

Factors influencing HIV seroconversion rate in Chinese heterosexual discordant couples: A systematic review and meta-analysis

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Research article

Keywords: HIV/AIDS; discordant couples; seroconversion rate; China; ART

Posted Date: May 3rd, 2019

DOI: <https://doi.org/10.21203/rs.2.9379/v1>

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Abstract

Background At present, there are few studies focusing on the factors affecting the seroconversion rate of serodiscordant couples, but the number of serodiscordant couples is increasing, which has become a serious global public health problem. We sought to identify factors contributing to HIV seroconversion of the uninfected spouse in couples serodiscordant for the virus. **Methods** We used a systematic literature search to identify studies describing serodiscordance and seroconversion among couples in which one partner was infected with HIV. We conducted a meta-analysis of 18 published articles in which we combined the random-effects models to identify factors contributing to seroconversion. Forest plots, sensitivity analysis and Egger's regression asymmetry test were performed by STATA SE-64 (version 12) to measure the overall results, stability of results and bias. Heterogeneity was tested by I² statistic. **Results** The overall seroconversion rate was lower in the ART-receiving group [odds ratio (OR) = 0.34, 95% confidence interval (CI) (0.16; 0.71)], demonstrating that ART is effective in preventing HIV transmission. Farmers had greater odds of HIV transmission than those who were not farmers [OR = 1.28, 95% CI(1.07; 1.52)]. Further, the serodiscordance rate was higher in intravenous drug abusers [OR = 0.76, 95% CI(0.66; 0.87)]. However, HIV patients and AIDS patients had no statistical differences in serodiscordance rates [OR = 1.38, 95% CI(0.81; 2.35)]. **Conclusions** These findings suggest that promoting early and long-term access to ART treatment, developing a rural HIV prevention model, and focusing on families of drug addicts may be beneficial interventions for reducing HIV transmission. Further research should explore the effects of ART intervention in different periods (HIV/AIDS).

Background

Human Immunodeficiency Virus(HIV) seriously impacts global public health through the pandemic's influence on morbidity and mortality. By the end of 2017, there were 78 million reported HIV/AIDS(Acquired Immune Deficiency Syndrome) infections worldwide, and the mortality caused by AIDS or its complications reached 35 million [1]. In China, the situation is not optimistic—China had about 780,000 living HIV/AIDS patients by the end of 2011 [2]. Research has shown that heterosexual transmission, superseding injection drug use, has played a dominant role in all modes of transmission, and around 1/3 of those infected by this method were infected by a spouse [3,4]. HIV serodiscordant couples, defined as one partner who is HIV-negative and the other who is HIV-positive, are at a high risk of becoming infected without any intervention of protective measures [5].

Unprotected sex between discordant couples provides a chance for transmission and has become a predominant source of new infections [6], necessitating the identification of factors associated with seroconversion rates. Use of antiretroviral therapy (ART), condom use, gender of index case, HIV viral load, and age of index case are associated with transmission between discordant couples [7]. One study showed that the seroconversion rate is higher in couples who had not received ART and lower in couples who had received ART, and that the effect of ART is remarkable in the first year but then stalls with the extension of the follow-up period [8]. However, less attention has been given to additional factors, such as disease stage and occupation (e.g., farmer).

Because there is high risk of acquiring HIV from an HIV-positive partner, clear effective prevention strategies and interventions are particularly significant to not only protect the HIV-negative partner, but also to reduce the society-wide AIDS prevalence. Therefore, we evaluated the effectiveness of potential factors associated with HIV seroconversion in serodiscordant couples using a systematic review and meta-analysis of published articles, applying subgroup analysis to eliminate the effects of confounding factors.

Methods

2.1. Search strategy and selection criteria

We defined HIV serodiscordant couples as heterosexual couples in which one partner was HIV-infected while the other was not infected. The definition for couples was a partner who had a legal effect or those in a traditional marriage or stable, long-term sexual relationship. Legal marriage referred to marriage registered at the Civil Affairs Bureau and protected by the constitution. Traditional marriage referred to extremely remote areas where there was no capacity to register. HIV-positive was defined as an individual who tested positive for HIV antibody by western blot.

We systematically searched the literature published between June 1981 and May 2018 using the following Chinese and English databases: China National Knowledge Infrastructure (CNKI), Wanfang, Weipu and Pubmed, Embase and SinoMed. The following keywords were used to search for relevant articles: HIV/AIDS, serodiscordant, seroconversion rate, ART, and transmission. Articles whose study area were not in China were not included. We excluded articles that presented only qualitative data, or presented quantitative data in a manner that did not allow calculation of seroconversion rate. Articles that did not identify areas of study, methods of study, or demographic baseline characteristics or those with anti-HIV antibody tests not verified by western blot were excluded. For different articles from the same study, we only used the most complete data. We also did a manual search to address unpublished and gray literature. In addition, we included the most recent study if the integrity of data from articles was similar. A flow diagram of preferred reporting items for systematic reviews and meta-analyses describing the article selection process is shown in Figure 1.

2.2 Data extraction

We used a standard form to extract the following information from each article: 1) name of first author; 2) publication date; 3) study area; 4) study region; 5) study date; 6) number of couples; 7) ART; 8) routes of infection; 9) seroconversion rate; 10) occupation; and 11) disease stage. Basic characteristics of the articles are shown in Table 1.

2.3 Statistical analysis

We chose the following items as the main output indicators: 1) seroconversion rate in couples receiving or not receiving ART; 2) seroconversion rate in couples with different occupations (farmer or non-farmer),

disease stage (HIV or AIDS) and infection route (intravenous drug use or heterosexual intercourse). Study methods contained both retrospective and prospective analyses, so odds ratio (OR) values were used to select effect quantities. Subgroup analysis was performed if heterogeneity was high. We used Cochrane Collaboration's tool for randomized controlled trials (RCTs) and Newcastle-Ottawa scale for non-RCTs to assess study quality. We estimated the possibility of heterogeneity between studies with I² statistic and used random-effects models for meta-analysis whether heterogeneity was high or not. Given that the number of included articles was not large, Egger's regression asymmetry test was chosen to assess potential for publication bias. We used sensitivity analysis to determine whether results were substantially altered or not. Statistical analyses were performed using STATA SE-64 (version 12) .

Results

3.1. Systematic review

The literature search yielded 18 articles for data extraction and analyses; 14 articles were in Chinese and 4 in English [7–23]. Study methods included case-control, cohort, and cross-sectional studies. Study provinces in China were Henan, Guangxi, Xinjiang, Zhejiang, Anhui, Yunnan, and Sichuan. Research subjects were HIV serodiscordant couples, and the HIV prevalence rate was available in each article. In total, 15 articles included data on ART, 11 articles provided data on occupation, 6 articles included infection route of the index partner, and 3 articles indicated disease stage of index partner.

3.2. Effect of ART

Whether infected individuals received ART and their respective seroconversion rates were provided in 15 articles detailing 110,098 HIV serodiscordant couples. Seroconversion rate was higher in couples who did not receive ART in 14 articles, while 1 article reported the opposite result. Heterogeneity test showed high heterogeneity (I² =99.0%; P < 0.001) between articles, so we used a random effects model. Meta-analysis showed that ART was effective in preventing HIV transmission, as overall seroconversion rate was lower in the ART-received group [OR = 0.34; 95% CI (0.16, 0.71)]. The forest plot in Figure 2A shows detailed results.

Considering the high heterogeneity in Yunnan and Henan provinces, we performed subgroup analysis to identify causes of heterogeneity. Data from Henan showed similar results [OR = 0.43; 95% CI (0.35, 0.52)] as overall articles, with no significant heterogeneity (I² =0.0%; P = 0.819) (Figure 3). However, data from Yunnan suggested no statistical significance [OR = 0.39; 95% CI (0.08, 1.77)], with high heterogeneity (I² = 91.2%; P < 0.001).

Sensitivity analysis was conducted to measure stability of the results. After each article was neglected, analysis showed no significant difference in the results (Figure 4A). Further, Egger's regression asymmetry test revealed no significant publication bias (t = 0.59; P = 0.564) (Figure 5A).

3.3. Effect of occupation

Occupation of couples, classified as farmer or non-farmer, was evaluated in 11 articles with data on 60,284 couples. In those 11 articles, 9 reported that the serodiscordant rate among farmers was higher than that for non-farmers, while 2 articles found a lower serodiscordant rate in farmers. The heterogeneity test indicated no significant heterogeneity ($I^2 = 21.9\%$; $P = 0.234$). Mean meta-analysis showed farmers had more opportunity for HIV transmission than non-farmers [OR = 1.28; 95% CI (1.07, 1.52)] (Figure 2B). When any individual article was ignored in sensitivity analysis, the results did not change (Figure 4B). However, Egger's regression asymmetry test indicated strong publication bias ($t = 1.91$; $P < 0.1$) (Figure 5B).

3.4. Effect of infection route

Infection route of index partner (heterosexual sex or intravenous drug use) was reported in 6 articles with data on 52,206 couples. Of these 6 articles, 5 reported increasing serodiscordant rate in patients infected by heterosexual sex. Articles showed no heterogeneity ($I^2 = 0.0\%$; $P = 0.478$). The serodiscordant rate was higher for those infected by intravenous drug use [OR = 0.76; 95% CI (0.66, 0.87)] (Figure 2C). Sensitivity analysis revealed that 1 article had so much weight that results [OR = 0.88; 95% CI (0.70, 1.11)] showed no difference between transmission routes (Figure 4C). Further, Egger's regression asymmetry test found publication bias ($t = 0.04$; $P < 0.1$) (Figure 5C).

3.5. Effect of disease stage

Disease stage data were offered in 3 articles containing data on 2400 couples of which 2 articles reported a higher serodiscordant rate in HIV patients than AIDS patients. The remaining 1 article reported contradictory results. These articles did not show heterogeneity ($I^2 = 0.0\%$; $P = 0.542$). After analyzing the main extracted data, HIV patients and AIDS patients were not statistically different [OR = 1.38; 95% CI (0.81, 2.35)] (Figure 2D). Sensitivity analysis showed that results were stable (Figure 4D). However, Egger's regression asymmetry test indicated the presence of publication bias ($t = 6.45$; $P < 0.1$) (Figure 5D).

Discussion

HIV is one of the most influential infectious diseases in the world, and the spread of HIV virus through HIV serodiscordant couples is a transmission route that cannot be ignored. Risk of HIV transmission is determined by factors such as the possibility of exposure to the infected individuals and explicit sexual activity [24]. Some studies have even carefully described the specific mechanisms of HIV sexual transmission [25]. In this study, we analyzed a total of four factors related to HIV transmission among HIV serodiscordant couples: whether or not they received ART, occupation (farmers or non-farmers), infection route of index case (intravenous drug abuse or heterosexual intercourse), and disease stage (HIV or AIDS). Among these factors, ART, occupation and infection route of index case had a significant relationship with the HIV seroconversion rate in HIV serodiscordant couples.

Our meta-analysis shows that the HIV seroconversion rate in couples who received ART was lower than in couples who did not receive ART. However, not all studies confirmed the effect of ART. One study showed that after 2 years of ART, 33% of the patients experienced virological treatment failure [26]. Another study conducted in Zhejiang province showed that from 2009 -2013, the HIV seroconversion rate increased slightly in the ART group (from 0.0/1000 PY in 2009 to 3.0/1000 PY), but decreased in those without ART (from 24.10/1000 PY in 2009 to 5.56/1000 PY in 2013) [15]. These results may be explained by the Chinese government's emphasis on HIV transmission in families, with HIV testing of couples being a key task since 2010. In addition to increased intervention capacity of grassroots workers, these measures have reduced the risk of HIV infection in untreated couples. Further, couples that receive ART are tested once a year, although the time interval between HIV seroconversion and ART may be shorter—making results appear as if the preventive effect of ART has not yet been achieved.

Factors affecting ART outcomes are increasingly being reported. Several studies included in our analysis explored the effects of ART interventions in the HIV infection and AIDS stages, but due to different definitions of disease staging, we could not conduct a meta-analysis of this outcome. A large-scale clinical trial of ANRS 12249 in South Africa found that early initiation of ART had no effect on HIV incidence [27], which is contrary to existing theoretical knowledge. During the follow-up of patients receiving ART therapy, we found that they have further improved their awareness of AIDS and become more aware of the safety of sexual behavior, such as the reduction of sexual intercourse and the increase of condom use. Therefore, early and long-term acceptance of ART can not only reduce the viral load in patients, but also carry out health education in the process of intervention. Although the effectiveness of ART needs to be subdivided and explored from different angles to achieve long-term suppression of HIV in patients who need lifetime ART, it is still considered necessary to promote ART therapy in general.

The disease stage of AIDS doesn't always mean the higher seroconversion rate than HIV infection. According to general theoretical knowledge, patients with AIDS have fewer CD4 cells, more copies of the virus, and a greater probability of HIV transmission. However, the clinical symptoms of patients with AIDS could be more serious. Such couples likely use more measures to protect the uninfected partner from HIV infection, partially offsetting other adverse effects of AIDS. In addition, related studies have found that not all HIV-infected individuals are identified, especially patients with acute and early infections, which are the most infectious [26]. If one individual of a couple was infected with HIV and the symptoms had not yet manifested, the infectiousness of HIV may be underestimated. Indeed, because HIV has an incubation period, patients vary in the length of time from diagnosis of HIV infection to development of AIDS. Evidence to describe the difference in risk of seroconversion between these periods could guide medical resources more effectively.

The HIV-infected population in rural central China is likely the largest known HIV-infected cohort in the world [28]. Due to the limitations of the medical environment and the challenges in identifying these cases, this subset of HIV serodiscordant couples may have an increased HIV seroconversion rate. Meta-analysis of occupation also showed that HIV seroconversion rate was significantly higher in farmers. A less educated index case is more likely to pass the HIV virus to others due to a lack of awareness [29]. At

present, rural regions that represent a major portion of HIV cases are important considerations for disease control. However, due to the low level of education and lack of health knowledge, farmers are resistant to HIV interventions and the vast majority of rural residents do not understand government policies and social health service resources. Our results highlight the need for an AIDS prevention model specifically targeted at farmers, with a focus on increasing awareness of and education about AIDS.

Analysis by infection route of the index case revealed that those who injected drugs were more likely to transmit the HIV virus than those having heterosexual intercourse. Further, the effect of ART in patients infected through heterosexual intercourse is better than in those infected by injection drug use [26]. Patients infected by drug injection have poor cognitive ability and treatment compliance, which may partially account for these results [30]. This suggests that drug injection has become a significant factor in seroconversion. Some people addicted to drugs choose to share syringes to meet their needs, despite knowing the risk of HIV infection. Spouses of injecting drug users may also be willing to take the risk despite not injecting drugs themselves. Relevant institutions should pursue interventions that reduce injection drug use and educate drug users on the risk of spreading HIV to their spouses.

Our results are novel; we have not found any other studies that explore factors that may influence HIV seroconversion rate. Further, our research content is relatively comprehensive and studies not only the effects of ART (the most popular topic of research), but also factors that are often overlooked, such as infection route of the index case, which is sometimes related to the HIV seroconversion rate. Other factors that should theoretically be related to HIV seroconversion rate, such as disease stage, may have no effect. In addition, our inclusion of external intervention factors and patients' own conditions make the results more accurate.

This study also had some limitations. We found large heterogeneity in ART studies. Subgroup analysis indicated heterogeneity may arise from the study area, which was over-dispersed. Sensitivity analysis of infection route of index case indicated no difference between the two routes when we excluded a heavily weighted article, indicating that this article likely influenced overall results. Therefore, more research is needed on the infection route of index case. Egger's regression asymmetry tests showed different degrees of publication bias in all results except ART. In addition, it was impossible to require all the included articles to be prospective studies because few articles examined factors affecting the HIV seroconversion rate. The varied research methods of included articles may also have complicated our results. Yet, after combining analysis of the existing literature with the test of heterogeneity and sensitivity, we consider these results persuasive.

Conclusions

This study explored four influencing factors related to HIV seroconversion rate in heterosexual discordant couples. We found positive results of ART, occupation and infection route and negative results of disease stage. We conclude that promoting early and long-term access to ART treatment, developing a rural HIV prevention model, and focusing on families of drug addicts are important avenues for intervening on HIV

transmission. Further research should explore the effects of ART intervention in different periods (HIV/AIDS).

Abbreviations

HIV=Human Immunodeficiency Virus

AIDS=Acquired Immune Deficiency Syndrome

ART=antiretroviral therapy

CNKI=China National Knowledge Infrastructure

OR=Odds Ratio

CI=Confidence Interval

RCTs=Randomized Controlled Trials

Declarations

Ethics approval and consent to participate:Not applicable.

Consent for publication:Not applicable.

Availability of data and material:The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:The authors declare that they have no competing interests.

Funding:This work was supported in part by the Natural Science Foundation of China (U1503123, 11571273), the National S&T Major Project Foundation of China (2017ZX10201101) and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

Authors' contributions:All authors have contributed significantly and all authors are in agreement with the content of the manuscript. Conception and design of study: ZH P. Acquisition of laboratory or clinical: HX and KJ S. Analysis of data: WN. Drafting of artical: HX and KJ S. Critical revision: WN. Final approval: ZH P, HX, KJ S, WN. All authors read and approved the final manuscript.

Acknowledgements:Not applicable.

Authors' information:Not applicable.

References

1. United Nations. Global Issues—AIDS. 2017. <http://www.un.org/en/sections/issues-depth/aids/index>. Accessed 15 November 2018.
2. Wang LY, Qin QQ, Ding ZW, Cai C, Guo W, Li DM, et al. Current situation of AIDS epidemic in China. *Chin J AIDS STD*. 2017; 23:330–333.
3. Piot P, Bartos M, Ghys PD, Walker N, Schwartländer B. The global impact of HIV/AIDS. *Nature*. 2001; 410:968–973.
4. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med*. 2000; 342:921–929.
5. Yang RR, Gui X, Benoit JL, Xiong Y. The comparison of human immunodeficiency virus type 1 transmission between couples through blood or sex in central China. *Jpn J Infect Dis*. 2010; 63: 283–285.
6. Ji GP. Risk behaviors and influencing factors of HIV cases who know their HIV infection status. *Chin J AIDS STD*. 2004; 10:151–153.
7. Yang RR, Gui X, Xiong Y, Gao SC, Yan YJ. Five-year follow-up observation of HIV prevalence in serodiscordant couples. *Int J Infect Dis*. 2015; 33:179–184.
8. Jia ZW, Mao YR, Zhang FJ, Ruan YH, Ma Y, Li J, et al. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003-11): a national observational cohort study. *Lancet*. 2013; 382:1195–1203.
9. Yang CB. Analysis of sexually transmitted HIV after AIDS single-yang family receiving antiviral therapy. *Sichuan Med J*. 2014; 35:1594–1595.
10. Liu XC, Li ZY, Fu JC, Chen L, Lu JB, Zhao JX, et al. Analysis on current status of seroconversion of HIV/AIDS pairs of spouses positive family and single positive family, Yuxi City, 2006-2013. *Prev Med Trib*. 2015; 21:354–356.
11. Tang HL. Study on the main factors of HIV transmission among sero-discordant couples and a Bernoulli process model to model its transmission. Doctoral thesis. Chinese Center for Disease Control and Prevention, Beijing, China. 2014. <http://kns.cnki.net/kns/detail/detail.aspx?FileName=1015525963.nh&DbName=CDFD2015>. Accessed 15 November 2018.
12. Liu HX. Study on the preventive effect of highly active antiretroviral therapy on HIV sexual transmission among sero-discordant couples. Doctoral thesis. Chinese Center for Disease Control and Prevention, Beijing, China. 2015. <http://kns.cnki.net/kns/detail/detail.aspx?FileName=1016000099.nh&DbName=CDFD2016>. Accessed 15 November 2018.
13. Zhu QY, Yang XY, Jiang H, Tan GJ, Xiong RS, Liao LJ, et al. Efficacy of antiviral therapy on prevention of HIV transmission among sero-discordant couples in Guangxi Zhuang autonomous region. *Chin J Epidemiol*. 2015; 36:1401–1405.
14. Chen FF, Wang L, Han J, Wang LY, He WS, Guo W, et al. HIV sero-conversion rate and risk factors among HIV discordant couples in Zhumadian city, Henan province. *Chin J Epidemiol*. 2013; 34:10–14.

15. Chen L, Pan XH, Yang JZ, Xu Y, Zheng JL, Jiang J, et al. Incidence rate of HIV transmission in HIV discordant couples in Zhejiang province, 2009-2013. *Chin J Epidemiol.* 2015; 36:857–861.
16. Dong YL, Tang JL, Nong GD, Mao YF. Follow up intervention effect of “one-stop service” in Zhongshan County on HIV sero-discordant family. *J Applied Prev Med.* 2016; 22:336– 338.
17. Chen FF. Study on the role and risk factors of HIV antiviral therapy on sexual transmission among couples under treatment in Zhumadian. Doctoral thesis. Chinese Center for Disease Control and Prevention, Beijing, China. 2016. <http://kns.cnki.net/kns/detail/detail.aspx?FileName=1016282244.nh&DbName=CDFD2017>. Accessed 15 November 2018.
18. Zhang J. Analysis on HIV sero-conversion and risk factors among HIV discordant couples in Yili, Xinjiang. Master’s thesis. Xinjiang Medical University, Wulumuqi, Xinjiang, China. 2016. <http://kns.cnki.net/kns/detail/detail.aspx?FileName=1016102593.nh&DbName=CMFD2016>. Accessed 15 November 2018.
19. Feng MX, Liu M, Liu J, Chen J. Antiretroviral therapy to block transmission in HIV discordant couples: a meta-analysis. *Chin J AIDS STD.* 2015; 21:668–672.
20. Qi JL. An epidemiological study of HIV sexual transmission in married spouses in Yunnan province. Master’s Thesis. Kunming Medical University, Kunming, Yunnan, China, 2012; doi: 10.3760/cma.j.issn.0254-6450.2012.02.010
21. Li HR, Wang Z, Yang L. Risk factors associated with HIV transmission between spouses in Henan. *Chin J AIDS STD.* 2008; 14:39–41.
22. Smith MK, Westreich D, Liu HX, Zhu L, Wang L, He WS, et al. Treatment to prevent HIV transmission in serodiscordant couples in Henan, China, 2006 to 2012. *Clin Infect Dis.* 2015; 61:111–119.
23. He N, Duan S, Ding YY, Rou KM, McGoogan JM, Jia MH, et al. Antiretroviral therapy reduces HIV transmission in discordant couples in rural Yunnan, China. *PLoS One.* 2013; 8:e77981.
24. Baggaley RF, Boily MC, White RG, Alary M. Risk of HIV-1 transmission for parenteral exposure and blood transfusion: a systematic review and meta-analysis. *AIDS.* 2006; 20: 805–812.
25. Joseph SB, Swanstrom R, Kashuba AD, Cohen MS. Bottlenecks in HIV-1 transmission: insights from the study of founder viruses. *Nat Rev Microbiol.* 2015; 13:414–425.
26. Ma Y, Zhao DC, Yu L, Bulterys M, Robinson ML, Zhao Y, et al. Predictors of virologic failure in HIV-1-infected adults receiving first-line antiretroviral therapy in 8 provinces in China. *Clin Infect Dis.* 2010; 50:264–271.
27. HIV Prevention Trials Network. HPTN responds to results from ANRS 12249 TasP study presented at AIDS. 2016. <https://www.hptn.org/news-and-events/press-releases/hptn-responds-to-results-from-anrs-12249-tasp-study-presented-at>. Accessed 15 November 2018.
28. Dou Z, Chen RY, Wang Z, Ji G, Peng G, Qiao X, et al. HIV-infected former plasma donors in rural Central China: from infection to survival outcomes, 1985-2008. *PLoS One.* 2010; 5(10): e13737.
29. Zhang FJ, Dou ZH, Yu L, Ma Y. An ambispective cohort study of the natural history of HIV infection among former unsafe commercial blood and plasma donors. *Chin J Epidemiol.* 2008; 29:9–12.

30. Gordillo V, Del AJ, Soriano V, González-Lahoz J. Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *AIDS*. 1999; 13:1763–1769.

Tables

Table 1. Characteristics of studies included in research.

Article number	First author	Publication date	Study region	Study date	Number of couples	Seroconversion rate(%)
1	Chengbin, Yang	2014	Sichuan	2009-2012	466	6.87
2	Xiaochun, Liu	2015	Yunnan	2006-2013	314	4.14
3	Houlin, Tang	2014	Yunnan	2011-2012	120	33.33
4	Huixin, Liu	2015	Henan	2008-2013	4241	1.93
5	Huixin, Liu	2015	Henan	2008-2013	1093	2.2
6	Qiuying, Zhu	2015	Guangxi	2008-2014	7694	5.12
7	Fangfang, Chen	2013	Henan	2006-2011	4813	2.64
8	Lin, Chen	2015	Zhejiang	2009-2013	1966	1.12
9	Yulian, Dong	2016	Guangxi	2010-2014	190	0.53
10	Fangfang, Chen	2016	Henan	2008-2014	4689	2.18
11	Jing, Zhang	2016	Xinjiang	2009-2015	1574	3.11
12	Mnegxian, Feng	2015	China	1987-2014	39574	4.25
13	Jinlei, Qi	2012	Yunnan	2012	300	40.67
14	Huarong, Li	2008	Henan	2012	417	11.99
15	Weijia, Zhong	2013	China	2003-2011	38862	4.2
16	Rongrong, Yang	2015	Hubei	2005-2007	753	0.66
17	M. Kumi Smith	2015	Henan	2006-2012	4916	3.19
18	He, Na	2013	Yunan	2009-2011	813	2.09

Figures

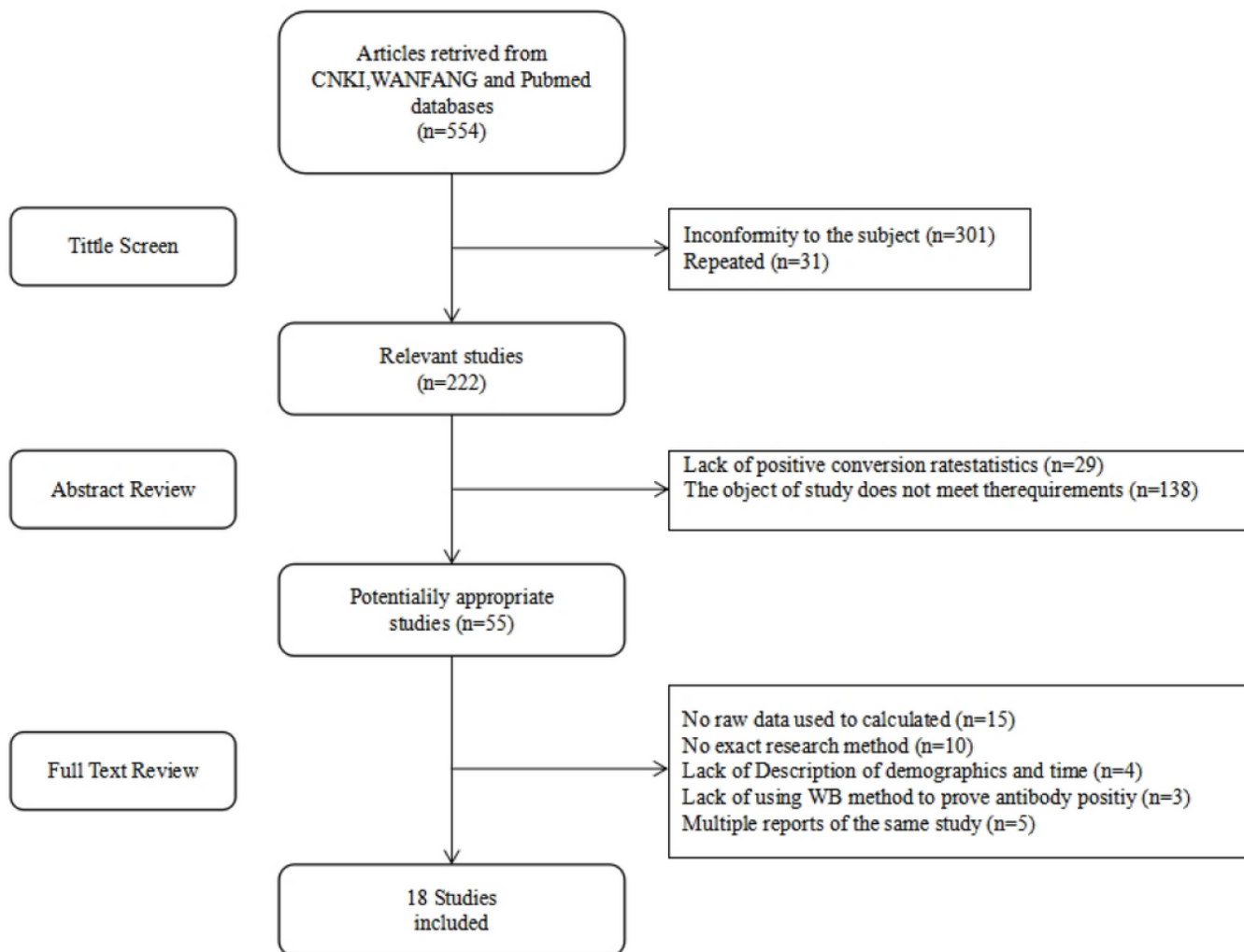


Figure 1

Procedure of the selection process.

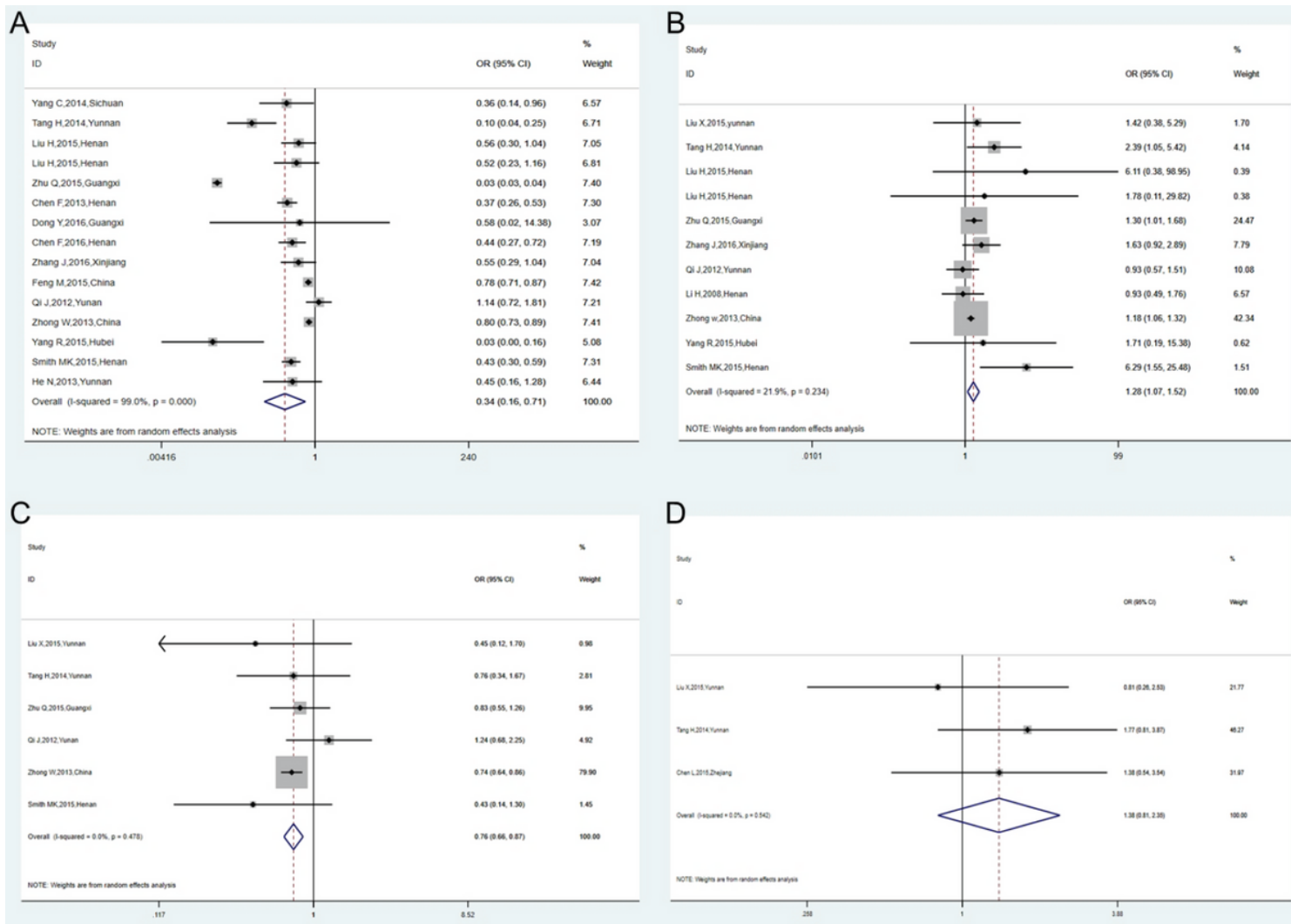


Figure 2

(A) Forest plot of ART. (B) Forest plot of occupation. (C) Forest plot of infection route. (D) Forest plot of disease stage.

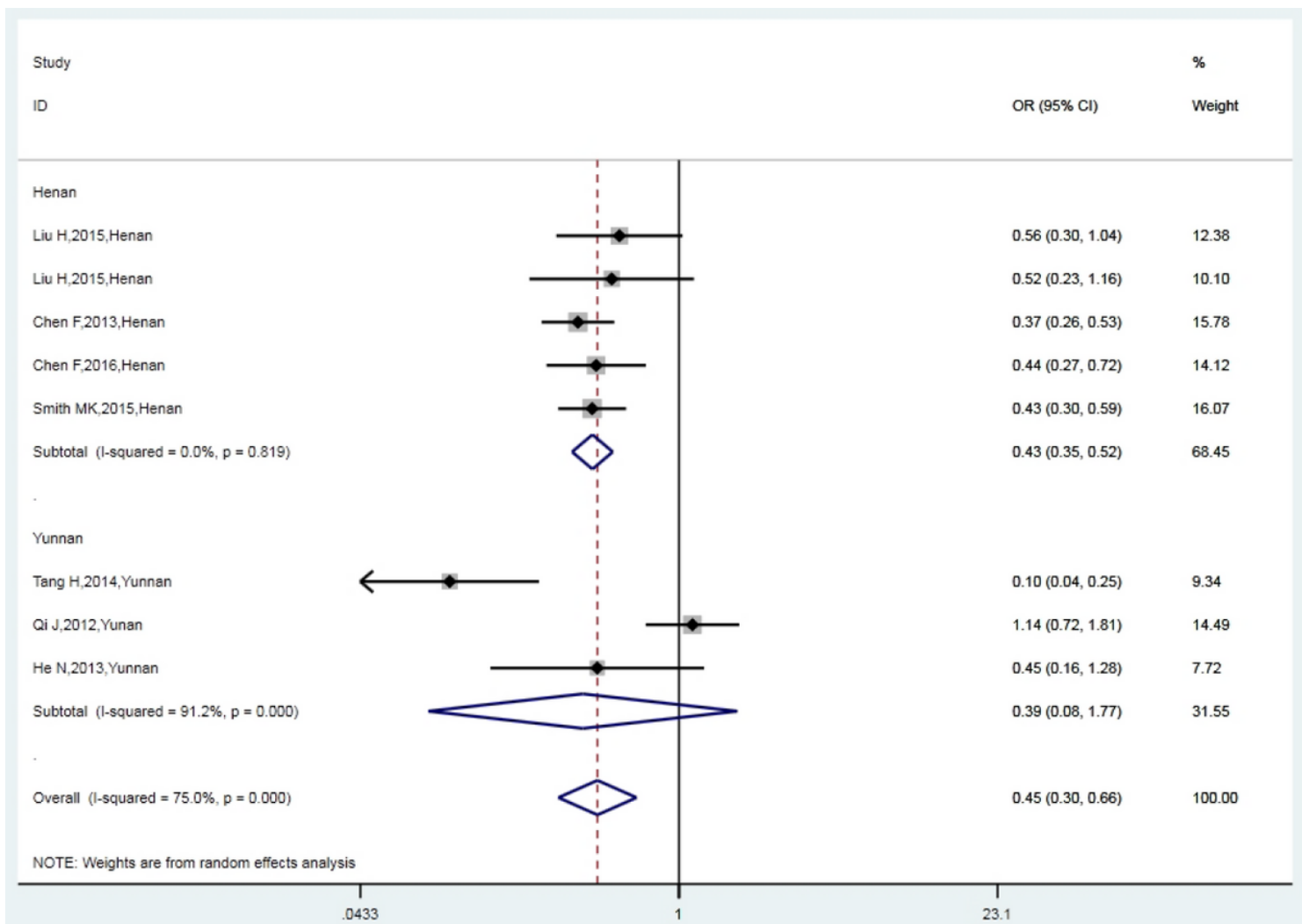


Figure 3

Subgroup analysis of province.

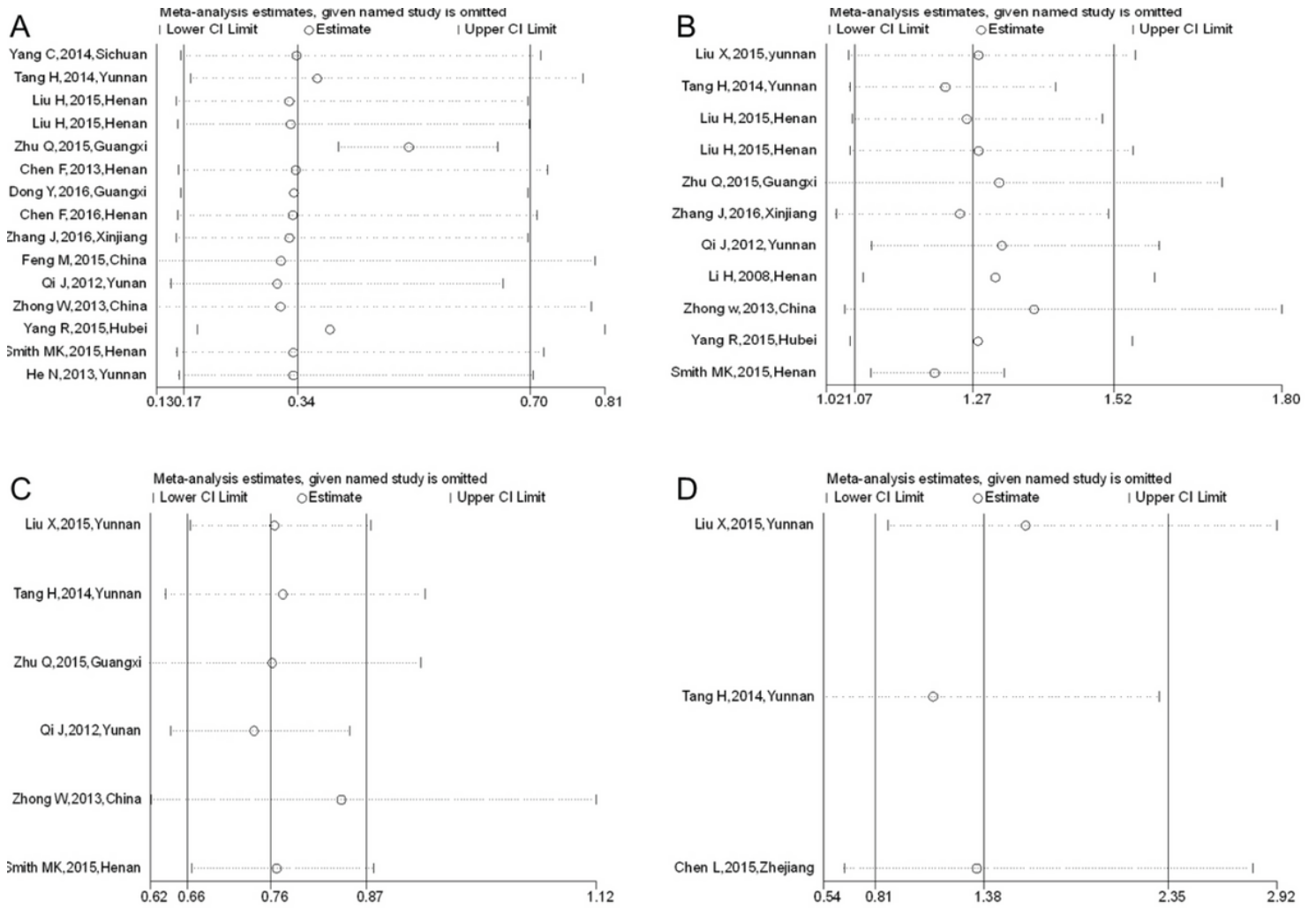


Figure 4

(A) Sensitivity analysis of ART. (B) Sensitivity analysis of occupation. (C) Sensitivity analysis of infection route. (D) Sensitivity analysis of disease stage.

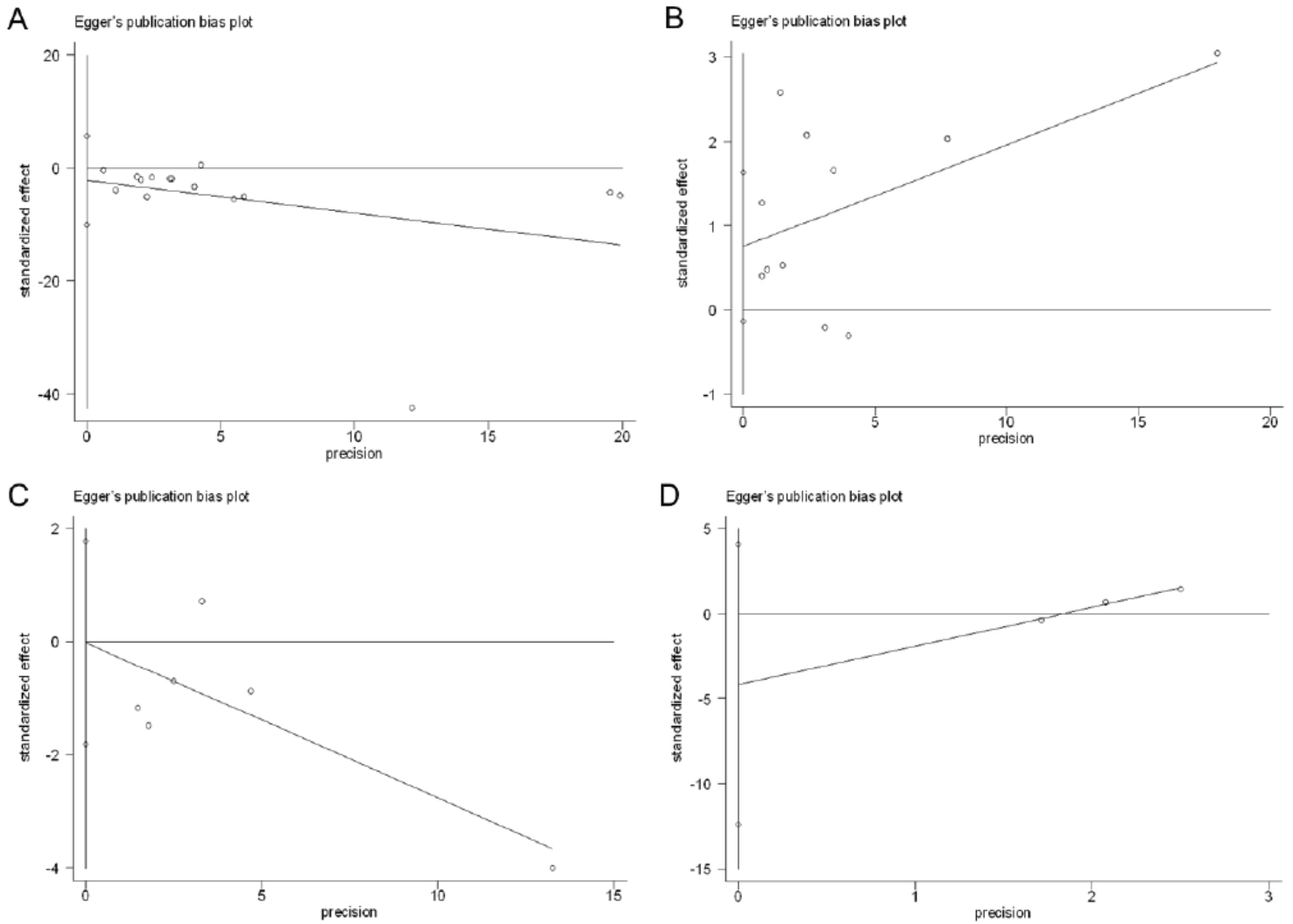


Figure 5

(A) Egger's regression asymmetry test of ART. (B) Egger's regression asymmetry test of occupation. (C) Egger's regression asymmetry test of infection route. (D) Egger's regression asymmetry test of disease stage.