

Research Article

Bleaching and Withdrawal: A Modeling Approach for Assessing the Role of Bleaching and Individual Withdrawal on Controlling HIV among Intravenous Drug Users

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Abstract

Bleaching of syringes has been advocated to prevent HIV transmission among injection drug users (IDUs). In this paper, a simple mathematical model is developed to assess the role of bleaching and individual withdrawal on controlling HIV among intravenous drug users. A threshold dimensionless quantity known as the reproductive number (R_0) has been derived and qualitatively used to assess the impact bleaching and individual withdrawal of symptomatic HIV carriers (from drug injection misuse activity) on controlling HIV epidemic among intravenous drug users. Latin Hypercube Sampling has been used to assess the amount and type of change inherent in the model as captured by the terms that define the (R_0). At best this study suggests that bleaching is more effective on controlling HIV among intravenous drug users compared to withdrawal of symptomatic HIV carriers from drug injection misuse activity. Furthermore, the study suggest that, the use of antiviral drugs can substantially reduce the rate at which individuals progress to full blown AIDS, thereby increasing the life expectancy of individuals within the community.

Keywords: HIV; Intravenous drug users; Bleaching; Withdrawal; Reproductive number; Sensitivity analysis

Introduction

Injection of illicit drugs is a key pathway for the transmission of HIV, and is the primary mode of transmission in certain regions, such as Eastern Europe, Russia and south Asia. For instance, in Russia more than 90% of new HIV infections are caused by this type of exposure, and 37% of injecting drug users (IDUs) are believed to be HIV positive [1,2,3]. Worldwide estimates suggest that as many as 3 million IDUs are HIV positive, [1] and that injection of illicit drugs has contributed substantially to wider morbidity and mortality [2]. The first recognizable HIV outbreak in China occurred among injecting drug users (IDUs) in the city of Ruili, Yunnan province in 1989 [4], following which the epidemic rapidly expanded throughout Yunnan and neighboring provinces. By 2009, an estimated 740,000 people were infected with HIV in China, including 105,000 with AIDS [5]. The strategy of disinfecting syringes to prevent HIV emerged in California in the 1980s. East Coast epidemics among IDUs (especially in New York) made public health officials fear that HIV would be a major threat to California IDUs [6,7]. Although, bleaching have been encourage for more than twenty years, several studies are demonstrating high HIV prevalence among IDUS [1,2,3]. In 2002, over a decade after the epidemic commenced, needle and syringes programs (NSPs) were initiated by various agencies throughout China as a harm reduction strategy. Despite the large investment in NSPs, it is estimated that less than 25% of IDUs in Yunnan obtain their injecting equipment through NSPs [8,9] and rates of sharing of injecting equipment remains as high as 45% [10]. NSPs have been shown to be a safe and effective means to reduce HIV transmission in some developed and developing country settings [11-17].

If it is done carefully and thoroughly, disinfection can reduce the amount of live HIV in a syringe [6]. However, the repeated use of needles and syringes necessarily compromises their sterility and safety. The aim of this paper is to use a simple mathematical model to assess the role of bleaching and individual withdrawal on controlling HIV among intravenous drug users.

A Mathematical Framework and Approach

Based on epidemiological status, the population of injection drug users is sub-divided into the following subgroups: Susceptible (S), newly-infected individuals in primary or acute sero-conversion stage (P) (less than 28 days of infection), symptomatic HIV carriers (I), and AIDS stage (A). Thus, the total population is given by, N = S + P + PI + A. The susceptible population is increased by the recruitment of individuals (assumed susceptible) into the population through peer pressure, self motivation or any other reasons at rateA. Susceptible individuals are infected with HIV through sharing contaminated needles or syringes at rate $\lambda = \frac{\beta(1-\theta)[P+\eta(1-q)]}{\beta}$, where β is the $\overline{N}-qI$ probability of getting infected whenever a susceptible individual uses a contaminated needle, syringe or any other tools that might be used to share intravenous drugs, $0 < \eta < 1$ accounts for the relative infectiousness of symptomatic HIV carriers (I) in relation to newly-infected individuals in acute sero-conversion stage (P). The role of bleaching is modeled by a factor of, (1- θ), with, $0 \le \theta \le 1$, $\theta = 0$ it implies that bleaching is 0% effective to prevent HIV infection among injecting drug users, while θ = 1 implies that bleaching is 100% effective to prevent HIV infection among injecting drug users. A fraction, q of symptomatic HIV carriers is assumed to withdraw from intravenous drug injection activity. The fraction q appears in both the numerator and the denominator of the incidence term. Further, it is assumed that individuals progress from the acute sero-conversion stage (P) to the asymptomatic stage (I) at rate γ . Progression from the asymptomatic stage (I) to the AIDS stage (A)

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occurs at rate ϕ . Natural mortality occurs in all classes at rate μ , and AIDS individuals suffer an additional disease-induced death at rate δ . Parameters in the model are summarized and explained in Table 1, and the model is depicted in the transfer diagram in Figure 1. All the parameters in the model are assumed to be nonnegative.

From the descriptions and assumptions on the dynamics of the epidemic made above, the following are the model equations.

$$S = -(+\mu)S, S(0) = S_0 \ge 0,$$

$$P' = S - (+)P, P(0) = P_0 \ge 0,$$

$$I' = P - (+)I, I(0) = I_0 \ge 0,$$

$$A' = I - (+)A, A(0) = A_0 \ge 0.$$
(1)

Since system (1) monitors human population, it is assumed that all the state variables are nonnegative for $t \ge 0$. Hence; we consider system (1) to be biologically-feasible in the region.

$$D = \left\{ (S, P, I, A) \in \mathbb{R}^4_+ : N \le \frac{\Lambda}{\mu} \right\}$$

It can be shown that all solutions of the system starting in D remain in D for all $t \ge 0$. Thus, D is positively-invariant and sufficient to consider the dynamics of the flow generated by (1) in this positively invariant domain D. It can be shown that unique solutions exist in D for all positive time. Thus, the model is epidemiologically and mathematically well posed (see [20] for further discussion).

Reproductive Number

The basic reproductive number (or, R_0) is defined as the number of secondary cases generated by a primary case when the virus is introduced in a population of fully susceptible individuals at a demographic steady state [21]. That is, R_0 measures the power of a disease to invade a population under conditions that facilitate maximal growth. If, $R_0 > 1$ then the epidemic progresses. If, $R_0 > 1$, the epidemic dies out. The higher the reproductive number, the faster the infecting

Parameter Definition	sym- bol	Units	Point estimate	Range	Source
Bleaching	θ	-	0.5	0.0-1.0	Assumed
Transmissibility	β	-	0.6	0.11-0.95	[24]
Recruitment rate	Λ	People/year	500	-	Assumed
Natural mortality	μ	/year	0.0142	0.01-0.02	[18]
Modification factor	η	-	0.7	0.1-1.0	[19]
Duration of acute phase	γ	/year	0.077	0.038-0.077	[23]
Proportion of with- drawals	q	-	0.5	0.0-1.0	Assumed
AIDS related mor- tality rate	δ	/year	0.33	-	[18]
Rate of progression to AIDS stage	φ	/year	0.125	0.01-0.125	[18]

Table 1: Model parameters and their interpretations.



agent runs out of susceptible individuals (i.e., the faster it decreases). For system (1) the basic reproductive number is given by the unit-less expression:

$$R_0 = \frac{\beta(1-\theta)}{(\gamma+\mu)} \left[1 + \frac{\eta\gamma(1-q)}{(\phi+\mu)} \right]$$
(2)

The threshold quantity, R_0 measures the average number of new secondary HIV cases generated by a single HIV infective intravenous drug user, when introduced in a susceptible population in the presence of aforementioned control measures are in place. The effectiveness of interventions (medical or behavioural) is evaluated by the ability of the program to reduce, R_0 . Ideally, one would like to bring the system to the point where, $R_0 < 1$.

Analysis of the Reproductive Number

In this section, I will analyse the impact of bleaching and individual withdrawal, as means of controlling HIV among intravenous drug users in the absence of any antiretroviral therapy.

Case 1: (No bleaching and withdrawal). In the absence of bleaching $(\theta = 0)$ and withdrawal (q = 0), the reproductive number reduces to, R_1 which is given by

$$R_{\rm I} = \frac{\beta}{(\gamma + \mu)} \left[1 + \frac{\eta \gamma}{(\phi + \mu)} \right] \tag{3}$$

Case 2: (Bleaching only). In the absence of withdrawal (q = 0), the

reproductive number reduces to, R_2 , which is given by

$$R_2 = \frac{\beta(1-\theta)}{(\gamma+\mu)} \left[1 + \frac{\eta\gamma}{(\phi+\mu)} \right]$$
(4)

Case 3: (Withdrawal, only). In the absence of bleaching ($\theta = 0$), the reproductive number reduces to, R_3 which is given by

$$R_{3} = \frac{\beta}{(\gamma + \mu)} \left[1 + \frac{\eta \gamma (1 - q)}{(\phi + \mu)} \right]$$
(5)

Comparing equations (3-5), one can easily observe that $R_0 < (R_2, R_2) < R_1$, suggesting that bleaching and individual withdrawal of symptomatic HIV carriers from drug injection misuse have a positive impact on controlling the spread of HIV among intravenous drug users. Further analysis on these reproductive numbers suggests that implementing both strategies may have a more influence on reducing the disease among intravenous drug users.

Uncertainty and Sensitivity Analyses

The uncertainty analyses were used to assess the variability in the empirical, R_0 distribution generated from the variability in parameter estimates. The sensitivity analyses assess the amount and type of change inherent in the model as captured by the terms which define, R_0 . If, R_0 is very sensitive to a particular parameter, then a perturbation of the conditions that connect the dynamics to such a parameter may prove useful in identifying policies that reduce the transmission of HIV among injection drug users. Sensitivity and uncertainty analyses are common in the study of the role of variability in tipping-point phenomena [22-26].

Partial rank correlation coefficients (PRCC) were calculated to estimate the correlation between values of, R_0 and the seven model parameters across one thousand (1000) random draws from the empirical distribution of, R_0 and its associated parameters. A large

PRCC is indicative of high sensitivity to parameter estimates, while a small PRCC reflects low sensitivity [22-26]. The signs of PRCC values determine whether a parameter is correlated directly or inversely to the reproductive number (R_0).

Figure 2 illustrates that reproductive number (R_0) is most sensitive (inversely) to bleaching, and directly to the rate of progression to AIDS stage. Comparing voluntary withdrawal of symptomatic HIV carriers and bleaching, I observe that the reproductive number is more sensitive to bleaching than individual withdrawal; this suggests that effective bleaching may be more important on controlling HIV among injection drug users compared to voluntary withdrawal of symptomatic HIV carriers. By effective bleaching herein, I mean following current bleach policy, as recommended by the health experts. Although, voluntary withdrawal of symptomatic HIV carriers is not most sensitive (inversely) to the reproductive it should not be discouraged, since it has show that it contributes to the reduction of the magnitude of R_0 . Results on Figure 2 further suggests that, the use of antiviral drugs can substantially reduce the rate at which individuals progress to full blown AIDS, thereby increasing the life expectancy of individuals within the community.

Figure 3, below illustrates the effect of bleaching on controlling HIV among intravenous drug users. The results suggest that an increase on the level of bleaching results in a decrease on the reproductive number. Thus, bleaching will be an important intervention strategy for controlling HIV among intravenous drug users, (in the absence of antiviral drugs). If the level of bleaching can be 50% effective of all the time or more, then the disease will be controlled.

Discussion

Injecting drug use has been associated with severe health and social







Figure 3: Monte Carlo Simulation of 1000 sample values illustrating effectiveness of bleaching. Results in Figure 3, suggests that if the level of effective bleaching is greater than 50%, then the disease can be controlled.

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harms. High rates of disease, death, crime, and the accompanying costs are drug-related harms experienced throughout the world. Injecting drug use has also been identified as a key risk characteristic for HIV infection in many countries around the world. Explosive epidemics of HIV have emerged in various settings, demonstrating that HIV can spread rapidly once established within communities of people who inject drugs. The dynamics of injecting drug use-driven HIV epidemics present unique challenges, giving policy makers and health authorities little time to respond in an effort to contain outbreaks of HIV infection. Here, a simple deterministic mathematical model for assessing the role of bleaching and individual withdrawal of symptomatic HIV carriers from drug injection misuse activity is presented. A threshold dimensionless quantity known as the reproductive number (R_0) has been derived. It (R_0) has been used to assess the role of bleaching and withdrawal on controlling HIV among injecting drug users. The reproductive number (R_0) measures the average number of new secondary HIV cases generated by a single IDU in a population where the aforementioned control measures are in place. If $\overline{R_0} \le 1$, then HIV will not persist, while if $R_0 > 1$ the disease will persist. At best this study suggests that bleaching is more effective compared to withdrawal on controlling HIV among intravenous drug users. The study further suggests that antiviral drug may be use on controlling HIV among intravenous drug users.

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