ATENÇÃO: Este modelo **NÃO** representa uma prova integral, apenas parte dela.

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CENTRO DE LÍNGUAS – EXAME DE PROFICIÊNCIA EM LÍNGUA INGLESA
IB
MARÇO/2019

Nome:

RG:

Assinatura:

DOUTORADO

PARTE II: SOMENTE PARA CANDIDATOS AO DOUTORADO

- Responda em **INGLÊS**.
- **NÃO** copie trechos do texto ou a questão será **ANULADA**.
- O critério de correção avaliará:
  - Estruturas gramaticais;
  - Coerência;
  - Vocabulário;
  - Pertinência ao assunto proposto.
  - Esta questão **vale de 0 a 10 pontos**.
- Observação:
  - A Parte I possui peso 2 e a Parte II possui peso 1.
  - A **Nota Final** será a média ponderada das duas provas (Parte I e Parte II):

$$\mathbf{NF = \frac{(Parte\ I \times 2) + (Parte\ II \times 1)}{3}}$$

Nested Model Reveals Potential Amplification of an HIV Epidemic Due to Drug Resistance

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Disponível em : www.elsevier/locate/epidemics

By the end of 2010, there were around 34 million people living with human immunodeficiency virus (HIV) worldwide, with an estimated 2.7 million new infections in 2010 alone (UNAIDS, 2011). Since 1995, an estimated 2.5 million deaths had been averted in low- and middle-income countries by implementing prevention measures and using antiretroviral therapy (ART) (UNAIDS, 2011). ART coverage in low- and middle-income countries is around 47% of eligible people living with HIV, with several countries achieving universal coverage (UNAIDS, 2011). ART represents a crucial epidemic intervention since, besides slowing down disease progression and increasing survival periods, it decreases transmissibility (Cohen et al., 2011). Although there are clear recommendations available for treatment eligibility of HIV-infected patients (World Health Organization, 2010), alternative cost effective treatment strategies are constantly under evaluation; for instance, frequent HIV testing of at-risk population with immediate administration of treatment (Granich et al., 2012).

ART was implemented after the use of a single antiretroviral (zidovudine in 1987) led to the emergence of drug resistance (Clavel and Hance, 2004). Drug-resistant (DR) viruses, strains that have the ability to replicate in the presence of drugs, are favored by the fast replication rate of the virus and its lack of proofreading mechanisms (Margeridon-Thermet and Shafer, 2010). The main predictors for acquired drug resistance are suboptimal antiviral therapy and incomplete therapy adherence (Bangsberg et al., 2006). It has been estimated that first-line ART fails to suppress viremia in around 20% of patients, with DR strains present in the majority of cases (Barth et al., 2010).

Although drug resistance normally carries fitness costs for the virus, DR strains are transmitted even in ART-naïve individuals (Hué et al., 2009). Pretreatment DR is associated with virological failure after ART is initiated (Hamers et al., 2011a). Drug resistance prevalence is directly influenced by ART coverage: the prevalence of transmitted drug resistance is around 9- 15% in Europe and USA and around 5.6% in Sub-Saharan Africa (Hamers et al., 2011b). Transmitted DR is a concern as a DR strain may persist in a patient for several years without the selective pressure of ART (Jain et al., 2011; Little et al., 2008) and may lead to virological failure when treatment starts (Wittkop et al., 2011). Even if a wild-type (drug-sensitive, DS) strain replaces the DR strain as the more abundant virus, latently infected CD4+lymphocytes (Richman et al., 2009) and viral mutations (Bonhoeffer and Nowak, 1997) are feasible mechanisms for sustaining the persistence of DR. Most studies, using mathematical models for the analysis of epidemic dynamics of drug resistance, have omitted this potential impact of transmitted drug resistance (Baggaley et al., 2006; Blower et al., 2005; Sánchez et al., 2005; Smith et al., 2010; Wagner and Blower, 2012) — a notably exception is the study by Supervie et al. (2011). These models tend to assume that an individual can develop drug resistance or reverse to drug sensitive, depending on treatment status, but the difference between transmitted and acquired drug resistance is ignored; thus the risk of developing drug resistance when ART is administered is the same regardless of being initially infected with a DS strain or being originally infected with DR and reversed to DS.

Using a novel mathematical modeling framework, we study the impact of treatment-related variables such as ART coverage and timing when ART is initiated, on an epidemic of HIV and on drug resistance dynamics. An age-of-infection epidemiological model, with homogeneous population and random-mixing, is employed. The epidemic model receives feedback, in terms of infectiousness and infectious period, from a within-host model of two-strain viral dynamics following the general framework of nested models (Mideo et al., 2008). It also incorporates the change in infectiousness in each of the three stages of HIV infection.

Importantly, the model assumes that individuals receiving ART may or may not develop drug resistance but the DR strain would always be selected during ART if initial infection was with DR strain. The effect of both within-host parameters, e.g., the fitness cost of drug resistance, and between-host parameters, e.g., ART coverage, on epidemic outcomes such as cumulative infections and DR prevalence are reported.

According to the text ***Nested Model Reveals Potential Amplification of an HIV Epidemic Due to Drug Resistance****, the HIV epidemic could grow due to drug use. Discuss this point of view by presenting the arguments used in the text. Write between 90 to 100 words.*

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