

**Age-Specific Multi-State Drug Initiation Models:
Insights from Considering Heterogeneity**

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AGE-SPECIFIC MULTI-STATE DRUG INITIATION MODELS: INSIGHTS FROM CONSIDERING HETEROGENEITY¹

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ABSTRACT

This paper introduces several models concerning drug initiation and drug epidemics that extend traditional single and multi-state dynamic models by considering explicitly the age distribution of users. This age-specificity brings up more realistic models, because it is certainly true that behavior can depend on age and also the influence among one another can depend on age and the age difference. Furthermore prevention programs – especially school-based programs – can be targeted to certain age classes. These models allow to reproduce the dynamics of drug epidemics in more detail. The models can be used either for studying the features of drug initiation or for discovering how best to allocate resources to prevention programs over different age classes.

1 INTRODUCTION

Often models of drug initiation and drug use are based on the same principles as epidemiological models. At first sight it is not clear why drug use and infectious diseases have much in common. Initiation into consumption of an illicit drug is usually a deliberate decision of an individual, whereas the act of infection by a pathogenic agent (e.g., the common cold virus) usually takes place without the infected individual having any awareness of the process. In contrast to a drug epidemic, most individuals infected by a certain disease undergo the same run of

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infection, i.e., almost all individuals either recover or get immune or remain infected. Recovery from drug consumption may be diverse for different users. It may be a healing process, if the user was addicted, or the user's free choice to quit consumption, or the result of drug enforcement policies [1].

Nevertheless, drug use is clearly contagious in the sense that use by some individuals affects the probability that others will use through multiple mechanisms. In a very literal sense, most users are introduced to a drug by a friend or relative; the more drug users there are, the more likely an individual is to be offered the drug [2]. At a market level, the larger the market, the more diluted the enforcement risk, and the safer it is to try drugs [3]. At a reputational level, experiences of others can be instrumental in shaping perceptions of the riskiness of drugs, and those perceptions in turn influence initiation [4]. Indeed, the very fact that the mechanism of *transmission* does not involve physical contact or interaction means that the dynamics of contagion can be more complex and more interesting.

Looking at drug use and the process of initiation in more detail, it is clear that the decision of a non-user to start consumption depends strongly not only on the individual's immediate, personal social environment, but also on the overall reputation of a drug in society, e.g., as portrayed in movies or news media. That means, an individual might want to use drugs even if none of the individual's associates encourages that desire. And, conversely, an individual may fear drugs even if no one he or she knows has suffered harm from them.

This rough explanation shows already the complexity of drug initiation and the large number of parameters influencing this process. The complexity grows if the age-dependency of those factors is taken into consideration. The disadvantages of complex models stem from the lack of data for parameter identification and the difficulties in analyzing them. Hence, in this paper as we introduce age-dependency into models of drug use, we strive to keep other aspects of the models relatively simple.

More specifically, the additional insight considered and quantified in this paper is that the influence of a drug user on a non-user vulnerable to initiation can depend on the ages of both individuals. A sixteen year old might look up to and seek to emulate an eighteen year old, but rebel and try to do exactly the opposite of what his or her parent's generation is perceived to be doing. So drug use by an 18 year old might encourage a 16 year old to initiate even though drug use by a 38 year old might discourage it. Or perhaps for some drugs and some situations, use by a 38 year old is a stronger endorsement than is use by an 18 year old. Whichever one believed, there is no way to incorporate such effects into existing models. There are age-specific epidemiological models in the literature [5,6], but as mentioned above, the process of contagion is different for drug initiation. Therefore, those models are not capable of describing the dynamics of a drug epidemic.

This paper describes a new class of models that can consider such effects in an explicit quantitative framework and gives some initial results. Furthermore, control models of prevention, which are based on the descriptive age-specific drug initiation models, are introduced.

2 BASIC ASPECTS OF DRUG INITIATION MODELS

We start with a very general description of the basic features of drug initiation models. These features are the foundation for the further developments of initiation models towards age-structured models, which are presented in section 3. Some heterogeneity is already introduced in this state by dividing the population into multiple groups (see section 2.2), but that is qualitatively different than the models with an *infinite number* or *continuous distribution* of states that we introduce later.

2.1 Homogeneous Modeling of the Population – Single-State Model

The simplest model of drug use in a population distinguishes only between individuals who are not consuming drugs, and individuals who are using drugs. It is common in such models to ignore variation in the overall population size. That means the number of deaths is equal to the number of births. In that case, the only things we have to consider are the flows from the non-user group to the user group and back. (See figure 1.)

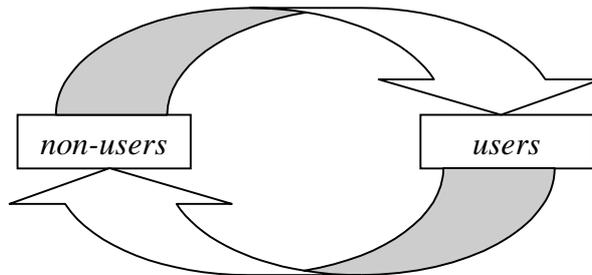


Figure 1: Simple user – non-user model

The flow from the non-user to the user group – the initiation rate – is influenced by several features:

- a basic initiation rate representing the probability that a non-user starts drug consumption without any influence from others. This basic initiation rate is drug-specific, but also cultural-specific. That means we have

to consider different initiation rates for different drugs, but also for different cultural context. Apart from that, this basic initiation rate may also depend on time (e.g., higher basic initiation rates in the late sixties than in the early fifties for cocaine in the US).

- the reputation of the drug in the society. Reputation is determined by the number of drug consumers, but it is not necessarily the case that more drug users always means a more favorable reputation. For some drugs there could be a threshold. Beneath that threshold the reputation increases with the number of users, but above the threshold it decreases because a very high number of drug users could underscore the problems caused by drug consumption.
- the effect of prevention programs. Prevention programs can reduce the initiation rate, but only down to a certain level. Unfortunately, no program can reach all people, and not all people reached change their behavior.

The flow from the user group to the non-user group also consists of different parts:

- the flow implied by the zero population growth assumption. (If we assume all newborns are in the non-user group, then there must be a flow from the user to the non-user group representing the death of users and their replacement by newborns who are not users.)
- a basic rate at which drug users quit their consumption.
- the effect of treatment. With more treatment the flow from users to non-users is increased, but only up to a certain threshold. (Similar to the effects of prevention programs on the initiation rate.)

Remark. If the user group represents all people who have consumed drugs at least once in their life, then the flow from the user to the non-user group consists only of the part due to the zero population growth.

When considering models with a constant population size it is only necessary to analyze one of the groups; all individuals who are not in this group, must be in the other one by definition. Therefore, the dynamics of this model depends only on one state, and the analysis becomes accordingly simpler.

2.2 Multi-State Models

One type of a more detailed model distinguishes not only between drug users and non-users, but also between different kinds of users and possibly also between different kinds of non-users. In Everingham and Rydell [7] such a multi-state model is explained, where users are split into light and heavy user groups. The

light drug users consume drugs at most once per week; the heavy users consume several times per week or more often

Even that simple binary distinction generated many insights, but there are other ways of splitting the population in multiple groups. A principle constraint on such elaborations is data availability; e.g., if there is no distinction in the data between the amounts and the frequencies people use drugs, then it makes no sense to introduce different levels of drug consumption into the models.

Although the population is split up in several groups, they all can be combined again in two sets of groups, namely those groups representing the non-user population and those representing the drug consumers (see figure 2).

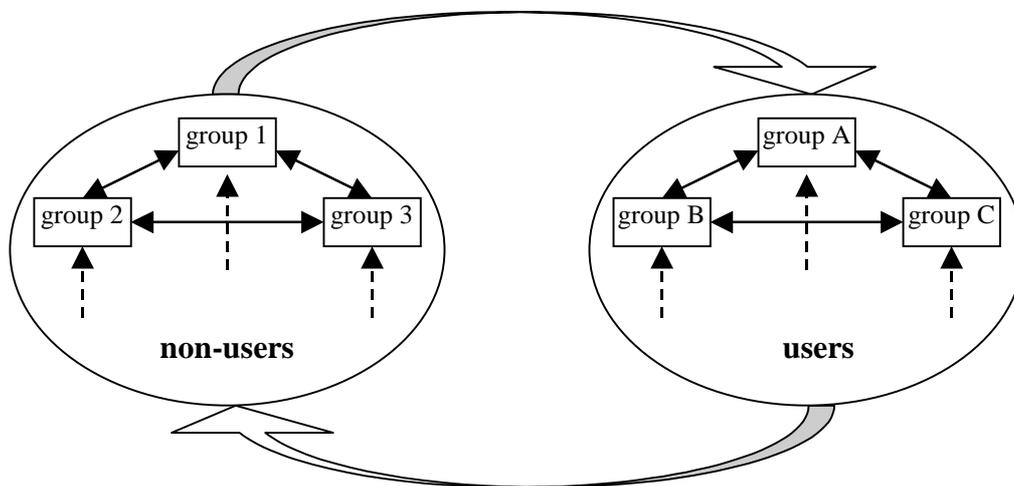


Figure 2: Multi-stage model with subgroups of users and non-users

Some examples of groups within the non-user population are:

- general non-users
- non-users who have been exposed to a prevention program
- former users
- ...

and for the user population:

- light users
- heavy users
- users under treatment
- ...

In the multi-state models there are not only transitions between non-users and users but also within these groups, e.g. from light users to heavy users. One can

generate very complex models with many different states, but as mentioned above it is only useful to develop a model which can be supported by the available data. Highly differentiated data acquisition allows modeling of drug dynamics in greater detail.

3 DESCRIPTIVE AGE-SPECIFIC MODELS OF INITIATION

The central contribution of this paper is to introduce another form of heterogeneity to the models, specifically to take into consideration the age of the individuals. This extension brings up much more realistic models, because it is certainly true that behavior can depend on age. E.g., people between 13 and 25 years of age are much more likely to start drug consumption than are people over 40. It is also true that not all people have the same influence on a person of a certain age. That influence can depend on their age and/or the age difference. Furthermore prevention programs – especially school-based programs – can be targeted to certain age classes. Therefore, such an extension is useful, although the increased complexity makes it much more difficult to analyze such models and gain practical results [8].

A simple way to introduce age is to split the population into different age groups. This leads to so-called compartment models such as those described in section 2.2, but with a large number of population groups [9]. A more general method is to include age as a second parameter in addition to time. So a continuous age distribution of the population can be fully taken into consideration. The analysis of the model becomes in some way easier, because there are fewer groups to consider, but in some sense also more complicated, because this method leads to a system of partial differential equations – a further development of the so-called McKendrick equation [10].

3.1 Age-Specific Single-State Models

As a first step we extend the simplest model with 2 groups (i.e., non-users and users) to consider age-specific reputational feedback on initiation. The details of the underlying model change a little bit. We assume that there is a fixed birth cohort size, which moves only into the non-user group at age 12. (I.e., any use before age 12 is ignored.) There are no deaths during the subsequent lifetime of 60 years, so all individuals live from age 12 to age 72. Then they are removed from the model, either by death or because they are presumed no longer to affect drug use. Additionally we assume that there is no recovery from drug use, so the back-flow from users to non-users can be neglected (see figure 3). Obviously people do cease use, so the practical implication of this simplification is that the pool of us-

ers is more properly understood to be the pool of ever users, not the pool of current or past-year users.

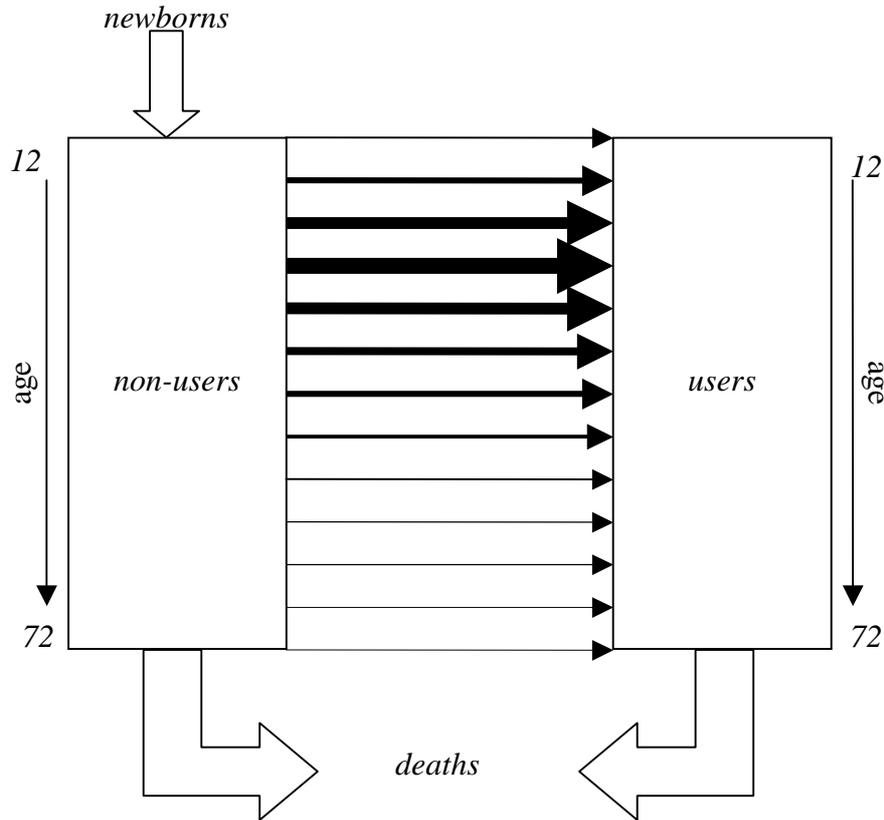


Figure 3: Schematic representation of a simple age-specific model (thicker arrows indicate higher initiation rates)

The initiation rate consists of three factors (see section 2.1): the basic initiation rate, the reputation, and the prevention. All those factors depend on age. Prevention programs always suppress initiation, but the reputation effect can influence initiation in either direction. (See figure 4.)

In the simpler model without age differentiation, the reputation was construed as an overall image held by the society as a whole, but now we adopt a more differentiated view because the reputation is age-specific. In other words, at any given point in the drug epidemic people of different ages can have different perceptions of the drug. Furthermore, the influence a given user has on someone

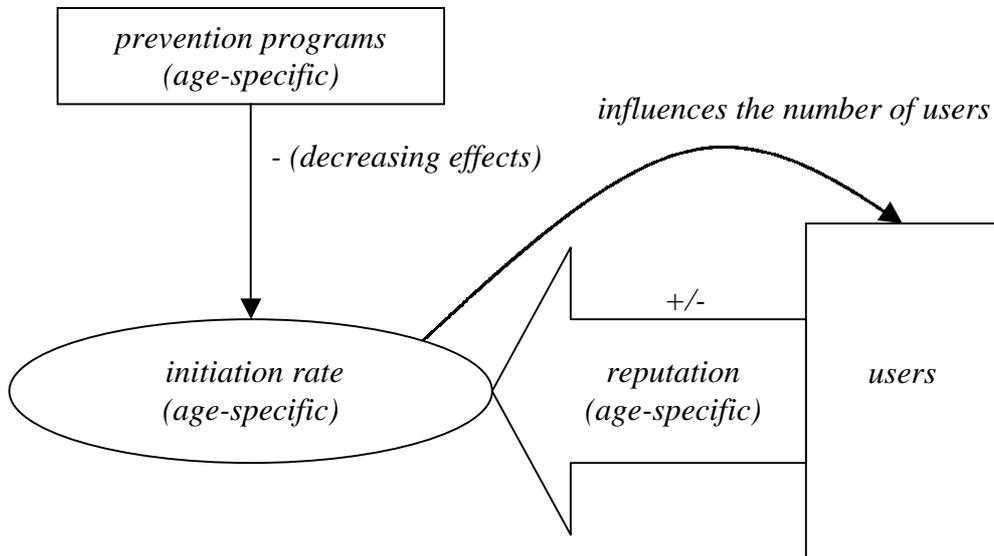


Figure 4: Influences on the initiation rate

else's perceptions of the drug can depend on the person's age and the age difference. So the main factor for the reputation is how much influence a user of age b has on a non-user of age a , and whether this influence is positive or negative. This influence relation can be a socially- or culturally-specific factor. We believe that at least for the typical drug in Western Europe or North America this influence may be described as follows:

- Young people are more sensitive to peer pressure, so the older a non-user is, the weaker the influence of any other user on that individual.
- The influence depends primarily on the age difference between the user and non-user.
- Especially for young non-users (who have the highest underlying proclivity to initiate drug use):
 - Persons who are at the same age or a little bit older set examples, therefore their influence is very high.
 - Persons who belong to their parents' generation may evoke a contrarian response or at least have only a small impact and therefore have a very low and maybe even a negative influence.

The reputation of the drug that is effective on a non-user of age a is the compound influence of the users over all ages.

The feedback from considering the influence of users on the initiation rate of non-users can generate a very interesting behavior in the model. The drug users never vanish completely, because neither a low reputation, nor an expensive pre-

vention program can reduce initiation down to zero. In most cases, when no prevention program is applied, the number of users becomes stabilized and reaches an endemic equilibrium. On the other hand, it is also possible to end up with an oscillation of repeated waves of drug use, if the influence of the parents' generation is negative.

The intuitive explanation for this modeled behavior is the following. If there are few older drug users, then their negative influence on the younger potential users is very small. Therefore initiation of new drug users at younger ages is high. (Initiation by older individuals is low and relatively insensitive to others' use.) Some years later, those former young drug users grow older and cause a strong negative reputation of the drug for the new young non-users. This keeps the initiation rate very low and results in a large non-user group in younger and eventually middle ages. Eventually the older users disappear, which reduces their negative influence on initiation, and the cycle can begin again.

Figure 5 shows these cycles graphically. In particular, it plots the proportion of an age cohort that has never used as a function of time. Troughs in this graph represent peaks in use because everyone is either a user or a non-user. People in the youngest age groups are primarily non-users at all times, as is indicated by the plateau in the graph for those ages. Initiation occurs primarily in the adolescent years (indicated by the "cliff" at those ages), but the ultimate lifetime prevalence of drug use varies from birth cohort to birth cohort (indicated by the series of ridges). The time differences between peaks of drug use are about 1-2 generations depending on the influence of users on non-users. The amplitude is about 10-20% of a birth cohort size.

As mentioned before, this reputation factor depends strongly on the social structure, i.e. it may have completely different forms for drug epidemics in other countries or times. This example shows, however, that a model with just one state but a heterogeneous age structure can produce cycles of drug use of the sort observed historically [11]. Furthermore, this cycling is not the only possible outcome, so one can explore conditions under which cycling occurs and contrast them with conditions under which drug use approaches a constant steady state. Still more complex behavior can be obtained by further refining the state space, as we will discuss next.

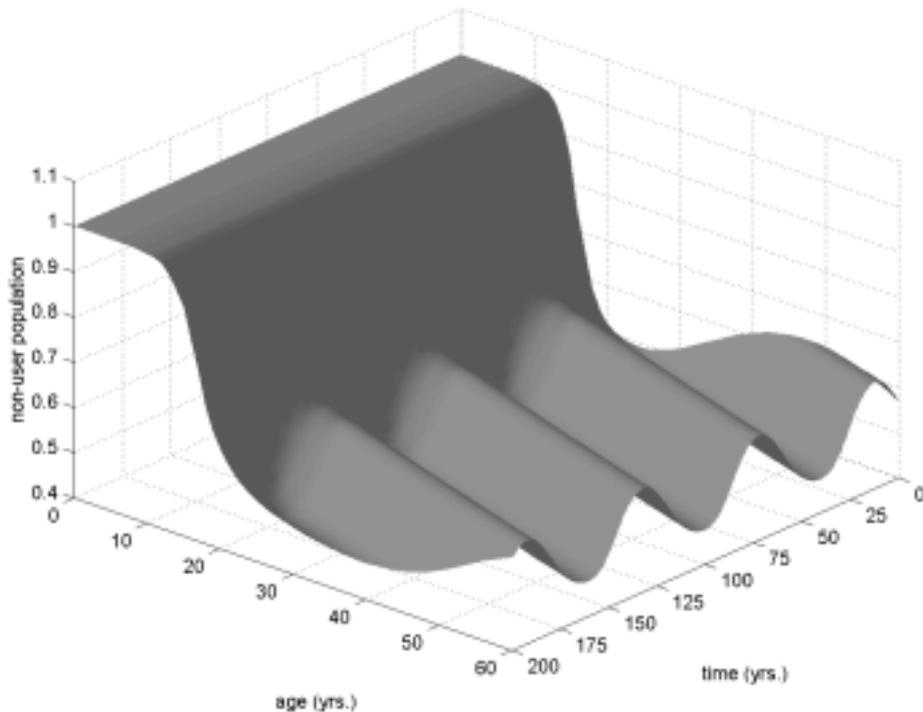


Figure 5: Oscillation in the non-user population due to the negative influence of the parents generation (These results are based on data on marijuana initiation in the United States. The user group represents those people who have consumed marijuana at least once in their life)

3.2 Age-Specific Multi-State Models

One way to refine the model above is by splitting the user and/or non-user groups into subgroups as shown in section 2.2. Following the lead of Everingham and Rydell [7] and Behrens et al. [12], we consider in particular distinguishing between light and heavy users. This yields three population groups: non-users, light users, and heavy users [13]. A key motivation for this distinction is the assumption that *light* users, who may be using the drug for recreational reasons, can create a positive impression of the benefits of drug use, whereas the *heavy* or addicted users who manifest the adverse effects of drug use create a negative impression. Hence, the underlying assumption of this model is, the more light users

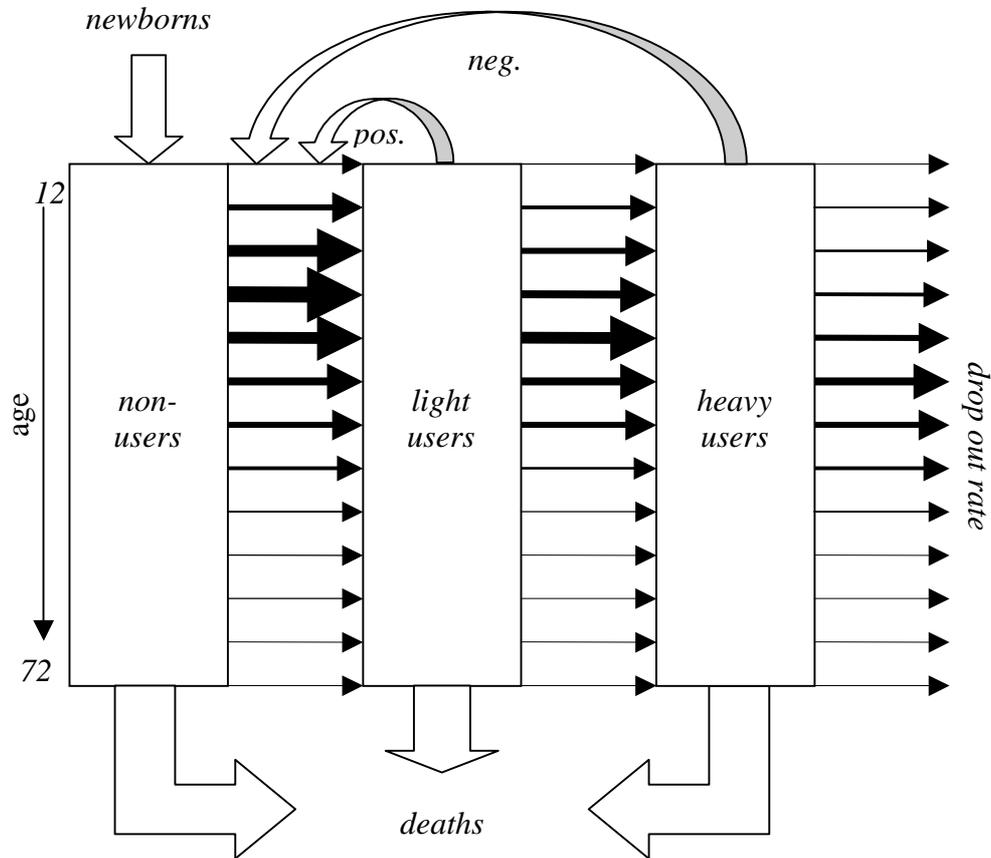


Figure 6: Schematic diagram of an age-specific L-H-model (thicker arrows indicate higher initiation and transition rates)

there are, the better the reputation of the drug is, but the more heavy users there are, the worse the drug's reputation and, hence, the lower the initiation rate. (See figure 6.)

As this model includes age, the reputation is age specific, and again the main factor is the impact of light and heavy users of age a on the initiation rate of a non-user aged b . We assume there is a big influence if the age difference is small, and a small impact if the age difference is large, which reflects the fact that people have more social contacts within their own age group than with other age groups.

Similar to the previous model of section 3.1, the L-H-model shows different types of behavior depending on the magnitude of the negative influence of heavy users on reputation. If this negative influence is very small then drug use converges to a single, high equilibrium level of drug use. If it is very large, then initiation is uniformly low and use converges to a single, low equilibrium level.

However, if the influence of heavy users is in a moderate range, this model produces cycles of greater and lesser drug use [13]. Intuitively, the reason is pretty much the same as for the model presented in section 3.1. A high number of heavy users reduce the initiation rate for younger non-users, but as they grow older and disappear, their negative impact wanes and a new wave of drug consumers is created, which results later on in a high number of heavy users again.

As mentioned in section 2.2, this is only one way to extend the model. Other groups can be included as long as data are available for estimating the age-specific transition rates between those groups.

4 OPTIMIZATION OF AGE-SPECIFIC MODELS OF PREVENTION

The models above were descriptive. Their main contribution was showing how age-specific reputational effects can generate cycles of greater and lesser drug use. From a policy perspective, one is interested not only in describing drug epidemics, but also in controlling them. Since resources are always constrained, a common and fruitful question is to ask how drug control interventions should be managed in order to achieve some reduction in use at the least possible cost.

There is an emerging literature on these resource allocation questions, but to date much has focused on trading off spending on different types of interventions (e.g., treatment vs. enforcement [14,15]) or trading off interventions at different points in a drug control epidemic [16,17], or trading off the benefits of attacking different local markets [18,19]. For school-based prevention programs, another interesting variant of this question pertains to the appropriate age at which to intervene.

By and large enforcement and treatment interventions cannot be age specific. One can impose different sanctions on juvenile vs. adult offenders, and treatment policies that are contingent on the number of past treatment episodes have some age discriminating power, but for school-based drug prevention the ability to target on particular ages is much greater. Except for the extent to which students skip or fail grades, there is almost a one-to-one mapping between grade level and age. So one can ask, at which grade (age) should most school-based intervention efforts be targeted.

This is in fact a complex and multi-faceted question. Theoretically one would want to factor in differential school attendance by age (due to dropping out and truancy) and how intervention effect sizes vary with age. Here we consider just a subset of those issues, but one that cannot be analyzed directly without an age heterogeneous model. How should the fact that baseline initiation rates vary over time and the fact that past initiates can promote further initiation, particularly of people from the same birth cohort, affect the ages of intervention?

To address this question, the previously introduced models are converted into an optimal dynamic control formulation [13]. A variety of objectives can be considered, e.g. the total costs of drug use including the social costs caused by the drug consumers and the costs of running the prevention programs themselves. Initially it was assumed that a prevention program only affects the initiation rate while the program is being run. When the program is stopped, the initiation rate immediately returns to the rate that would have pertained in the absence of any prevention program. For this simple case, in which the prevention programs have no *memory effects*, the results are predictable. In general, expenditures should be directed to the age classes with the highest initiation rates (see figure 7). However, the spending profile does not match the initiation profile exactly. Because of the contagious character of drug use, prevention interventions should be shifted a bit toward younger ages.

One way to include prevention programs with a memory effect is to split the non-users group into two parts, a group of people who have already received a prevention program, and another group that has not. So the implementation of a prevention program results in a flow from one of those groups into another. A backwards flow could be included to represent forgetting or decay in program

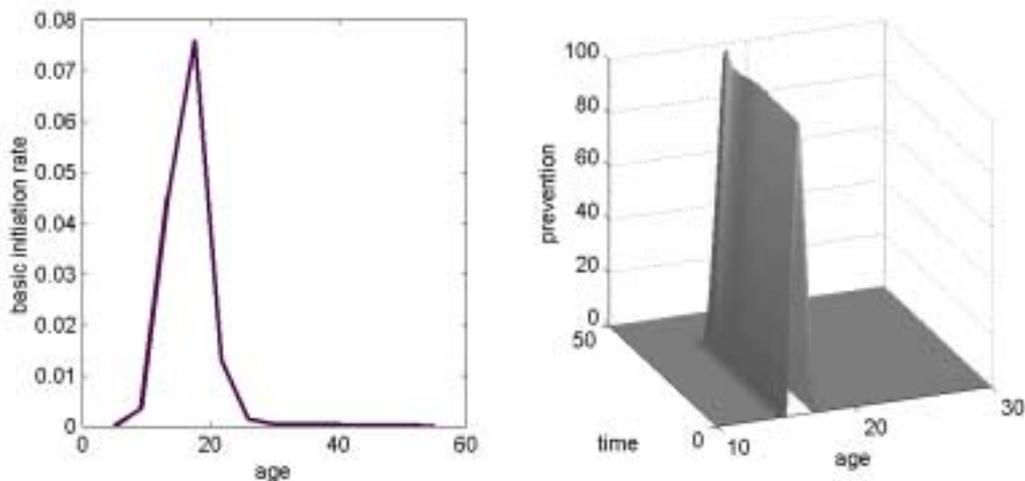


Figure 7: The graph on the left shows the age-specific basic initiation rate, which was used for the calculations. The graph on the right shows a typical result for an age-specific prevention program without a memory effect. (The small age range of the prevention program emerges from the relatively low social costs of drug users. Assuming higher social costs provokes a wider age range.)

effect. Presumably people who have taken part in a prevention program would be modeled as having a reduced drug initiation rate compared to those who have not taken part. This kind of model can be compared to some extent with vaccination models, where the vaccinated part of the population is in one group. After some time the vaccination effects fade away and people are again susceptible.

This type of model falls in the class of section 3.2, and also for this kind of prevention program an optimization can be performed regarding to some objective. Hence, the most important age classes for applying a prevention program can be calculated, so that the best effects can be obtained. (The analysis of these optimal control models is underway at the moment.)

5 CONCLUSIONS

Introducing age-specific aspects to drug initiation models allows one to develop more complex models that give detailed insights into the principles of drug epidemics and their control. The simple single-state model of section 3.1 already shows a big advantage of age-structured models: the complex dynamics of an drug epidemic can be simulated using a model based on simple, manageable assumptions, such as distinguishing between just two groups of people. The behavior of the solution (cycles or constant equilibrium) depends on the type of age-specific feedback. To gain similar results with traditional multi-state models that do not differentiate by age a larger number of groups would be necessary.

In particular, the age-specific concept allows one to incorporate an age-specific reputation effect (feedback from number of users on the initiation rate) which depends on how much influence a user of age b has on a non-user of age a , and whether this influence is positive or negative.

Another advantage of age-specificity is the ability to investigate age-structured strategies for prevention and to optimize them. Although section 4 addresses only programs without a memory effect, the extension to other types of prevention is straight forward and fits into the scope of models presented in this paper. This kind of investigation is our main focus at the moment.

Many issues concerning population dynamics include heterogeneity, either spatial or temporal. The age distribution of a population can change sometimes very quickly, and can be completely different in different regions. Hence, it is necessary that a model for adapting strategies to these different cases incorporate the age-distribution of population groups. The age-specific models presented in this paper are a first step towards including more heterogeneity in drug epidemic models. Further extensions would be to use finer group classifications or to introduce the duration of use as a third parameter, because some aspects of drug initiation depend on how long an individual has been in his/her current group. E.g., the

probability of an individual moving from light to heavy use may be related to the duration of his/her drug consumption. Theoretically such extension can be developed from the models of this paper, but at this state of science the analysis of those models encounters difficulties on two sides: the availability of data for the large number of parameters and the numerical limitation due to computational power.

In summary the age-specific models presented in this paper allow more detailed insight into the dynamics of drug epidemics, and by formulating them as optimal control models they can be used to increase the effects of prevention programs by improving their targeting.

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