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Research Article

Assembly of Single Substance Use Epidemiological Models

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Abstract

Substance use/abuse is a public health concern with a long history and mathematical modelling is an important tool to study its epidemiology. Recently, a study showed that adding 2 processes into a 6-compartment model with 15 processes can drastically affect the conclusions, illustrating the importance of a more complete but complicated model. A systematic review in 2022 presented 24 ordinary differential equations (ODE) models of substance use/abuse epidemiology. This study aims to assemble these 24 ODE models, for single substance use only, by stepwise analysis and assembly. Multiple substance uses and comorbidities are deemed out of scope. The assembled model consists of 11 compartments [(i) susceptible without or refusing health education (S), (ii) susceptible with or accepted health education (C), (iii) light drug users (L), (iv) heavy drug users (H), (v) users under in-patient treatment (Ti), (vi) users under out-patient treatment (To), (vii) users in remission (Re), (viii) drug sellers (D), (ix) susceptible who matured (M), (x) users who quit permanently (Q), and (xi) removed (R)] with 42 processes and 40 parameters. We present the assembled model, SubstanceUseModel, as a Python command-line script where model parameters can be changed using command-line arguments, to improve its usability. This can form the basis for further model development in the field.

Keywords: Substance Use Epidemiology; Substance Abuse Epidemiology; Ordinary Differential Equations (ODE) Models; 5th Order Dormand-Prince; Python Command-line tool

Introduction

Substance use and/or abuse is a public health issue for most of human history [1]. These substances can range from socially acceptable and legal substances, such as nicotine and alcohol; to non-prescription products, such as cough mixture [2] and sports supplements [3]; to prescription medications, such as methadone [4] and Adderall [5]; to illicit and illegal substances, such as heroin and cocaine [6]. Hence, the terms "substance use", "substance abuse", "drug use", and "drug abuse" are used interchangeably. Recent studies suggest non-negligible prevalence in substance use/abuse. For example, Mansoor., *et al*. [7] reported 68.1% tested positive on urine drug screen among 8734 adult trauma patients hospitalized in West Virginia, USA, between 2006 and 2016. Abate., *et al*. [8] conducted a meta-analysis on 29 articles amounting to 22012 Ethiopian students aged 18 to 25 and found 32.28% overall prevalence of psychoactive drug abuse. Alenazi., *et al*. [9] surveyed 400 Saudi Arabian male high-school students aged 15 to 21 in 2021, using a self-administered questionnaire, and found 9.8% drug use. Olanrewaju., *et al*. [10] surveyed 400 Nigerian university students aged 15 to 29 in 2020 with questionnaire and found 45.7% drug use. Chapagain., *et al*. [11] performed a questionnaire survey on 1125 East Nepalian higher secondary school students in 2018 and reported 18.1% of the surveyed students were current drug users. A review by Bryson [12] in 2018 found a disturbing trend that prevalence of substance use/abuse in anaesthesiologists is higher than in general population and is increasing since 2000.

Since Mackintosh and Steward [13] introduced mathematical modelling into the study of substance use/abuse epidemiology, multiple models have been formulated to study different aspects of substance use/abuse epidemiology [14] under varying assumptions. Recently, Tang and Ling [15] demonstrated that adding 2 processes into an existing model of 6 compartments [(i) susceptible (S), (ii) light drug users (L), (iii) heavy drug users (H), (iv) users under treatment (T), (v) drug sellers (D), and (vi) removed (R)] with 15 processes [16] may result in substantial distribution among the compartments. This suggests that a more complete but complicated model may yield more reliable insights than a simpler model.

A systematic review by Wang., *et al*. [14] in 2022 presented 24 models using ordinary differential equations (ODE). In this study, we present an assembled model of single substance use/abuse only epidemiology by stage-wise analysis and assembly of the remaining 23 ODE models, presented in Wang., *et al*. [14], using Tang and Ling's model [15] as basis. Multiple substance use, also known as polydrug use; and comorbidities, such as substance use and infections, are deemed out of scope. The assembled model, SubstanceUseModel, consists of 11 compartments [(i) susceptible without or refusing health education (S), (ii) susceptible with or accepted health education (C), (iii) light drug users (L), (iv) heavy drug users (H), (v) users under in-patient treatment (Ti), (vi) users under out-patient treatment (To), (vii) users in remission (Re), (viii) drug sellers (D), (ix) susceptible who matured (M), (x) users who quit permanently (Q), and (xi) removed (R)] with 42 processes and 40 parameters.

Method

Tang and Ling's model [15], which is an adaptation of Njagarah and Nyabadza's model [16], was used as the baseline drug epidemiological model for sequential model assembly. Each subsequent model was analyzed for compartments and processes that are not present in the previous model and added (see supplementary materials for stage-wise analysis and assembly of models). For example, compartments and processes found in Knolle's model [17] were added to Tang and Ling's model [15], resulting in a new base model for addition from the next model. The sequence of models analyzed and added to Tang and Ling's model [15] were (i) Knolle's model [17], (ii) Caulkin., *et al*. 2009 model [18], (iii) Caulkin., *et al*. 2010 model [19], (iv) White and Comiskey's model [20], (v) Mulone and Straughan's model [21], (vi) Nyabadza and Hove-Musekwa's model [22], (vii) Wang., *et al*. model [23], (viii) Kalula and Nyabadza's model [24], (ix) Nyabadza., *et al*. model [25], (x) Muroya., *et al*. model [26], (xi) Mushanyu., *et al*. model [27], (xii) Yang., *et al*. model [28], (xiii) Mushanyu., *et al*. model [29], (xiv) Wangari and Stone's model [30], (xv) Mushanyu., *et al*. model [31], (xvi) Ma., *et al*. model [32], (xvii) Li and Ma's model [33], (xviii) Naowarat and Kumat's model [34], (xix) Su., *et al*. model [35], (xx) Memarbashi and Pourhossieni's model [36], (xxi) Liu and Liu's model [37], (xxii) Saha and Samanta's model [38], and (xxiii) Duan., *et al*. model [39]. The assembled model was implemented as a Python command-line script and simulated using 5th order Dormand-Prince method [40] with fixed time step as previously described [41].

Results and Discussion

Stepwise analysis and assembly of 24 models

The systematic review by Wang., *et al*. [14] in 2022 presented 24 ODE models for substance use and/or abuse epidemiology. Of which, Njagarah and Nyabadza's model [16] is adapted into Tang and Ling's model [15] (Figure 1 and Supplementary materials S1), resulting in 23 remaining models [17-39] for step-wise analysis and assembly. Tang and Ling's model [15] consist of 6 compartments [(i) susceptible (S), (ii) light drug users (L), (iii) heavy drug users (H), (iv) users under treatment (T), (v) drug sellers (D), and (vi) removed (R)] with 17 processes and 17 parameters.

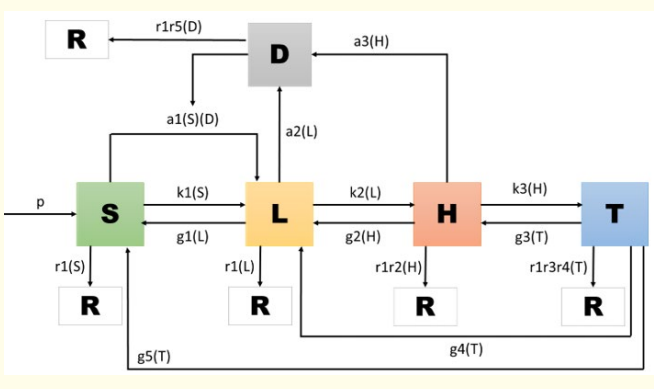

Figure 1: Tang and Ling's Model [15]. It consisted of 6 compartments [(i) susceptible (S), (ii) light drug users (L), (iii) heavy drug users (H), (iv) users under treatment (T), (v) drug sellers (D), and (vi) removed (R)] with 17 processes and 17 parameters.

Of the 23 models, 13 models had been addressed by the model at the analytical step. They are (i) White and Comiskey's model [20] (Supplementary materials S7 and S8), (ii) Mulone and Straughan's model [21] (Supplementary materials S9), (iii) Wang., *et al*. model [23] (Supplementary materials S12), (iv) Muroya., *et al*. model [26] (Supplementary materials S17), (v) Yang., *et al*. model [28] (Supplementary materials S20 and S21), (vi) Mushanyu., *et al*. model [29] (Supplementary materials S22 and S23), (vii) Wangari and Stone's model [30] (Supplementary materials S24 and S25), (viii) Mushanyu., *et al*. model [31] (Supplementary materials S26 and S27), (ix) Ma., *et al*. model [32] (Supplementary materials S28 and S29), (x) Naowarat and Kumat's model [34] (Supplementary materials S30 and S31), (xi) Memarbashi and Pourhossieni's model [36] (Supplementary materials S35 and S36), (xii) Liu and Liu's model [37] (Supplementary materials S37 and S38), and (xiii) Saha and Samanta's model [38] (Supplementary materials S39 and S40).

Of the 10 remaining models, 3 models are deemed out of scope – (i) Caulkin., *et al*. 2010 model [19] (Supplementary material S6), which examined social cost of drug use using Caulkin., *et al*. 2009 model [18]; (ii) Su., *et al*. model [35] (Supplementary material S34), which examines the shuttling between single drug use (heroin), multidrug use, and synthetic drugs; and (iii) Duan., *et al*. model [39], which examines heroin and HIV coinfection.

Hence, 7 models are incorporated stepwise into Tang and Ling's model [15]. These include (i) Knolle's model [17] (Supplementary materials S2 and S3), which added policing efforts to move light drug users (L) into treatment (T). (ii) Caulkin., *et al*. 2009 model [18] (Supplementary materials S4 and S5), which added maturing (M) and quitting (Q) from susceptible (S) and light drug users (L) respectively. (iii) Nyabadza and Hove-Musekwa's model [22] (Supplementary materials S10 and S11), which added transfer of treated users (T) and light drug users (L) into remission (Re), and from remission (Re) to light (L) or heavy (H) drug use. (iv) Kalula and Nyabadza's model [24] (Supplementary materials S13 and S14), which added transfer from susceptible (S) to heavy drug use (H), and treated users (T) that quit drug use (Q) permanently. (v) Nyabadza., *et al*. model [25] (Supplementary materials S15 and S16), which added susceptible (S) seeking out drugs and entering light drug use (L) without the need for sellers (D). (vi) Mushanyu., *et al*. model [27] (Supplementary materials S18 and S19), which considered that treatment (T) can be separated into out-patient treatment (To) or in-patient treatment (Ti); hence, light (L) or heavy (H) drug users can enter into either out-patient treatment (To) or in-patient treatment (Ti) depending on various factors. In addition, out-patient treatment (To) can be transferred to in-patient treatment (Ti) and vice versa. (vii) Li and Ma's model [33] (Supplementary materials S30 and S31), which separates susceptible (S) into susceptible without health education (S) and susceptible with health education (C).

Amendments to the model

Four amendments are made to the model. Firstly, the process from susceptible without health education (S) to heavy drug user (H) should also depend on the availability of drugs in the system to bring this process in line with S to light drug user (L). Secondly, it was found that users in remission (Re) never gets removed (R); hence, a process was added from Re to R. Thirdly, susceptible without health education (S) could enter heavy drug use (H) but susceptible with health education (C) could not go enter heavy drug use (H); hence, a process was added for C to H. Lastly, same proportion of L and H goes into in-patient treatment (Ti); hence, a parameter was added to allow for different proportions of L and H goes into in-patient treatment (Ti). The assembled model is then known as SubstanceUseModel (Figure 2).

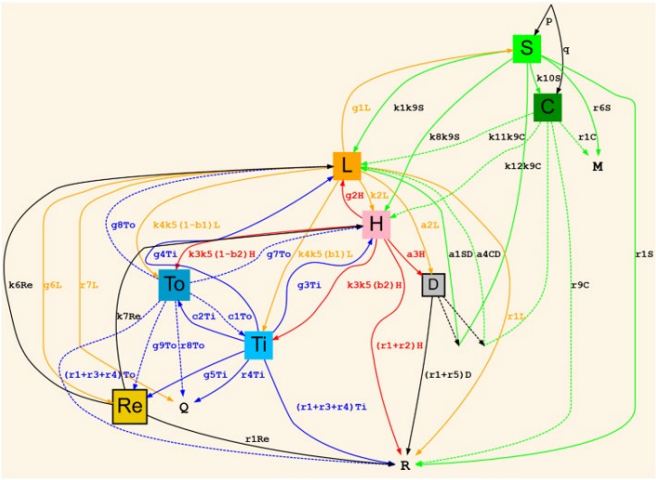

Figure 2: Substance Use Model.

Substance UseModel consists of 11 compartments [(i) susceptible without or refusing health education (S), (ii) susceptible with or accepted health education (C), (iii) light drug users (L), (iv) heavy drug users (H), (v) users under in-patient treatment (Ti), (vi) users under out-patient treatment (To), (vii) users in remission (Re), (viii) drug sellers (D), (ix) susceptible who matured (M), (x) users who quit permanently (Q), and (xi) removed (R)] with 42 processes and 40 parameters (Table 1). Therefore, the ODE rate equations for the 11 compartments can be written as

- Susceptible without health education: $\frac{dS}{dt} = (p + g1L) - (a1SD + k1k9S + k8k9S + k10S) - (r1S + r6S)$
- Susceptible with health education: $\frac{dC}{dt} = (q + k10S) - (a4CD + k9k11C + k9k12C) - (r1C + r9C)$
- Light drug users: $\frac{dL}{dt} = (a1SD + a4CD + g2H + g4Ti + g8To + k1k9S + k6Re + k9k11C) - (a2L + g1L + g6L + k2L + k4k5(b1)L + k4k5(1 - b1)L) - (r1L + r7L)$
- Heavy drug users: $\frac{dH}{dt} = (g3Ti + g7To + k2L + k8k9S + k9k12C + k7Re) - (a3H + g2H + k3k5(b2)H + k3k5(1 - b2)H) - ((r1 + r2)H)$
- In-patient treatment: $\frac{dTi}{dt} = (c1To + k3k5(b2)H + k4k5(b1)L) - (c2Ti + g3Ti + g4Ti + g5Ti) - ((r1 + r3 + r4)Ti + r4Ti)$
- Out-patient treatment: $\frac{dTo}{dt} = (c2Ti + k3k5(1 - b2)H + k4k5(1 - b1)L) - (c1To + g9To + g8To + g7To) - ((r1 + r3 + r4)To + r8To)$
- Remission: $\frac{dRe}{dt} = (g6L + g5Ti + g9To) - (k6Re + k7Re)$
- Drug sellers: $\frac{dD}{dt} = (a2L + a3H) - ((r1 + r5)D)$
- Matured: $\frac{dM}{dt} = (r6S + r9C)$
- Quit: $\frac{dQ}{dt} = (r4Ti + r7L + r8To)$
- Removed: $\frac{dR}{dt} = (r1S + r1C + (r1 + r5)D + r1L + (r1 + r2)H + (r1 + r3 + r4)Ti + (r1 + r3 + r4)To).$

Parameter	Default Value	Description
p	0.05	Recruitment rate from general population into susceptible population without health education (S).
q	0.15	Recruitment rate from general population into susceptible population with health education (C).
k1	0.2	Rate at which susceptible population without health education (S) become light drug users (L) without the effects of drug barons (D).
k2	0.5	Rate at which light users (L) escalates to heavy drug use (H).
k3	0.4	Proportion of heavy drug users (H) exposed to police search.
k4	0.2	Proportion of light drug users (L) exposed to police search.
k5	1	Intensity of policing / police search.
k6	0.05	Rate of relapse from remission (Re) to light drug use (L).
k7	0.01	Rate of relapse from remission (Re) to heavy drug use (H).
k8	0.01	Rate of susceptible population without health education (S) become heavy drug users (H) without the effects of drug barons (D).
k9	1	Availability of drugs in the system.
k10	0.3	Rate at which susceptible population without health education (S) accepts health education (C).
k11	0.1	Rate at which susceptible population with health education (C) become light drug users (L) without the effects of drug barons (D).
k12	0.001	Rate of susceptible population with health education (C) become heavy drug users (H) without the effects of drug barons (D).
b1	0.2	Proportion of light drug users (L) caught for in-patient treatment (T_i). Therefore, the proportion of light drug users caught for out-patient treatment (T_o) is (1-b1).
b2	0.8	Proportion of heavy drug users (H) caught for in-patient treatment (T_i). Therefore, the proportion of heavy drug users caught for out-patient treatment (T_o) is (1-b2).
g1	0.2	Rate at which light users (L) quit and become susceptible without health education (S) again.
g2	0.4	Rate at which heavy users (H) become light users (L), which includes amelioration.
g3	0.01	Rate at which in-patient treatment (T_i) reverted to heavy drug use (H).

g4	0.02	Rate at which in-patient treatment (T_i) reverted to light drug use (L).
g5	0.2	Rate at which in-patient treatment (T_i) enter remission (Re).
g6	0.015	Proportion of light drug users (L) entering remission (Re) on their own accord.
g7	0.015	Rate at which out-patient treatment (T_o) reverted to heavy drug use (H).
g8	0.025	Rate at which out-patient treatment (T_o) reverted to light drug use (L).
g9	0.2	Rate at which out-patient treatment (T_o) enter remission (Re).
a1	0.4	Effective contact rate between drug barons (D) and susceptible population without health education (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).
a4	0.2	Effective contact rate between drug barons (D) and susceptible population with health education (C).
r1	0.2	Per capita mortality rate of population.
r2	0.001	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	0.1	Rate at which in-patient treatment (T_i) permanently quit (Q).
r5	0.02	Removal rate of drug barons (D), which constitutes mainly to law enforcement.
r6	0.005	Rate of susceptible without health education (S) maturing into non-susceptible (M)
r7	0.01	Rate of light users (L) quitting drug use permanently (Q).
r8	0.1	Rate at which out-patient treatment (T_o) permanently quit (Q).
r9	0.01	Rate of susceptible with health education (C) maturing into non-susceptible (M).
c1	0.001	Rate of out-patient treatment (T_o) entering in-patient treatment (T_i).
c2	0.01	Rate of in-patient treatment (T_i) entering out-patient treatment (T_o).

Table 1: Parameters for SubstanceUseModel.

Default values for the parameters (Table 1) were set based on reasonable values and with the following assumptions:

- Higher proportion of general population enter susceptible population with health education (C) compared to without health education (S); that is, $p < q$.
- Per capita mortality rate of population equals to recruitment rate from general population to susceptible; that is, $r1 = (p + q)$.
- Higher proportion of heavy drug users (H) exposed to police search compared to light drug users (L); that is, $k3 > k4$.
- Intensity of policing equals to availability of drugs; that is, $k5 = k9$.
- Higher rate at which susceptible population without health education (S) become light drug users (L) without the effects of drug barons (D) compared to with health education (C); that is, $k1 > k11$.
- Higher rate at which susceptible population without health education (S) become light drug users (L) without the effects of drug barons (D) compared to with heavy drug users (H); that is, $k1 > k8$.
- Higher rate of relapse from remission (Re) to light drug use (L) compared to relapse into heavy drug user (H); that is, $k6 > k7$.
- Higher rate at which susceptible population with health education (C) become light drug users (L) without the effects of drug barons (D) compared to heavy drug user (H); that is, $k11 > k12$.
- Higher proportion of heavy drug users (H) caught for in-patient treatment (T_i) compared to light drug users (L); that is, $b2 > b1$.
- Higher rate at which in-patient treatment (T_i) reverted to light drug use (L) compared to heavy drug use (H); that is, $g4 > g3$.

- Higher rate at which out-patient treatment (T_o) reverted to light drug use (L) compared to heavy drug use (H), and higher rate of out-patient treatment (T_o) reverted to drug use (L or H) compared to in-patient treatment (T_i); that is, g7 > g8, g7 >g3, and g8 > g4.
- Same rate of in-patient (T_i) and out-patient (T_o) treatment enter remission (Re); that is, g5 = g9.
- Higher effective contact rate between drug barons (D) and susceptible population without health education (S) compared to with health education (C); that is, a1 > a4.
- Higher rate at which heavy users (H) convert from consumer to seller/promoter (D) compared to light drug user (L); that is, a3 > a2.
- Same rate at which in-patient (T_i) and out-patient (T_o) permanently quit (Q); that is, r4 = r8.
- Higher rate of susceptible with health education (C) maturing (M) compared to without health education (S); that is, r9 > r6.
- Higher rate of in-patient treatment (T_i) entering out-patient treatment (T_o) compared to out-patient treatment (T_o) entering in-patient treatment (T_i); that is, c2 > c1.

Usage of model implemented in python

The usefulness of command-line tool has been previously described [42-46], triggering the impetus to implement the assembled model as a command-line tool, called SubstanceUseModel (filename = SubstanceUseModel.py), where initial conditions and model parameters can be changed from the default values by command-line argument. The model is implemented in Python programming language and the command-line argument parser uses argparse, which is part of Python standard library. Fifth order Dormand-Prince ODE solver [40] is incorporated into SubstanceUseModel; hence, only dependent on a local Python installation. Command-line usage and options are given in Supplementary material S44. Our simulation result (Figure 3) suggests that our command-line tool can execute without errors.

Conclusion

We present a single substance use/abuse only (multiple substance use and comorbidities are deemed out of scope) ODE model with 11 compartments, 42 processes and 40 parameters by stepwise analysis and assembly of 24 ODE models. The model, SubstanceUseModel, is presented as a Python command-line script where parameters can be changed using command-line arguments.

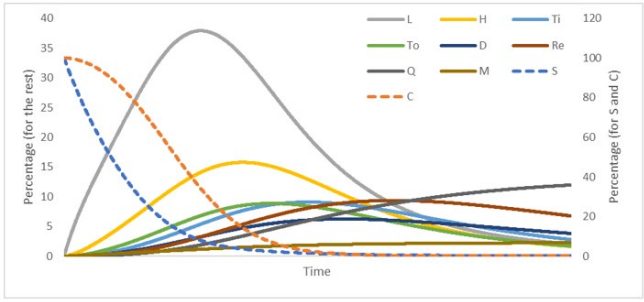

Figure 3: Simulation Results of SubstanceUseModel on Default Parameters. Only 10 of the 11 compartments are shown – Removed (R) is not shown.

Supplementary Materials

Codes and results for this study can be downloaded at https://bit.ly/SUM_Code. Supplementary materials for this study can be downloaded at https://bit.ly/SUM_Suppl.

Conflict of Interest

The authors declare no conflict of interest.

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Note

Sean SK Yap and Wei Jun Choy are joint first authors.

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