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## Mini Review

### **DRUG RESISTANCE MAY ACCELERATE AN HIV EPIDEMIC AS SHOWN BY THE NESTED MODEL**

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#### **ABSTRACT**

The most effective strategy for controlling the HIV epidemic is the use of antiretroviral therapy (ART). However, the emergence of drug-resistant strains may diminish ART's potential advantages. Individually, the viral dynamics of drug-sensitive and drug-resistant strains may play a significant role in the development and spread of drug resistance in a population. Using a nested model that connects both dynamical levels, we investigate how an infected person's viral dynamics affect the HIV epidemic's dynamics. An epidemiological model of HIV incorporates a time-dependent transmission rate between hosts that receives feedback from a model of two-strain virus dynamics within a host. Model parameters like the time at which ART is initiated, the percentage of cases treated, and the likelihood that a patient develops drug resistance have the greatest impact on total infection and the prevalence of drug resistance, according to our analysis of the model's resulting dynamics.

**Keywords:** HIV; Drug-resistant; epidemiological model

#### **INTRODUCTION**

Importantly, increasing the percentage of cases treated can increase the total number of infected individuals for small values of the risk of a patient developing drug resistance. This pattern is the result of striking a balance between treating a patient and increasing the likelihood of subsequent (untreatable) drug-resistant infections if the patient is not treated. An epidemic model takes into account significant aspects of virus dynamics within a host with the current modeling framework. In order to determine the most effective way to use antiretroviral therapy (ART), this strategy provides useful insights into the dynamics of drug resistance during an epidemic of HIV. There were approximately 34 million people worldwide who were infected with the human immunodeficiency virus (HIV) at the conclusion, and there were an estimated 2.7 million new infections. since antiretroviral therapy and preventative measures have prevented an estimated 2.5 million deaths in low- and middle-income nations. Approximately 47% of eligible HIV-positive individuals in low- and middle-income countries receive ART, and several countries have achieved universal coverage. Because it reduces transmissibility and slows disease progression, ART is a crucial epidemic intervention. It also increases survival rates. Alternative cost-effective treatment strategies are constantly being evaluated, despite the fact that HIV-infected patients have clear

treatment eligibility recommendations; for instance, providing at-risk populations with frequent HIV testing and prompt treatment [1-3].

## **DISCUSSION**

If therapies lose effectiveness due to inappropriate drug use, significant investments in drug development may be undermined; Drug resistance can develop wherever inappropriate use occurs, which has consequences for patients everywhere. An instructive illustration of this is the evolution of drug resistance in malaria. Antifolate medications became widely used as a result of this, and resistance to them soon developed. Artemisinin-based medications, which are currently the most widely used first-line treatment for malaria, are on the verge of repeating this pattern. Multiple first-line treatments for malaria are still almost never used, in part because of worries about higher costs for supply chains and programs. Global policy inaction on this issue is a result of the absence of rigorous analysis comparing the benefits and operational costs of using multiple drugs.

Numerous mathematical modeling studies have attempted to comprehend the impact of using multiple therapies simultaneously in a population on the emergence and spread of drug resistance in response to concerns about the evolution of drug resistance and the global health threat it poses. These studies have demonstrated that the development of drug resistance is slowed and delayed when a greater number of therapies (drugs) are administered to the population at the same time. This is primarily due to two factors: a) the low short- and long-term drug-specific selection pressure brought on by the abundance of drugs on the market; and b) the slower degradation of the mean fitness of the parasite population, which makes it more difficult for new types of resistance to enter and spread. In addition, the practice of administering multiple medications concurrently enables a greater proportion of the population to be treated without compromising the ability to treat cases that may be untreatable due to high resistance levels in the future.

Despite the fact that these studies demonstrate that increasing drug variety slows the emergence and spread of drug resistance, it also results in increased operational costs. In the pharmaceutical industry, volume discounts are a common practice. This means that more kinds of drugs for the same disease would cost more per unit. Also, when demand is uncertain, a wider range of drugs for a particular disease means more safety stocks, which means more money spent holding inventory. In contrast, there is a demand variability pooling effect that allows one to hold less safety stock in order to maintain the same level of customer (patient) service when all patients are treated with the same drug. For a given number of sourced treatments, an increased drug variety increases the cost of acquiring the drugs, the cost of holding inventory, and, in some cases, the cost of training healthcare workers. When multiple drugs are used to treat a specific disease, this study examines the tradeoff between risk of drug resistance and operational costs [4-6].

## **CONCLUSION**

Following the development of drug resistance as a result of the use of a single antiretroviral, ART was implemented. The virus's rapid replication rate and absence of proofreading mechanisms favor drug-resistant (DR) strains, which can replicate in the presence of drugs. Suboptimal antiviral therapy and incomplete therapy adherence are the primary predictors of acquired drug resistance. Approximately 20% of patients fail to respond to first-line antiretroviral therapy, with DR strains prevailing in the majority of cases.

Despite the fact that the virus typically suffers from drug resistance, DR strains can still be transmitted to ART-naïve individuals. After starting ART, DR prior to treatment is associated with virological failure (Hamers et al., 2011a). Prevalence of drug resistance is directly impacted by ART coverage: In Europe and the United States, the prevalence of transmitted drug resistance ranges from 9 to 15 percent, while it is only 5.6 percent in Sub-Saharan Africa. Because a DR strain may persist in a patient for several years without the selective pressure of ART, transmitted DR is a concern because it may result in virological failure when treatment begins. Latently infected CD4+ lymphocytes and viral mutations are plausible mechanisms for maintaining the persistence of DR, even if a wild-type (drug-sensitive, DS) strain replaces the DR strain as the more prevalent virus. The majority of studies that analyze the epidemic dynamics of drug resistance using mathematical models have omitted this potential impact of transmitted drug resistance, with the exception of the study by Little et al. The distinction between transmitted and acquired drug resistance is ignored in these models, which tend to assume that a person can become drug resistant or drug sensitive depending on their treatment status; Therefore, the risk of developing drug resistance during the administration of ART is the same whether the patient was initially infected with a DS strain or with DR and reversed to DS.

We investigate the impact of treatment-related variables like ART coverage and the timing of ART start-up on an HIV epidemic and drug resistance dynamics using a novel mathematical modeling framework. An age-of-infection epidemiological model is used, with random mixing and a homogeneous population. In accordance with the general framework of nested models, a within-host model of two-strain viral dynamics provides the epidemic model with feedback regarding infectiousness and infectious period. It also takes into account the alteration in infectiousness that occurs during each of the three stages of HIV infection. Importantly, the model assumes that individuals receiving ART may or may not develop drug resistance; however, if the initial infection was with the DR strain, the DR strain would always be selected during ART. It is reported that epidemic outcomes like cumulative infections and DR prevalence are influenced by both within-host parameters, such as the fitness cost of drug resistance, and between-host parameters, such as ART coverage. The impact of ART efficacy and its initiation at the individual level on between-host transmission rates and infectious periods, for example, can be incorporated into an epidemic by the current modeling framework.

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