughout the study period among young labour migrants, the changes in condom use behaviour with sex workers are not consistent (use of condoms increased with Indian FSW but declined over time among Nepalese FSW). Also, changes over time in other risk factors (age of the first injection, place of solicitation, injection frequency) were not consistent between epidemic zones in Nepal.



—◆— i. East Terai Highway —■— ii. West to Farwest Terai Highway —▲— iii. Kathmandu valley —×— iv. Pokhara valley

Figure 11. Trends in HIV prevalence, risk behaviours and comprehensive HIV/AIDS knowledge among young people who inject drugs aged 16–24 years, by epidemic zones and year of survey, Nepal 2003–2012 (N=2767). p values in the East and West-to-Far West Terai highway were calculated after excluding 2003 and 2005 survey data.

Table 6. HIV prevalence, risk behaviors and comprehensive HIV/AIDS knowledge among young MSM/TG in Kathmandu valley and male labour migrants aged 16-24 years in West-To-Farwest hills, by year of survey, Nepal 2004-2012 (N= 1887)

Characteristic	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	p-trend
MSM/TG	2004	2007	2009	2012	
Comprehensive HIV/AIDS Knowledge	35 (23-48)	52 (37-67)	47 (32-61)	53 (35-71)	0.084
Condom use among MSM/TG in last anal sex with male sex partner	-	72.1 (62-82)	66.8 (52-81)	80.1 (77-84)	0.098
Condom use among MSM/TG with non-paying male partner at last anal sex	71.4 (60-83)	71.5 (62-81)	71.1 (56-86)	84.9 (60-99)	0.361
Condom use among MSW* with casual male client at last anal sex	82.6 (55-99)	98.7 (86-99)	97.3 (95-97)	86.6 (76-97)	0.225
Condom use among MSW* with regular male client at last anal sex	77 (40-99)	93 (81-99)	82 (67-98)	97 (95-99)	0.150
HIV prevalence	5.9 (3-9)	4.3 (0.01-10.6)	0.2 (0.002-0.5)	0.7 (0.6-0.8)	0.005
Male labour migrants	2001	2006	2008	2012	
Comprehensive HIV/AIDS Knowledge	-	0.6 (0.002-1.4)	19 (14-23)	11 (7-15)	<0.01
Had sex with FSW in Nepal [†]	-	3 (1-5)	2 (0.03-3.0)	10 (6-13)	<0.01
Condom use at last sex with FSW in Nepal	-	40 (10-70)	75 (33-99)	56 (37-76)	0.001
Had sex with FSWs in India [†]	-	7 (3.9-9.3)	5 (8.1-15.9)	10 (6-13)	0.103
Condom use at last sex with FSW in India	-	73 (54-91)	83 (62-99)	84 (69-98)	0.059
HIV prevalence (%)	0.0	0.6	0.0	0.4	-

[†] In the last 12 months; CI, Confidence interval; MSM/TG, Men who have sex with men/ Transgender; MSW*, Male sex workers.

5 DISCUSSION

The findings of this thesis demonstrate that the following issues act as a threat to achieving positive results in the spectrum from input (interventions) to impact (declining HIV prevalence as well as AIDS-related deaths among key populations and PLHIV in the study countries) (Figure 4). A high prevalence of unprotected sex and a high proportion presenting late for HIV care delaying linkage to ART, was widely prevalent among PLHIV in seven study countries. The experience of adverse conditions (poor social support, economic vulnerability) increased the odds of unprotected sex among FSW. Although HIV prevalence and risk behaviours are declining over time among young key populations, those who had become HIV-positive were not so likely to engage in HIV care or had poor ART adherence.

The results from this thesis demonstrate that four out of every 10 PLHIV in the seven studied countries practise unsafe sexual behaviours with different partners (regular and casual partners) (Paper I). The prevalence of these unsafe sexual behaviours among PLHIV with casual partners differs widely between study countries, i.e. from 16% in Lao PDR to 60% in the Philippines. A 40% of PLHIV presented late for HIV care (CD4 count of <200 cells/uL) but delayed linkage to care varied greatly between the study countries (6% in Lao PDR to 46% in Vietnam) (Paper II).

Almost a quarter of the studied FSW had unprotected sex with their clients in the 22 Terai highway districts of Nepal that share an open border with India, but the HIV prevalence was still low in comparison to FSW in other Asian countries (Paper III). Analyses of surveillance survey data from the last 12 years (2001-2012) suggest that the decline in HIV prevalence is paralleled by a reduction in risk behaviours among young key populations aged 16-24 years in Nepal. In Nepal, the decline in HIV prevalence over the past decade was remarkably significant and consistent with an increase in condom use and safer use of clean needles and syringes.

Condom use behaviour among PLHIV (Paper I)

Paper I found that women and key populations (MSM, PWID and FSW) were more likely to practice inconsistent condom use behaviours with different partners in line with previous studies (9, 88). Various factors such as poverty and rooted gender inequities in the region increase the risk of survival sex and low self-esteem, including poor condom negotiation skills among FSW (89-91). An unsafe working environment (unavailability of condoms, policing policies) also influences condom use behaviours among sex workers in the region

(32). Many countries in the region also lack plans and efforts to address unsafe sex among refugee and internally displaced persons (92-94).

We found that the experience of physical assault among PLHIV was associated with inconsistent condom use, which is consistent with other published studies (95, 96). The experience of physical assault increases sexual risk-taking behaviours (inconsistent condom use) through different pathways such as forced sex with a perpetrator and reduced capacity to negotiate condom use (97). A poor HIV treatment literacy (not knowing that condoms are still needed if both partners are HIV positive), having a regular partner whose HIV status was either positive or unknown, and not being on ART (the overall ART coverage was 24% but varied from 3% in Lao PDR to 33-34% in Nepal and Philippines) also increased inconsistent condom use among PLHIV. This indicates that the benefits of treatment as prevention is limited in study countries.

Retention in HIV care between HIV testing and ART initiation (Paper II)

We found different barriers and facilitators associated with various steps of the HIV care continuum associated with predisposing (young age, no formal education, sex work, transgender identity, prisoners, transgender identity, alcohol/injecting drug use, HIV treatment literacy), enabling (enrolled in health insurance program), need (perceived poor health status, self-referral for HIV testing, referral from a health worker and diagnosis of tuberculosis/HIV co-infection) and health system (good client-provider communication, fear of confidentiality breach, public hospital as the place of HIV diagnosis) factors.

Previous research has found that PLHIV belonging to key populations (PWID, TG, FSW and prisoners) are less likely to remain in HIV care because of criminalization of their behaviours, because of unsafe work environments for sex workers, and, because of discrimination based on sexual orientation (98-101). Unavailability or intermittent delivery of poor quality HIV services in prison and the brief nature of prisoners (102) often results in poor ART access, adherence and retention in HIV care among prisoners. Those PLHIV who were not sure whether their medical records were kept confidentially in the health centres, delayed uptake of ART and linkage to HIV care (meeting health workers within 30 days of HIV diagnosis) (Paper II). Confidentiality breach by health workers is widely prevalent in many countries in the region despite the availability of guidelines the protection of privacy of PLHIV (103-105). PLHIV satisfied with the information provided by the health workers about the illness were more likely to adhere to treatment (Paper II), which is consistent with previous studies (106, 107).

PLHIV enrolled in a health insurance program were more likely to engage in care and initiate ART (Paper II). Social protection with different names (Vietnamese Social Security Social Health Insurance Program etc.) targeting PLHIV—which provides CD4 cell count tests free of charge, monthly cash allowance for daily necessities and common drug provision—are implemented in four study countries (Indonesia, Vietnam, Philippines and Lao PDR). However, the coverage and awareness among PLHIV of such social protection programs is limited in those countries (18-20). Despite the implementation of different social protection programs, PLHIV living in Indonesia, Lao PDR and Vietnam often experience a catastrophic financial burden while seeking various HIV-related services, such as viral load tests, hospital admission fees or diagnosis and treatment of comorbid diseases (6, 17, 18). Although PLHIV receive free HIV treatment (ART) from the public system, insurance that covers general health care costs among PLHIV does not exist neither in Bangladesh nor in Nepal. PLHIV in Pakistan can enrol in a health insurance program, but information on the coverage and effectiveness of this program in reducing the financial burden related to HIV services is not available.

Synergistic effects of micro-level structural factors and HIV risk (Paper III)

The prevalence of HIV among FSW in Nepal was lower than among sex workers in other countries (HIV prevalence in India 13.7% and Thailand 11.9%) (16). Available interventions may contribute to a lower HIV prevalence among FSW in Nepal. The micro-level social structural factors related to physical (experience of undesirable events), social (poor social support and condom negotiation skills), and economic (unprotected sex to make more money) act in a dose-response relationship to increase unprotected sex among Nepalese sex workers (Paper III). Other studies in the Philippines, USA, and Vietnam have also found that physical, social and economic level factors interact and are associated with unprotected sex among FSW (42, 108, 109).

Trends in HIV prevalence and risk behaviours among young key populations (Paper IV)

Young key populations in Nepal are experiencing declining trends of HIV prevalence and risk behaviours in different epidemic zones (Paper IV). However, other countries in the region (Cambodia, Pakistan and Thailand) are experiencing different scenarios, such as higher levels of risk behaviours and increased HIV incidence and prevalence (25, 110-112). Similarly, the practice of multiple risk behaviours among young key populations (e.g. MSM/TG sometimes both use drugs and also sell sex, and drug users also sell sex) is widely

prevalent in Cambodia, Pakistan and Thailand (25, 111, 114) but less so in Nepal (113). The aforementioned differences in the burden of HIV in Nepal compared to other nations in the region may be attributed to several factors including an improved social capital and high coverage of interventions early on already since the inception of the epidemic. A favourable policy environment to protect the health and rights of key populations also exists in Nepal (13, 37). However, much preventive work remains to be done, for example the change in other risk determinants (mean age at first injection, injection frequency, solicitation place) is not consistent between epidemic zones overtime in Nepal.

5.1 METHODOLOGICAL CONSIDERATIONS

Paper I and Paper II

In Papers I and II, a community-based participatory research (CBPR) approach (84), called CAT-S (community access to HIV treatment care and support services study) was used to design, implement and use of research findings. CBPR promotes the collaboration between researchers, community and organisations to identify the problem of interest and propose its solutions. Participation from the community was highly prioritised in the different phases of the research (prioritising the problem/research question, planning/implementing the field activities, analysing collected data and disseminating the results for advocacy and proper response) to enhance the ownership of the process. The Agency for Healthcare Research and Quality define CBPR as: *“Community-based participatory research is a collaborative research approach that is designed to ensure and establish structures for participation by communities affected by the issue being studied, representatives of organizations, and researchers in all aspects of the research process to improve health and well-being through taking action, including social change.”*(115)

CAT-S is a collaborative effort of community members, organisational representatives (Asia-Pacific Network of People Living with HIV/AIDS) and researchers (85). PLHIV from the seven study countries actively participated in different phases of the research such as the planning phase (formulation of priority such as treatment access, identification of study sites and preparation of documents for ethical approval), the field work phase (recruitment and training of the field researchers, implementation of field work), and the action phase (development of effective advocacy messages based on study findings and dissemination of

findings at national level). The use of CBPR has both advantages and disadvantages. One lesson learnt after the implementation of CBPR was that PLHIV are not only the target population of the research but could and should also manage the research and contribute to generating evidence and prioritisation of response activities. Their experiences of day-to-day life e.g. challenges in terms of accessing treatment, also helped us to refine the study variables. Their involvement in the study also contributed to recruiting hidden and marginalised PLHIV who were experiencing the double burden of their HIV status and belonging to a key population (MSM, TG, and/or sex workers). However, the major limitation of using CBPR was that the use of evidence for advocacy and response prioritization was not uniform across the study countries. The overall process in terms of utilising our study findings may affect the interest and capacity among community leaders regarding understanding the bigger picture and in terms of implementing research results.

Some other limitations also exist in the findings of Papers I and II due to the design and the methodology used for data collection. An assessment of retention in HIV care over time was not feasible due to the analysis of baseline data. Paper II gives the proportion of PLHIV who initiated ART and factors associated with this. However, considering that PLHIV are supposed to stay on ART for life, information on the proportion of PLHIV who initiate ART but and who also remain on treatment over time it is very important to assess treatment effectiveness since some stop treatment or drop out of care. In addition, some outcomes of interest such as ART initiation could have been overestimated, if the characteristics of the study participants differed from those who did not participate or refused to take part in the study. For example, study participants may be more aware of available treatment options and more likely to initiate ART than other PLHIV because of their association with a national network of PLHIV. If so, the real problems are even bigger than what we have estimated.

The collection of information about sensitive issues (sexual behaviour, sexual orientation, sex work) as well as the retrospective nature of interviewing, may result in social desirability bias and recall bias. PLHIV may tend to report socially acceptable responses, so-called 'good norms or behaviours', such as the use of condoms and not having sex with multiple partners etc. The effect of such bias may result in underestimation of non-use of condoms with different partners. Some study variables that require recalling information from the past, such as CD4 level at the first HIV diagnosis, may be reported less accurately by PLHIV who were diagnosed with HIV a long time back. Different strategies were used to reduce the effects of the various biases mentioned above, such as informing study participants of the importance of responding accurately and their responses would be treated confidentially. .

Papers III and IV

We have analysed secondary data from surveillance surveys to answer the research questions of Papers III and IV. The disadvantage of secondary data is the unavailability of all the required variables in a usable format. For example, in Paper III there were no variables related to structural factors that operate at macro level limiting data analysis.

The sampling techniques (two-stage cluster sampling and RDS) used to enrol study participants may also have influenced the estimate of the outcome of interest. The mapping phase to develop the sampling frame in two-stage cluster sampling is influenced by the information provided by community people or local organisations. If the characteristic of sex workers who were not recorded or who were missed during the mapping phase is different from those who were interviewed, then that might cause a selection bias which results in either an under -or an overestimation of the outcome of interest. Another scenario is if the particular cluster is missed during the listing of clusters,. Then there is a risk that FSW who work in missed clusters (for example FSW operating from rented apartments) have different characteristics with regards to the outcome of interest than those FSW who work in other clusters (for example dance bars, massage parlours). The collection of sensitive information through face to face interviews may also result in social desirability bias. However, considering that a significant proportion of key populations in Nepal have no formal education, a self-administered questionnaire was not viable.

RDS is widely used to enrol hidden and marginalised populations such MSM/TG and PWID. It is assumed that use of RDS produces unbiased estimates if its key assumptions are met. However, in some cases, RDS could have reached only one subset of the study population e.g. if there is no cross-referral between young and old or between different ethnic groups. Various strategies to minimise recruitment bias were used in the RDS surveys among key populations in Nepal for example making sure that seed characteristics were diverse and also consistent with baseline surveys.

The results of a trend analysis are influenced by several factors such as the natural course of an HIV epidemic, social desirability bias over time, sampling technique and HIV testing strategy. At the start of an HIV epidemic, individuals with high-risk behaviours are more likely to become infected rapidly, and new infections dwarf mortality due to the chronic nature of HIV and the slow progression rate from HIV to AIDS. As the epidemic progresses, HIV incidence declines due to lower risk behaviours among remaining at risk individuals, even despite a lack of preventive interventions. However, such effects is unlikely to affect the

results in Paper IV because the young people who participated during this study period were from different birth cohorts compared to those young people infected in the early years of the epidemic. This phenomenon has also been pointed out by The International group on analysis of trends in HIV prevalence and behaviours in young people (116).

The effects of social desirability bias in IBBS surveys was minimised by the non-collection of personal identifiers, and all interviews were anonymous. The collection of both biological and behavioural information through different methods (rapid tests and face to face interviews) also reduced any effects of social desirability bias. The results of biological samples were confirmed through external quality assurance after completion of data collection in the IBBS surveys (Papers III and IV).

6 CONCLUSIONS

- Non-use of condoms with different (regular and casual) partners was highly prevalent among PLHIV in the seven study countries (Paper I). Inconsistent condom use with different partners among PLHIV was associated with previous experience of physical abuse, poor HIV treatment literacy and not being enrolled on ART (Paper I). In addition to FSW and drug users, refugees were also more likely to report inconsistent condom use with regular and casual partners (Paper I).
- A high proportion of PLHIV presented late for HIV care (CD4 cell less than 200/ μ l). Moreover, delayed linkage to care (not having one or more documented CD4 tests within three months of an HIV diagnosis) was common among PLHIV. However, engagement in HIV care, ART initiation and adherence to ART was at an acceptable level (more than or equal to 80%) (Paper II).
- PLHIV with good HIV treatment literacy were more likely to initiate ART. Health system factors such as good client-provider communication related to HIV treatment enhances adherence to HIV treatment. Young PLHIV (16-24 years) were less likely to engage in HIV care, not start ART and also had poor adherence to ART. Similarly, prisoners were less likely to engage in HIV care. PLHIV not enrolled in any health insurance program were less likely to engage in care and not initiate ART (Paper II).
- Micro-level social structural factors related to physical (experience of undesirable events), social (poor social support and condom negotiation skills) and economic (unprotected sex to make more money) levels act synergistically to increase the likelihood of unprotected sex among female sex workers in Nepal (Paper III).
- HIV prevalence and risk behaviours are declining or have stabilised at a low level ($\leq 3\%$) among young key populations (PWID, MSM/TG, FSW and male labour migrants) in Nepal. However, changes in other risk determinants such as mean age at starting first injection, injection frequency, place of commercial sex solicitation, mean age when leaving for work abroad, were not consistent between epidemic zones in Nepal (Paper IV).

7 PROGRAMMATIC AND POLICY IMPLICATIONS

- *Enhance the treatment as prevention benefits of ART.* HIV programs should prioritise early detection of HIV and to enrol PLHIV who are not on ART on treatment as soon as possible, as well as making PLHIV aware of the health and prevention benefits of ART.
- *Target missed key populations such as refugees and prisoners with prevention and treatment services.* Currently, the national plans of most of the countries in the region lack clear strategies to address inconsistent condom use among refugees. Also many countries in the region lack HIV services in prison meaning that ART often is interrupted when PLHIV belonging to key populations (PWID, FSW) are incarcerated. Implementing HIV programmes into the prison setting is crucial to ensure that ART is delivered uninterrupted during incarceration to prevent illness, secondary HIV transmission and ARV drug resistance.
- *Design and implement interventions to address the gap of timely identification of PLHIV and linking them to HIV care.* Paper II clearly suggests that the biggest problem lies in the late presentation of PLHIV for HIV care. Proper implementation of the ‘test and treat’ strategy would help to address the issue of delayed linkage of PLHIV in HIV care.
- *Design and implement sustainable social protection programs.* Paper II demonstrates that PLHIV without health insurance were less likely to engage in care and to not initiate ART. Efforts should be made to more easily enrol PLHIV in such protection programme, and to improve the coverage of health insurance for PLHIV.
- *HIV prevention programme should incorporate strategies to address the negative effects of social structural factors.* Existing behavioural interventions lack elements to address the social structural factors that increase the likelihood of unprotected sex. Future efforts should include strategies to address negative micro level social structural factors (for example poor social support, poor condom negotiation skills, economic vulnerability) to make behavioural interventions more effective. Only distributing condoms will not stop risky behaviours among sex workers.
- *Prioritise young PLHIV-friendly HIV care services.* The current blanket approach does not adequately address the specific treatment needs and demands of young PLHIV. Thus, needs assessments among young PLHIV should be prioritised to improve their retention in HIV care.

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