

INPLASY PROTOCOL

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None declared.

Treatment failure and associated factors among people living with HIV on antiretroviral therapy in China: A meta-analysis

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Review question / Objective: Our study aimed to conduct a meta-analysis on observational studies to estimate the current situation of treatment failure rates and its influencing factors in China, so as to provide data support for decision makers and stakeholders to evaluate treatment effects and formulate targeted intervention strategies.

Condition being studied: Treatment failure was likely to cause drug resistance and even death through drug-resistant mutation, and early detection of treatment failure can prevent the occurrence of drug resistance to some extent. Before 2007, there was scarce fund support for VL testing in China, which was provided through transfer payment since 2007. However, due to the limitations of staff and the capabilities of laboratory testing, the proportion of PLHIV receiving VL testing in 2007 was still low with 9.1%, and then increased gradually reaching 71.3% by 2010. Because of failing to guarantee each PLHIV was tested for VL each year, there was lack of comprehensive evaluation on the ART effect among PLHIV nationwide. There have been some studies on treatment failure abroad. In Ethiopia, the treatment failure rate was high and was affected by treatment adherence, WHO clinical stages, exchange of treatment regimens and opportunistic co-infection in a systematic review and meta analysis. In resource limited areas, the CD4+T lymphocyte (CD4) count and treatment adherence affected treatment failure. In china, there have been many different studies on treatment failure among people living with HIV on antiretroviral therapy, and the treatment failure and influencing factors from different studies vary widely, ranging from 0.0% to 42.6%.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 October 2022 and was last updated on 17 October 2022 (registration number INPLASY2022100066).

INTRODUCTION

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METHODS

Participant or population: People living with HIV on antiretroviral therapy in China.

Intervention: None.

Comparator: None.

Study designs to be included: All observational studies related to treatment failure among PLHIV receiving ART in China were included, including cross-sectional, case-control, retrospective cohort, prospective cohort and ambi-directional cohort studies.

Eligibility criteria: Studies with wrong research design (non-observational studies), wrong outcomes (drug-resistance or viral suppression), molecular mechanism of HIV drug-resistance mutations, wrong study population (pregnant women or people co-infected with opportunistic diseases), Newcastle-Ottawa Scale Quality Assessment Tool (NOS) quality score less than 6 or wrong research areas (Taiwan, China) were excluded.

Information sources: A total of six databases were used for comprehensive search to obtain relevant studies on treatment failure among PLHIV in China by Sept.2022, including PubMed, Web of Science, Cochrane Library, WanFang, CNKI, and SinoMed. Database searches were supplemented by citation searches and manual searches in order to trace important historical and gray studies. The search method was mainly composed of MeSH and free word research. The complete search formula was ("People's Republic of China" OR "Mainland China" OR "Inner Mongolia" OR "China"[MeSH]) AND ("HIV"[MeSH] OR "HIV-1" OR "HIV-2" OR "HIV1" OR "HIV2" OR "HIV infections"[MeSH] OR "Human Immunodeficiency Virus" OR "Acquired Immunodeficiency Syndrome"[MeSH] OR "Acquired Immune Deficiency Syndrome Virus" OR "Acquired Immuno Deficiency Syndrome Virus" OR "Acquired Immuno-Deficiency Syndrome Virus" OR "AIDS") AND ("Antiretroviral Therapy, Highly Active"[MeSH] OR "HAART" OR "Combination Antiretroviral Therapy") AND ("Treatment Outcome"[MeSH] OR "Treatment failure" OR "Virological failure" OR "Immunological failure" OR "Clinical failure" OR "Failure" OR "Less CD4 count" OR "Viral load").

Main outcome(s): treatment failure, treatment failure was assessed through virological and (or) immunological based on the latest WHO guidelines in 2016. Virological failure referred to VL>1000copies/ml, and immunological failure referred to that the CD4 count decreased to or below baseline value, or

remained below 100cells/ μ l after receiving ART for 6 months.

Additional outcome(s): The potential influencing factors of treatment failure, mainly including treatment adherence, baseline CD4 count, ART regimens, WHO clinical stage, age and gender.

Quality assessment / Risk of bias analysis: NOS standard was used for the quality assessment of cross-sectional and cohort studies. This tool mainly included three sections. The first section mainly evaluated the selection of the research population, with a total score of 4 points; the second section mainly evaluated the comparability between groups, with a total score of 2 points; the third section mainly focus on the assessment of research outcomes and statistical methods, with a total score of 3 points. The total NOS score was 9 points, and the higher the total score, the better the quality of the study. If one observational study was scored as below 6 points, it was considered low quality and would be excluded from our meta-analysis.

Strategy of data synthesis: Data information of included studies such as the year of publication, first author, study type, sample size and other information were extracted in Microsoft Excel format, and the meta-analysis including the pooled treatment failure and influencing factors among PLHIV on ART in China was completed in R4.1.2. Normality test was conducted by Lilliefors method, and the data conforming to non-normal distribution would be converted to arcsine. Heterogeneity among different rates was evaluated by Cochrane Q test and I² statistics. I²≥50% was considered as significant heterogeneity, and a random effect model would be used to pool treatment failure rate, OR value and 95% Confidence Interval (CI). Bonferroni method was used for pairwise comparison among multiple groups, and Mann Kendall test for time trend test. The funnel plot and Egger's test were used to evaluate publication bias.

Subgroup analysis: The sources of heterogeneity can be explored by both

meta-regression and subgroup analysis based on the year of publication (<2016 vs.≥2016), study area (the eastern, central and western), study population (adults vs. children), study type (cross-sectional vs. cohort study), sample size (≤1000 vs.>1000), the duration of treatment (≥12 months, <12 months and mixed) and treatment failure criteria (virological, immunological and mixed).

Sensitivity analysis: Sensitivity analysis was conducted by deleting each study.

Language restriction: None.

Country(ies) involved: China.

Keywords: HIV/AIDS, Treatment Failure, Factors, China.

Contributions of each author:

Author 1 - Dandan Niu - The author made contributions in data curation, formal analysis, methodology, writing-original draft and writing-review & editing.

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Author 3 - Fangfang Chen - The author made contributions in writing-review & editing.

Author 4 - Decai Zhao - The author made contributions in methodology.

Author 5 - Hehe Zhao - The author made contributions in data curation, formal analysis.

Author 6 - Shi Wang - The author made contributions in data curation.

Author 7 - Yushan Hou - The author made contributions in data curation.

Author 8 - Fan Lyu - The author made contributions in writing-review & editing.