

## Abstract

Hypertension is a major risk factor for cardiovascular disease and various other comorbidities. Similarly, both bacterial and viral infections have established relationships with hypertension, though those relationships are dependent on each individual infection. This study aimed to determine if the current body of clinical trials has sufficiently researched the effects of treatment on patients living with hypertension and infectious diseases (IDs) by analyzing the inclusion and exclusion of ID terms in hypertension clinical trials found on [clinicaltrials.gov](https://clinicaltrials.gov). This study revealed an overwhelming disparity regarding the inclusion of IDs in hypertension clinical trials, with 83.67% of ID terms found within the exclusion criteria of hypertension clinical trials. Researchers identified a significant difference ( $p < .001$ ) between the inclusion and exclusion of ID terms in hypertension clinical trials via regression analysis. Based on the results of this study, it's evident that researchers should prioritize the inclusion of infections in hypertension clinical trials to optimize treatment outcomes in patients living with hypertension and concomitant infection(s).

## Background

Hypertension is a primary risk factor for cardiovascular disease (CVD) and numerous other comorbidities. In many instances, hypertension has also been associated with an increase in the prevalence or severity of bacterial and viral infections, although that effect varies per each individual infection. For example, hypertension may actually reduce the likelihood of COVID-19 while increasing the severity of acquired infections in hypertensive persons (Li et al., 2021). While COVID-19 is still a relatively new viral infection, hypertension has been consistently reported as a predictor of poor treatment outcomes in COVID patients (Basu et al., 2021, e047561). Other infections, such as *H pylori* bacterial infection, may also increase the prevalence of hypertension (Xiong et al., 2020, 1389). COVID-19 and *H pylori* represent a fraction of infections that can influence hypertension incidence.

While the pathophysiology of hypertension and infectious diseases (IDs) tend to be drastically different, some concerns may exist regarding treatment modalities, especially in those with numerous conditions or diseases. For example, COVID-19 directly impacts the renin-angiotensin system, specifically angiotensin-converting enzymes (ACE), thus disrupting blood pressure regulation and contributing to glomerulopathy, affecting kidney function (Savedchuk et al., 2022, 1618) which could influence treatment methods. Overall, ACE inhibitors traditionally used to treat blood pressure do appear to be safe in COVID-19 patients, though this may not be true for all IDs (Tieyeh et al., 2022, e74). Overall, it's important to ensure that researchers investigate the efficacy of co-treatments in unique cases such as hypertension and concomitant IDs.

## Methods and Results

This study aimed to determine the proportional inclusion and exclusion of IDs in hypertension clinical trials. Researchers used all completed interventional clinical trials from 1990 to 2022 available on the national clinical trials repository, [clinicaltrials.gov](https://clinicaltrials.gov), to analyze the inclusion and exclusion frequency of IDs in hypertension clinical trials. Data was collected and organized using Python 3.9.10 to reflect the frequency of inclusion and exclusion for each respective infection term. All data were subsequently organized and analyzed using Microsoft Excel to identify patterns within the data and to conduct a regression analysis. Table 1 represents the leading ID terms found within hypertension clinical trials which is further illustrated in Figure 1.

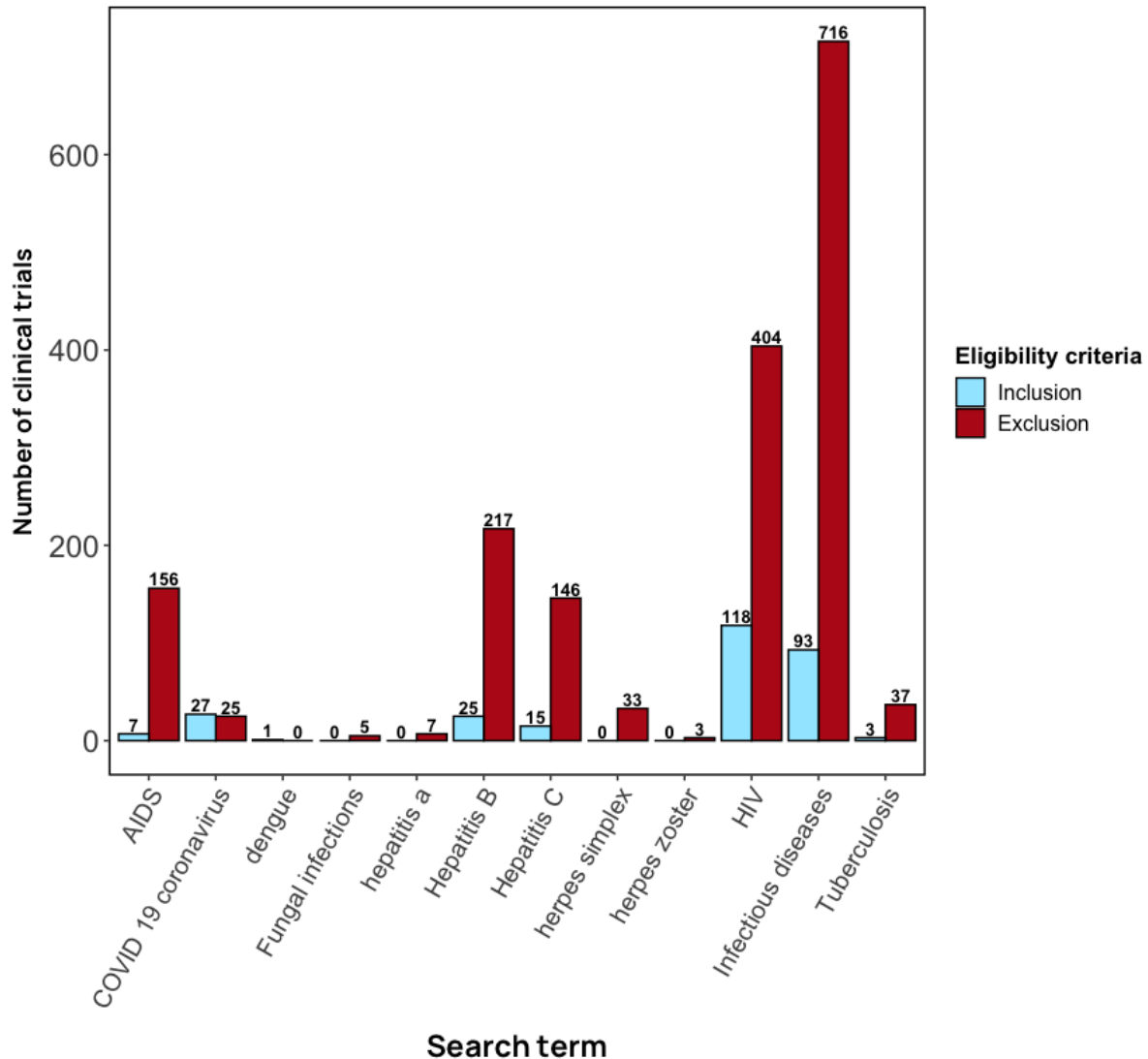
Table 1. Inclusion and exclusion frequencies of the most common IDs and the respective inclusion rates in hypertension clinical trials.

| Term                | Inclusion | Exclusion | Total | Inclusion Rate |
|---------------------|-----------|-----------|-------|----------------|
| Infection           | 126       | 586       | 712   | 17.70%         |
| Hepatitis           | 37        | 228       | 265   | 13.96%         |
| Infections          | 5         | 87        | 92    | 5.43%          |
| Conjunctivitis      | 8         | 48        | 56    | 14.29%         |
| Autoimmune diseases | 3         | 41        | 44    | 6.82%          |
| Tuberculosis        | 4         | 36        | 40    | 10.00%         |
| Herpes simplex      | 4         | 25        | 29    | 13.79%         |
| Pneumonia           | 16        | 23        | 39    | 41.03%         |
| Aids                | 6         | 16        | 22    | 27.27%         |
| Infectious diseases | 2         | 16        | 18    | 11.11%         |
| Immunosuppression   | 6         | 11        | 17    | 35.29%         |
| Meningitis          | 1         | 6         | 7     | 14.29%         |

Figure 1. Comparison of inclusion and exclusion frequencies of renal-related terms in hypertension clinical trials.

### Search Terms in Hypertension Clinical Trial Eligibility Criteria:

(Based on interventional trials initiated between 1990 and 2020.)



(Source: [www.clinicaltrials.gov](http://www.clinicaltrials.gov))

### Results and Discussion

Hypertension is a notable cardiovascular condition with established relationships to numerous IDs. This study found an overwhelming and statistically significant difference between the inclusion and exclusion of ID terms in hypertension clinical trials. Of 1378 ID terms, 1153 (83.67%) were excluded from hypertension clinical trials, yielding a mere 16.33% inclusion rate. Of these terms, “infection”, “hepatitis”, and “infections” were excluded the most frequently and with comparable inclusion rates of 17.7%, 14.0%, and 5.4%, respectively. Of all terms, “pneumonia”, “AIDS”, and “immunosuppression” were included at the highest rate at 41.0%,

27.3%, and 35.3%, respectively. All terms were collectively analyzed by inclusion and exclusion frequency via regression analysis which found a significant difference ( $p < .001$ ) between these frequencies.

Overall, it's clear that there have been historical disparities regarding the inclusion of IDs in hypertension clinical trials. Previous research has established clear relationships between the prevalence and magnitude of hypertension and various IDs which prompts the need for clinical trials in patients with concomitant conditions. Future clinical trials should actively consider the inclusion of IDs in hypertension clinical trials to balance the current disproportions and improve treatment outcomes.

### **References**

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