

Risk factors associated with HIV infection among men who have sex with men in China: a meta-analysis

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Abstract

Background: Although human immunodeficiency virus (HIV) prevalence in the general population is very low in China, high infection rate has been reported among men who have sex with men (MSM). We conducted a meta-analysis to identify HIV infection associated risk factors among MSM in China, thus we can further understand the high-risk population and provided basic information to further develop specific and effective interventions of HIV prevention.

Methods: A comprehensive literature search was conducted in several public databases, the relevant articles which published from January 2010 to June 2018 were identified, and a meta-analysis was performed according to these included studies. The odds ratio (OR) and its 95 % confidence intervals (CI) of each risk factor among MSM in China were pooled by using a random-effects model or fixed-effects model when appropriate.

Results: A total of 23 articles were included and analyzed. The pooled results revealed that non-local residency (OR=2.31, 95% CI: 1.05, 5.08), education less than junior high school (OR=1.73, 95% CI: 1.36, 2.21), engaging in commercial sex (OR=2.99, 95% CI: 1.02, 8.72), preferred receptive sexual role (OR=2.43, 95% CI: 2.09, 2.83), having anal bleeding during anal intercourse (OR=2.22, 95% CI: 1.60, 3.07), having no HIV test in the last 12 months (OR=2.17, 95% CI: 1.45, 3.25), having unprotected anal intercourse (UAI) in the last 6 months (OR=2.06, 95% CI: 1.69, 2.50), recreational drugs use (OR=1.90, 95% CI: 1.53, 2.36), preferred versatile sexual role (OR=1.69, 95% CI: 1.35, 2.21), inadequate HIV related knowledge (OR=1.63, 95% CI: 1.26, 2.11), having multiple sexual partners (MSP) in the last 6 months (OR=1.35, 95% CI: 1.24, 2.47), having infection of syphilis (OR=3.22, 95% CI: 3.02, 3.44) and diagnosed with sexually transmitted infections (STI) in the last 12 months (OR=1.71, 95% CI: 1.30, 2.26) were significantly and positively related to HIV infection.

Conclusions: Continuous education and further interventions such as Pre-Exposure Prophylaxis (PrEP) should be prioritized for those MSM who engaged in high-risk behaviors.

Background

Acquired immune deficiency syndrome (AIDS), caused by infection with human immunodeficiency virus (HIV), remains a significant public health problem with an estimated 1.1 million death (1) and more than 1.5 million newly identified infections each year globally(2). In China, more than one hundred thousand people were newly identified with HIV infection annually in the past few years and the number continued to grow(3–9). Although HIV prevalence in the general population is very low (0.055% in 2017) (10), high infection rate has been reported among men who have sex with men(MSM) in China(11). Previous studies reported the prevalence increased significantly from 0.9% in 2003 to 7.3% in 2017, peaking at 8.0% in 2015 among MSM in China(10–13) *Fig. 1a*. Meanwhile, with the changing of transmission mode from primarily blood-born spreading to sexual contract(11, 14), the proportion of transmission among homosexuals has continued to gain ground among all groups, rising from 0.3% before 2005 to 28.25% in

2015 before coming down a little in 2016 and 2017.(3–9) *Fig. 1b.* compared to 2006, when homosexual transmission only accounted for 2.5% of total cases that year, that's a 91.2% increase cumulatively. MSM has become not only an emerging population susceptible to HIV infection but also one of the priority populations for HIV prevention and control in China.

Fig. 1 a: HIV prevalence among MSM in China, 2003–2017

1 b: Distribution of transmission modes of newly identified HIV/AIDS cases in China

Previous studies (15, 16) have revealed risk factor associated with HIV incidence, with sample sizes ranged from 80 to 1044 and most of surveys conducted in large and medium sized Chinese cities. All studies included were conducted before 2013. However, studies on risk factors associated with HIV infection among MSM in China have not been systematically reviewed in past 5 years. By updating the review of risk factors among Chinese MSM, we can further understand the high-risk population, provide scientific evidence for comprehensive prevention and control of HIV/AIDS, and underpin new strategies for HIV intervention of MSM in China. Therefore, we conducted a meta-analysis to identify risk factors associated with HIV infection among MSM in China.

Materials And Methods

Search Strategy

We conducted a comprehensive literature search in PubMed, EMBASE, Chinese National Knowledge Infrastructure (CNKI) and WANGFANG Data to identify the relevant both English and Chinese language articles which published from January 2010 to June 2018. The search included Medical Subject Headings (MeSH) terms for 'HIV', 'AIDS', 'risk behaviors', 'risk factors', 'men who have sex with men', 'MSM', 'China' and 'Chinese'. Truncation and wildcard operators were also used in the search strategy. Meanwhile, we reviewed citations in retrieved articles to search for the relevant studies included in the analysis from the initial selection.

Eligibility Criteria

Inclusion criteria. The criteria for inclusion of studies were (i)peer-reviewed studies published either in English or Chinese language journals prior to June 2018; (ii)quantitative epidemiological studies, including observational studies which conducted among MSM in China; (iii)studies measured the HIV infection associated behavior or factors, and the observed association in standardized form of odds ratio (OR) or risk ratio (RR). In this paper, OR stands for these risk estimates; (iv) studies had sufficient discussion of results for proper data abstraction.

Exclusion criteria. Studies were excluded from this paper if any of the following criteria apply: (i) review articles, editorials, newspapers, modelling studies, case reports and conference report; (ii) studies that specified only one subpopulation, such as students, sex workers, recreational drug users, etc., and only one HIV infection associated factor, such as unprotected anal intercourse(UAI), inadequate HIV knowledge, multiple sexual partners(MSP, defined as having more than two male sexual partners), etc., (iii) studies were lack of OR, RR value and related confidence intervals(CI) for risk estimates.

Quality Assessment

The Agency for Healthcare Research and Quality (AHRQ) an 11-item checklist tool was used to assess bias in cross-sectional or prevalence studies(17). An item would be scored '0' if it was answered 'NO' or 'UNCLEAR'; if it was answered 'YES', then the item scored '1'. Study quality was assessed as follows: low quality (0–3); moderate quality (4–7); high quality (8–11). The Newcastle-Ottawa Quality Assessment Scale(NOS) tool was used for quality assessment in cohort studies and case control studies(18, 19). Studies were judged with 8 questions on three broad perspectives by a 'star system': the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies respectively. Study quality was assessed as follows: low quality (0–3 star); moderate quality (4–6 star); high quality (7–9 star).

Study Selection and Data Abstraction

Two reviewers (J. P. and Y. R.) screened all retrieved articles and completed study selection and data abstraction independently against the eligibility criteria. Data information was extracted from all eligible studies and entered into a standardized excel spreadsheet, included: first author, publication year, study year, location, study design, sampling methods, sample size, age range, HIV prevalence, HIV incidence, education, migration, HIV test, syphilis status, sexually transmitted infections(STI) status, HIV knowledge, UAI, anal bleeding during anal intercourse, preferred sexual roles, number of male sexual partners, sex with female partners, recreational drugs use behavior and commercial sex behavior. Not all variables were included in each study, discrepancies and contradictions were resolved by discussions.

Data Analysis

All the meta-analyses were performed using Review Manager 5 statistical software (RevMan 5, Cochrane Community, London, United Kingdom). The pooled OR and 95% CI for each risk factor presented in the form of forest plots. Statistical significance was defined as two-tailed $\alpha < 0.05$. Given prevalence was $< 10\%$, the prevalence ratio was used as a proxy for OR given that for rare outcomes, RR approximates an OR(20). Two studies(21, 22) reported HIV infection related factors with RR which were converted to OR directly.

Heterogeneity among stratified group was primarily assessed by the Chi squared (χ^2) based Cochran Q statistic ($p < 0.10$, statistical significant was considered) and I squared (I^2) test (13). I^2 values (from 0 to 100%) of 25%, 50% and 75% represented low, moderate and high heterogeneity, respectively(23). If heterogeneity was high ($I^2 \geq 75\%$) and significant (p value < 0.10 using Q test), the random-effect model was used for summary risk estimate. Otherwise, the fixed-effect model was used(24, 25). Sensitivity analyses were conducted to assess the impact of excluding studies which had high heterogeneity or low quality.

Results

Search results

Overall, 1891 potentially related studies were identified from abovementioned database. After de-duplication, 1489 articles were screened in titles and abstracts and 1351 articles were excluded per our selection criteria. Then, 138 articles were reviewed in full. Finally, a total of 23 articles were included and analyzed. The PRISMA flow diagram for included studies showed in *Fig.2*.

Fig.2: Study selection

Characteristics of Included Studies

The summary information of studies included in this meta-analysis and evaluation of study quality is shown in *Table 1*. Of the 23 included articles, 14 articles were published in Chinese(21, 26–38) and 9 in English(22, 39–46). These studies mainly conducted from 2008 to 2015 and the sample size ranged from 250 to 47,231. The age of these participants ranged from 16 to 85 years. Most of studies recruited study participants utilized a combination of recruitment methods. All the included studies were observational studies. Nineteen were cross-sectional studies, 3 were cohort studies and one was case-control study. Twenty studies reported the HIV prevalence and two cohort studies reported the HIV incidence. For consistency, one cohort study(42) was treated as cross-sectional data, with reporting on baseline data. Thirteen out of twenty-three included studies met the criteria of “high quality” and ten studies met “moderate”.

Table 1: Characteristics of 23 studies included in the Meta-analysis

HIV Prevalence

Of the included studies, 20 studies reported HIV prevalence. One cohort study reported baseline data with HIV prevalence in two cities separately(42). The HIV prevalence varied from 2.85%(38) to 15.54 %(36) (median 9.54%) in individual studies.

Risk factors associated with HIV infection

Table 2 shows the summary of the meta-analysis for demographic and behavioral factors related to HIV infection. Using the random effects model, the risk factors include: having UAI in the last 6 months, commercial sex behavior, having sex with female partners in the last 6 months, non-local residency (defined as not having permission for permanent residence), having no HIV test in the last 12 months.

Using the fixed effects model, factors associated with HIV infection are: having MSP in the last 6 months, recreational drugs use behavior, education less than junior high school, diagnosed with STI in the last 12 months, having infection of syphilis, having anal bleeding during anal intercourse, preferred receptive or versatile sexual roles, and inadequate HIV related knowledge. Risk factors associated with the HIV infection were obtained through subgroup analysis of included eligible articles. (*Supplementary Materials S1a and S1b*)

Table 2: Meta-analysis of risk factors associated with HIV infection among MSM in China

Demographic factors

The pooled results revealed that non-local residency (OR = 2.31, 95% CI: 1.05, 5.08) and education less than junior high school (OR = 1.73, 95% CI: 1.36, 2.21) were significantly and positively related to HIV infection.

HIV related knowledge and behavioral factors

Engaging in commercial sex (OR = 2.99, 95% CI: 1.02, 8.72), preferred receptive (OR = 2.43, 95% CI: 2.09, 2.83) or versatile (OR = 1.69, 95% CI: 1.35, 2.21) sexual roles, having anal bleeding during anal intercourse (OR = 2.22, 95% CI: 1.60, 3.07), having no HIV test in the last 12 months (OR = 2.17, 95% CI: 1.45, 3.25), having UAI in the last 6 months (OR = 2.06, 95% CI: 1.69, 2.50), recreational drugs use (OR = 1.90, 95% CI: 1.53, 2.36), inadequate HIV related knowledge (OR = 1.63, 95% CI: 1.26, 2.11) and having MSP in the last 6 months (OR = 1.35, 95% CI: 1.24, 2.47) were found to be the risk factors for HIV infection among MSM in China.

STI status

Having infection of syphilis (OR = 3.22, 95% CI: 3.02, 3.44) and diagnosed with STI in the last 12 months (OR = 1.71, 95% CI: 1.30, 2.26) were positively related to HIV infection.

Sensitivity analysis

There were significant heterogeneities of results across studies in effect analysis of having UAI in the last 6 months ($I^2 = 79\%$, $p < 0.00001$), engaging in commercial sex ($I^2 = 84\%$, $p = 0.002$), having sex with female partners in the last 6 months ($I^2 = 82\%$, $p = 0.0007$), non-local residency ($I^2 = 99\%$, $p < 0.00001$) and having no HIV test in the last 12 months ($I^2 = 94\%$, $p < 0.00001$). However, sensitivity tests did not reveal any individual study that exerted impact on the overall estimate.

Discussion

HIV Prevalence

The HIV prevalence among MSM in China has increased continuously for the last decade. The average HIV prevalence estimated in the included studies was 9.19% (95%CI: 7.68%, 10.69%), which was higher than the average prevalence of 7.27% (95%CI: 6.83%, 7.71%) in a nationwide survey during 2011 to 2017. The individual prevalence of HIV infection included in this study varied widely from 2.85%(38) to 15.54% (36). The observed disparity reflects differences in study years, sample size and study locations. The study in Guilin(38) from 2008 to 2009, one of the earliest studies in the included studies, reported the lowest HIV prevalence of 2.85% with 632 subjects. At the same time, a national study survey of more than 47,000 MSM in 61 Chinese cities reported HIV prevalence of 4.9%(45). The latest study(26) completed in 2015 and published in 2018 with 2,531 subjects in Harbin reported an HIV prevalence of 14.30%. The highest HIV prevalence reported among our included studies was 15.54%(36) in Chengdu which was conducted in 2011 with 251 MSM participants.

Risk factors associated with HIV infection

The results of this study suggest that having UAI is a major risk factor for HIV infection. On average, 49.32% (95% CI: 41.17%, 57.48%) Chinese MSM have engaged in UAI among our included studies. This is consistent with the previous meta-analysis(47) that pooled prevalence rates of UAI with any male partner was 53%(95% CI: 51%, 56%). One study which focused on the global epidemiology of HIV infection in MSM population, published in 2012 by Chris Beyrer, et al., revealed that UAI was consider to be the key reason of HIV infection and other STIs' transmission among MSMs in China(48). The consistent high UAI proportion among MSM in China indicated that the measures of prevention/intervention for Chinese MSM in the past decade did not sufficiently reduce this high-risk behavior, as indicated by the consistently increasing HIV prevalence among MSM in China(10–13). Therefore, other effective intervention methods besides education, promotion and condom distribution, should be considered.

Recreational drugs such as rush poppers, ketamine and methamphetamine, has quickly emerged and increasingly become popular in recent years among MSM(49). The pattern of drug use among Chinese MSM population has changed from using traditional drugs (such as opium, heroin) to the abuse of synthetic drugs (such as methamphetamine, ketamine), and towards the newly emerged drugs (e.g., rush

poppers)(50, 51). Several studies' results revealed that rush poppers were the most popular recreational drug among MSM in many areas over the last several years(51–54). As newly emerged drugs, rush poppers are not defined as an illicit drug in China and are easy to access with low price from internet(54, 55). Recreational drug users can have enhanced feelings of sexual desire, stamina and intoxicating highs(50). Under the effect of recreational drugs, drug users are more likely to have sexual disinhibition and engage in high risk behaviors, such as having multiple sexual partner(56), participating in group sex(57), engaging in UAI and commercial sex(52, 58), which may further facilitate HIV transmission. In our study, pooled results showed that recreational drug users had a 1.9 times higher risk of HIV infection than nonusers. Interestingly, one study found that recreational drug users were reported as more likely to have HIV testing experience than non-users (58), perhaps due to increased anxiety over HIV infection post exposure. Another study found MSM with high education level were more likely to get recreational drugs(59). One possible factor could be that better educated MSM may be better at using internet to acquire both information and source of synthetic drugs.

Role preference in anal sex is an important aspect of identities and sub-cultures among MSM populations(60). With regard to different anal sex behavioral patterns, there are three types of sex role including insertive (top), receptive (bottom), and versatile (either top or bottom). Among Chinese MSM, these roles correspond with '1', '0' and '0.5', respectively(61). Our study found those MSM who preferred receptive or versatile sexual roles during anal sexual intercourse are at higher risk for HIV infection. Bottoms are often in a submissive position during anal sex and younger than those who have the top role, which may in turn result in a lower awareness or reduced ability in terms of self-protection(62). On the other hand, the MSM who engaged exclusively or predominantly in receptive anal intercourse would be more likely to use recreational drugs and have unprotected receptive anal intercourse (URAI) (63), as the effects of recreational drugs in relaxing the anal sphincter and in reducing pain during anal intercourse(64–66), which carries a higher risk for HIV infection in the absence of condom use. For those who engaged in both receptive and insertive anal intercourse, studies show versatile sexual roles could have more occasional sex partners or engage in UAI frequently(60, 62, 67). In that case, the person who is easily infected through URAI could have greater possibility of transmission through unprotected insertive anal intercourse (UIAI)(68).

Have syphilis infection which was reported as a risk factor related to HIV infection by most studies (n = 17) in our review. The relationship between HIV and syphilis has been extensively studied(69–71). Some studies' results revealed that syphilis infection would act as a cofactor for HIV infection(72–75), which could facilitate HIV spread in the MSM population. Similarly, the findings of our study show that have been diagnosed with STI in the last year.

Other STIs were also recognized as risk factors associated with HIV infection in the MSM population. STIs are being studied more in their relations to high-risk behaviors for HIV infection, especially anal STIs such as rectal *Neisseria gonorrhoeae* (rGC) and rectal *Chlamydia trachomatis* (rCT)(76). In the United States, the median prevalence of *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) among MSM attending STI Surveillance Network clinics in 2010 (including rectal, urethral, and oropharyngeal

infections with these pathogens) were 15.5% and 13.0%, respectively(77). Meanwhile, the prevalence estimates in MSM as high as 38% for rGC(78) and 24% for rCT(79), have been documented; these results revealed that HIV-positive status was significantly associated with the prevalence of rCT(76). However, few studies have reported the burden of rCT, rNG or HSV infections and their correlation with HIV infection in Chinese MSM. Limited data and records of anal STI make it difficult to pinpoint risk associated with STIs and develop more precise intervention for MSM in China. Therefore, it is worthwhile for us to dissect causes of infection among various STI pathogens and different sites, as they will provide tools of detection for potential HIV transmission among MSM.

Intervention for HIV Prevention

HIV prevention intervention among MSM in China has mainly focus on publicizing HIV related knowledge, having education and providing HIV healthcare including HIV counselling, HIV testing, free condom and lubricant distribution and referral service. However, as we can see, classic interventions are insufficient to stem the tide of rising HIV epidemic among MSM in China.

On one hand, some studies have suggested that those MSM who had lower education level and lack of HIV related knowledge such as HIV transmission routes were more likely to engage in UAI(80–82). And these two factors were also positively associated with HIV infection revealed in our study. Obviously, for these population, publicity and education are needed but the content should include comprehensive sex education and not be limited to HIV related knowledge. One recent survey indicated that, even in the college, only half of the respondents received school-based sex education before(83). This suggests that comprehensive sex education need to cover the college population as well, which should include HIV/STI related knowledge, usage of condom, sexual orientation and safe sex, etc. The approach should also be diverse to include peer education, community education and online education through apps, etc.

On the other hand, researches also shown that separation of knowledge and behavior is quite common among MSM(84–86), that is, despite high level of knowledge and awareness of HIV and prevention methods, many still act in contrary to what they know. For this population, having high risk behaviors can't be attributed to lack of related knowledge, so other alternative interventions for HIV prevention such as Pre-Exposure Prophylaxis (PrEP) should be offered. PrEP is when people at high risk for HIV take HIV medicines daily to lower their chances of getting infected(87). It has been validated in high-risk populations through multiple clinical trials and led to regulatory approval of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) by the Food and Drug Administration (FDA) for PrEP in the United States(88–91) as well as other regulatory agencies. The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) have offered guidance about TDF/FTC as a PrEP treatment. As of March 2018, PrEP has been approved in over 50 countries globally (92) but not in China. Multinational PrEP trials have not included Chinese sites. The first study to assess the PrEP uptake preferences and associated factors with a National Internet Survey in China was published in 2019(93). The results indicated that only 22.4% of participants had heard of PrEP. Near half of the participants

(49.6%) doubted PrEP and only a quarter (26%) would be definitely willing to take PrEP. Other cross-sectional studies also reported low to moderate acceptability of daily or long-acting injectable PrEP use among Chinese MSM(94–96). These results suggests that an effective roll-out of PrEP among MSM in China will require broader educational and promotional campaigns to promote awareness about PrEP (97). Professional training about the benefits and effectiveness of PrEP and the successful experiences of PrEP promotion should be provided to health care sectors, community and social network in the first place to raise awareness and motivation of using PrEP among MSM and healthcare providers. Convenient access to information and PrEP drugs should be also provided. Target populations, such as those MSM who had high education level and adequate HIV related knowledge but engage in high risk behaviors, should be able to easily get access to these drugs while protecting their privacy.

Additionally, since we identified syphilis and STIs infection were consistently shown as risk factors for HIV infection, HIV prevention interventions should be provided at STI clinics, not just free HIV testing, HIV counselling and sex education but also the knowledge and information of PrEP and drugs to those MSM with high risk of HIV infection.

Limitations

There are some limitations in this study. Firstly, our results are based on most of cross-sectional data, which provide HIV prevalence. We did not attempt to have meta-regression for HIV prevalence. Because the objective of this study was not to obtain a single summarized HIV prevalence and most of included studies were conducted in large and medium sized Chinese cities at different study year. The pooled HIV prevalence may not objectively represent HIV prevalence among MSM in China. Secondly, the heterogeneities of included studies are also cause of different sample size, sampling method, study year, etc. For example, 12 studies were conducted in a single city in China with small sample size, 10 studies were conducted in more than one city and one is a national-wide study among 61 cities with large sample size. Moreover, the data collected on demographic factors were insufficient like age and income, due to limited raw data provided in studies and the inconsistency of range intervals for age and income. Further studies into how the relationship between age, income and HIV should be considered. Lastly, though publication bias was not formally assessed in our study, as analytical methods to test for publication bias, such as funnel plots and funnel plot asymmetry tests, may not be appropriate for observational data(98). But the possibility of publication bias could not be excluded.

Conclusions

Our study identified some associated risk factors for HIV infection among MSM in China and thus provided some basic information to further develop specific and effective interventions of HIV prevention. As underlined in our study, current intervention approaches such as routine education, behavior interventions should still be strengthened for those MSM who had lower education level and lack of HIV related knowledge. Further interventions such as PrEP should be prioritized for those MSM who engaged

in high-risk behaviors despite high level of HIV knowledge. Continuous education and PrEP drugs should be included in an HIV intervention package for those MSM with STI infection at STI clinics.

Supplementary Files

***S1a*: Factors associated with HIV infection (RE Forest plot)**

***S1b*: Factors associated with HIV infection (FE Forest plot)**

Abbreviations

AIDS: Acquired immune deficiency syndrome

HIV: Human immunodeficiency virus

MSM: Men who have sex with men

CNKI: Chinese National Knowledge Infrastructure

MeSH: Medical Subject Headings

OR: Odds ratio

RR: Risk ratio

UAI: Unprotected anal intercourse

MSP: Multiple sexual partners

CI: Confidence intervals

AHRQ: The Agency for Healthcare Research and Quality

NOS: The Newcastle-Ottawa Quality Assessment Scale

STI: Sexually transmitted infections

URAI: Unprotected receptive anal intercourse

UIAI: Unprotected insertive anal intercourse

rGC: rectal *Neisseria gonorrhoeae*

rCT: rectal *Chlamydia trachomatis*

GC: *Neisseria gonorrhoeae*

CT *Chlamydia trachomatis*

PrEP: Prevention such as Pre-Exposure Prophylaxis

TDF/FTC: Tenofovir disoproxil fumarate/emtricitabine

CDC: The Centers for Disease Control and Prevention

WHO: The World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

JP, HYQ and YR participated in the design of the study and data collection. JP and YR conducted the statistical analysis. JP, HYQ and LQZ conceived of the study and helped to draft the manuscript. All authors read and approved the final manuscript.

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Tables

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Figures

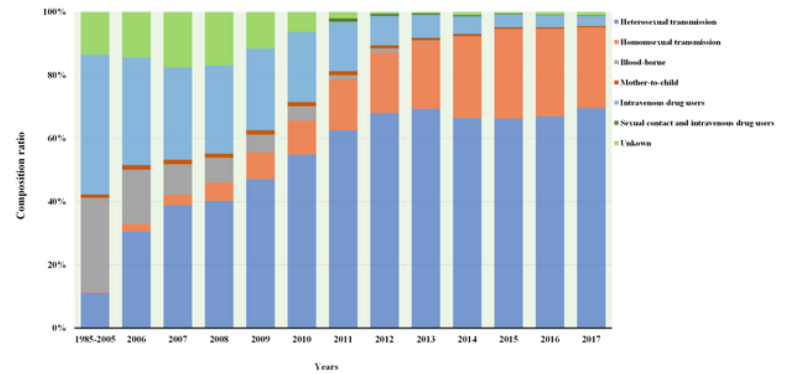
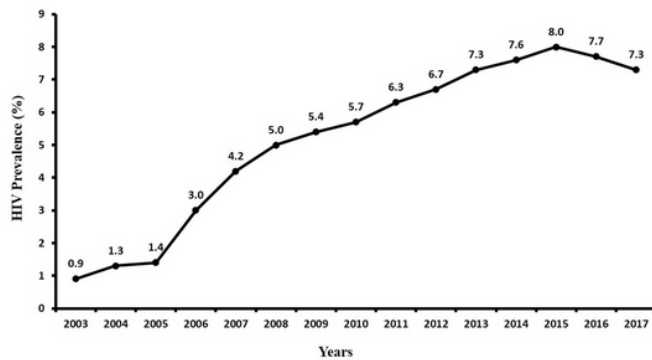


Figure 1

1 a: HIV prevalence among MSM in China, 2003-2017 1 b: Distribution of transmission modes of newly identified HIV/AIDS cases in China

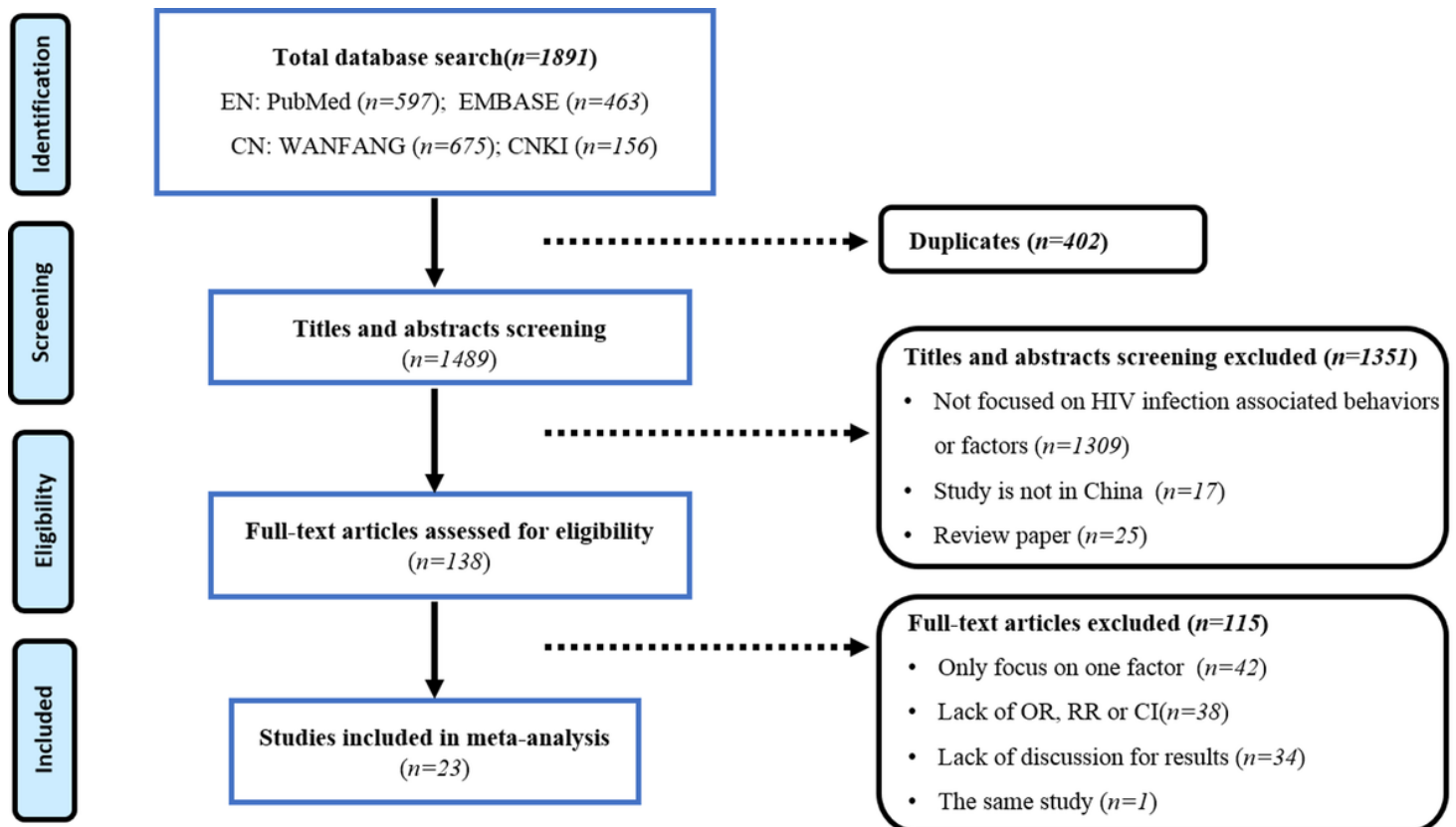


Figure 2

Study selection

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