

Abstract

Human immunodeficiency virus (HIV) is a retrovirus that disrupts immune function and is often considered a sexually transmitted infection. Due to HIV's effects on the immune system, persons living with HIV (PLWH) are typically at a greater risk of acquiring other infectious diseases (IDs). Additionally, PLWH can experience adverse effects to common HIV treatment methods. Based on the relationship between HIV and other infectious diseases, this study aimed to identify inclusion and exclusion trends of infectious diseases in HIV clinical trials. This study identified 6118 terms related to IDs with 4461 (72.92%) found within the exclusion criteria of HIV clinical trials. A subsequent analysis identified hepatitis-related terms to be a major contributor to the exclusion frequency and rate. Hepatitis terms accounted for 2288 (51.29%) of all exclusion terms and yielded an 80.11% exclusion rate in HIV clinical trials. Contrarily, herpes-related terms were identified in lower volumes and with a more substantial inclusion rate (58.28%). Based on the collected data, this study identified a significant difference between the inclusion and exclusion data which indicates a greater need for the inclusion of IDs, specifically hepatitis-related infections, in HIV clinical trials.

Background

Human immunodeficiency virus (HIV) is a retrovirus that disrupts immune function, increasing the risk of infectious disease for many persons living with HIV (PLWH). HIV is especially problematic in those with hepatitis viruses. Research shows that HIV accelerates hepatitis C virus (HCV) infection and can cause hepatotoxicity if PLWH and concomitant HCV are treated with highly active antiretroviral therapy (HAART) (Rockstroh et al., 2004, 437). Hepatotoxicity has also been identified in PLWH and concomitant hepatitis B virus (HBV), yet very little data exist regarding HIV and HBV co-infection (Hoffman & Thio, 2007, 402), indicating that alternative treatment methods have not been explored thoroughly for PLWH with comorbid hepatitis infections.

While HIV and hepatitis co-infections tend to reduce treatment efficacy in PLWH, other infectious diseases aren't impacted as severely. For example, combined antiretroviral therapy (cART) may reduce the incidence of herpes zoster in PLWH, though herpes zoster increases the risk of HIV acquisition four-fold (Erdmann et al., 2018, 70). Herpes simplex, on the other hand, is estimated to increase HIV risk by three times, although combination treatments like cART are deemed more of a necessity than a liability, as exhibited in hepatitis co-infections (Looker et al., 2020, 240).

Overall, it's clear that the immunosuppressant effects of HIV can increase the risk of other infectious diseases. Even so, treatment efficacy tends to vary based on the pathophysiology of the co-infection. Given the increased prevalence of co-infections and that most co-infections require combination treatments, it's important for clinical trials to target these populations to reduce the rate of mortality and prevent adverse treatment effects as those found in PLWH with comorbid hepatitis (Hoffman & Thio, 2007; Rockstroh et al., 2004, 437).

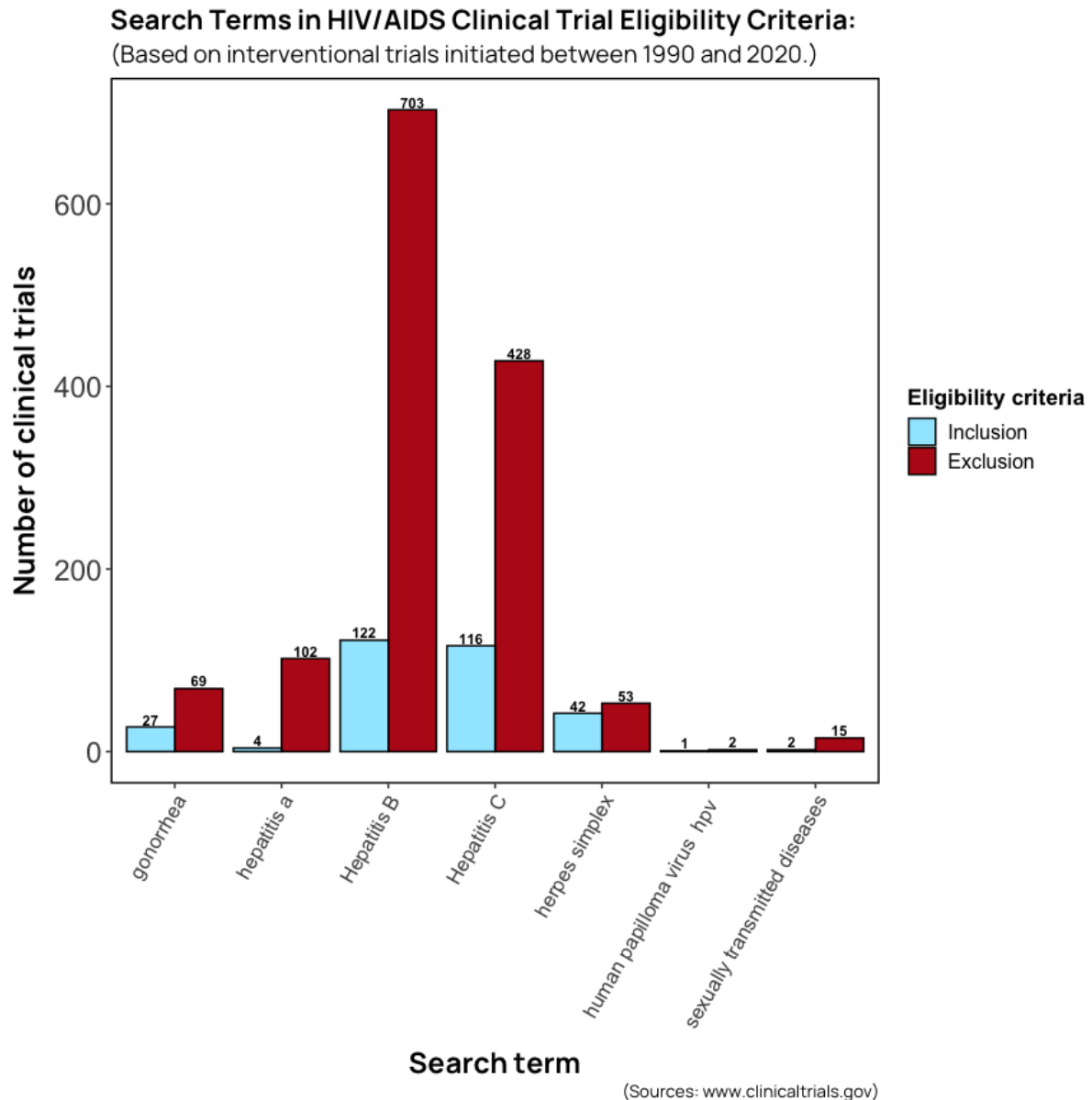
Methods

The aim of this study was to identify trends within the inclusion and exclusion frequencies of infectious disease terms in HIV clinical trials to identify any potential disparities. Using clinicaltrials.gov, researchers extrapolated data from all completed interventional trials from 1990 until 2022 using Python 3.9.10. All terms were collected and tallied for inclusion and exclusion frequencies to assess the proportional relationship independently and collectively. After collecting and organizing all data, a secondary analysis was conducted using Microsoft Excel to include a t-test paired for two sample means, regression analysis, and Pearson correlation. The inclusion and exclusion frequencies of the most voluminous infectious disease terms are represented in Table 1 while the proportional distribution of hepatitis terms is presented and compared to other IDs in Figure 1.

Table 1. Inclusion and exclusion frequencies of the most common IDs identified in HIV clinical trials.

Infectious Disease Term	Inclusion Frequency	Exclusion Frequency	Total Frequency	Inclusion Rate
Hepatitis	234	1033	1267	0.184688239936859
AIDS	503	755	1258	0.399841017488076
Hepatitis b	199	711	910	0.218681318681319
Hepatitis c	130	431	561	0.231729055258467
Infections	161	360	521	0.309021113243762
Tuberculosis	43	330	373	0.115281501340483
Pneumonia	146	104	250	0.584
Hepatitis a	5	102	107	0.0467289719626168
Gonorrhea	28	69	97	0.288659793814433
Meningitis	8	60	68	0.117647058823529

Figure 1. Comparison of inclusion and exclusion frequencies and proportions of hepatitis viruses compared to other IDs in HIV clinical trials.



Results and Discussion

The results of this study identified that the overall inclusion rate of IDs in HIV clinical trials was insufficient although some conditions were represented more proportionally than others. In total, 6118 terms related to IDs were found within the inclusion and exclusion criteria of HIV clinical

trials with 4461 (72.92%) excluded and 1657 included (27.08%). IDs were collectively 2.63 times more likely to be excluded from HIV clinical trials. These data were statistically significant based on regression analysis ($p < .001$) and t-test significance ($p < .01$). Additionally, a large effect was identified via Pearson correlation (0.8462). While the data analysis indicated a clear disparity between the inclusion and exclusion of IDs in HIV clinical trials, it would be naive to ignore the independent data showing higher inclusion rates of IDs such as herpes (51.29%), pneumonia (58.4%), bacterial infections (58.82%), AIDs (39.98%), and general infectious diseases (51.61%). The most concerning disparities existed for hepatitis (2288 terms, excluded 80.11%) and tuberculosis (373 terms, excluded 88.5%).

In conclusion, this study identified a substantial difference between the inclusion and exclusion terms of IDs in HIV clinical trials. Previous research has substantiated the prevalence, risk, and importance of IDs in PLWH (Hoffman & Thio, 2007; Rockstroh et al., 2004, 437) yet notable disparities still exist in the representation of IDs in HIV clinical trials. Moving forward, a greater emphasis should be placed on the inclusion of IDs like hepatitis in HIV clinical trials to improve treatment outcomes and reduce the incidence of adverse effects related to combined treatments.

References

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