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Research Article

Relapse Processes are Important in Modelling Drug Epidemic

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Abstract

Global drug epidemic is an important public health issue. Mathematical modelling is vital for gaining insights, which may inform policymaking. Several modelling studies fail to adequately address relapse, which includes rapid relapse into heavy or light drug use, and relapse after extended sobriety. Here, we study the impact of relapses by incorporating relapse processes into an existing 6-compartment model. Our results show that the proportions of drug users are higher with relapse processes than that without relapse processes; yet, the proportion of rehabilitation is lower with relapse than without relapse. This highlights the importance of relapse processes in modelling drug epidemic.

Keywords: Drug Epidemic Model; Relapse; ODE; Sensitivity Analysis

Introduction

US Department of Health and Human Services together with US Centers for Disease Control and Prevention, and US National Center for Health Statistics [1] report a 31% increase in age-adjusted rate of drug overdose deaths from 2019 to 2020 before COVID-19. This increasing trend is echoed in other countries [2, 3] and may have been exacerbated by COVID-19 pandemic [4-6]. Hence, drug epidemic is currently one of the most important public health issues [7].

Mathematical modelling concepts of epidemiology introduced by Mackintosh and Steward [8] have been used in the last four decades to study various aspects of drug epidemic [9]. As each model is formulated to study a specific aspect, each model has its own set of deficiencies. For example, the model by Tang., *et al*. [10] does not consider relapse, which is an important aspect of addiction management [11]. While relapse is considered by Njagarah and Nyabadza [12], only relapse into heavy drug user is considered. There is no consideration of relapse after exiting treatment, which can be modelled as reversion into from treatment population into light drug user population; or relapse after extended sobriety, which can be modelled as reversion into from treatment population into susceptible population.

In this study, we aim to study the effects of relapse by adding added the reversion of treatment population to susceptible population and light drug user population using the simplified model of Njagarah and Nyabadza [12]. Our simulation results show that the trend of drug users is inverted from that of proportion in treatment – there are more drug users in the model with relapse than the model without relapse but the population of drug users undergoing treatment (drug users in rehabilitation) is lesser in the model with relapse than the model without relapse. This highlights the importance of relapse processes in modelling drug epidemic.

Materials and Methods

Model formulation

The model we used in this study was based on a simplified model by Njagarah and Nyabadza [12]. In Njagarah and Nyabadza [12], the conversion of susceptible (S) to light drug user (L)

without drug pushers/sellers (also known as drug barons, D) is the probability of contact between the susceptible population (S) and the drug user populations comprising of light drug users (L), heavy drug users (H), and users in treatment or rehabilitation (T). This interaction is simplified to a constant rate (k1) of recruitment from susceptible population to light drug user population (Figure 1). On top of rapid relapse into heavy user as modelled by Njagarah and Nyabadza [12], rapid relapse following treatment into light drug use and reversion of rehabilitated population into susceptible population were added. Hence, the extended model (Figure 1) can be written in the following ordinary differential equations (ODEs) with the parameters are listed in table 1.

$$\frac{dS}{dt} = (p + g1L + g5L) - (k1S + a1SD) - r1S$$

$$\frac{dL}{dt} = (k1S + a1SD + g2H + g4T) - (k2L + a2L + g1L) - r1L$$

$$\frac{dH}{dt} = (k2L + g3T) - (a3H + k3H + g2H) - (r1 + r2)H$$

$$\frac{dT}{dt} = (k3h) - (g3T + g4T + g5T) - (r1 + r2 + r4)T$$

$$\frac{dD}{dt} = (a2L + a3H) - (r1 + r5)D$$

$$\frac{dR}{dt} = r1S + r1L + (r1 + r2)H + (r1 + r2 + r4)T + (r1 + r5)D$$

Figure 1: Model of Drug Epidemic. This model was adapted from a simplified model by Njagarah and Nyabadza [12]. The simplified model was extended with red dotted lines, g4(T), and g5(T) in this study. Compartments: S, susceptible; L, light drug users; H, heavy drug users; T, drug users under treatment or rehabilitation; D, drug sellers/pushers/barons; and R, removed or dead.

Parameter	Nominal Value	Description
p	0.02	Recruitment rate from general population into susceptible population (S).
k1	0.28	Rate at which susceptible population (S) become light drug users (L) without the effects of drug barons (D).
k2	0.56	Rate at which light users (L) escalates to heavy drug use (H).
k3	0.223	Rate at which heavy users (H) enters rehabilitation (T).
g1	0.2	Rate at which light users (L) quit and become susceptible (S) again.
g2	0.4	Rate at which heavy users (H) become light users (L), which includes amelioration.
g3	0.25	Rate at which rehabilitated users (T) reverted to heavy drug use (H).
g4	0.325	Rate at which rehabilitated users (T) reverted to light drug use (L).
g5	0.283	Rate at which rehabilitated users (T) reverted to susceptible (S).
a1	0.4	Effective contact rate between drug barons (D) and susceptible population (S).
a2	0.04	Rate at which light users (L) convert from consumer to seller/promoter (D).
a3	0.08	Rate at which heavy users (H) convert from consumer to seller/promoter (D).
r1	0.02	Per capita mortality rate of population.
r2	0.0014	Removal rate of heavy users (H) due to events related to drug usage.
r3	0.003	Removal rate of rehabilitated users (T) due to events related to drug usage.
r4	0.2	Rate at which rehabilitated users (T) permanently quit.
r5	0.028	Removal rate of drug barons (D), which constitutes mainly to law enforcement.

Table 1: Parameters Used in the Model.

Model analysis

Both simplified and extended models were implemented and simulated using 5th order Dormand-Prince method [13] with fixed time-step as previously described [14]. Fifty units of time was simulated with time-step of 0.1. The sensitivity of each parameter was estimated by sensitivity analysis using one factor a time method [15,16] by doubling the parameter value, followed

by comparing the values of the populations with that of either the simplified or extended model at ten units of time using mean absolute error (MAE), [17].

Results and Discussion

Relapse into substance abuse after treatment is an important aspect of substance abuse treatment, which warrants numerous studies [18-21]; and studies have suggested a neurological [22], genetic [23], and hormonal [24] basis for relapse. Rapid relapse into substance abuse immediately following treatment is possible as shown by Mussulman., *et al*. [25], where 25% of the 942 participants relapsed into smoking within one day from hospital discharge. Cornelius., *et al*. [26] studied 59 patients treated for alcohol and drug disorder and found that the median time for relapse is 59 days after completing treatment for two-thirds of the patients, with possibility of multiple relapses [27]. These suggest three possible avenues of relapse: (i) immediate relapse into heavy user which had been modelled by Njagarah and Nyabadza [12], (ii) immediate relapse into light user, and (iii) relapse after a period of sobriety. The last of the two had been incorporated into the extended model for this study. More importantly, the prevalence of relapse suggests its importance in modelling drug epidemic. Indeed, Tang., *et al*. [10] acknowledge that the lack of relapse as a major drawback of their study. Hence, this study aims to examine the importance of relapse.

Figure 2: Simulation Results of Simplified and Extended Model. Panel A shows the results of the simplified model while Panel B shows the results of the extended model. S, L, H, T, D represents the compartments of susceptible, light drug users, heavy drug users, rehabilitated drug users, and drug barons; respectively.

Figure 3: Comparing the Simulation Results Between Simplified and Extended Models. Panels A, B, C, and D show light drug users, heavy drug users, rehabilitated drug users, and drug barons; respectively.

A first examination of our simulation results suggests similar results with or without relapse processes (Figure 2). However, an important difference emerges by examining each population (Figure 3). Our results show that the proportion of light drug users (L), heavy drug users (H), and drug barons (D) are higher in the extended model with relapse processes than that from the simplified model without relapse processes but the proportion of rehabilitation (T) is lower in the in the extended model than that from the simplified model. The inversion of rehabilitated drug user prevalence to that of drug users and drug barons may have significant implications for drug user monitoring.

One of the fundamental problems in managing drug epidemic is its underground nature – the actual quantity of drugs sold, and the number of drug users are not easily available [28]. A common method is by classical sampling, which is to use drug trafficking arrest rates and incentivized self-reporting rates to estimate the actual quantity of drugs sold, and the number of drug users, respectively. For example, needle exchange rates [29] and self-reporting [30,31] may be used to estimate the number of intravenous drug users. These methods can be used together with capture-recapture procedure to provide better estimates [32-34]. However, these methods are equivalent to exposure of illicit drug users to official statistics, which is synonymous to knowing the number of drug users in treatment (T). The actual proportion of drug users (L and H) and sellers (D) remains unknown. Yet, our results show that the proportion of known drug users (equivalent to T) to unknown drug users (equivalent to L and H) may differ depending on whether relapse is considered.

Similarly, the orders of the top 5 most sensitive parameters are different in both models (Figure 4). The order of top 5 most sensitive parameters from the simplified model is k3 (rate of heavy user going for treatment) > a2 (rate of light user to seller) > g2 (rate of heavy user becoming light user) > a3 (rate of heavy user to seller) > k2 (rate of light user going heavy), while that from the extended model is a2 (rate of light user to seller) > k2 (rate of light user going heavy) > a3 (rate of heavy user to seller) > g2 (rate of heavy user becoming light user) > r1 (per capita mortality rate). Despite the difference in order, there is a consistent pattern of fluctuation between the heavy and light users (g2 and k2) and the prevention of drug users becoming sellers (a2 and a3).

Modelling is an important tool to gain a handle on drug epidemic, which has potential to inform policy making [35,36]. Our results demonstrate that the exclusion of processes may have an impact on the simulation results. Of the 48 models reviewed by Wang., *et al*. [9], 23 (48%) models are based on ordinary differential equations. Hence, the integration of these models may provide a more accurate representation of the actual drug epidemic.

Figure 4: Sensitivity of Parameters.

Conclusion

The exclusion of relapse processes in drug epidemic models may result in different simulation results, leading to potentially different conclusions.

Supplementary Materials

The scripts and data files from this study are available at https://bit.ly/RelapseDrug.

Conflict of Interest

The authors declare no conflict of interest.

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