Original Paper

A Database of Randomized Trials on the HIV Care Cascade (CASCADE Database): Descriptive Study

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Abstract

Background: The Joint United Nations Programme on HIV/AIDS has set targets for 2025 regarding people living with HIV. For these targets to be met, 95% of people with HIV would need to know their HIV status, 95% of people with HIV would need to be receiving antiretroviral therapy, and 95% of people on antiretroviral therapy would need to be virally suppressed. Some countries are on track to meet these targets. However, within and across countries, several vulnerable populations may not meet these targets. This is in part because several approaches to improving the cascade of care after an HIV diagnosis are not tailored to and are not appropriate for vulnerable populations, such as men who have sex with men, sex workers, people who inject drugs, Black people, people in prisons, women, and youth. To inform research, policy, and practice, there is a need for curated data on HIV care cascade research.

Objective: The CASCADE database is a repository of randomized clinical HIV trials. It was designed to inform, support, and improve HIV care cascade research, systematic reviews, and evidence maps.

Methods: PubMed, Embase, CINAHL, PsycINFO, Web of Science, and the Cochrane Library were searched to obtain randomized trials that were designed to address at least one of the following care cascade outcomes: the initiation of therapy, adherence to medication, retention in care, and engagement in care. Data were screened and extracted in duplicate using DistillerSR software (Evidence Partners Incorporated) and were cataloged based on the following features: year, income level, setting, the delivery of the intervention, the population receiving the intervention, intervention type, and the level of pragmatism of the intervention.

Results: A total of 298 HIV clinical trials are included in the CASCADE database, of which 162 (54.4%) were conducted in high-income countries, and 116 (38.9%) targeted vulnerable populations. Adherence to antiretroviral therapy was the most investigated HIV care cascade outcome (216/298, 72.5%), followed by retention in care (34/298, 11.4%). CASCADE has a user-friendly interface with simple and advanced search features. The CASCADE database has inspired 2 methodological papers and 13,567 website visits from over 10 countries.

Conclusions: CASCADE is the first database dedicated to trials that focus on the HIV care cascade, and it can be used for systematic reviews, evidence maps, and methodological research. It is freely accessible, and the data can be downloaded in CSV format.

Introduction

From 2020 to 2021, about 37.7 million people were living with HIV worldwide, of which 28.2 million were accessing antiretroviral therapy (ART) [1]. Deaths from HIV-related causes have reduced by about 47% in the last decade [1]. People at higher risk of HIV infection, who are also referred to as *key populations* (eg, sex workers, men who have sex with men, people who inject drugs, and transgender people), account for 65% of all HIV infections [1].

Success in curbing morbidity and mortality due to HIV is measured based on the proportion of people achieving key steps in the HIV care cascade. The Joint United Nations Programme on HIV/AIDS (UNAIDS) has set targets for 2025 regarding people living with HIV. It is expected that by 2025, a total of 95% of people living with HIV will know their status, 95% of people who know their status will be on ART, and 95% of people on ART will achieve viral suppression [1]. For countries to meet these goals, targeted policies and interventions are required to enhance the uptake of testing for HIV; engagement in care; adherence to medication; and, ultimately, viral suppression. With close to 40 years of HIV research and innovation, enormous strides have been made toward reaching these targets in many countries [2-4]. However, there are concerns that even if countries meet these targets, stigma, discrimination, and structural barriers may prevent key subpopulations from meeting these targets. For instance, many countries have punitive laws and policies against people living with HIV, and gender inequalities and violence compromise access to care for many [5]. Further, successful research may never be implemented in the real world because the interventions are too complex, resource intensive, or insufficiently tailored [2].

As we strive to ensure that all of the UNAIDS targets are met globally (ie, across countries and within subpopulations), we must understand what needs to be done to ensure that all people living with HIV can meet these targets. Evidence syntheses can help with identifying knowledge gaps and shortcomings from the existing evidence base and highlighting areas where further research is needed [6]. To this end, and as part of an overview of systematic reviews to improve treatment initiation, adherence to ART, and retention in care for people living with HIV [5], we built the CASCADE database.

The CASCADE database [7] was born from efforts to create evidence maps on the HIV care cascade. This database is a "one-stop shop" for randomized trials of interventions that improve the initiation of treatment, adherence to medication, and retention and engagement in care. The database can be used to write literature reviews, conduct systematic reviews, conduct methodological research, create evidence maps, or simply learn about HIV care cascade research.

Methods

Database Implementation

The trials were identified by using a standard evidence synthesis methodology. The first set of trials were identified from an overview of systematic reviews on strategies for improving the HIV care cascade [8,9]. In brief, we searched PubMed, Embase, CINAHL, PsycINFO, Web of Science, and the Cochrane Library for systematic reviews published from 1995 to 2018, including at least 1 randomized trial of an intervention that was designed to improve the initiation of ART, adherence to ART, or retention in care. The second and subsequent sets of trials were identified through targeted searches for trials on the HIV care cascade that were published in the same databases from 2018 to August 2021. Only trials that were published as full texts and had participants who were people living with HIV that reported at least 1 care cascade outcome were eligible. All retrieved searches were deduplicated. Screening and data extraction were conducted in duplicate using DistillerSR software (Evidence Partners Incorporated).

The database is composed of 1 back-end table, which includes the following data: year, income level, the vulnerable population of focus, who delivered the intervention, the setting in which the intervention was delivered, the intervention type, and the level of pragmatism of the intervention (ie, how close it is to real-world care). The vulnerable population, who delivered the intervention, the setting of the intervention, and the intervention type are not mutually exclusive (ie, trials may belong to more than 1 category).

Database Functionalities

Simple Search

The simple search function identifies any key words in the title or abstract, including author and journal names.

Advanced Search

The advanced search function allows users to filter the results of a search based on the following features:

- Year: The platform allows the user to specify a start year and end year for the search and is based on the year of publication of the trial.
- Income level: This drop-down menu allows the user to select trials from countries with different income levels, as
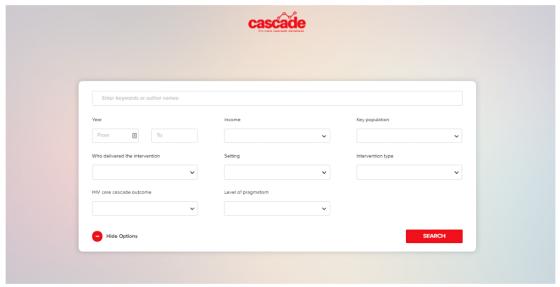
defined by the World Bank, and includes high-income, upper-middle–income, low-middle–income, and low-income countries [10]. There is also a mixed category for studies conducted in multiple countries with different income levels.

- Key population: Trials are organized according to whether they primarily included people from any key population (ie, African, Caribbean, or Black people; commercial sex workers; men who have sex with men; prisoners; people who inject drugs; women; and youth).
- The person who delivered the intervention: The database distinguishes among trials of interventions delivered by clinicians, lay workers, or peers.
- The setting: Trials may be for interventions delivered in a clinic or community-based setting.

- Intervention type: A variety of intervention types are included, such as changes in health care delivery, counseling, education, electronic interventions, incentives, mobile health, outreach, peer navigation or support, and psychotherapy.
- Care cascade outcome: Users may select 1 of 4 care cascade outcomes—the initiation of treatment, adherence to ART, retention in care, and engagement in care.
- Level of pragmatism: The level of pragmatism—a measure of how well a trial matches usual care—was determined for each trial by using the RITES (Rating of Included Trials on the Efficacy-Effectiveness Spectrum) tool [11]. Trials may be situated along a continuum ranging from having a strong emphasis on efficacy to having a strong emphasis on effectiveness.

The layout of the advanced search page is shown in Figure 1.

Figure 1. Image of the advanced search layout on the CASCADE website.

Tips

On the tips page, we display information on how to use the database and the types of trials that are included in each category. The layout of the tips page is shown in Figure 2.

Figure 2. Image of available tips on the CASCADE website.

User Interaction

All of the trials have hyperlinks that take users to the PubMed page or journal page of the identified articles. Search results can also be downloaded as a CSV file. Users are encouraged to suggest studies that could be added by emailing hccd@mcmaster.ca.

Results

As of December 30, 2021, CASCADE includes 298 HIV clinical trials that were published between 2015 and 2021. About half of these trials were conducted in high income countries (n=162, 54.4%), and 116 (38.9%) focused on a vulnerable population. About half of the interventions were delivered exclusively by clinicians (158/298, 53%) and were clinic-based interventions (173/298, 58.1%). The most frequent types of interventions were combinations (136/298, 45.6%), and adherence was the most common HIV care cascade outcome (216/298, 72.5%). About half of the trials (136/298, 45.6%) had a balanced emphasis on both efficacy and effectiveness. The key features of the trials in the database are outlined in Table 1.

In addition to the protocol for the overview of systematic reviews and the published overview [7,8], the CASCADE database has inspired 2 methodological papers. The first is an assessment of how HIV pilot studies are conducted [12], and the second evaluates the virological measures used in HIV clinical trials [13].

In the last year, as of June 24, 2022, the database has had 13,567 visits, with most visitors accessing the database from the United States, Canada, Singapore, Germany, the United Kingdom, China, Ireland, France, Lithuania, and the Netherlands.

Table 1. Characteristics of trials in the CASCADE database (N=298).

Variable	Trials, n (%)
Income level	
High	162 (54.4)
Upper middle	51 (17.1)
Low middle	39 (13.1)
Low	31 (10.4)
Mixed	15 (5)
Population	
General population of people with HIV	185 (61.1)
Vulnerable population	116 (38.9)
The people who delivered the intervention	
Clinicians exclusively	158 (53)
Laypersons exclusively	45 (15.1)
Peers exclusively	25 (8.4)
Combinations	70 (23.4)
Setting of intervention	
Clinic-based intervention	173 (58.1)
Community- and clinic-based intervention	44 (14.8)
Community-based intervention	46 (15.4)
Other	35 (11.7)
Type of intervention	
Changes in health care delivery	40 (13.4)
Counseling	36 (12.1)
Education	13 (4.4)
Incentives	9 (3)
Mobile health	34 (11.4)
Outreach	4 (1.3)
Peer navigation or support	9 (3)
Psychotherapy	17 (5.7)
Combinations of any types of interventions	136 (45.6)
Care cascade outcome	
Adherence	216 (72.5)
Retention	34 (11.4)
Engagement	8 (2.7)
Initiation	14 (4.6)
More than 1 cascade outcome	26 (8.7)
Level of pragmatism	
Strong emphasis on efficacy	1 (0.3)
Rather strong emphasis on efficacy	35 (11.7)
Balanced emphasis on both efficacy and effectiveness	136 (45.6)
Rather strong emphasis on effectiveness	80 (26.8)
Strong emphasis on effectiveness	46 (15.4)

Discussion

Principal Findings

CASCADE is a database of 298 HIV clinical trials that were published between 2015 and 2021. With 13,567 visits as of June 24, 2022, it is a widely used resource for clinical trials on the HIV care cascade. We plan to update the database on a semiannual basis, and we will continue to develop it based on user feedback. Updates will include formal searches for new trials and previously unpublished trials, and we will contact the authors of the included trials to suggest additional trials. Additional information that could be added for each trial include a detailed description of the intervention based on the TiDieR (Template for Intervention Description and Replication) checklist [14], risk of bias assessments, the indication of whether the study is a pilot study or a full trial, graphical displays, and other features. We will also validate the completion of the database against future systematic reviews. Further development is contingent on user interest and resources.

Comparison to Prior Work

To the best of our knowledge, there is no other database dedicated to randomized trials of the HIV care cascade. Other existing HIV databases either store data on the prevalence and incidence of HIV [15] or are dedicated to storing HIV genetic sequences [16,17]. Within the Cochrane Library, the Cochrane Controlled Register of Trials can be used to identify completed published and unpublished randomized trials, and ongoing trials.

Specific filters can be applied to identify HIV trials. However, these trials are not categorized by the following: income level, the vulnerable population of focus, who delivered the intervention, the setting in which the intervention was delivered, the intervention type, and the level of pragmatism of the intervention [18].

Limitations

We faced challenges in categorizing trials that were not accessible as full texts, either because they were only published as conference abstracts or because the full texts were not available through our institutional libraries and the interlibrary loan system. We will continue to seek these full-text articles to include and curate these trials. Further, as this database is focused on the HIV care cascade, it does not include research on preventive interventions, such as pre-exposure prophylaxis and postexposure prophylaxis.

Conclusion

CASCADE is the first database dedicated to trials on the HIV care cascade. It includes information that can be used to learn about interventions, supplement systematic reviews, create evidence maps, and conduct methodological research. By looking at the bigger picture, this database can help researchers explore the similarities and differences among HIV clinical trials that may help explain why some interventions are more successful than others, highlight knowledge gaps, and inform future research.

Authors' Contributions

LM and DJ wrote the first draft. All other authors (GZ, HE-K, NR, MY, MCG, VA, BZ, AL, MW, and OM) reviewed subsequent drafts and approved the final version.

Conflicts of Interest

None declared.

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Abbreviations

ART: antiretroviral therapy
RITES: Rating of Included Trials on the Efficacy-Effectiveness Spectrum
TiDieR: Template for Intervention Description and Replication
UNAIDS: Joint United Nations Programme on HIV/AIDS

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