

Incidence of HIV and HCV in Injecting Drug Users: Systematic and Meta-analysis Review protocol

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Protocol

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Abstract

introduction: HIV and HCV is a health concern in the world. Therefore, this systematic review and meta-analysis protocol study is aimed to estimate the incidence of HIV and HCV among People who inject drugs (PWID) by applying mathematical modeling. The primary purpose of this systematic review is to identify and review existing studies of HIV and HCV incidence in people who inject drugs, that use mathematical modeling. Methods and analysis: Studies including cohort, cross-sectional, case-control studies which were conducted to estimate incidence of HIV and HCV based on mathematical or evaluated effectiveness of mathematical models will be considered to enroll the review; a comprehensive search with Cochrane approach would be applied to identify relevant studies in electronic databases in the period of 2000 to 2019. This protocol was prepared according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) and we will search PubMed, EMBASE, OpenGrey, WOS, SCOPUS, and Cochrane Library with no restriction of language. Study selection and data extraction will be performed by two independent reviewers. Assessment of risk of bias will be implemented using three quality test tools including Newcastle Ottawa Scale and ROBIS scale for cross-sectional studies and quantitative studies quality test tool for observational and interventional studies for other study Publication bias will be assessed by funnel plots, Begg's and Egger's tests. Heterogeneity will be evaluated using the I² statistic and the χ^2 test. In addition, subgroup analyses will be conducted for population and the secondary outcomes.

Background

Strengths and limitations of this study

- ▶ The present systematic review is the first to examine models for the incidence of HIV and HCV in injecting drug users by searching various databases.
- ▶ To minimize potential bias, each process of initial screening, data extraction and quality evaluation will be performed by two independent reviewers.
- ▶ The study is not limited in that only study in specific language; therefore, it's not exposed to language bias.
- ▶ this review includes just studies using mathematical model therefore may ignore some studies working on HIV and HCV incidence in people who inject drugs.

Despite significant progress in treatment of diseases during the past decade, HIV infection has still remained as a major health concern globally and it is predicted to be the third main cause of death throughout the world by 2030 (1). According to global statistics in 2015, 36.7 million people worldwide were infected with HIV (1). Although epidemiological evidence indicated a decreasing trend of HIV

infection in many developing countries during last few years, HIV prevalence is indeed increasing in developing countries (2).

UNAIDS global strategy of 2016-2021 has focused on key population with high risk behaviors towards HIV infection and applying affective interventions on them to prevent increasing the incidence of HIV infection (3).

One of the main groups at risk for HIV infection is injecting drug abusers. According to published reports around the world, an average of 13.3% of injecting drug users are infected by HIV with a remarkable rate of 28.8% in South East Asia and 23% in Eastern Europe (4).

Sharing injection equipment not only threatens the user and his/her partners with HIV infection (5), but also counts as one of the main means of HCV transmission. Numerous interventions have been conducted on reducing high risk behaviors injection equipment sharing (6-9). One of the main interventions to reduce high risk behaviors and the consequence diseases like HIV and HCV among injecting drug users is implementation of harm reduction programs (10, 11).

Harm reduction interventions in the case of substance abuse insist in programs aligned with reducing health, social, and economic risks among patients through needle exchange programs. Main purpose of needle exchange program is to prohibit patients from sharing needle and syringe, provide education regarding safe injection and distribution of condoms, and refer them to methadone maintenance treatment centers, if necessary(12).

Although harm reduction programs have had successful results in controlling injection drug epidemic, this factor has still remained challenging (13-15). Evaluating the effectiveness of harm reduction programs among injection drug users is a necessity to provide more appropriate strategies and prevent HIV and HCV infection among injection drug users. Studies focused on evaluating the effectiveness of harm reduction programs – especially needle exchange programs (NSP) - are often conducted using either cost-effectiveness or efficacy evaluation by modeling approaches (16).

Modeling approach has an important role in evaluating economic and demographic effects on diseases epidemiology, estimating effectiveness of interventions, providing précised information to policy makers in order to make decisions and deal with the challenges ahead and controlling diseases (17-18).

Despite several initial pilot studies on effectiveness of needle and syringe exchange program, results are quite conflicting and different between studies, and there is still no strong evidence on the effectiveness of needle and syringe exchange program in prevention of HIV and HCV infection.

According to some studies, these programs could make changes in high risk behaviors and prevalence of HIV and HCV, while others indicate that such programs are ineffective or have a reverse effect and actually cause high risk behaviors and raise prevalence of HIV and HCV infection (10, 12, 19, and 20).

Providing scientific evidence of a systematic review could assist policy makers and health planners to identify appropriate health policies, better recognition of resources, planning prevention interventions and promoting society health in general. Therefore, a systematic review of HIV and HCV incidence in people who inject drugs, may clarify the underlying causal mechanisms, which can be used to determine priorities in the fields of research and prevention of incidence and prevalence HIV and HCV.

Objective: The objective is to estimate the incidence of HIV and HCV by using studies applying mathematical modeling.

Review question(s):

1. Which models of HIV and HCV incidence consider more inclusive model?
2. What is the incidence of HIV and HCV applying mathematical model in people who inject drugs?
3. What are the parameters of these models, and their implications for the prevention of HIV and HCV incidence in people who inject drugs?
4. What areas need more research?
5. Are mathematical models applied to estimate incidence of HIV and HCV among injection drug users?

Method

This is a protocol to complete a systematic review study. A comprehensive search with Cochrane approach as explained below would be applied to identify relevant studies in electronic databases in the period of 2000 to 2016 according to the search strategy. Studies will be searched in PubMed, EMBASE, OpenGrey, WOS, SCOPUS and Cochrane Library.

Initially, at least two authors will evaluate studies according to title and abstract and the next step would be to evaluate the chosen full texts. Studies that comply with the inclusion criteria will be entered to the review. Then, quality assessment of papers will be done by two authors using two quality assessment tools including Newcastle Ottawa Scale for cross-sectional studies and quantitative studies quality test tool for observational and interventional studies (21). Next step would be to extract required information from studies, and results will be explained in descriptive tables.

Research Population:

All studies that provided mathematical models to estimate incidence of HIV and HCV in people who inject drugs would be entered to the review.

Eligibility criteria (inclusion and exclusion criteria)

Inclusion Criteria:

Inclusion criteria based on PICO's (Cochrane standard) are:

P (Participants or population): Studies with injection drug users as the study population. Any studies that have been done on injection drug users in all settings will be enrolled for review. Therefore, the Drop in Centers (DIC) and stamp grounds will be considered both.

I (Intervention): Studies aimed to determine incidence of HIV and HCV through mathematical models.

C (Comparison): Comparing evaluation of HIV and HCV incidence through mathematical models versus other models.

O (Outcome): Estimate incidence of HIV and HCV among injection drug users based on mathematical models; only studies which were conducted to estimate incidence of HIV and HCV based on mathematical models will be considered to enroll the review.

S: Cohort studies and studies that evaluated effectiveness of mathematical models in estimate of incidence of HIV&HCV in Injecting Drug Users. This systematic review will include all cohort studies, clinical trials, and cross-sectional studies. Since main focus of this study will be on estimate of HIV and HCV incidence through mathematical models, only studies that applied mathematical models in order to evaluate HIV and HCV incidence will be enrolled in the review.

Exclusion Criteria:

Studies with target groups other than injection drug users, qualitative studies and studies with a secondary analysis will be excluded from the review. Also, studies that estimated HIV and HCV incidence directly or through laboratory tests and self-reports will be excluded from the study.

General Objective:

Estimate incidence of HIV and HCV based on mathematical models among injection drug users.

Specific Objectives:

Estimate incidence of HIV based on mathematical models among injection drug users.

Estimate incidence of HCV based on mathematical models among injection drug users.

Information sources

Research Evidence and Search Strategy:

This review will do research to identify relevant studies regarding estimate of HIV and HCV incidence, with high sensitivity without considering any language limitations and publication status (published, unpublished, in press, and in progress). We will consider time limitation for publishing dates of papers; Studies in the period of 2000 to 2016 will be evaluated.

In addition to searching electronic resources like PubMed, EMBASE and Cochrane Library, a manual search will also be conducted to identify studies that are not in the above mentioned database. All results will be downloaded and managed by EndNote software. Duplicate records will be recognized and removed.

Electronic Searches:

In order to identify the most relevant studies on incidence of HIV and HCV in electronic databases, a professional team, with members who are mastered in harm reduction programs and studies conducted on injection drug users will co-operate.

In addition, the integration keywords in keyword databases such as MeSH, Emtree, DeCS will be used.

Various forms of words, synonyms, plural words, abbreviations and acronyms for “distribution of syringe”, “harm reduction”, “effectiveness”, etc... will also be used in the titles and abstracts. Meanwhile, common terms in the field of harm reduction and studies regarding injection drug users will be used. We will also use truncation and keyword combinations like “AND” and “OR” together.

English database search strategy (electronic search strategy) is provided in the attached table. We will modify our search strategy for other databases, applying syntaxes and appropriate words. We will update the search six months ahead of publishing the systematic review paper.

Searching Other Resources:

We will apply below method in aim of identifying the most possible number of relevant researches:

- Search for review studies with relevant titles and their references in the period of 2000 to 2016.
- Electronic search in EMBASE, MEDLINE and CENTRAL.
- Manual search in journals not indexed in MEDLINE and EMBASE.
- Search for clinical trials recorded in valid worldwide clinical trials records.
- Search in the Web of Science.
- Search in the Grey Literature and the Opengrey.
- Contacting the first or corresponding authors of papers regarding harm reduction and addiction via e-mail and kindly request them to provide relevant published and non-published records.
- Manual search in relevant congress abstracts.

Study Selection:

After being identified, studies will be entered to EndNote software. Initial screening will be based on titles and abstracts. The second phase of screening will be according to the check list that matches including

criteria (the check list will consist of three sections: study design, participants and the results).

Questions will be designed for each section based on inclusion criteria. Finally, articles that meet study questions and inclusion criteria will be entered to the review for further evaluation and data extraction.

A pre-determined form, that will be filled out after the evaluation by two of the authors separately, will be used to choose articles.

Full texts of studies that were recognized by both authors as eligible will be procured. Full texts of studies that are recognized eligible only by one author will be evaluated based on inclusion criteria and in case of that further information is needed, we will contact their first or corresponding authors to collect required information. Then, a third author will be consulted, in aim for making final decision regarding whether to or not enroll the article into the systematic review.

Assessing the quality of articles:

Assessment of risk of bias will be implemented using two quality test tools including Newcastle Ottawa Scale for cross-sectional studies and quantitative studies quality test tool for observational and interventional studies

Extraction and Data Management:

Two of the study authors will separately extract data in accordance with the designed form using information provided in articles. Data of papers that only report results of one study will be combined together into one single study. Articles in languages other than English or Persian will be translated into Persian and same earlier mentioned process will be administered on those.

Data extraction will be done through collecting results of relevant studies and recording in the relevant forms. Data collection form includes authors name, type of the study, place of the study, year of publication, study population, number of study samples, and applied Methodology in the study. Ultimately, this Data will be entered into an Excel file 2010 sheet and some tables will be designed and filled accordingly, based on the type of studies.

Method of Analysis:

After completing the data extraction phase, results of the selected papers will be categorized and summarized in descriptive tables. Publication bias will be assessed by funnel plots, Begg's and Egger's tests. Heterogeneity will be evaluated using the I² statistic and the χ^2 test. In addition, subgroup analyses will be conducted for population and the secondary outcomes. All meta-analyses will be performed using Stata V.12 software.

Assessment of heterogeneity:

To assess the viability and meta-analysis feasibility, heterogeneity between studies will be evaluated. For this purpose, the Forest Plots and Chi-Square test and I^2 statistics will be used to assess the level of heterogeneity.

In case the level of interval confidence for evaluating effectiveness overlaps a little among studies, or I^2 statistics is higher than 40% or P Value in Chi-Square test for two heterogeneity is less than 0.1, then there is a heterogeneity between the studies, and it is not possible to conduct meta-analysis, and otherwise it is.

Patient and public involvement

Patients and the public were not involved with the development of this protocol. The results will be published in open-access, peer-reviewed publications.

Discussion

This systematic review will provide an incidence of HIV and HCV in people who inject drugs, using mathematical models. The synthesis of review findings in the present study will assess the limitations of identified studies as well as any limitations in our own review methodology. Once a large volume of studies have been identified as a result of the first search, we will use a multiple reviewer team to minimize the risk of bias. A team of multiplayers is beneficial in reducing the time needed to complete the study. It is expected that the findings of this review will be of interest to physicians, psychiatrists, harm reduction professionals and those who are in contact with injecting drug users. The findings of this review study may also be compared with findings from other studies on this issue. Finally, in the discussion, key findings, study limitations, implications and recommendations for future research and practical/clinical considerations for specialists will be presented.

Declarations

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Contributors ZJS,SA,AS,BA,SaK drafted the protocol. MN, AR commented on and suggested revision to the protocol. All author approved the final revision of the protocol.

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Competing interests None declared.

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Declaration of interest The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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Search Strategy in English Databases:

Titles **Ti:**needle sharing [MeSH Terms] AND HIV [MeSH Terms] OR Models, Theoretical [MeSH Terms] OR HIV Infections [MeSH Terms] OR Injecting Drug Users OR Mathematics [MeSH Terms] OR HCV

Ti: Needle-Exchange Programs [MeSH Terms] AND HIV [MeSH Terms] OR Models, Theoretical [MeSH Terms] OR HIV Infections [MeSH Terms] OR Injecting Drug Users OR Mathematics [MeSH Terms] OR HCV

Ti: syringe exchange programmes AND HIV [MeSH Terms] OR Models, Theoretical [MeSH Terms] OR HIV Infections [MeSH Terms] OR Injecting Drug Users OR Mathematics [MeSH Terms] OR HCV

Ti: syringe exchange

Titles, Abstracts and Keywords **Ti & abs& key:** HIV [MeSH Terms]

Ti & abs& key: Models, Theoretical [MeSH Terms]

Ti & abs& key: [MeSH Terms]

Ti & abs& key :HIV Infections [MeSH Terms]

Ti & abs& key: Injecting Drug Users