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HIV/AIDS-related stigma reduction intervention in China, a systematic review

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Master of Public Health

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Thesis Committee Chair

An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

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Abstract

HIV/AIDS-related stigma reduction intervention in China, a systematic review

By Siqiao Zhang

Introduction:
HIV/AIDS-related stigma continues to be one of the most impactful factors on the physical and mental well-being of people living with HIV/AIDS. The identification of key effective strategies aiming to reduce HIV/AIDS-related stigma is an indispensable step in combating the HIV/AIDS epidemic.

Methods:
The article conducted a systematic review of existing studies that assessed the effectiveness of interventions reducing HIV/AIDS-related stigma in the Chinese population. Four electronic databases were searched to retrieve relevant studies, including PubMed, EMBASE, COCHRANE library, and PsychInfo. Studies with an intervention design conducted in mainland China, Hong Kong, Taiwan or Macao, and aimed to reduce HIV/AIDS-related stigma as primary or secondary outcome were included. Studies without intervention effectiveness assessments and sufficient pre- and post-intervention data were excluded.

Results:
Among 371 peer-reviewed articles identified, 11 articles were retained for the systematic review. 91% of the studies were assessed as high-quality studies. 90% of high-quality interventions found statistically significant HIV/AIDS-related stigma reduction outcomes. The majority of interventions utilized more than one strategy approach. Most interventions were individual-oriented, only two studies intervened at multi-faceted socio-ecological levels. However, target population and intervention location lacked variation and representativeness. Outcome measurements lacked consistency, posing challenges in comparing effectiveness across interventions. Intervention duration and dosage varied widely, making it challenging to examine the sustainability of the effectiveness of interventions.

Conclusion:
The article revealed considerable progress in reducing HIV/AIDS-related stigma in the past two decades. Identified gaps and challenges that continue to hamper our collective efforts in ending the HIA/AIDS epidemic are needed to be addressed in future research. The development of standardized and culturally appropriate stigma measures is needed to allow comparison of effectiveness across interventions. Research resources on developing and implementing interventions with multi-faceted structural designs and mixed-strategy approaches are needed to reduce HIV/AIDS-related stigma among the Chinese population.

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CHAPTER 1. INTRODUCTION

1.1 Introduction and rationale

Ever since the first onset of the HIV epidemic in the early 1980s, HIV infection continues to be one of the significant public health issues in the world, leading to more political and scientific mobilization than any other disease. According to the latest report from World Health Organization (WHO), by the end of 2017, approximately 36.9 million people worldwide are living with HIV/AIDS, with an estimated 0.8% prevalence among adults aged between 15 and 49 years old. Due to the advances in HIV treatment and continuous investment in scientific research in the past three decades, HIV infection has now become a manageable chronic disease, and the life expectancy of people living with HIV/AIDS (PLWHA) has been prolonged (Deeks, Lewin & Havlir, 2013). The increasing number of PLWHA presents challenges in improving the quality of life and satisfying the need for lifetime treatment and care of the expanding seropositive population.

However, the public health efforts in improving the quality of life of PLWHA have been undercut by the severe magnitude of stigma and discrimination towards HIV infected people observed throughout the world. The 2015 UNAIDS report reveals that given the available data collected from 35% of countries in the world, more than half of the people report having discriminatory attitudes towards people living with HIV. Evidence indicates that one in eight HIV-infected people report ever been rejected in healthcare settings (UNAIDS, 2015).

More than 3 decades after the first outbreak of HIV infected case, HIV/AIDS-related stigma persists and continues to be one of the most impactful factors on the physical and mental well-being of people living with HIV/AIDS, spouses and family members, and people at high risk of HIV infection (i.e. men having sex with men, commercial sex workers,

injection drug users, and migrant workers) (Zukoski & Thorburn, 2009). HIV/AIDS stigma has introduced a wide range of barriers to healthcare seeking behaviors, including, voluntary HIV testing, early detection of HIV, linkage to and retention in HIV care, disclosure of HIV status, willingness and acceptability of oral-PrEP, which all eventually increase disease transmission (Brown, Macintyre & Trujillo, 2003; Alemus et al., 2013; Ma et al., 2007).

With 501,000 people living with HIV/AIDS and 0.037% national prevalence, China remains as a low HIV epidemic country (Avert, 2019). However, due to China's massive population, the number of PLWHA and people at risk of HIV infection outnumber countries with high HIV prevalence. Moreover, China is still far behind reaching UNAIDS 90-90-90 target, suggesting great challenges in the progress of reducing new infections, ensuring sustained treatment, and improving quality of life among PLWHA (UNAIDS, 2014a).

HIV/AIDS-related stigma is a significant barrier that continues to hamper China's efforts in combating the AIDS epidemic. Evidence indicates that 73% of rural Chinese have a discriminating attitude against PLWHA and believe having HIV is shameful (Zhang et al., 2016b). The 2014 China Country Progress Report regards China's severely stigmatized attitudes around HIV/AIDS as one of the five major challenges in future efforts in combating the HIV epidemic (UNAIDS, 2014b). The complexity of HIV/AIDS stigma varies by cultural background, and studies found that PLWHA in China face more severe HIV/AIDS stigma when comparing to those in western countries due to Chinese conservative culture settings (Mahajan et al., 2008; Zhang et al., 2016a).

In the past decade, HIV/AIDS stigma reduction programs received little attention, funding, and resources, resulting in limited success in the efforts of eliminating HIV/AIDS stigma in the world (Mahajan et al., 2008). The number of intervention studies aimed at alleviating HIV/AIDS stigma among the Chinese population is limited as well. However, in recent years, there is a shift of focus in stigma-related studies, and eliminating HIV/AIDS-

related stigma and discrimination became one of the two main objectives proposed in the new UNAIDS 2016-2021 Strategy (UNAIDS, 2015). Developing and delivering effective stigma-reduction programs proves to be one of the primary priorities in future efforts in combating the HIV epidemic in both China and countries throughout the world.

1.2 Problem statement

Consistent with other countries in the world, HIV remains as one of the most stigmatized diseases in China, and the level and categories of HIV/AIDS-related stigma widely observed in China are different from what is found in western countries (Mahajan et al., 2008; Zhang et al., 2016a). While increasing attention and efforts in developing and implementing HIV/AIDS stigma reduction interventions has been noticed in African and western countries, limited reviews have been published to evaluate the effectiveness of these interventions delivered in China (Grossman & Stangl, 2013). Given the magnitude of HIV/AIDS stigma observed in the Chinese population and its negative influence on PLWHA, family members and partners of PLWHA, it is timely to review interventions aiming at reducing HIV/AIDS-related stigma among Chinese.

1.3 Purpose statement

In this paper, we systematically review HIV/AIDS-related stigma reduction intervention studies conducted among the Chinese population. The objectives of this thesis are to describe 1) interventions aimed at reducing HIV/AIDS-related stigma in the Chinese population, 2) summarize shared characteristics and differences, 3) identify effective components of these interventions, and 4) discuss lessons learned and implications for future efforts in reducing HIV stigma in China.

1.4 Significance statement

Three decades into the HIV epidemic, HIV/AIDS has now become a manageable chronic disease, and the number of PLWHA is steadily increasing due to the advances in

antiretroviral therapy. However, the stigma around HIV/AIDS continues to hamper efforts in preventative programmes, such as engaging people at risk in regular testing, promoting biomedical preventative drugs, retaining PLWHA in continuous treatment, encouraging status disclosure, and etc. The current systematic review of existing stigma-reduction programmes implemented in China will inform best practices to reduce HIV/AIDS stigma, guide future work in devising and delivering effective stigma reduction programmes and, ultimately, to help reduce new infections among key affected populations, ensure best treatment outcome, and improve quality of life among PLWHA.

CHAPTER 2. LITERATURE REVIEW

2.1 Status of HIV/AIDS Epidemics in China

According to the latest data published in 2014, China remained a low HIV epidemic country with only 501,000 people living with HIV/AIDS, roughly 0.037% of the national prevalence (Avert, 2019). However, given China's enormous population, even with low HIV prevalence rate, the total number of people living with HIV and people at risk of HIV infection in the country is comparable to sub-Saharan African countries with high HIV prevalence rate (Yang, Wu, Schimmele & Li, 2015). The HIV epidemic in China is also characterized by its highly imbalanced geographic distribution, with certain regions having significantly higher HIV prevalence rates. The 2017 CDC data revealed that the top five provinces with the highest HIV infection rates are all sitting along the southwest border of China, regions with major drug smuggling routes passing through (Thepochtimes, 2019).

In recent years, a spike of new infections in young populations and infections through MSM (men having sex with men) sexual activities are alarming and presents severe challenges of providing targeted intervention programs in key affected populations such as injection drug user (IDU), MSM, and young students aged 15-24 (Avert, 2019). Furthermore, the high level of stigma and discrimination against PLWHA throughout the country places obstacles in HIV preventive behaviors and undermines the public health efforts in stemming the epidemic.

The UNAIDS 90-90-90 target aims to end HIV epidemic worldwide by 2020, through having 90% of people living with HIV aware of their HIV status, 90% of people diagnosed with infection receive antiretroviral treatment, and 90% of people on treatment are virally suppressed (UNAIDS, 2014a). China, unlike its neighboring country, Thailand, is still far

behind in reaching UNAIDS 90-90-90 target despite heavy investments in HIV testing and ART therapy provision in the past decades. A study conducted in Shandong province indicates that only 60% of people infected knew their status, among these, 42% were on highly active antiretroviral therapy (HAART), and only 60% of HARRT-treated people and 15% of all infected people were virally suppressed (AIDSMAP, 2016; Zhang et al., 2016c).

2.1.1 IDU populations

The first outbreak of indigenous HIV infection was observed among rural IDU populations in Yunnan province, the southern border area between China and Myanmar (Zhang & Ma, 2002; Wang et al., 2015). The HIV epidemic in IDUs quickly spread to neighboring provinces along the southwestern boarders of China, mainly through two major drug smuggling routes originated from Myanmar and Vietnam. IDUs and tainted plasma transfusion quickly became two major transmission routes in the 1990s, the early years of the HIV epidemic in China. As of 2017, five provinces sitting closest to the borders of Myanmar, Vietnam, and Central Asia still have the highest HIV prevalence compared to central provinces (Sullivan & Wu, 2007).

The increasing trend of infection through drug injection has been effectively addressed, with the proportion of people who inject drugs (PWID) among PLWHA slightly dropping from 6.33% in 2013 to 6.00% in 2014 (UNAIDS, 2014b). Moreover, the proportion of infection through drug injection among all newly infected HIV cases declined substantially from 34.1% in 2006 down to 3.4% in 2017 (SCDC, 2018). With the massive scale-up of harm reduction programmes delivered across the country in the past decade, by the end of 2014, a total of 767 methadone maintenance treatment (MMT) programmes and 814 needle-syringe programmes (NSP) have been established across 28 and 14 provinces, respectively (UNAIDS, 2014b; AVERT, 2019).

While considerable progress has been made to target transmission through IDUs, new challenges and gaps remain, including the emergence of "new-type drug", also known as the synthetic drugs, such as amphetamine-type stimulant (ATS), and the drastically increased number of young drug users aged between 15-24. In order to maximize existing prevention effects and prepare for future trends in drug consumptions, further efforts are needed in studying characteristics of "new-type drug" users, adjusting existing intervention programmes, and targeting young drug users (Liu et al., 2014).

2.1.2 Illegal commercial plasma donor

Unlike most countries in the world, the key affected populations in China not only include injection drug users (IDUs), commercial sex workers, and men having sex with men (MSM). Illegal commercial plasma donors have also contributed greatly in the early phase of HIV/AIDS epidemic in China. At the beginning of the 1980s, national blood shortage opened up the so-called "liquid gold" market and led to the emergence of massive-scale illegal blood trading industries in China (He & Detels, 2005). Thousands of small blood trading stations were established in rural villages, collecting blood from impoverished farmers and peasants. Unsanitary practices such as using shared needles, inadequately sterilized equipment, and blending various plasma within a single container, have led to the rapid spread of HIV infection among these donors.

As these illegal blood companies traded contaminated blood to the government-run blood banks and various underground blood banks, the transmission of HIV has become unstoppable and untraceable among people all over the country. Between 1985 and 2005, nearly one-third of the national HIV infections were attributed to the illegal commercial plasma industry (Wang et al., 2013). Henan province, one of the most impoverished and populous provinces in China, became the epicenter of this shockingly enormous outbreak of AIDS, resulting in the tragedy of "AIDS village," where the majority of villagers were

infected and died from HIV/AIDS. The initial surveillance found the HIV prevalence among former plasma donors ranged from 9.1% to 17% in Henan province. Fortunately, the transmission through illegal blood transfusion has gradually reduced after government involvement stepped in in the late 1990s. Multiple forceful regulations were immediately put into practice, including shutdowns and penalties of illegal blood trading stations, training of healthcare workers, and education campaigns through mass media and community. And the final newly infected case of former plasma donor was reported in 2012, suggesting a successful elimination of HIV transmission through tainted plasma transfusion (Chen et al., 2015).

The large-scale prevention programme aiming at educating people and publicizing HIV/AIDS-related information, on the one hand, is one of the biggest contributors to the substantive achievements in eliminating illegal commercial blood transfusion. However, on the other hand, mass media propaganda and education campaigns also create extreme negative social representations of HIV-infected people, and such influence persists and intensifies for decades, impeding our progress in eliminating stigma and discrimination against HIV/AIDS-related individuals.

2.1.3 Migrant workers

At the end of 2017, the number of rural-to-urban migrate workers in China has reached 288 million, accounting for 22% of the total population (China Labour Bulletin, 2019). The HIV prevalence among rural-to-urban migrant workers is approximately 1.8 times higher than non-migrant rural workers (Hong et al., 2006). Due to low educational attainment, inadequate exposure to preventative health behaviors, and limited access to healthcare, migrant workers are especially vulnerable to risky behaviors and HIV infections. Several studies suggest that the increasing number of floating workers played an important role in contributing to China's sporadic geographic distribution of HIV infections, with infected

migrant workers returning home without knowing their HIV status and transmitting the virus to their sexual partners (Yang et al., 2015; Wu et al., 2014). A 2008 HIV surveillance report of Nantong, a major migrant exporting city in China, demonstrates an increasing trend in HIV prevalence among returning migrant works (Zhuang et al., 2012).

The demographic characteristics of migrant workers predispose them to perform more risky behaviors and increase their susceptibility to HIV infection. Reports show that the majority of migrant workers are young, unmarried males or people living apart from their partners and children (Hong et al., 2006). Risky behaviors such as frequent sexual activities with multiple commercial sex workers, misunderstanding of the usage of condoms, constant relocation between different cities, and low awareness of safer sex are commonly seen among migrant workers, which not only increases their vulnerability to HIV infection but also presents challenge in public health intervention efforts (Hong et al., 2006; Yang et al., 2015). Due to their high mobility and limited access to healthcare, HIV prevention programmes have difficulty reaching targeted migrant workers and delivering continuous and effective preventative services (Yang et al., 2015).

2.1.4 Men having sex with men (MSM)

Sexual transmission has become the main transmission route in contributing to newly reported infection in China in the past decade (Liu et al., 2015). And risky sexual behaviors among MSM is one of the biggest factors in changing the HIV transmission distribution in China (Xu et al., 2016). According to the latest data from China CDC, sexual transmission accounted for 94.7% of the newly infected HIV cases in 2017, 69.4% of them are heterosexual, and 25.3% of them are homosexual (SCDC, 2018). From 2001 to 2011, HIV prevalence among MSM increased by 450%, from 1.4% to 6.3%, with an estimated 1.1% annual increase. The estimated proportion of MSM among newly infected HIV cases increased from 12.2% in 2007 to 25.3% in 2017 (Dong et al., 2014; SCDC, 2018). And the

proportion of new infection attributable to MSM is higher in some major cities: 61.7% in 2011 to 73.9% in 2016 in Beijing, 43% in 2011 to 63.9% in 2016 in Shanghai (Dong et al., 2014; SCDC, 2017).

An upsurge of newly infected cases found among young students aged between 15 to 24 has become one of the challenges in the efforts to reduce new infections. Reports show that 95% of these new infections were contracted through MSM sexual activities (Avert, 2019). The new infection rate among young men having sex with men (YMSM) increased by 35% annually. A 2014 study conducted in 3 major cities found that HIV incidence among YMSM is 18.9% in Guiyang, 10.6% in Beijing, and 5.6% in Shanghai (Dong et al., 2014). As MSM sexual activities are taking over other transmission routes in big cities with an increasing trend among younger population, intervention and prevention programs targeted at youth, especially male students, has become a primary priority of China's future response to AIDS epidemic.

2.2 HIV/AIDS stigma

Stigma surrounding health issues is defined as "a social process or related personal experience characterized by exclusion, rejection, blame, or devaluation that results from experience or reasonable anticipation of an adverse social judgment about a person or group identified with a particular health problem" (Weiss & Ramakrishna, 2006, p. 536). Numerous studies indicate that despite limited funding and resources allocated to HIV/AIDS stigma reduction programmes, the complexity in and of itself and its various manifestations in different cultural contexts increases the difficulties in achieving effective intervention outcomes (Mahajan et al., 2008). HIV/AIDS stigma is multilayered and combined with already stigmatized behaviors such as condom usage, commercial sex behaviors, homosexual sex practices, and susceptible populations such as migrant workers, sex workers, and men having sex with men (Sengupta et al., 2011). Meanwhile, a number of mixed underlying

factors at the individual, interpersonal, community or societal level, such as lack of correct understanding about the disease, misconceptions about HIV transmission routes, outdated perceptions of treatment options, extensive fear of its incurable nature, and deep-rooted discrimination against specific groups, further aggravates the negative impacts of HIV/AIDS stigma (CDC, 2018; Sengupta et al., 2011; Stangl et al., 2013).

2.2.1 Stigma

Ever since the publication of Goffman's influential work on stigma in 1963, a large body of research has been done to explore the nature, complexity, and consequences of stigma. Erving Goffman suggested that stigma arises when people experience "discrediting" social status, creating a discrepancy between the "actual social identity" and the "virtual social identity" (Stangl et al., 2013; Goffman, 1963). Such gaps between "whom we think we are" and "how we are seen" by the society is considered a "spoiled identity", and "cuts stigmatized people off from the society and from himself, so that he stands as a discredited person against an unaccepting world" (Stangl et al., 2013, p.2; Goffman, 1963).

Building on Goffman's argument on the internalizing impact of stigma, Link and Phelan provided a more comprehensive understanding of stigma by incorporating sociocultural perspectives and the underlying influence of social, political, and economic factors (Link & Phelan, 2001). They proposed the following sequence of components behind the development of stigma 1) labeling human difference; 2) mainstream cultural beliefs "linking labeled persons to negative stereotypes"; 3) separating "us" from "them"; 4) experiencing loss of status and discrimination (Link & Phelan, 2001; Stangl et al., 2013).

Despite a profusion of scientific literature on stigma, there is a lack of coherent and sustainable definition of stigma, presenting challenges in developing standardized stigma scales, assessing the impact of stigma on the effectiveness of HIV prevention programmes, and devising effective stigma-reduction programs (Deacon, 2006; Mahajan et al., 2008).

2.2.2 Classification of HIV/AIDS-related stigma

The classification of stigma into perceived, internalized and enacted, was commonly used in HIV/AIDS-related stigma-reduction studies targeting PLWHA (Cao et al., 2006; Brown et al., 2003; Stangl et al., 2013). Perceived stigma is defined as expected or imagined discriminating attitudes from the surrounding communities (Brown et al., 2003). Examples of outcomes related to perceived stigma include the reluctance of HIV testing and HIV status disclosure due to the fear of potential discrimination from friends, colleagues, and families.

Internalized stigma or self-stigma refers to stigmatizing beliefs towards oneself after incorporating conventional negative images from the society. In other words, internalized stigma happens when one person takes in stereotypes and myths about PLWHA and applies these ideas to himself. Examples of internalized stigma include feelings of shame, fear of status disclosure, social isolation, despair, and even suicidal ideation (CDC, 2018). People with internalized stigma are found to be reluctant to care-seeking and nonadherent to treatment, resulting in less effective treatment outcomes and impaired quality of life.

Enacted stigma refers to personal experience with someone else's discriminating behaviors against stigmatized individuals (Zhang et al., 2016; Phillips, Moneyham, & Tavakoli, 2011). Examples of enacted stigma include gossip, blaming, social isolation, refusal of healthcare services (Ma, Chan & Loke, 2018).

2.3 Impact of HIV/AIDS stigma

A large body of research suggests that HIV/AIDS stigma is a persisting and forceful barrier to various HIV preventive behaviors such as early status identification, and HIV status disclosure and poses significant threat to care-seeking behaviors, quality of life among PLWHA, and quality of services offered to PLWHA within the healthcare settings (Sengupta et al., 2011). The extensive magnitude of negative impacts of HIV stigma is universal worldwide, including countries in sub-Saharan African with the highest HIV prevalence. The

ubiquitous nature of HIV stigma strengthens the urgent need to reduce HIV/AIDS-related stigma in the progress of ending the AIDS epidemic (Brown, Macintyre & Trujillo, 2003).

2.3.1 Impacts on PLWHA individual

Numerous studies have found evidence that the persistent stigma surrounding HIV and AIDS was significantly associated with adverse mental outcomes including depression, anxiety, and even suicidal ideation. A recent study reported that the prevalence of moderate to severe depression among people living with HIV/AIDS in China was as high as 62% (Wang et al., 2014). Consequently, poor mental health may exacerbate the progression to AIDS and decrease survival rate due to its impact on retention, adherence to therapies, and uptake of services provided (Schuster et al., 2012; Li, Mo, Wu & Lau, 2017). In addition to adverse effects on physical and mental health, HIV/AIDS-related stigma also negatively influences quality of life among people living with HIV. Stigma manifestation includes social isolation and rejection by relatives, friends, and colleagues, and loss of employment.

2.3.2 Impacts on the uninfected, including family and community

As conceptualized by Goffman (1963), stigma extends to people associated with the stigmatized subject. Family members of PLWHA are also experiencing different levels of stigma due to their relationship with a PLWHA. Apart from the burden of caring for an HIV-infected patient, family members also experience similar forms of discriminatory attitudes and behaviors, such as social isolation, refusal of service, gossip, loss of status, and etc. A qualitative study conducted among 33 families living with HIV, found that all of the families recounted experiences with stigma, such as avoidance from friends, children losing friends, and discrimination from work (Bogart et al., 2008). Since family members are reluctant to disclose HIV status to avoid the potential likelihood of experiencing courtesy stigma, a type of stigma experienced by people associated with stigmatized individuals, they are less likely to get involved in targeted stigma-reduction programmes, which further aggravates their

perceived stigma, negatively influencing their mental well-being and quality of life, people (Bogart et al., 2008).

2.4 Characteristics of HIV/AIDS stigma in China

PLWHA in China face a more severe degree of stigma than those living in western countries. Evidence indicates that 73% of rural Chinese have discriminating attitudes against PLWHA and believe having HIV is shameful (Zhang et al., 2016b). China's low national HIV prevalence was found to be contributing to the escalated stigmatization towards PLHWA (Zhang et al., 2016b). Studies have found that PLWHA living in HIV endemic places experienced intensified stigma and discrimination compared to those living in high-prevalence regions due to "lower tolerance of variations shared among the public, less anonymity, and greater fear of HIV" (Zukoski & Thorburn, 2009, p. 267).

Different transmission routes of HIV infection play an important role in determining the likelihood of experiencing stigma among PLWHA. Studies found that former plasma donors and people who contracted from the spouse or stable partners are considered "blameless" and have lower levels of perceived, internalized and enacted stigma (Zhang et al., 2006b). People who contracted through more "blamable" transmission routes such as drug injection, casual sex activities, multiple sex partners, and homosexual behaviors are associated with a higher likelihood of experiencing discriminatory attitudes and behaviors (Zhang et al., 2006b; Cao et al., 2006). However, as sexual transmission and drug injection became the top two main transmission routes contributing to newly infected cases in recent years, the increasing incidents of "blamable" behaviors strengthen the association between HIV/AIDS and already stigmatized events and further aggravates stigma surrounding HIV/AIDS.

Another characteristic of China's HIV/AIDS-related stigma is the AIDS phobia phenomenon that is commonly seen in China. Unfortunately, empirical investigations of AIDS phobia are limited, and a majority of recent works focusing on AIDS phobia were

conducted in China. People with AIDS phobia experience a combination of the following symptoms: repeated HIV testing after suspected exposure and irrational and consistent fear of HIV positive despite negative HIV results (Harrell & Wright, 1998; Scragg, 1995). This is relevant to HIV/AIDS-related stigma because AIDS phobia appears to be one of the manifestations of HIV/AIDS-related stigma that is commonly seen among the Chinese population. It is brought to the surface by a combination of underlying factors, such as lack of knowledge on HIV/AIDS, misconception about HIV transmission routes, and existing stigma surrounding PLWHA.

2.5 Literature gap

There is a limited number of existing studies aiming at reducing HIV/AIDS-related stigma. Thus, studies systematically summarizing and evaluating the effectiveness of HIV/AIDS stigma reduction intervention is limited as well. The 2003 systematic review conducted by Brown and colleagues is the first study assessing a variety of HIV/AIDS-related stigma reduction interventions from a global perspective. Brown et al. (2003) included 22 interventions that had primary or secondary components measuring changes in perceived stigma towards PLWHA or changes in healthcare providers' willingness to treat PLWHA. The study found improved tolerance toward PLWHA in the short term and the promising effect of the contact with affected groups approach (Brown et al., 2003). Additionally, the authors categorized HIV/AIDS-related intervention strategies into 4 different groups: the information-based approach, the skills-building approach, the counseling approach, and the contact with affected groups approach. The categorization was commonly utilized by future interventions in designing and assessing intervention strategies.

The second study conducted by Sengupta et al. (2011) aimed to determine the effective components of 19 identified HIV/AIDS-related stigma reduction interventions. The study broadened their search strategy to include studies that may or may not target HIV/AIDS-

related stigma and found that only 2 out of 14 effective studies with a statistically significant stigma reduction were assessed as good quality studies. Sengupta et al. (2011) called for more studies targeting HIV/AIDS-related stigma reduction specifically and stressed the urgent need for developing standardized stigma measures and good quality randomized controlled studies.

The third systematic review conducted by Stangl and colleagues in 2013 identified 48 studies from 28 countries. Unlike the previous two studies, Stangl et al. (2013) evaluated discrimination reduction and stigma reduction independently and included structural and biomedical intervention strategy into the review. They found significant stigma reduction in a majority of studies and identified several gaps, including the lack of intervention impact in multiple socio-ecological levels, the lack of control groups in study design, the lack of consistency and standardization in stigma measuring instruments, and the lack of variety in stigma targeted for intervention (Stangl et al., 2013).

Although both the 2011 Sengupta review and the 2013 Stangl review included a few studies that were conducted in China, the number of existing reviews targeting the Chinese population specifically is very limited. The current review is one of the first studies to systematically summarize and evaluate HIV/AIDS-related stigma reduction interventions among the Chinese population. It was conducted based on the lessons learned from the previous three systematic reviews and aimed to expand the understanding of reducing HIV stigma within the Chinese cultural and societal context. This study also aimed to fill some gaps identified in previous studies, such as excluding studies without a control group and assessing sustained effect between baseline and post-intervention at longer follow-ups.

Considering the enormous Chinese population and the intensified stigma and discrimination surrounding HIV/AIDS in China, the potential negative health effects of HIV stigma on PLWHA and at-risk population is alarming. Therefore, in order to inform future

HIV/AIDS-related programs to better understand the effective components in reducing HIV stigma and improve HIV-related health outcomes in China, the current study aims to summarize and evaluate various components of HIV stigma reduction intervention implemented among the Chinese population and generate recommendations for future efforts.

2.6 Summary

Eliminating stigma and discrimination against HIV/AIDS has become one of the top global health priorities in ending the AIDS epidemic. Apart from the ambitious 90-90-90 target, UNAIDS also proposed a vision for "getting to zero" in its strategic plan for ending the AIDS epidemic, including "zero new infections," "zero AIDS-related deaths," and "zero discrimination" (Grossman & Stangl, 2013). While the negative effects of HIV/AIDS-related stigma on HIV preventive behaviors, HIV treatment cascade, and care continuum have been studied and confirmed in numerous studies, evidence on effective stigma-focused interventions among the Chinese population is needed for the government to allocate limited resources and incorporate stigma reduction programs into national AIDS strategic plans. Therefore, summarizing existing stigma reduction programs and identifying key effective components are essential steps for achieving future advances in the scientific evidence base in this research filed and developing effective interventions that could be scaled up by the government.

CHAPTER 3. METHODOLOGY

3.1 Search strategy

A comprehensive systematic review was conducted to identify existing studies that assess the effectiveness of interventions reducing HIV/AIDS-related stigma. Four electronic databases were searched to retrieve relevant studies: PubMed, EMBASE, COCHRANE library, and PsychInfo. Various combinations of the following 21 MeSH terms and/or keywords were used when searching each database: HIV/AIDS ("HIV" OR "AIDS" OR "Acquired Immunodeficiency Syndrome" OR "PLWHA" OR "People living with HIV/AIDS" OR "STI" OR "STD" OR "sexually transmitted disease" OR "sexually transmitted infection"), stigma ("stigma" OR "discrimination" OR "attitude"), China ("China" OR "Chinese"), Intervention ("intervention" OR "evaluation" OR "evaluate" "trail" OR "effectiveness" OR "effect"). In addition, articles were manually searched from the reference lists of all retrieved articles and peer-reviewed articles focusing on HIV/AIDS-related stigma in China.

Citations and abstracts of identified peer-reviewed articles were first exported to Endnote (a citation software) for organization and duplication removal, and then uploaded to Covidence (a systematic review software) for eligibility screening and data extraction.

3.2 Inclusion criteria

The PRISMA guideline was used to guide article and study selection (Figure 1). The following inclusion criteria was used to identify relevant studies: 1) the study utilized intervention design, 2) the intervention took place in mainland China, Hong Kong, Taiwan, or Macao, 3) published in peer-reviewed journals from inception to March 2019, 4) published in both English and Chinese, 5) HIV/AIDS-related stigma reduction as primary or secondary

outcomes, 6) clear description of HIV/AIDS-related stigma measurement scale regardless of its validated or non-validated status, and 7) with experimental or quasi-experimental or pre-post study designs.

3.3 Exclusion criteria

Studies were excluded if they were:1) not an intervention design (e.g, conference abstract or a cross-sectional study design or without quantitative measures), 2) only discuss the development and implementation of interventions but with no assessment of effectiveness of the HIV/AIDS-related stigma reduction interventions, and 3) insufficient pre- and post-intervention data on HIV/AIDS-related stigma.

3.4 Data Synthesis

Due to the lack of standardized scale used during HIV/AIDS-related stigma measurement, a meta-analysis of identified articles included in the current review was not conducted. Articles that met inclusion criteria were exported into excel spreadsheet and organized according to the following information: 1) study characteristics (e.g., title, author, year of publication, study participants, location where the intervention was implemented, and sample size, and study design); and 2) intervention characteristics (e.g., intervention strategy, measure of stigma, intervention dosage, strategy approach, socio-ecological level, and intervention outcomes).

3.4.1 Socio-ecological framework

In order to identify targeted societal level of each study, a socio-ecological framework was used to categorize selected studies into four categories: individual, interpersonal, community, and public policy (McLeroy, Bibeau, Steckler, & Glanz, 1988; Stangl et al., 2013).

The social-ecological framework is often used to demonstrate the dynamics of HIV/AIDS-related stigma in multiple scientific literatures because it helps identify key

affected levels where stigma reduction is mostly needed (Zhang et al., 2016b; Stangl et al., 2013).

1) At the individual level, people with older age, low educational attainment, non-adherence to ART, and poor physical or mental well-being are more likely to experience HIV/AIDS-related stigma.

2) At the interpersonal level, people receiving little social support from families and friends are more susceptible to negative impact of HIV/AIDS-related stigma.

3) At the organizational level, stigma occurs when receiving discriminating attitudes from workplace or healthcare settings

4) At the community level, cultural norms and negative society attitude influence the extent of stigma experienced by stigmatized people.

3.4.2 Intervention strategy approach

To further facilitate data synthesis, four intervention categories introduced by Brown et al. (2003) were used to categorize selected studies:

1) Information-based approaches, delivering fact-based information through various communicating channels, including pamphlets, videos, lectures, media, peer education, and discussion groups (Brown et al., 2003).

2) Skills building, learning strategies (e.g., role play, game, imaginary skills, group desensitization, and etc.) to improve perspective-taking and reduce negative attitudes (Brown et al., 2003; Mak et al., 2017).

3) Counseling approaches, providing counseling services and group supports to encourage positive behavior (Brown et al., 2003).

4) Contact with affected groups, creating interaction opportunities between participants and PLWHA to improve empathy for affected groups and practice perspective-taking (Brown et al., 2003; Mak et al., 2017).

The characteristics of selected studies are demonstrated in Table 1.

3.5 Quality assessment

A Modified Downs and Black checklist, validated by Stangl et al. (2013), was used to assess the quality of all selected studies on the following four domains: reporting, external validity, internal validity (bias), and internal validity (confounding). The 27th item assessing power of the study on the original Downs and Black checklist was removed due to small sample sizes in some of the selected studies. The modified checklist consists of 26 questions with each question worth 1 point (Appendix 1).

CHAPTER 4. RESULTS

A total of 371 peer-reviewed articles were identified from electronic databases and additional records. Sixty-five of them were removed due to duplication, 272 were further excluded during the title and abstract screening. A total of 34 articles remained for further evaluation of full texts. Among them, 12 articles met the inclusion criteria (Figure 1).

Of note, Li et al. (2010a) and Rice et al. (2012) presented findings from the same 2-year intervention on food market vendors implemented in Fuzhou, China. In order to avoid duplicate analysis of the intervention, the Rice et al. (2012) article was removed, and the Li et al. article was retained for further analysis. Therefore, a total of 11 articles remained for systematic review (Figure 1).

4.1 Study characteristics

4.1.1 Geographic distribution

All of the 11 included articles were conducted in provinces situated along the southeastern, southwestern, and eastern coastline of China. Seven studies were conducted in Southeastern China: two in Fujian province (Li et al., 2010a; Li et al., 2013), and three in Hong Kong (Yiu et al., 2010; Abdullah et al., 2005; Mak et al., 2015). Six studies were conducted in Eastern China: two in Jiangsu province (Operario et al., 2016; Li et al., 2011), two in Shanghai (Li et al., 2010b; Liu et al., 2015), and two in Anhui province (Operario et al., 2016; Liu et al., 2006). Two studies were conducted in the Southwestern region, Yunnan province (Li et al., 2013; Wu et al., 2006). While all selected articles were conducted in high prevalence regions in China, some key affected regions, such as Sichuan Province, still lack research attention (Table 1).

4.1.2 Target population

The selected HIV/AIDS-related stigma reduction interventions targeted various groups of populations. The most common targeted populations were healthcare providers (Operario et al., 2016; Wu et al., 2006; Yiu et al., 2010; Li et al., 2013; Mak et al., 2015), children and students (Abdullah et al., 2005; Li et al., 2010b; Li et al., 2011), and female sex workers (FSWs) (Liu et al., 2015). Other target populations include market vendors (Li et al., 2010a) and rural married residents (Liu et al., 2006) (Table 1).

4.1.3 Study design

Among 11 selected studies, five studies utilized Randomized Controlled Trials (RCT) (Li et al., 2010a; Li et al., 2013; Liu et al., 2015; Mak et al., 2015; Operario et al., 2016;), five studies utilized Quasi-Experimental designs (QE) (Abdullah et al., 2005; Li et al., 2010b; Li et al., 2011; Wu et al., 2008; Yiu et al., 2010), and one study utilized pre-test and post-test design (Liu et al., 2006) (Table 1).

4.2 Stigma outcome measures and study findings

Table 2 organizes 11 selected studies by the study population, sample size, socio-ecological level the study focused on, intervention strategies, stigma measures (number of items included and whether or not they have been validated), and statistical findings. Ten out of 11 studies reported a statistically significant change in HIV/AIDS-related stigma reduction.

Of note, among all 11 selected studies, only five studies used validated multi-item stigma reduction scale, ranging from 4 to 15 items (Abdullah et al., 2005; Li et al., 2013; Mak et al., 2015; Operario et al., 2016; Yiu et al., 2010). Of the five studies that used validated multi-item scale, four studies found a statistically significant reduction in HIV/AIDS-related stigma in the intervention group at $p < .05$ or lower, regardless of their intervention strategy, duration, and dosage (Abdullah et al., 2005; Li et al., 2013; Mak et al., 2015; Yiu et al., 2010). As the only study in this review that did not find a statistically significant stigma reduction

toward PLWHA, Operario et al. (2016) only observed a slightly more positive attitude towards PLWHA among the intervention group (M=8.5 [SD=3.43]) compared with the control group (M=7.15 [SD=3.10]) (Table 2).

Among six studies that used self-developed and un-validated scale, three of them measured HIV/AIDS stigma with 1-4 items and three studies included 5 to 17 items in its scale (Li et al., 2010a; Li et al., 2010b; Li et al., 2011; Liu et al., 2006; Liu et al., 2015; Wu et al., 2008). All six studies with self-developed scales reported statistically significant changes in stigma reduction at p < .05 or lower (Li et al., 2010a; Li et al., 2010b; Li et al., 2011; Liu et al., 2006; Liu et al., 2015; Wu et al., 2008) (Table 2). Additionally, one study found a statistically significant stigma reduction in 3 out of its 7 scale items (Liu et al., 2015). The lack of uniformity in standardized and validated stigma measures makes it challenging to evaluate the effectiveness of stigma reduction across different interventions (Table 2).

A majority of studies (91%, 10/11) demonstrated the effectiveness of HIV/AIDS-related stigma reduction in the intervention group regardless of the intervention strategy, duration, and dosage. However, three studies reported the lack of sustained effectiveness of the intervention in stigma reduction at longer follow-up (Li et al., 2010a; Li et al., 2013; Yiu et al., 2010). One study observed statistically significant stigma reduction among the intervention group compared to the control group (estimated difference= 1.663, p<.0001) at the 6-month follow-up but found no statistical difference between the two groups at the 12-month follow-up (Li et al., 2013). In another study, the percentage of participants supporting the notion "PLWHA deserve to be punished" reduced from 46.5% at baseline to 34.4% at 12-month follow-up and 20.5% at 24-month follow-up in the intervention group as compared to 48.0% at baseline, 43.6% at 12-month follow-up, and 38.8% at 24-month follow-up in the control group (p<.0001) (Li et al., 2010a). One study reported statistically significant changes

in one experimental group, not the other, but the effect fades in both experimental groups at the 6-week follow-up (Yiu et al., 2010).

Additionally, statistical findings from one study suggest that improvement in HIV/AIDS knowledge level and intention to change risky behavior was more significant than other measurement components, including changes in negative attitudes and stigma towards PLWHA (Li et al., 2010b). Li et al. (2010b) found that compared with stigma attitude reduction, the intervention was more effective in improving knowledge level and self-protection efficacy (Table 2). The pre- and post-test score change was most obvious in knowledge (STDβ = 2.76, 95%CI [2.40, 3.12]) and self-efficacy (STDβ = 1.64, 95%CI [1.23, 2.05]) as compared to attitudes (STDβ = 0.84, 95%CI [0.23, 1.58]). Stigma reduction interventions usually take place as a secondary outcome in knowledge improvement and behavior change programs due to funding mechanism and resource allocation (Li et al., 2010b).

4.3. Intervention characteristics

4.3.1 Intervention duration and dosage

The duration of selected interventions varied widely, with the shortest intervention lasted for a single 15-minutes counseling session targeted at rural married couples in Anhui Province (Liu et al., 2006) and the longest intervention lasted for two years targeted at food market vendors in Fujian Province (Li et al., 2010a) (Table 2).

Previous research suggested that the number of sessions and duration of the intervention are two crucial factors affecting the effectiveness of interventions on stigma reduction (Abdullah et al., 2005; Brown et al., 2003). For example, Abdullah et al. (2005) included a single 90-min education session integrated with fact-based lectures, pamphlets, and videos in its intervention. The intensive 90-min duration and the single session made it challenging to cover multidimensional aspects of HIV/AIDS-related topics and was tiring for participants to

fully engage in the activities (Abdullah et al., 2005). The Li et al. study (2010b) implemented a 3-month peer-led education intervention and found non-significant changes in stigma reduction as compared to statistically significant changes in improving knowledge and self-efficacy, implying that stigma against PLWHA is a multidimensional concept that is not as easily improved at the knowledge level. Hence, longer intervening duration, repeated sessions, and a multi-faceted intervention design tailored for stigma reduction might be used as strategies for future interventions tackling stigma reduction (Table 2).

4.3.2 Socio-ecological level

It was consistently found that interventions intervening at two or more societal levels rather than a single societal level were more effective in modifying stigmatizing attitudes against PLWHA (Liu et al., 2006). Among 11 selected studies, nine interventions (82%) were individual-oriented (Abdullah et al., 2005; Li et al., 2010a; Li et al., 2010b; Li et al., 2011; Liu et al., 2006; Liu et al., 2015; Mak et al., 2015; Wu et al., 2008; Yiu et al., 2010. Only two interventions, Li et al. (2013) and Operario et al. (2016), intervened at multi-sociological levels, combing the individual and organizational level. Both multi-faceted studies were conducted in healthcare settings, where hospital policies are prone to adaption to ensure universal precaution (Stangl et al., 2013) (Table 2).

4.3.3 Strategy approach

Interventions usually used two or more strategy approaches to reduce HIV/AIDS-related stigma. Eight interventions (73%) utilized two approaches, two interventions (18%) utilized three approaches, and only one intervention utilized a single approach to reduce HIV/AIDS-related stigma. All selected studies utilized information-based approach in intervention designs with a variety of channels disseminating educational information to different populations, including pamphlets for male students at Police Training Institutes (Abdullah et al., 2005) and media advertisements for female sex workers (FSWs) (Liu et al., 2015).

However, previous findings suggested that education-only programs that were successful in improving knowledge related to HIV/AIDS were found to be less effective in reducing stigmatizing attitudes toward PLWHA (Yiu et al., 2010). Previous findings indicated that "no single effort is sufficient" (Brown et al., 2003, p.62). The Abdullah et al. (2005) study, for example, utilized a single information-based strategy and found that intervention with a single strategy is not as effective as those incorporating multiple strategy approaches (Stangl et al., 2013; Abdullah et al. 2005) (Table 2).

Three studies combined information-based strategies with a contact with affected groups approach by providing participants with not only educational sessions but also opportunities to interact with PLWHA (Yiu et al., 2010; Operario et al., 2016; Mak et al., 2015). Contact with affected groups approach can be administered in many different forms, including face-to-face interaction, attending a presentation hosted by PLWHA (Yiu et al., 2010; Operario et al., 2016), in-vivo or video-based interaction between participants and stigmatized groups (Mak et al., 2017; Mak et al., 2015). The promising effect of information and contact combined interventions in tackling HIV/AIDS-related stigma has been confirmed in many previous works (Mak et al., 2015; Mak et al., 2017; Operario et al., 2016). For example, Yiu and colleagues (2010) implemented the knowledge-only program and the knowledge-contact program among nursing students in Hong Kong universities, specifically aiming to compare the effectiveness of improving negative attitudes toward PLWHA between a single strategy approach and combined strategy approach. The study found a statistically significant reduction in stigmatizing attitudes in the knowledge-contact group compared to the knowledge-only group (Yiu et al., 2010) (Table 2).

Contact and skills building are the two most common methods to promote perspective-taking and empathy with stigmatized people (Mak et al., 2017). In addition to the information-contact approach, seven selected studies also combined information-based with

skills-building approaches to improve perspective-taking among participants (Li et al., 2010a; Li et al., 2010b; Li et al., 2011; Li et al., 2013; Mak et al., 2017; Operario et al., 2016; Wu et al., 2008). For example, Li and colleagues incorporated role-play and games into the intervention group. The study yielded a statistically significant reduction of prejudicial attitudes among POLs (intervention) versus non-POLs (control) (Li et al., 2013). Operario et al. (2016) included all three approaches (information based, skills building, contact with affected groups) into its intervention designs to improve physicians' clinical performance, counseling skills, and patients satisfaction. The study suggested that improved interaction between patients and physicians lead to decreased reinfection of sexually transmitted disease (STDs) (Operario et al., 2016) (Table 2).

4.3.4 Popular opinion leaders (POL) model

Li and colleagues (2010a) utilized community popular opinion leaders (C-POLs) as advocates to disseminate information within its population. Building upon the Diffusion of Innovations Theory, the C-POL model aims to diffuse information in a non-discriminated way through daily conversations among trained target populations (Li et al., 2010a; Li et al., 2013; Rice et al., 2012). C-POLs are often nominated by gatekeepers based on the following characteristics: reputable, empathetic, dependable, and confident (Rice et al., 2012). Since POLs are selected within its population, they share similar cultural norms and perceptions with the target populations. Interventions using the POL model benefit from POLs' ability to "mobilize the whole community and penetrate its social network" (Li et al., 2010a, p. 120). The effect of community intervention using POL model has been assessed among different scale and target populations. For example, Li and colleagues engaged C-POLs in its intervention design and achieved a statistically significant reduction of prejudicial attitudes among POLs (intervention) versus non-POLs (control) (estimated difference = 1.663, p<.001) (Li et al., 2013).

4.4 Quality appraisal

All selected studies were assessed with modified Downs and Black checklist (Table 3). The scores range from 13 to 20, with a mean score of 17.3. Studies receiving scores below 13, the median score, was considered a low-quality study. Studies receiving scores above 13, the median score, was considered a high-quality study (Stangl et al., 2013). Overall, 10 out of 11 studies were high-quality studies. Only one study (Abdullah et al., 2005) received 13 scores. 90% of high-quality studies found a statistically significant reduction in stigmatizing attitudes toward PLWHA (Appendix 1).

4.5 Result summary

To summarize, the current review indicates that a rigorous study design such as randomized controlled trial (RCT) or quasi-experimental with the control group and a validated, multi-item measuring scale are key elements when designing and implementing an HIV/AIDS-related stigma reduction intervention. While rigorous study designs help to minimize confounding bias and selection bias within the study, validated and multi-item scales help to increase the meaningfulness of the statistically significant reduction in HIV stigma post-intervention (Sengupta et al., 2011).

In addition, longer intervention duration, multiple intervention sessions, combined strategy approach, and intervening at multiple socio-ecological levels are promising components if these interventions are to be effective in reducing HIV/AIDS-related stigma. A single strategy approach is proven to be insufficient in stigma change; combining an information-based approach with either the skills-building approach or the contact approach appears to be more effective in stigma reduction through promoting perspective-taking and empathy towards PLWHA. Appropriate duration of each intervention session implemented with a consecutive number of sessions appears to be more effective in stigma reduction than a single intense session.

When comparing and evaluating the effectiveness across all identified studies, the present study found target population lacked variation and representativeness, with eight out of 11 studies targeting healthcare providers or students alone. Outcome measurements lacked consistency, posing challenges in comparing effectiveness across interventions. Additionally, length of follow-ups varied widely, making it challenging to examine the sustainability of the effectiveness of interventions.

CHAPTER 5. DISCUSSION AND RECOMMENDATION

The present study systematically reviewed HIV/AIDS-related stigma reduction interventions conducted in China. The statistically significant stigma reduction outcomes from the selected studies demonstrate considerable progress has made so far. Yet the current review also identified gaps and challenges that need to be addressed in the future efforts targeting stigma reduction among the Chinese population.

Ten out of 11 selected studies utilized rigorous experimental design such as randomized controlled trials (RCTs) and quasi-experimental with control groups, with only one study (Liu et al., 2006) using a pre-test and post-test design. Ten out of 11 selected studies were assessed as high-quality studies based on the Modified Downs and Black checklist. Among high-quality studies, a high percentage (90%) of interventions found statistically significant HIV/AIDS-related stigma reduction outcomes. Additionally, multi-faceted structures and combined-approach strategies were more widely used in the existing studies, with 73% interventions used two approaches and 18% interventions used three approaches, leading to more effective intervention outcomes as compared to interventions with the individual-oriented and information-based approach.

5.1 Strengths

Existing literature is limited in number and scope in evaluating the effectiveness of HIV/AIDS-related stigma reduction in the Chinese population. The result of this review identifies feasibility and areas of improvement of implementing interventions targeting HIV/AIDS-related stigma. More importantly, apart from a few Chinese studies included in the 2011 Sengupta's review and the 2013 Stangl's review, the current review is one of the first studies that systematically reviewed the effectiveness of interventions reducing HIV/AIDS-related stigma targeting the Chinese population specifically. This study

incorporated recommendations from previous reviews into its own study design, aiming to provide a comprehensive understanding of the progress that has been made so far in improving stigmatizing attitudes toward PLWHA in China. The limited resources underscore the importance of conducting a systematic review that summarizes shared characteristics and differences of existing studies, identify effective components of these interventions, and discuss implications for future efforts in reducing HIV stigma in China.

As one of the first systematic reviews assessing effectiveness in reducing HIV/AIDS-related stigma among the Chinese population, the current study was designed upon existing reviews (Brown et al., 2003; Sengupta et al., 2011; Stangl et al., 2013). The study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline utilized by Sengupta et al. (2011) to guide article and study selection and assess external validity and internal validity of each intervention. A total of 21 MeSH terms were used to retrieve a sufficient amount of published literature related to the research problem from four electronic databases, including PubMed, EMBASE, COCHRANE library, and PsychInfo.

The study also incorporated the categorization of intervention strategies identified from the 2003 Brown's review and the socio-ecological framework adapted from the 2013 Stangl's review. Additionally, the Downs and Black checklist was used to conduct a quality assessment of all 11 included studies (Appendix 1). Unlike the scarcity of good-quality studies identified in the Sengupta review (2011), the current study found nine out of 10 effective studies to be high-quality studies. Additionally, different from the Stangl et al. study, where a majority of included studies didn't have a control group, nine out of 11 identified studies in the current review utilized either an RCT study design or a quasi-experimental with control group to minimalize selection and confounding bias.

Comparison of intervention effectiveness across all studies was challenging due to the heterogeneity in the target population, outcome measures, and intervention strategy. Therefore, in order to generate a detailed and comprehensive evaluation of the effectiveness of selected interventions from all aspects, the current review organized intervention characteristics by various variables, including the geographic distribution, target population, study design, intervention duration and dosage, measurement scales, length of follow-up, five socio-ecological levels, and strategy approaches (Table 2).

The result of the present study demonstrates the potential feasibility and efficacy of HIV/AIDS-related stigma reduction intervention in China. The high percentage of high-quality studies with a statistically significant changes in stigma reduction sends an encouraging message for future research investment. Given the magnitude of HIV/AIDS stigma observed in the Chinese population and its negative influence on PLWHA, family members and partners of PLWHA, we call for more research attention on intervention studies aiming at reducing HIV/AIDS-related stigma among Chinese.

5.2 Limitations

First, there is a limited number of existing studies examining HIV/AIDS-related stigma reduction as their primary outcomes. Existing interventions primarily concentrated on improving HIV knowledge, risky behavior, and infection prevention, with limited works specifically studying the stigma-reduction field. In order to gather sufficient data to generate a comprehensive systematic review, the current study expanded the inclusion criteria to allow for studies sought to reduce HIV/AIDS-related stigma as a secondary outcome.

Second, the geographic distribution of existing HIV/AIDS-related stigma reduction interventions did not align well with the geographic variation of the HIV/AIDS epidemic in China. Although all selected articles were conducted in regions with high HIV prevalence rates, including provinces situated along the Southeastern, Southwestern, and Eastern

coastline of China, certain key-affected areas were missing. For example, Sichuan province is a region with the most PLWHA in China but received little few research attentions. There is also inadequate data focusing on Northeastern, Central, and Northwestern China. Additionally, existing studies demonstrate limited variation in the target population, with a predominant concentration on healthcare providers (5 studies), youth, and students (4 studies). A large proportion of at-risk population, including MSM, migrant workers, commercial sex workers received minimal research resources. Only one intervention target FSWs (Liu et al., 2015).

Third, selected studies are limited in their variation in intervention duration and dosage. Intervention duration could range from 15 minutes (Liu et al., 2006) to 2 years (Li et al., 2010a). Follow-up periods could range from 6 weeks to 9 months. Most study designs reported one or more follow-ups, while some study designs didn't specify any follow-ups. The length of the intervention and arrangement of follow-ups are two important factors in evaluating the long-term effects of interventions. For example, one study observed a statistically significant reduction in stigmatizing attitudes toward PLWHA in the intervention group compared to the control group; however, the effect faded at the 6-weeks follow-up.

Fourth, the lack of validated and standardized HIV/AIDS-related stigma measurement poses a critical challenge in evaluating the effectiveness of each intervention design and comparing the effectiveness across different studies. The stigma measure utilized in selected studies varied considerably: only 5 of 11 selected studies used a validated stigma measure. The number of items included in the stigma measures also differed significantly, with one study (Li et al., 2010) having only one item in the stigma scale and another study (Yiu et al., 2010) having 15 items in the stigma scale. For studies using single item or unvalidated measuring instrument, statistical significance in stigma reduction might be less meaningful than those using validated and multi-item scales (Sengupta et al., 2011). Therefore,

developing "culturally appropriate" and "population-specific" measurements becomes one of the key priorities moving forward (Hong & Li, 2009; Stangl et al., 2013).

Fifth, another measurement limitation is the mostly used self-reported measure, a form of data gathering measure that is subject to social-desirability bias and other types of biases. Importantly, survey questions pertinent to sexual behaviors and HIV/AIDS are especially prone to receive social-desirability bias. However, self-reported measures appear to be one of the few practical methods that can examine topics including stigmatizing attitudes toward PLWHA (Liu et al., 2015). Since all of the selected studies relied heavily on self-reported surveys or questionnaires, future research needs to take account of the confounding effect of social-desirability bias when measuring the effectiveness of interventions and consider other assessment modalities.

5.3 Implications

5.3.1 Implication for future research

To address the gaps discussed above, the study will conclude by making recommendations for future HIV/AIDS-related research to better understand whether one intervention strategy is effective or not in reducing HIV stigma and improving HIV-related health outcomes in China. First, relatively few interventions targeting HIV/AIDS-related stigma reduction specifically have been conducted, creating barriers to identify key effective elements when designing and implementing stigma reduction interventions. Therefore, more stigma reduction efforts are needed so that various aspects of intervention components can be tested through a large number of studies. Designing stigma reduction intervention should also consider formative data and qualitative research to tailor intervention components for its specific target groups (Sengupta et al., 2011).

Second, the present study suggests that the combined strategy approach, longer intervention duration, and multiple intervention sessions are relatively more effective in

improving stigmatizing attitudes surrounding PLWHA. However, such findings lacked representativeness and were not able to generalize to larger groups of people or different setting of population. Therefore, we need funding resources and research attention invested in interventions that can be scaled up in large sample size and are applicable to people in similar cultural settings.

Third, when evaluating a statistically significant reduction in stigma, it is important to consider the long-term difference in stigma reduction between the control group and the intervention group in order to examine the sustainability of intervention effectiveness. It is recommended that future research includes more extended intervention duration and well-planned follow-up periods to examine whether the effectiveness in stigma reduction fade at longer follow-ups.

Fourth, statistically significant interventions using an unvalidated or single-item measuring instrument is not sufficient in demonstrating the effectiveness of stigma reduction. This generates an urgent need for developing standardized HIV/AIDS-related stigma to compare the effectiveness across different studies. Additionally, even without the development of a standardized instrument, validated and multi-item measures are recommended for future research to ensure the quality of intervention outcomes.

Lastly, a majority of studies identified in this review lack a demonstration of the public health significance of stigma reduction interventions. It is important for future research to demonstrate whether studies with a statistically significant stigma reduction also find improvement in HIV/AIDS-related health behaviors, including improved testing behaviors, higher levels of knowledge and understanding about HIV/AIDS, better adherence to and retention in HIV treatment. Future studies need to examine the relationship between reduced HIV stigma and improved HIV/AIDS-related health outcomes to better demonstrate the public health significance of their interventions. Additionally, it is crucial to test whether

these improved attitudes and behaviors are applicable to situations where people make actual encounters with PLWHA (Brown et al., 2003). A majority of studies utilized self-reported measures to assess changes in behaviors toward PLWHA, such as using a self-administered questionnaire to assess healthcare providers' behavioral changes in providing equal services to patients with or without HIV/AIDS. Future studies need to design alternative behavioral indicators in order to minimize the confounding effect of socio-desirability bias caused by heavy reliance on self-reported measures.

5.3.2 Public health significance

The stigma around HIV/AIDS continues to hamper efforts in preventative programmes, such as engaging people at risk in regular testing, promoting biomedical preventative drugs, retaining PLWHA in continuous treatment, encouraging status disclosure, etc. The HIV/AIDS-related stigma, an extraordinarily complex yet essential field of research, creates enormous barriers to all groups, from PLWHA to people at low-risk of infection, and pose tremendous threat to the overall health outcomes related to HIV/AIDS in the entire population.

Despite the large body of research reinforcing the negative influence of HIV stigma on HIV/AIDS-related health outcomes, interventions tailored for HIV stigma reduction is limited. The scarcity of good-quality interventions remains an obstacle for exploring components that are most effective at improving stigmatizing attitudes towards PLWHA. Therefore, in order to improve HIV preventative and treatment outcomes, efforts in updating and expanding our understanding of effective HIV/AIDS-related stigma reduction intervention through scaled-up research should be elevated as top priorities in HIV/AIDS-related programs.

The current systematic review of existing stigma-reduction programmes implemented in China will inform best practices to reduce HIV/AIDS stigma, guide future work in devising

and delivering effective stigma reduction programmes and, ultimately, to help improve HIV/AIDS-related health outcomes, reduce new infections among key affected populations, ensure best treatment outcome, and improve the quality of life among PLWHA.

5.4 Conclusion

The present systematic review focusing on HIV/AIDS-related stigma reduction interventions in China found considerable progress achieved in the past two decades, including the high percentage of high quality studies with a statistically significant stigma reduction, the high percentage of interventions using combined strategy approaches, and the high percentage of interventions using rigorous study designs. Though a number of gaps and challenges remained addressed moving forward, the statistically significant stigma reduction outcomes of reviewed studies demonstrated the feasibility and efficacy of implementing intervention tackling HIV/AIDS stigma in China. Overall, it was found that rigorous study designs and validated, multi-item measuring instruments are key elements when designing and implementing HIV/AIDS-related stigma reduction intervention. Longer intervention duration, multiple intervention sessions, combined strategy approach, and intervening at multiple socio-ecological levels are effective components of intervention aiming at reducing HIV/AIDS-related stigma.

Researchers, policy makers, stakeholders, and funding agencies are encouraged to recognize reducing HIV/AIDS stigma as an indispensable step in improving HIV/AIDS-related health outcomes. Future HIV/AIDS stigma reduction interventions are recommended to address the existing gaps in this field of research based on the following implications: 1) scaling up the number of interventions targeted HIV stigma reduction; 2) improving generalization of existing studies to allow intervention components to be successfully replicated in similar cultural settings; 3) designing longer durations of follow-ups to better evaluate sustained effectiveness of intervention; 4) developing and utilizing of standardized

and multi-item HIV/AIDS-related stigma measures; 5) and lastly examining how statistically reduced stigma affect HIV/AIDS-related health outcomes. We hope the effective components of interventions and recommendations generated in the current systematic review can be useful for future efforts in HIV/AIDS programs.

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Figure 1. PRISMA flowchart of search strategy
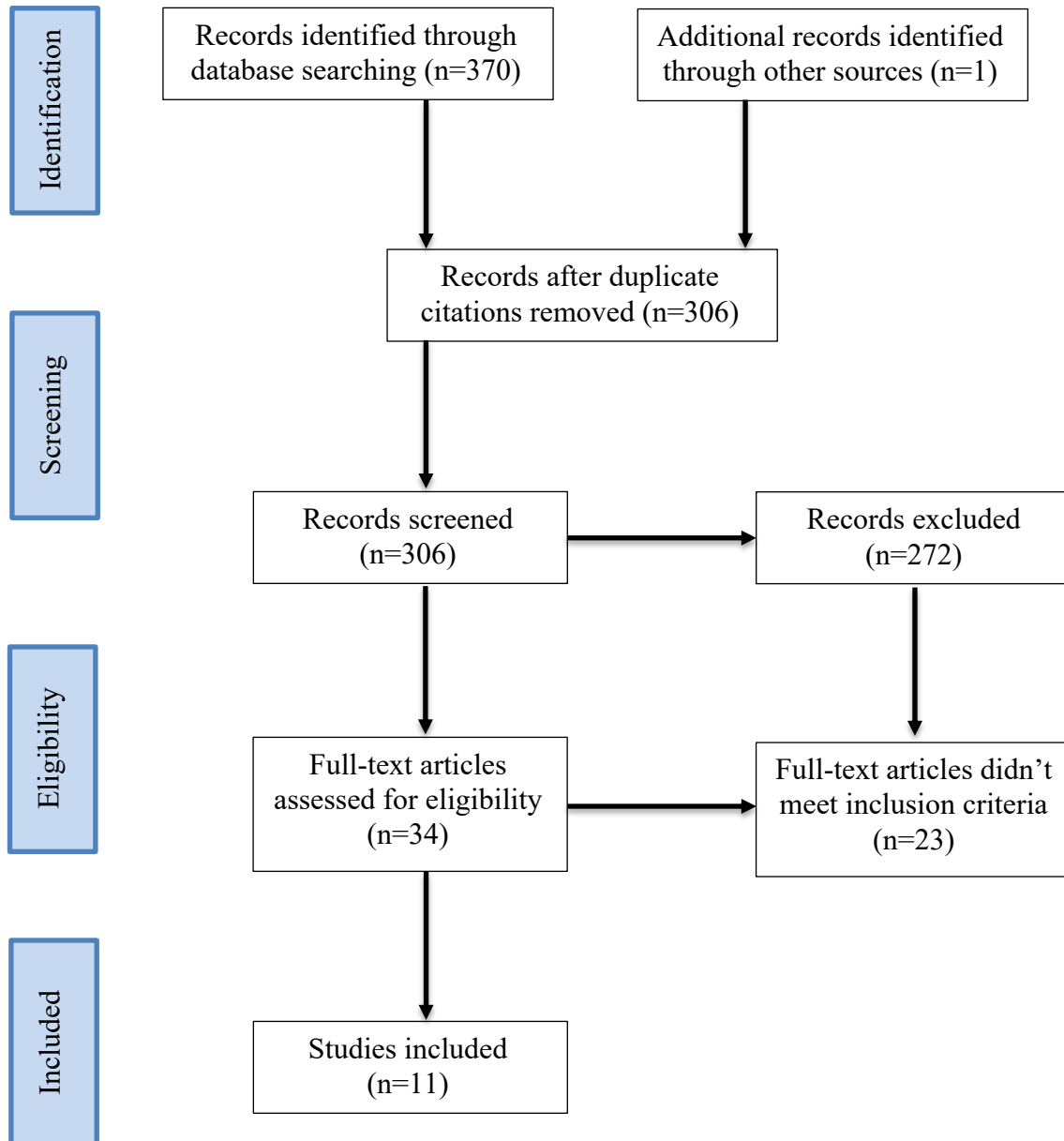
Table 1. Characteristics of included studies (n=11)

Study Design	
Randomized Control Trial	5
Quasi-experiment with control group	4
Quasi-experiment without control group	1
Pre-post study	1
Study participants	
Healthcare providers	5
Female sex workers	1
Food market vendors	1
Rural married residents	1
Children/Students [b]	4
Study location	
Anhui province [a]	2
Jiangsu province [a]	2
Yunan province	2
Fujian province [a]	2
Shanghai	3
Hong Kong	3
Intervention strategies	
Information based	11
Skills building	7
Counseling	2
Contact with affected groups	3

[a] Two selected articles implement interventions in two provinces during the study: Li et al. (2013) in Fujian and Yunnan Province; Operario et al. (2016) in Anhui and Jiangsu Province.

[b] One selected article (Yiu et al., 2010) target nursing students in Universities in Hongkong. Therefore, it is counted twice in the following two categories: Healthcare providers and Children/students.

Table 2. Summary of HIV/AIDS stigma reduction intervention by study population, stigma measure, and outcomes from 11 studies

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Abdullah et al., 2005 Police training institutes in Hong Kong	Male students from Police Training School (n=136) 72(intervention) 68(comparison)	*Information based* *Individual level* To increase knowledge and attitudes towards PLWHA and improve behavioral changes in safer sex practices and risk perception. A total of 90-min educational session integrated with presentation, pamphlets, video, and question discussion.	*Design:* Quasi-experimental design with pre- and post-test at 4 months follow-up. Participants were assigned into intervention and comparison groups based on class and living schedules. *Measure: (Validated)* Attitudes towards PLWHA (4 items)	Both intervention and comparison groups had significantly higher attitudes scores at 4-month follow-up. Median attitudes score increased from 12 at baseline to 16 at follow-up in intervention as compared to 10 to 13 in comparison group (p<.05). The improvement in attitudes towards PLWHA in both groups was potentially due to the following two reasons: 1) the small sample size and potential contamination of the comparison group 2) the enlightening effect of the baseline survey itself.
Li et al., 2010a Food markets in Fuzhou, Fujian province	Market vendors (n=4510) 2262(intervention) 2248(comparison)	*Information based, skills building* *Individual level* To reduce stigmatizing attitudes towards PLWHA through community-based dissemination of information and improved perception of HIV. Community popular opinion leader (C-POL) were identified among each market and trained to act as AIDS prevention advocates. With 4 weekly sessions and 10-12 reunion session over 2 years, C-POLs were trained through approaches including interaction, discussion, role-play, and modeling. C-POLs disseminated HIV/AIDS-related information to other market vendors in the intervention group. Both groups administered assessments at baseline and follow-ups.	*Design:* Randomized controlled trial with 12-month follow-up and 24-month follow-up. *Measure: (Un-validated)* Attitudes toward PLWHA (4 items, including "A person with HIV must have done something wrong and deserves to be punished")	The intervention group significantly reduced HIV/AIDS-related stigma at 12-month follow-up and the effect showed a 2-fold increased at 24-month follow-up. Whereas no changes were observed in the control group. For example: percentage of participants supporting the notion "PLWHA deserve to be punished" reduced from 46.5% at baseline to 34.4% at 12-month follow-up and 20.5% at 24-month follow-up in the intervention group as compared to 48.0% at baseline, 43.6% at 12-month follow-up, and 38.8% at 24-month follow-up in the control group (p<.0001).

Table 2. continued

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Li et al., 2010b Junior high school in Shanghai	Children of migrant workers (n=2237) 1130(intervention) 1097(comparison)	*Information based, skills building* *Individual level* To increase knowledge level regarding HIV/AIDS and other sexually transmitted diseases (STDs), improve attitudes against PLWHA, and protection self-efficacy through peer-led education intervention. School-based lecture, one session every two weeks for three months. The intervention group held peer-led sessions incorporating group discussion, brainstorming, case study, and games. The control group held regular teacher-led sessions imparting knowledge to students without active learning and participation.	*Design:* quasi-experimental with control group, no follow-up *Measure: (Un-validated)* HIV/AIDS-related knowledge (14 items) Attitudes toward PLWHA (7 items) Protection self-efficacy (4 items)	The intervention group found statistically significant improvement in knowledge, attitudes, and protection self-efficacy. However, the pre- and post-test score change was most obvious in knowledge (STDβ = 2.76, 95%CI [2.40, 3.12]) and self-efficacy (STDβ = 1.64, 95%CI [1.23, 2.05]) as compared to attitudes (STDβ = 0.84, 95%CI [0.23, 1.58]). No significant increase in attitudes scores observed in the control group.
Li et al., 2011 High school in Nanjing, Jiangsu province	High school students (n=304) 140 (experimental) 164 (control)	*Information based, skills building* *Individual level* To improve knowledge and perception regarding HIV/AIDS, reduce stigmatizing attitudes against PLWHA and risky behaviors. In the intervention group, trained instructors administered curriculum-based eight 90-min sessions including games, role-play. The control group received no lectures or activities	*Design:* Quasi-experimental with pre- and post-test at 6-month follow-up *Measure: (Un-specified)* HIV knowledge (13 items) Attitudes toward PLWHA (1 item "If I know someone who has HIV, I will stay far away from him/her") Intention to engage in sexual and risky behavior (1 item)	The intervention group found statistically significant changes in HIV knowledge (8.49 at baseline to 9.08 at 6-month follow up, p<.01) and reduction in stigma towards PLWHA (2.62 at baseline to 2.57 at follow-up, p<.05). No significant changes in intention to engage in sexual and risky behavior. No significant changes observed in the control group. The study also found that HIV knowledge improvement has mediation effects on stigma reduction.

Table 2. continued

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Li et al., 2013 Hospitals in Fujian, and Yunan Province	Healthcare providers (n=880) 456 (POLs) 424 (non-POLs)	*Information-based, skills building* *Individual, organizational level* To increase level of message diffusion, reduce stigmatizing attitudes against PLWHA, and reduce avoidance intention to serve PLWHA. With four 90-min weekly sessions over a month and three reunion session over the 12-month follow-up period. POLs were trained through group discussions, role-play, and games were incorporated in the training sessions. POLs initiated HIV/AIDS-related conversations with co-workers.	*Design:* Randomized controlled trials with 6-month and 12-month follow-up *Measure: (Validated)* Diffusion of HIV Care Message Scale (6 items) Prejudicial attitudes toward PLWHA (8 items) The Avoidance Intent Scale (8 items)	At 6-month follow-up, the study observed statistically significant reduction of prejudicial attitudes among POLs vs. non-POLs (estimated difference= 1.663, p<.0001) However, at 12-month follow-up, no statistically significant difference in reduction between POLs and non-POLs (estimated difference= .236 p= .546) was found.
Liu et al., 2006 Center for Marriage Certificate Issue in a rural county in Anhui Province	Married rural couples (n=605)	*Information based, Counseling* *Individual level* To understand the interrelationship pathways among knowledge, perceived worry, public stigma, felt stigma, and intention to disclose seropositive status. A 15-20-min-long counseling session was provided for participants. Each participant will be assigned to a counselor with the same gender. A baseline assessment and a post-test assessment were administered pre- and post-counseling.	*Design:* pre-test and post-test study *Measure: (Un-validated)* HIV/AIDS knowledge (13 items) Perceived worry of HIV/AIDS infection (6 items) Public stigma (7 items) Felt stigma (7 items) Intention of seropositive status disclosure (7 items)	Statistically significance was found in the following path: Knowledge -> worry (β= -.39) Worry -> public stigma (β= .27) Public stigma->felt stigma (β=.22) Felt stigma->disclose intention (β=- .20) Knowledge->felt stigma (β = -.1) No statistically significance was found in the following path: Knowledge->public stigma (p=.53) Knowledge->disclose intention (p=.30) Public stigma->disclose intention (p=.70) Significant improvement in knowledge level and reduction in perceived worries observed post-counseling. Reduction in public stigma and felt stigma were significant but with narrow 95% CI.

Table 2. continued

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Liu et al., 2015 Shanghai	Female sex workers (FSWs) (n=750) 375(intervention) 375(control)	*Information-based, counseling* *Individual level* To increase condom usage, HIV/AIDS knowledge level, reduce HIV/AIDS-related stigma, and reduce STI/HIV incidence Intervention included four educational videos (10-15 minutes), two 90-min group counseling, and one individual counseling.	*Design:* Randomized controlled trials with a 3-month follow-up and 6-month follow-up *Measure: (Un-validated)* HIV/AIDS knowledge (27 items) HIV/STD risk perception (2 items) Stigma towards PLWHA (7 items)	Intervention resulted in statistically significant attitudes improvement in three items: 1) allow children to be classmates with HIV-positive children; 2) eat in a restaurant where the cook is HIV positive; 3) work with HIV-positive co-workers. No statistically significant differences in attitudes changes between intervention group and control group in four items: 1) confidentiality of HIV positive status of family member; 2) care for a family member infected with HIV in the house; 3) non-disclose to family member once infected with HIV; 4) non-disclosure to sexual partners
Mak et al., 2015 Hong Kong	Healthcare providers (n=88) 46 (game-based) 42 (in-vivo contact)	*Information based, skills building, contact with affected groups* *Individual level* To assess the effectiveness of game-based intervention approach in reducing HIV/AIDS stigma and increase HIV/AIDS-related knowledge level. Both groups were given a 30-min didactic session on HIV/AIDS knowledge. Then, the intervention group employed game-based approach integrated with two interactive games to improve perspective-taking and empathy towards PLWHA The control group employed in-vivo contact approach by holding two 90-min sharing sessions hosted by 2 PLWHA.	*Design:* Randomized controlled trials with one-month follow up *Measure:* (Validated) HIV/AIDS-related knowledge (23 items) Stigmatizing attitudes toward PLWHA (14 items) Discrimination (7 items) Fear of infection (5 items) Willingness to treat (10 items)	Both game-based group and in-vivo contact group found significant changes in all outcomes in pre- to post-intervention.

Table 2. continued

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Operario et al., 2016 Hospitals in Anhui and Jiangsu Province	Healthcare providers (n= 249) 121(intervention) 128(control)	*Information based, skills building, contact with affected groups* *Individual, organizational level* To improve physicians' clinical knowledge related to HIV/STI and counseling skills To reduce HIV/STI infection rates, reduce negative attitudes toward PLWHA, and improve satisfaction with physicians among high-risk patients. Physicians in the intervention group received 1 week training integrated with lecture, group discussion, role play, and presentation from PLWHA; 2 months practicing; and 2 days booster sessions. Physicians in the control group received delayed training post-assessment. 633 (intervention) and 491 (control) gonorrhea or chlamydia positive patients from participating physicians' waiting rooms were recruited to complete assessments at baseline and follow-up.	*Design:* Cluster randomized controlled trials with 9-month follow-up for patients; 3-month, 6-month, and 9-month follow-up for physicians. *Measure:* (validated) Patients: Reinfection rates of gonorrhea or chlamydia HIV/STI knowledge (25 items) Attitudes toward PLWHA (12 items) Satisfaction with physicians (7 items) Physicians: Knowledge of HIV (48 items), syndromic management (48 items), antiretroviral treatment (25 items), risk reduction counseling (36 items) Management of opportunistic infection (41 items)	Physicians from both groups received statistically significant improvement in all outcome measures. Patients from both groups had no statistically significant difference in gonorrhea or chlamydia infection rates. Patients from intervention group had statistically significant reduced odds in reinfection and improved HIV/STD knowledge and satisfaction with physicians at 9-month follow-up. No statistically significant reduction in attitudes toward PLWHA was observed in patients from both groups, with only moderately more positive attitudes towards PLWHA among intervention groups compared with control groups

Table 2. continued

Reference, Location	Study population at baseline	Study objective and description of intervention	Study design stigma measure	Outcome
Wu et al., 2008 Hospitals in Yunnan Province	Healthcare providers (n=138) 68 (intervention) 70 (control)	*Information based, skills building* *Individual level* To reduce HIV/AIDS-related stigma among healthcare providers. One 4-hour session integrated with role plays, games, group discussion, testimony by HIV advocate, educational materials regarding HIV/AIDS.	*Design:* quasi-experimental with control with 3-month follow-up and 6-month follow-up *Measure: (Un-validated)* Attitudes and behavior toward PLWHA (3 items, including confidentiality of patients' HIV status; patients' right for doing or not HIV testing; negative attitudes toward PLWHA")	The odds for reducing negative attitudes towards PLWHA was 2.4 times higher among the intervention group than among the control group at the 6-month follow-up (p= 0.0395). Statistically significant odds ratios were found in physicians from intervention group in all 3 outcome measures.
Yiu et al., 2010 Universities in Hong Kong	Nursing students (n=102) 47(intervention) 55(control)	*Information based, contact with affected groups* *Individual level* To compare the effectiveness of reducing attitudes toward PLWHA between knowledge-only program to knowledge-contact program Knowledge-contact group:50-min lecture and sharing session with two PLWHA Knowledge-only group: 50 min lecture	*Design:* quasi-experimental without control, 6-week follow-up *Measure: (Validated)* HIV/AIDS knowledge (20 items) Stigmatizing attitudes toward PLWHA (15 items, for example, reluctance to treat HIV/AIDS positive patients)	A statistically significant improvement in HIV/AIDS knowledge level was found in both knowledge and knowledge-contact group. However, the effect significantly reduced in the knowledge-only group and sustained in the knowledge-contact group at follow-up. The knowledge-contact group had statistically significant reduction in stigmatizing attitudes compared to knowledge-only group. But the effect faded at follow-up in both groups.

Table 3. Quality assessment of 11 selected studies (Modified Downs and Black Checklist, 1998)

First author, publication date	Study design [a]	Summary score for quality critique
Abdullah et al., 2005	QE/C	13/26
Li et al., 2010a	RCT	19/26
Li et al., 2010b	QE/C	16/26
Li et al., 2011	QE/C	15/26
Li et al., 2013	RCT	17/26
Liu et al., 2006	Pre-post study	16/26
Liu et al., 2015	RCT	17/26
Mak et al., 2015	RCT	19/26
Operario et al., 2016	RCT	20/26
Wu et al., 2008	QE/C	18/26
Yiu et al., 2010	QE/NC	20/26

[a] QE/NC=quasi-experimental without control; QE/C=quasi-experimental with control; RCT=randomized controlled trials

Appendix 1. Modified Downs and Black checklist for the assessment of the methodological quality of selected studies
(Trac, MaArthur, & Jandoc et al., 2016)

Item	Criteria		Abdullah et al., 2005	Li et al., 2010a	Li et al., 2010b	Li et al., 2011	Li et al., 2013	Liu et al., 2006	Liu et al., 2015	Mak et al., 2015	Operario et al., 2016	Wu et al., 2008	Yiu et al., 2010
Reporting													
1	Is the hypothesis/aim/objective of the study clearly described?	Yes=1 No=0	1	1	1	1	1	1	1	1	1	1	1
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	Yes=1 No=0	1	1	1	1	1	1	1	1	1	1	1
3	Are the characteristics of the patients included in the study clearly described?	Yes=1 No=0	1	1	1	1	1	1	1	1	1	1	1
4	Are the interventions of interest clearly described?	Yes=1 No=0	1	1	1	1	1	1	1	1	1	1	1
5	Are the distributions of principal cofounders in each group of subjects to be compared clearly described?	Yes=1 No=0	0	1	1	1	1	0	1	1	1	1	1
6	Are the main findings of the study clearly described?	Yes=1 No=0	1	1	1	1	1	1	1	1	1	1	1
7	Does the study provide estimates of the random	Yes=1 No=0	0	1	0	0	1	0	0	1	1	0	1

	variability in the data for the main outcomes?												
8	Have all important adverse events that may be consequence of the intervention been reported?	Yes=1 No=0	0	0	0	0	0	0	0	0	0	0	0
9	Have the characteristics of patients lost to follow-up been described?	Yes=1 No=0	0	0	0	0	0	1	0	0	1	0	0
10	Have actual probability values been reported (e.g. 0.035 rather than<0.05)	Yes=1 No=0	1	1	0	0	1	1	1	1	1	1	1
External validity													
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes=1 No=0 Unable to determine =0	0	1	1	0	0	0	0	1	1	1	1
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes=1 No=0 Unable to determine =0	0	1	1	0	0	0	0	1	1	1	1
13	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	Yes=1 No=0 Unable to determine =0	0	1	1	1	1	1	1	1	1	1	1
Internal validity – bias													

14	Was an attempt made to blind study subjects to the intervention they have received?	Yes=1 No=0 Unable to determine =0	0	0	0	0	0	0	0	0	0	0	0
15	Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes=1 No=0 Unable to determine =0	0	0	0	0	0	0	0	0	0	0	0
16	If any of the results of the study were based on "data dredging", was this made clear?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	1	1	1	1	1	1
17	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	1	1	1	1	1	1
18	Were the statistical tests used to assess the main outcomes appropriate?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	1	1	1	1	1	1
19	Was compliance with the intervention/s reliable?	Yes=1 No=0 Unable to	0	1	0	1	1	1	1	1	1	1	1

		determine =0											
20	Were the main outcome measures used accurate (valid and reliable)?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	1	1	1	1	1	1
Internal validity- confounding (selection bias)													
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	Yes=1 No=0 Unable to determine =0	1	0	1	0	0	1	0	0	0	0	0
22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	0	1	1	0	1	1
23	Were study subjects randomized to intervention groups?	Yes=1 No=0 Unable to determine =0	0	1	0	0	0	0	1	1	1	1	0
24	Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was	Yes=1 No=0 Unable to determine =0	0	0	0	0	0	0	0	0	0	0	0

	complete and irrevocable?												
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes=1 No=0 Unable to determine =0	1	1	1	1	1	1	1	1	1	0	1
26	Were losses of patients to follow-up taken into account?	Yes=1 No=0 Unable to determine =0	0	0	0	1	1	1	1	0	1	1	1