Contents

Executive Summary

The authors of this report believe that modelling can lead to better policy making.

Models can help:

- estimate the size of a problem

- understand what factors might be important in determining the spread of diseases or other health problems

- assess which prevention strategies result in the greatest gain

- shape policy questions, future data collection or research by

  – simulating how patterns of behaviour and harm may occur
  – identifying the greatest uncertainties
  – determining what evidence may be required to test simulation models.

We present three examples of models – statistical, system-dynamic, and agent-based – intended to illustrate the potential utility and benefits of modelling for understanding the dynamics of drug use, the harms associated with it, and its use in supporting policy making. The examples are not exhaustive. Each has limitations and each presents specific recommendations. But in general they demonstrate that modelling can generate useful insights even over a very constrained timescale.

1. Public health surveillance: case study statistical models

Drug use is a behaviour of interest in public health and is associated with social harms that we want to prevent. Policies should be judged on whether they manage to reduce total harm. There can be no doubt that drug use has increased substantially over the last 30 years, but it is not clear what has driven the increase or what preventive actions might have been successful in the past or would be successful in future. The number of opiate overdose deaths has increased 100-fold, from 9 in 1968 to nearly 1,000 in 2000, and model estimates suggest considerable growth in the number of opiate users and injecting drug users (IDUs) in the population, especially in the late 1970s and early 1990s. There can be few other social or health problems that have increased as dramatically in the population – to the extent that in several cities in the UK there may be over 1 in 100 young adults using heroin or crack.

Statistical techniques can transform routine data into estimates of trends in the number of problem drug users in the population, for use by policy makers and as parameters for models of the dynamics of drug use and the harms associated with it. However, these methods are unable to provide insights into why or how drug use has increased, or how it might better be prevented. Modelling new problem drugs will depend first on traditional surveillance and epidemiological studies identifying the drug and its potential association with health or social harms. Inevitably there are information gaps and there is a degree of uncertainty in some of the prevalence estimates which may limit their utility. This could be addressed by developing a co-ordinated information and surveillance strategy to make the best use of the available data and identify ways of closing the gaps in the evidence.

2. Infectious disease modelling among injecting drug users: case study Hepatitis C transmission in London, UK

The number of new Hepatitis C (HCV) infections in the UK, and the total number of cases, are largely driven by the behaviour and size of the injecting population. Indeed, over 90% of diagnosed HCV infections are attributed to injecting drug use; and infection rates are increasing among current injectors in the UK. In London, the prevalence of HCV is over 50% and incidence over 30% per year among drug injectors. HCV infection is an important public health concern because of its long-term consequences. After 30 years, approximately half of the people infected with HCV develop cirrhosis of the liver. Once it has developed, 1–5% of individuals per year progress to liver cancer (hepatocellular carcinoma) which often leads to death (50% after two years). Treatment is available and increasingly effective (over 50% clearing the virus), but expensive. Key questions that could be addressed by modelling are the amount of HCV morbidity in a population, the future need for treatment and its cost, and how best to target and increase coverage of interventions to reduce HCV transmission among IDUs, and therefore future morbidity.

To look at some of these issues, a system-dynamic model was developed of the transmission of HCV among IDUs. The model divides IDUs into susceptible (not yet infected); recent, chronic infected; and those who have cleared the virus. It includes information on the probability of infection if exposed to the virus through sharing an infected syringe, and the frequency of injection and sharing. Because of uncertainty in the behavioural and epidemiological data, the model was run with a range of different possible parameter values, and fitted against observed data on the prevalence of HCV among IDUs in London for different durations of injecting. The preliminary findings highlighted key uncertainties in both the biological and behavioural evidence needed to fully understand the transmission of HCV among IDUs in London. A key question raised by the model which has implications for public health action and policy makers, and which requires further information to answer, is how critical the delivery of injecting equipment and health education is to all injectors at the outset of their injecting career, or to a subgroup of 'high risk'

injectors, in order to have the greatest impact on reducing HCV infection. There is no question that the coverage of interventions needs to be increased to reduce HCV infection, but modelling will help us understand what level it needs to be increased to, and what specific population groups need to be targeted. Specific recommendations for improved data collection and future modelling work are given.

3.   Agent-based model – DrugChat

In this section, an agent-based model is developed that uses insights from ethnographic research to investigate the role of social networks, choice and social influence on drug use and on transitions from use to dependence. Instead of fitting model results to observed data, the simulation model creates findings and hypotheses to be tested against further research to take forward our understanding of how drug use may spread within communities. The model starts with a population of agents connected through social networks. Agents are either non-users, users, or addicts. Non-users and users choose to use drugs if they are offered on the basis of their attitudes to risk and to taking drugs, which are influenced by members of their social network and by their prior experience. The simulation follows the theoretical population through and can measure the number and proportion of the population that remain non-users, use drugs and become addicts, and changes in their attitude towards drugs. At the same time, it can illustrate types of individual histories of drug use that may be relevant to future ethnographic work.

The model could be extended to explore what might happen under other hypotheses, such as introducing a change in the probability of having a good experience from using drugs with increased use, incorporating the potential harms associated with use, adding dealing and a drug market, or allowing the dynamic creation of deviant networks based on shared attitudes to risk and drug taking. The priority given to these different developments could reflect policy interest, synthesis and collection of ethnographic knowledge, and ability to generate sensible agent biographies and aggregate use statistics.

Finally, modelling can help evidence-based policy by 'organising' data and drawing attention to consequences of social interaction that are hard to envisage. At the same time, modelling requires additional data in order to deliver these benefits.
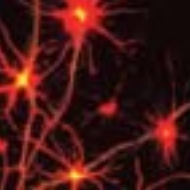
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Edmund Chattoe, Matthew Hickman, Peter Vickerman
Department of Sociology, University of Oxford
Centre for Research on Drugs and Health Behaviour, Imperial College
Health Policy Unit, London School of Hygiene and Tropical Medicine

1 Introduction

Modelling can enhance and contribute to the evidence base for public policy. Models can help:

- estimate the size of a problem
- understand what factors might be important in determining the spread of diseases or other health problems
- assess which prevention strategies may result in the greatest gain
- shape policy questions, future data collection or research by
  - simulating how patterns of behaviour and harm may occur
  - identifying where the greatest uncertainties lie
  - determining what evidence may be required to test simulation models.

Current policy-relevant questions that could be informed by modelling are concerned both with drug use and its harms. Modelling could be used to examine issues such as:

- What are the trends in consumption of heroin and crack-cocaine and their impact on crime?
- What is the best mix of treatment, criminal justice and other prevention activities for reducing drug-related deaths?
- What interventions might be successful in delaying onset or preventing progression to problematic drug use and the harms associated with drug use?

Equally, future questions will be concerned with how we monitor and prevent the spread of, or the risk of problems associated with, new or previously rare, potential harmful drugs such as new stimulants or methamphetamine.

What models cannot do, however, is to provide clear answers in the absence of empirical data or in the presence of great uncertainty about the nature of the relationship between behaviour and harm. Indeed, there is a danger, if the uncertainty is too great, that models may be uninformative and show too wide a range of possible outcomes.

There are several modelling approaches that can be used to look at these issues – statistical; system-dynamic; agent-based; economic; scenario- or complex system-based – but no ready-made menu about which approach may be best for which policy question. The Drug Policy Modelling Project (DPMP) in Australia provides a more comprehensive assessment of the range of approaches that can be used to describe the dynamic relationship between drug policy and a mix of interventions – law enforcement, treatment and prevention – on heroin use. Below we give three illustrations of the potential contribution of modelling: statistical model estimates of the prevalence and incidence of opiate use; a system-dynamic or infectious-disease model of a drug-related harm (Hepatitis C transmission and prevention among IDUs); and an agent-based model of the potential spread of drug use in a population. In addition, we discuss the available epidemiological data in England and Wales. These are only examples. It is important to note that system-dynamic models have been used to estimate trends in drug use (for example, cocaine use in the United States) and agent-based models have been used to assess harms (for example, to assess the dynamics of policing, price and consumption on mortality, and to model the transmission of drug-related harms); and other types of model can also be used to assess the dynamics of the drug-use population, and of harms and policies.

In the next section we give a brief introduction to modelling.

1.1 Contrasting approaches

Different styles of modelling can be characterised by what they assume about cause and effect and about the nature of the regularities that can be found in social systems. It is a mistake to think that some modelling approaches are more 'objective' than others simply because these assumptions are made less explicit. In fact, the applicability of a modelling technique hinges on the evidence we have for believing that such cause-and-effect relations and regularities occur in the social setting that we wish to understand.

This issue can be illustrated by comparing three different modelling approaches in terms of their assumptions concerning cause-and-effect and regularity. It is important to stress that these approaches are not better or worse in themselves, but are more, or less, appropriate for modelling particular kinds of social behaviour.

First, the main strengths of statistical modelling are its relative simplicity and the level of technical confidence that can be placed in the results. Most of the techniques involved are well established and may be supported by dedicated software. In its most general form, the task of statistical modelling is to detect and measure associations between quantitative variables. In the case studies presented here, the tasks of capture-recapture and back-calculation are to estimate hidden populations as accurately as possible from their recorded traces. This application is likely to work well, certainly in the case of capture-recapture, both because the

technique is being used to measure an association rather than explain it and because the association it seeks to measure is relatively free of behavioural elements. There is no reason to suppose that the different ways in which drug use can come to the attention of the police or hospitals are biased by drug user behaviour in a way that will systematically distort the measured association, particularly over short timescales. By contrast, the accuracy of the associations measured in the back-calculation analysis is conditional on the assumption that the main determinants of the observed association are 'physiological' (and thus relatively stable) rather than 'social'. If what 'drives' the system is (as in this case) the logic of a disease, it is reasonable to assume stability in the underlying parameters. If, by contrast, the system was driven by the evolution of social practices in drug use, it seems much less likely that the underlying associations would be stable enough to be measured with confidence. Effective applications of techniques such as those presented here can thus be contrasted with more problematic ones found elsewhere.

A common approach is to use regression analysis to measure associations between predisposing factors (unemployment, problem family history) and drug use[1]. In this case, there can be little argument with the mere measurement of association but explanations and predictions derived from these are far less convincing. It is clear that there is an 'explanation gap' between the observed association and the process that generates it. If we find an association between coming from a broken home and drug use, we can easily think of social reasons why this might be so (lack of control, psychological stress and so on), but the regression analysis does not differentiate between these. It is necessary to go away, collect more data on these variables, run another regression and hope the insights are confirmed after the fact. At the same time, the kind of explanations that are postulated and confirmed will determine the stability of the relationship for predictive purposes. It is reasonably plausible that psychological stress will always lead to some form of drug use but the drug choice (legal or illegal, for example) is likely to be a result of factors that are contextual, social and individual. In these circumstances, patterns of association found in statistical models might not constitute meaningful explanations, let alone be a stable basis for prediction.

Second, the main advantage of 'stocks and flows' approaches to modelling is that they recognise some of the key dynamic aspects of social processes while still retaining simplicity and the ability to use standard software. System dynamics[2-6] is the best-known example of an approach of this kind and is used in the case study presented here, but other approaches based on equation systems and Markov chains[7, 8] operate on the same principles. Instead of static variables, these techniques hypothesise flows between states. For example, light drug users may quit or become heavy drug users, while heavy drug users may quit (with more difficulty) or die. These transitions define evolving populations of different user types and capture key behavioural features of the system and its causal order. In this example, the transition from heavy use to non-use ought to be less common

than that from light use because it is harder to achieve. As with statistical models, the applicability of this approach hinges on assumptions about how social the process is that we are trying to model.

Ethnographic research[9-12] suggests that factors such as individual choice and social network position play important roles in determining drug-use biographies. In principle, these factors can simply be added to a 'stocks and flows' model by increasing the number of stocks (for example, 'well connected light user'). In practice, however, this leads both to technical problems with sampling and management of the model and doesn't really solve the conceptual difficulty, which is that certain forms of choice and social context are not well approximated by stocks of homogeneous actors and stable flows between them.

Infectious disease models are an important subset of system-dynamic or 'stocks and flows' models. Given the difficulty of directly measuring the dynamics of infections (such as HIV, Hepatitis B and C) among drug users, these provide an alternative approach to predicting the dynamics of disease transmission, and crucially the potential impact and cost-effectiveness of disease prevention interventions[13-18]. The power of this form of mathematical modelling lies in its ability to translate individual risk behaviour into patterns of disease transmission, and to explore what factors affect the transmission of a dynamic disease within a population over different timeframes including possible intervention strategies, and for different assumptions about risk behaviour, disease progression, behaviour change and policy intervention[19-24]. We develop a model of Hepatitis C (HCV), as an example and because of the central importance of drug use in the transmission and epidemiology of HCV in the UK. The model is used to illustrate possible insights this kind of model can give, and an extensive discussion is included, with recommendations, outlining how this modelling could be improved or extended, and what the urgent data needs are to improve its accuracy and power.

In addition, system-dynamic models have successfully modelled the cocaine epidemic in the US[8, 25]. They estimate consumption and fit rates of initiation, escalation to heavier use, cessation and average time of use to estimated trends in the prevalence of cocaine use. In one model, it was extended to trends in arrests and seizures[3]. We had originally intended to illustrate the use of a similar model for the UK. However, data from population surveys were not available in time.

Third, agent-based models attempt to tackle the 'explanation gap' discussed above by explicitly modelling the internal states, decision processes and social interactions of individuals. Instead of variables and parameters or 'types' and transitions, these models deal with simulated populations and their interactions. For example, the decision to use drugs may be influenced by subjectively perceived risk and that perception of risk may be determined by communication with others who have used drugs. This means that individuals in different social network positions will evolve potentially unique risk perceptions that will continue to change over time.
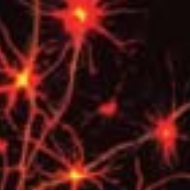
An agent-based model will make explicit assumptions about how these processes of communication and influence occur, based, for example, on ethnographic evidence. Thus, models of this kind are most suitable for helping us to understand social processes such as the etiquette of needle sharing discussed in the hepatitis case study. The downside is that agent-based models are relatively complex and cannot be built simply using standard software. This means that for processes believed not to be very 'social' (such as the other two case studies presented), an agent-based model may be a needless refinement. The final issue connected with agent-based modelling is potentially ambiguous as an 'advantage' or 'disadvantage'. Agent-based models require all assumptions about behaviour and interaction to be made explicit. This contrasts with some of the implicit assumptions about social regularity which are found in statistical and 'stocks and flows' models. (A profound but technical discussion of these in the context of statistical modelling can be found in Abbot (2001)[26].) On one hand, this process is very labour-intensive. On the other, it draws clear attention to things we don't yet know or don't fully understand.

To sum up, when we only want to know what is happening, statistical models may well be adequate. When we want to know why something is happening, a dynamic model will certainly be required. When the reasons why something is happening involve choices and social structure as well as individual attributes, an agent-based model may be required.

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2 Statistical models

A key piece of evidence for policy makers, used for targeting interventions and measuring total harm, is the prevalence or frequency of the problem. Estimates of the prevalence of problem drug use can be essential parameters in modelling the dynamics of the population and population need, and assessing the potential impact of interventions. For instance, modellers in the US have used estimates of the prevalence of light and heavy cocaine use over time to estimate the consumption of cocaine use, the duration of use, rates of cessation, and escalation between light and heavy use[1, 2]. Modellers in Australia and the UK have used estimates of the incidence and prevalence of opiate use (with other information) to estimate the spread of HCV infection in the population and potential future morbidity and mortality from HCV and treatment need[3, 4]. We have also used information on the prevalence of injecting in models to estimate the impact and cost-effectiveness of syringe distribution on HIV transmission, and impact of increasing the coverage of syringe distribution on endemic HIV prevalence[5, 6].

Smoking, alcohol, cannabis and some other forms of drug use are more than adequately measured directly through population surveys. This is not the case for injecting drug use, heroin or crack-cocaine use because of multiple response biases. Injecting drug users or crack-cocaine users are less likely than non-problematic drug users to live in households included in general household surveys, IDU/crack users may be less likely to participate in the survey even if asked, and injection or crack use may be less likely to be reported than other forms of drug use. For example, in 2002 the British Crime Survey, which surveyed about 30,000 subjects, found less than 50 subjects reporting heroin or crack use in the last month, which gave an estimate of 33,000 heroin or crack users in Britain[7]. This is less than the number of heroin users presenting to specialist drug treatment agencies, and less than an estimate of the number of crack users in London[8].

One solution is to develop and use indirect estimation methods[9] using routine data sources. Two examples are summarised below, with implications for surveillance and new problem drugs.

In the US, large-scale population surveys have been available since the 1970s. Data were collected on current and past use and age of first use, which together with year of survey can be used to estimate year of first use and time trends in the incidence and prevalence of drug use[10]. Such methods have been used to estimate

the growth in cannabis use and have been used to estimate trends in cocaine use[1, 11], but failed to detect any discernible change in heroin use from 1960 to 1990. This is implausible given the known, marked changes in heroin use and its harms over this period, and invalidates the method at least for heroin.

2.1 Indirect estimation: capture-recapture and back-calculation

The rationale for indirect estimation methods, based on statistical models, is that population surveys (or direct methods) are impracticable or unreliable, and a simple count of known cases will not suffice because an unknown number and proportion of IDUs and other problem drug users will not be in contact with any data source.

The starting point for indirect estimation is one or preferably many data sources on a sample of problem drug users. The aim of indirect estimation methods is to analyse the observed data set or combine it with other information to estimate the 'proportion of the [problem drug use] target population sampled within the observed data set', and thereby to arrive at an estimate of the prevalence. In other words, indirect methods use routine data sources as their raw material to estimate the sampling intensity i.e. the proportion of the total number of problem drug users observed or recorded by the data sources.

The problem with indirect methods is that they are 'inherently uncertain', often involving several untestable assumptions about the relationship between subjects recorded within the data sources and the underlying population of problem drug users; and that any statistical uncertainty (expressed in terms of 95% confidence intervals) is often far outweighed by model uncertainty or mis-specification.

In the next section, we give two examples of statistical models and indirect methods to highlight our current level of knowledge in order to illustrate both how the information might be used in other models and the implications for future surveillance of current and new problem drugs.

2.1.1 Case Study 1: Estimating the prevalence of IDU in three cities in England[12]

Tables 1–4 show the steps and output of the study. In Table 1, data are collected on problem IDUs in contact with different services: specialist treatment, police arrests, syringe distribution programmes, accident and emergency (A&E) departments, and a local survey of IDU recruited in the community. Table 2 shows the data sources being matched to identify subjects who were identified on only one or more than one of the data sources. All things being equal, the proportion of overlap is an indication of the size of the unobserved population. Statistical models are fitted to the data set, and the best-fitting model is used to predict or estimate the number of

IDUs in the population who in that year were not captured or identified by the data sources. Table 3 illustrates the combination of the observed and unobserved numbers of IDUs, which gives an estimate of the total number and prevalence. Then these estimates can be used to provide key public health indicators, such as the coverage of syringe distribution per IDU and per injection, the proportion of IDU in treatment, and the overdose mortality rate between sites (Table 4).

In this way, the prevalence of IDU and other forms of problem drug use can be estimated for many cities worldwide[13-17].

There are a number of observations that can be drawn from these studies.

- Prevalence of injecting, heroin, and crack use – at over 1% – among young adults is no longer rare in the UK cities sampled.

- The method works in the UK for heroin and IDU because routine data sources are available, these types of problem drug user predominate (especially in certain treatment and criminal justice data sets) and they have a reasonable probability of presenting or being captured by one of the data sources in their life course.

- The growth in crack-cocaine use, and the increase in numbers of these users in treatment and in contact with other data sets, means that for the first time we have been able to use capture-recapture methods to estimate their prevalence and the overlap with opiate use[8].

- However, these methods cannot work for drug users who have a very low probability of appearing on routine data sets, such as LSD users or even powder cocaine users.

- Indirect methods will probably not work for new drugs because they require data sources that identify and record their presence or use by problem drug users, and sufficient users in contact with routine data sources.

Reliance on routine data sources that only ever partially count the total number or prevalence of a disease or public health problem is a general problem, not just for problem drug use. One solution is to make explicit use of capture-recapture methodologies and invest in a mix of data sources that together can provide reliable estimates of prevalence[18]. At the very least, government investment in data sources should follow a common strategy and we strongly encourage (if it cannot be conditional) the provision of common data sets for record linkage and the regular estimation of the prevalence of heroin, IDU and crack use.

Table 1: Data on IDUs in contact with different services in three cities

Data Source	Brighton			Liverpool			London		
	Total	Female (%)	aged under 25 (%)	Total	Female (%)	aged under 25 (%)	Total	Female (%)	aged under 25 (%)
Treatment	193	11	13	654	26	8	2225	24	14
Arrest	82	40	30	232	25	11	755	19	20
Needle exchange	631	22	15	599	20	9	1627	22	14
Overdose at A&E	33	27	21	38	34	21	281	25	22
Survey	95	27	12	146	25	16	414	29	32
Total cases	1034	22	16	1669	24	10	5302	23	17
Individuals	857	24	16	1224	24	10	4252	24	17

Table 2: Data sets matched to identify subjects with data sources

Total subjects captured by data sources	Treatment	Arrest	Needle exchange	A&E and survey	Gender	Age
			(0: no; 1: yes)		(0: male; 1: female)	(0: <30; 1: 30+)
.[i]	0	0	0	0	0	0
.	0	0	0	0	0	1
.	0	0	0	0	1	0
.	0	0	0	0	1	1
8	0	1	0	0	0	0
15	0	1	0	0	0	1
13	0	1	0	0	1	0
4	0	1	0	0	1	1
144	0	0	1	0	0	0
232	0	0	1	0	0	1
57	0	0	1	0	1	0
3	1	0	1	1	0	0
3	1	0	1	1	0	1

i. '.' relates to the number of unobserved subjects of either gender or any age

Table 3: Combination of observed and unobserved IDUs to estimate total number and prevalence

		Brighton	Liverpool	Twelve London Boroughs	Inner London
Population (aged 15-44)		117,000	195,000	1,361,000	885,000
Observed		856	1,222	4,235	3697
Unobserved		1,448	1,688	12,547	10,987
Total		2,304	2,910	16,782	14,684
95% CI	Lower	1,500	2,500	13,800	10,700
	Upper	3,700	5,000	21,600	29,200
Prevalence		2.0%	1.5%	1.2%	1.7%
95% CI	Lower	1.3%	1.3%	1.0%	1.2%
	Upper	3.2%	2.6%	1.6%	3.3%

Table 4: Public health indicators

Estimated IDUs	Brighton 2,304		Liverpool 2,910		London 31,466	
Public Health Indicators	Number of events	Indicator	Number of events	Indicator	Number of events	Indicator
Proportion of injectors receiving structured treatment	363	16%	654	22%	7,500	24%
Annual number of syringes distributed per IDU per year (coverage per injection)	429,000	186 (27%)	566,500	195 (28%)	4,910,000	156 (22%)
Opiate overdose mortality rate	48	2.1%	28	0.96%	236	0.8%

2.1.2 Case Study 2: Estimating long-term trends in opiate use in England

Back-calculation methods have been applied very successfully to AIDS and other diseases with long latency periods, such as CJD[19]. They are underpinned by the assumption of an association between the end point, incidence and incubation distribution of a problem; and that knowledge of any two of these can be used to estimate the third. Thus, knowledge of time trends in AIDS cases and the progression between infection and AIDS can be used to estimate incidence of HIV. Figure 1 shows the components of a study that sought to estimate the long-term trends in opiate use in England[20]. First, a known end point is taken: trends in opiate overdose deaths. Second, information on the opiate overdose mortality rate and

cessation rate, which comprise the 'incubation distribution' – time between onset of opiate use and death – are obtained or assumed. Third, these data are combined to estimate the incidence of opiate use i.e. the number of opiate users there might be in the population, to generate the observed trends in opiate overdose deaths. Fourth, the estimated trends in incidence are combined with information on the incubation period to generate trends in the prevalence of opiate use.

Figure 1: Back-calculation: estimates of long-term trends in incidence and prevalence of opiate use[20]

Left axis	Right axis
Opiate overdose deaths	Prevalence (upper credibility interval)
	Prevalence (lower credibility interval)
	Incidence (upper credibility interval)
	Incidence (lower credibility interval)
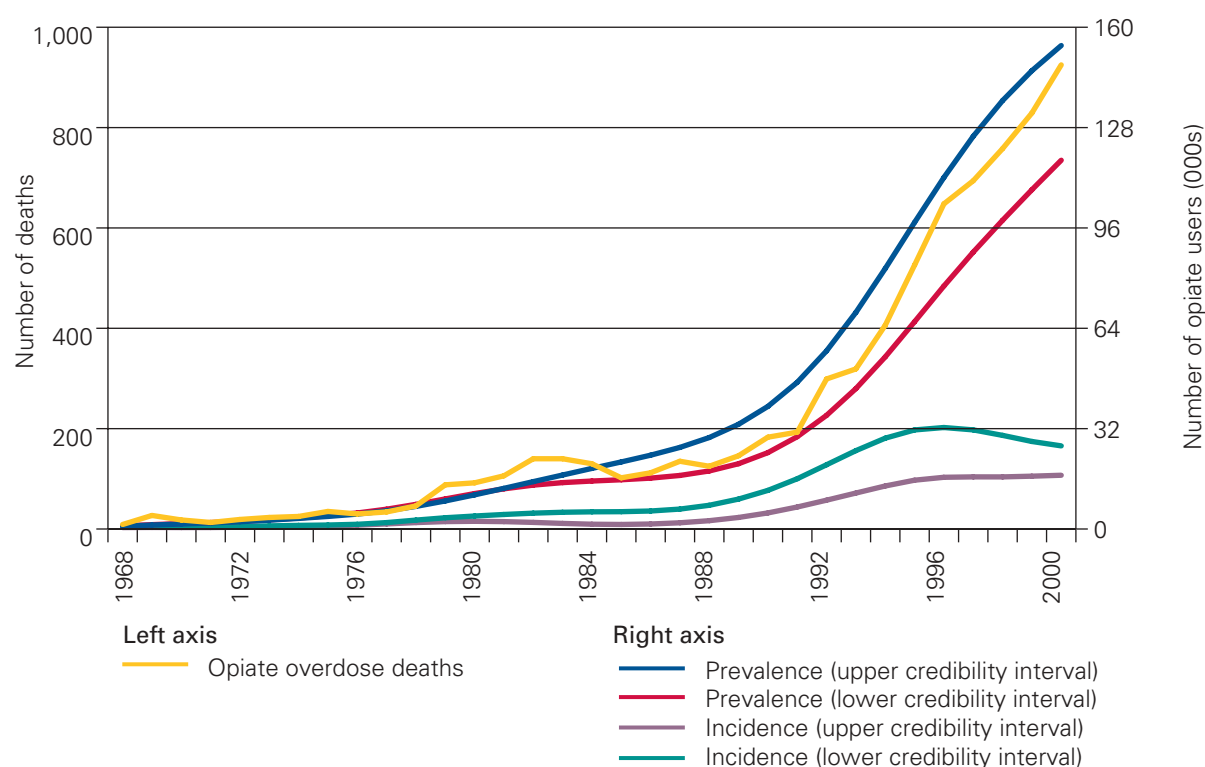
The findings raise a number of implications:

- Uncertainty in the projections of prevalence and incidence reflect model uncertainty over two key inputs: opiate overdose mortality rate by calendar year and age group, and cessation rate. The methods cannot be taken forward or uncertainty reduced without improved surveillance and investment in monitoring drug-related mortality and better data on the life course of injecting drug use. These factors are important in other models of drug use and may be of general interest for policy makers.

- If true, the findings suggest a dramatic increase in opiate use in England and Wales, especially in the 1990s. There can be few other social or health problems that have increased as dramatically in the population. Although the estimates by themselves cannot answer the question why opiate use has increased to such an extent, they can provide an end point for models to be fitted against. However, there is unlikely to be a simple relationship between candidate risk or protective

factors that could explain the many fold increase in use over the last 30 years[31]. Knowledge of individual susceptibilities, the impact of increased exposure, and the interaction between different risk and protective factors are insufficient to build an explanatory model.

- The back-calculation model estimates a population that, by definition, has a risk of opiate overdose death, and is likely to exclude 'recreational' or one-off users of opiates. Other methods or data sources – such as the use of population surveys – may be required to estimate this population and the total population that has used opiates.

- Similar output in Australia has been used in models of the transmission of HCV infection[4]. In applying these models to England and Wales, we suggest the model findings are highly sensitive to a few parameters which themselves are very uncertain: number and proportion of recreational IDUs and average injecting frequency.

- Back-calculation methods are unlikely to be useful for new or other drugs without trends in a specific end point.

2.2 Public health framework

Models also require data and knowledge on the nature and strength of the relationship between drug-using behaviours and specific outcomes, or between specific factors and the progression of problem drug use in order to be informative in assessing the potential impact of different policies. In this section we summarise the current data sources and evidence available for describing problem drug use.

One conceptual framework of drug use proposes that[21]:

Total harm = Average harm × Prevalence

This also follows the 'public health framework' for examining drug use and harm as outlined by the Institute of Medicine[22]. That is: a change in drug policy or specific public health intervention should be judged on whether it manages to reduce 'total harm' through its impact on the 'average harm' or overall 'prevalence' of use. Moreover, within a public health framework, drug use itself is a 'risk factor', the significance of which lies in its association with key public health harms (whether lung cancer, overdose, heart disease, infection, injury and violence, crime, mental and social functioning, or loss of earnings).[i] One theoretical argument brought against the 'legalisation' of cannabis or other drugs is that even if 'average harm' is reduced there may be no impact on total harm – or it may even rise – if there is a proportionally greater increase in prevalence than the decrease in average harm[23].

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i   Discussion of harms associated with drug use are covered in more detail in other sections.

The concepts within the model also are similar to the public health concept of 'attributable risk' and 'population attributable risk'[24]. The 'attributable fraction (AF)' measures the proportion or fraction of harm among exposed cases, in other words, how much harm could be prevented among those exposed. The 'population attributable fraction (PAF)' or 'etiologic fraction' is a measure of the proportion of harm in the population caused by the exposure, or of how much harm could be prevented by successfully eliminating the exposure. The information required to estimate AF or PAF is an estimate of the risk of disease given exposure, and the prevalence of exposure in the population. For example, over 90% of lung cancer among those who smoke can be attributed to smoking and approximately 80% of lung cancer in the population is due to smoking (http://www.hda.nhs.uk/documents/smoking_epidemic.pdf). Deaths associated with illicit drug use also impact greatly on the health of the population. In several European cities it has been estimated that over 1 in 100 injectors die annually (between 10 and 20 times higher than the general population) and contribute over 10% of deaths among young adults aged 15-44[25].

Smoking and alcohol use are associated with many diseases[24]. The quantification of harm from smoking and alcohol which have been so influential, for example, in Australia, and also conducted globally for the World Health Organisation (WHO), has been possible because of the availability of several large-scale cohort studies that follow up and compare mortality and morbidity among smokers, non-smokers and drinkers and non-drinkers, and because information on the frequency and prevalence of smoking and drinking is generally available directly from population surveys. Public health strategies and interventions that successfully reduce the prevalence of smoking or drinking in the population are likely to reduce the level of harm in the population, and there is growing evidence on which strategies are likely to be most successful.

In contrast, the same degree of information (either on the size of the population, the size of the risk associated with public health/social problems, or the effectiveness of interventions to reduce prevalence) is not as readily available for injecting or other forms of drug use in the UK or many other countries, limiting estimates of the quantity of harm in the population. Further, it is important that the level and proportion of crime, as a key social cost, associated with injecting and other illegal drug use is measured as well as health harms.

Birth cohort studies provide the best means of assessing the problems associated with common exposures – such as the link between cannabis use and school problems and adult schizophrenia – as they can adjust and allow for other potential risk factors that are related or antecedent to cannabis use[26, 27]. However, these types of study are likely to be biased and have insufficient power (due to small sample size, and differential loss to follow-up) to measure factors associated with injecting or crack use.

Thus, the complexity in the formulation of total harm, at least for injecting and some other types of problem drug use, lies in the measurement.

2.3 Routine data sources: measuring drug harms

The US has invested in school and general household surveys of problem drug use and other surveys of the consequences of drug use. These include two annual national surveys (Monitoring the Future, and the National Household Survey on Drug Abuse) and at least two national surveillance systems, one of drug-related crime through the Arrestee Drug Monitoring Programme, and the other of drug-related problems at emergency rooms and deaths (Drug Abuse Warning Network), as well as other one-off or periodic surveys[22, 28].

Notwithstanding the wealth of information provided, both the Institute of Medicine and the National Research Council noted a number of gaps in the available information, and made a number of recommendations to improve it. These may be relevant to the UK and include:

● Establish better evidence and monitoring of drug consumption and price. The uncertainty surrounding these data hinder economic models assessing the effectiveness of strategies to increase price and/or reduce consumption.

● Establish the nature of non-response in population surveys. At the moment, interpretation of trends over time requires a strong but unlikely assumption that non-responders are similar to responders.

● Increase opportunities for record linkage across surveillance systems, to corroborate and enhance the information provided.

● Increase effort to evaluate drug prevention initiatives – including evaluating universal versus targeted programmes focusing on initiation or transitions from use to abuse and dependence, and on modelling the potential impact of delaying the onset of drug use.

● Develop principles and procedures for information and surveillance systems on illegal drug taking and associated hazards.

● Investigate better (with long-term studies) the etiology, risk and protective factors associated with transitions to abuse and dependence.

2.4 Only connect: towards an information strategy

We recommend policy makers consider commissioning a similar review (across government departments and with multidisciplinary scientific input) to identify key gaps in our information and opportunities for greater integration of current information systems.

Table 5 outlines some of the data sources available. There are notable absentees from the list. The UK has no ongoing data on the distribution of syringes[29], the drug-related mortality rate[30], prices and the consumption of drugs, emergency room visits for drug-related problems, or the prevalence and incidence of problem drug use. We do not know whether current policies are having an impact on reducing the risk of death among IDUs or what the optimal level of substitution treatment and other interventions might be to minimise drug-related mortality. This could be addressed with a combination of epidemiological and modelling work. Further, we are missing unbiased estimates of a number of parameters, including the probability of arrest, ratio of light to heavy users, and the probability of treatment.

There is already substantial investment in drug-related information and surveillance. Investment in brand-new information systems is unlikely. What is missing, therefore, is an overarching strategy that can make the best of what data are collected, and to consider modifying existing data sources to provide added value. Some specific suggestions would include:

- Establish ongoing record linkage between criminal justice and health data sources:

  a Provide raw material for estimating the prevalence of opiate and crack-cocaine use.

  b Generate ongoing prevalence estimates for use in modelling.

  c Introduce recording of key event histories to multiple routine data sources, such as frequency and date of last arrest, treatment, imprisonment, HIV/HCV antibody test, overdose managed at A&E, hostel stay.

  d Combine the information to allow 'unbiased' estimates of the probability of these events among problem drug users, which can be monitored over time.

  e Provide raw material for other indirect estimations of prevalence

  f Provide parameters for models of the flow of problem drug users from onset, to arrest, imprisonment, treatment etc. and allow scenarios to be tested, for instance, on the potential impact of reducing time from onset to first treatment, increasing arrest.

- Establish new records of linkage and cohort studies to estimate mortality rates (based on existing data sources linked to the Office for National Statistics) of problem drug users over time:

  a Monitor drug-related mortality and whether prevention strategies have been effective in reducing the risk of death and the number of deaths

  b Estimate and monitor the Standardised Mortality Ratio of problem drug users compared to the general population, and Population Attributable Fraction of drug-related mortality.

    c Provide key parameter for estimating incidence and prevalence of opiate use over time.

    d Provide data for the modelling of drug-related mortality and what impact different strategies might have on reducing the number and risk of drug-related deaths.

- Link questions on population surveys with routine data sources on problem drug users such as the probability of arrest and treatment, and the frequency and consumption of the drug:

    a Provide parameters for combining direct and indirect estimations of cocaine use, and other more frequent types of drug use including that of amphetamine, MDMA.

    b Establish trends for models of drug use in the population.

- Establish and introduce standard questions on drug consumption and price for ongoing surveillance and surveys of problem drug users (including specialist drug treatment, community surveys, and arrestee monitoring):

    a Monitor changes in consumption and price of key drugs over time.

    b Provide parameters for economic models of the impact of different policies on price and consumption.

These examples build on or adapt existing data sources to provide more information on prevalence and incidence, and key events or harms during the life course. The routine data sources do not constitute an 'early warning system' per se, though misuse of new drugs will be identified if they lead substantial numbers to die, commit crime or seek treatment. The information derived may support estimates of the occurrence of drug use – such as the trends in opiate use shown above, or cocaine use – but cannot answer questions about what factors might be driving the change in numbers. To answer these questions requires further research on the causes of 'problem' drug use.

Many longitudinal studies have focused on the risks and protective factors associated with drug initiation, or with problems associated with cannabis use. There is less information on early-life risk, individual vulnerability and environmental factors that might increase exposure to drug use, and the onset of problem drug use such as heroin, crack-cocaine use or injecting. This limits any quantitative modelling work that could be used to model the dynamics of problem drug use, and how changes in policy that impact on environmental exposure, community and individual resilience might reduce future incidence and prevalence.

Table 5: Data sources available for surveillance of drug use and harms

Selected indicators	Source	Purpose	Limitations	Weblink
Drug use – population survey	British Crime Survey	Measure monthly/yearly/ lifetime drug use (cannabis, amphetamines, ecstasy, powder cocaine)	Inefficient and unreliable measure of rare and most problematic forms of drug use (heroin, crack and IDU). Data on age of first use or consumption is missing from historical surveys. No data on type of non-response	http://www. homeoffice.gov.uk/ rds/bcs1.html
	Crime and Justice Survey	Measure monthly/yearly/ lifetime drug use and age of first use (cannabis, amphetamines, ecstasy, powder cocaine)	Inefficient and unreliable measure of rare and most problematic forms of drug use (heroin, crack and IDU). No data on consumption. No data on type of non-response	http://www. homeoffice.gov.uk/ rds/offendingcjs. html
Health indicators and harms Drug-related deaths	Office for National Statistics (ONS) – mortality statistics/drug-related deaths	Measure number of drug-related poisonings and deaths mentioning specific drugs on the death certificate	Drugs cited on death certificate do not reflect full toxicology. Does not measure total number of drug-related deaths, or mortality rate	http://www. statistics.gov.uk/ pdfdir/hsq0205.pdf
	St. George's National Programme on Substance Abuse Deaths (npSAD) – surveillance of drug-related deaths from coroners	Measure number of drug-related poisonings and toxicology deaths reported by coroners	Undercount of number of drug-related poisonings – adds little to information provided by ONS. Does not measure total number of drug-related deaths, or mortality rate	http://www.sghms. ac.uk/depts/ addictive-behaviour/infores/ npsad.htm

Blood-borne viruses (BBV) due to IDU	Health Protection Agency laboratory reports of positive cases, clinical reports of AIDS	Measure number of AIDS cases, HIV cases in treatment, HIV, Hepatitis B virus (HBV), Hepatitis C virus (HCV) positive laboratory reports attributed to injecting drug use	Large-scale under-reporting of positive antibody tests from laboratories, data on exposure missing in many cases. Does not measure number of HBV or HCV infections in the population.	http://www.hpa. org.uk/infections/ topics_az/ injectingdrugusers
	Unlinked Anonymous Programme – survey of prevalence of BBV among IDUs in contact with treatment agencies	Measure prevalence of HIV, HBV, HCV among IDUs	Limited behavioural data. Mathematical models or other studies required to measure incidence of infection. Data on prevalence of IDU required to estimate number of infections in the population.	
Specialist drug treatment	National Drug Treatment Monitoring System – reports of problem drug users in contact with treatment agencies	Measure number of problem drug users presenting to specialist drug treatment agencies. Report drugs used in the last 4 months.	Undercount of number of problem drug users treated in primary care. No data on consumption or price.	http://www.nta. nhs.uk
Drug-related crime	Arrestee survey	Measure prevalence of arrests reporting, or positive for recent drug use. Estimate number of reported crimes committed by drug users.	Other information required to estimate total amount of drug-related crime. No estimates of total number of shop lifting crimes committed.	http://www. homeoffice. gov.uk/rds/ offendingarrest. html

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3 Case study: transmission of Hepatitis C in London, UK

3.1 Introduction to HCV and objectives for analysis

HCV is a blood-borne viral infection that affects the liver, causing chronic liver disease, including cirrhosis and liver cancer[1]. Worldwide, 170 million people are estimated to be infected with HCV, while 9 million are thought to be infected in Europe[2].

HCV can be transmitted through infected syringes or other injecting equipment[3-6]. Indeed, over 90% of diagnosed HCV infections are attributable to injecting drug use in the UK and infection rates are high among IDUs[7-9]. In addition, there is evidence that HCV can be transmitted sexually, but the risk is thought to be low compared to that through injecting[10-12]. Once an individual is infected with HCV, they enter an acute phase of infection that can last from 8 to 20 weeks[13-16]. During this time, the individual usually develops an antibody response[13, 14, 17-20]. Following the acute phase of infection, an infected individual will either develop chronic infection or will spontaneously self-cure. The majority do not self-cure, although the proportion who do not is highly variable – from 50% to about 80%[17, 20, 21]. Among the self-curers, there is evidence that the acute phase of infection may have lower viraemia than for chronically infected people[13, 17]. Conversely, there is a some evidence for a higher peak in viraemia in the acute phase of those individuals who develop chronic infection[13, 14, 17]. There is evidence that the self-curers develop a strong cell-mediated immune response, and that they can resist future infections[16, 22-26]. The chronically infected group remain infected for a long period of time.

HCV infection is an important public health concern because of its long-term consequences. After 30 years, approximately half the people infected with HCV develop cirrhosis of the liver and, once cirrhosis has developed, 1-5% of individuals per year progress to liver cancer (hepatocellular carcinoma) which often leads to death (50% after two years). The associated treatment costs for these conditions are great[27]. Despite this, limited evidence suggests that the mortality rate of HCV infected individuals is not elevated after 25 years of infection[28]. However, because many of the complications associated with HCV initiate after 20-30 years[29], it is likely that the mortality rate of infected individuals will increase after longer durations of follow-up.

Currently, there is no vaccine for HCV, but treatment is available and increasingly effective, with over 50% clearing the virus. However, current treatment regimes are expensive and long-term, lasting 6-12 months[29]. Indeed, the cost of treatment or care for an individual with chronic HCV infection is estimated to be €750 million for the European Union, and €100 million for the UK[27]. This emphasises the financial importance of preventing the transmission of HCV among IDUs.

In this analysis, a mathematical model for the transmission of HCV is developed for a specific setting (London, UK) to look at the impact of different prevention activities. The model is used to explore what factors affect the transmission of HCV in this setting, to estimate the proportion of IDUs that self-cure, and to explore the relationship between the endemic HCV sero-prevalence of an IDU population and the rate of syringe sharing. The model builds on previous studies that have developed mathematical models of the epidemiology of HCV[30], or have estimated the impact of harm-reduction interventions on HCV transmission[31]. Our analysis further illustrates, as did the study by Pollack (2001), how models can be used to guide policy. The strength of this analysis lies in the use of data from a specific setting, so the conclusions are directly relevant to policy makers from that setting. However, the analysis should be seen as preliminary, to illustrate how modelling can be used, and to highlight the implications of data uncertainty. Lastly, recommendations are made with regard to how the modelling could be taken forward to answer relevant policy questions, and suggestions are made on how to improve data collection to increase the accuracy of the modelling.

The basic methods and results and a full discussion of the findings are included in Section 3.4.

3.2 Methods

3.2.1 Background to study population

The prevalence and incidence of HCV among IDUs in London is high, with the prevalence of HCV being 53% in 2003[32], and the incidence of HCV being 41.8% among new IDUs for 2001-2003[33]. Indeed, there is evidence that the prevalence of HCV has increased recently, possibly due to an increase in syringe sharing[32], especially among newer injectors[33], and an increase in crack injecting[33]. In contrast, the prevalence of HIV among IDUs in London is low, 2.9% in 2003[32].

IDUs in London inject on average 700 times per year. However, syringe distribution does occur, with each IDU receiving on average 143 new syringes each year[34]. Each syringe is used a mean frequency of 3.5 times before disposal (median is 1.5 times). While 33% of IDUs report syringe sharing in the last month, 66% report having shared at least once in their life. The risk behaviour of IDUs in London is summarised in Table 6.
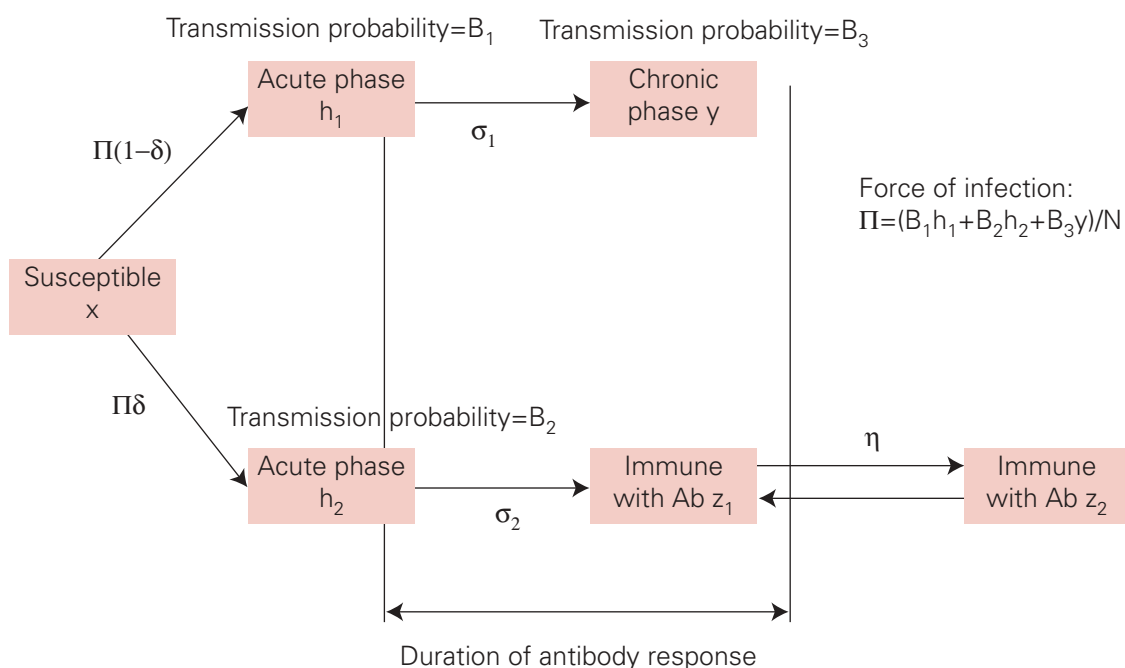
Table 6: Summary table of IDU risk behaviour

Data input	Parameter symbol	London
Frequency of injection per year	T	700
Number of syringes distributed per IDU per year	ε	143
Proportion of IDUs share syringes in the last 3-6 months	s	30-66%
How many times syringe used before disposal	f	3.5
Rate of cessation of injecting per year	μ	10%

There is little data on the frequency with which IDUs share syringes. However, if IDUs are assumed to receptively share syringes only when they do not have a syringe to use, then a proxy estimate for the frequency of syringe sharing can be estimated by calculating '$T - \varepsilon f$' i.e. the discrepancy between the total injection frequency and the product of the number of syringes distributed to each IDU and the number of times each syringe is used by that IDU. Using the data in Table 6, the average rate of syringe sharing per IDU per month was estimated to be about 16.

3.2.2 Description of HCV model

On the basis of the brief review of HCV above, we constructed a model to simulate the transmission of HCV in an IDU population. This initial form of the model is an adaptation of one developed by Kretzschmar and Wiessing[30]. Their model was modified to allow for two different types of acute infection, one leading to chronic infection and the other leading to self-cure, and to incorporate more explicitly the relationship between infection and sero-conversion. The motivation for incorporating two different acute phases was published evidence suggesting that the acute phase before chronic infection was different in terms of viraemia from the acute phase prior to self-curing[13, 14, 17]. Figure 2 shows a flow diagram of the model.

Figure 2: Flow diagram for HCV transmission model

Transmission probability=B_1 — Transmission probability=B_3

Acute phase h_1 — σ_1 — Chronic phase y

$\Pi(1-\delta)$

Force of infection:
$\Pi=(B_1h_1+B_2h_2+B_3y)/N$

Susceptible x

$\Pi\delta$

Transmission probability=B_2

Acute phase h_2 — σ_2 — Immune with Ab z_1 — η — Immune with Ab z_2

Duration of antibody response

Arrows portray possible transformations of susceptible or infected IDUs, and the parameters next to these arrows are the rate of flow per capita between these states.

The IDU population is divided into those who are susceptible to HCV infection (*x*), those who are recently HCV infected and are in the initial acute phase of infection (*h*), and those who have progressed into the chronic phase of infection (*y*) or have become immune (*z*). IDUs are assumed to share syringes at a constant rate and susceptibles are infected at a per capita rate π, dependent on the number of IDUs they share syringes with, and the proportion who are in the acute or chronic phase of infection. The simple assumption regarding syringe sharing was made because of the lack of detailed data on syringe-sharing patterns among IDUs in London. All susceptibles who become infected progress to the acute phase of infection. However, a proportion δ are assumed to progress to the acute phase that leads to self-curing, and the remainder '1 – δ' progress to the acute phase that develops into chronic infection. The duration of the different acute phases is 1/σ, with a subscript 1 denoting those that develop chronic infection and a subscript 2 denoting self-curers. The chronically infected are assumed to remain infected until death. Self-curers are assumed to remain immune for life, but may sero-revert after an average duration 1/η [26, 35-37].

For simplicity, we have not included behavioural heterogeneity in the initial version of the model, or allowed for the sexual transmission of HIV because it is not

thought to be a substantial risk[10-12]. The model in Figure 3 is defined by the following differential equations:

$$\frac{dx}{dt} = \Omega - x(\pi + \mu)$$

$$\frac{dh_1}{dt} = \pi x(1 - \delta) - h_1(\sigma_1 + \mu)$$

$$\frac{dh_2}{dt} = \pi x \delta - h_2(\sigma_2 + \mu)$$

$$\frac{dy}{dt} = \sigma_1 h_1 - \mu y$$

$$\frac{dz_1}{dt} = \sigma_2 h_2 - z_1(\mu + \eta)$$

$$\frac{dz_2}{dt} = \eta z_1 - \mu z_2$$

IDUs leave the population at a per capita rate μ due to death or if they stop injecting, and new susceptible IDUs are recruited at a constant rate Ω. The force of infection Π is dependent on the number of IDUs in the acute and chronic phase of HCV infection, the probability of HCV transmission per syringe- or equipment-sharing incident for each phase of infection, and the injection-equipment sharing behaviour of the IDUs:

$$\pi = \frac{1}{N}\left[h_1 B_1 + h_2 B_2 + y B_3\right], \;\; where \;\; B_i = m\left(1 - (1 - \beta_i)^n\right)$$

where m is the number of syringe-sharing partners they have per month, n is the number of times they receptively share a syringe with each of these partners, and β_i is the HCV transmission probability per syringe-sharing act. N is the size of the IDU population.

3.2.3 Biological parameters for the model

Following a review of the literature, estimates were obtained for the biological parameters required by the model. Due to the large degree of variation in different estimates for specific parameters, uncertainty ranges were produced for each. Table 7 shows the model parameter uncertainty ranges. The rate of leaving the population (μ) was assumed to be the sum of the rates of overdose, sepsis and rate of cessation (about 10% per year). For simplicity, the rate of recruitment of new IDUs (Ω) was assumed to be equal to the rate of leaving.

Table 7: Biological parameter values for HCV model

Model parameter definition		Parameter notation	Parameter range used	Specific estimates	References
Transmission probability per syringe-sharing act in chronic infection phase		$\beta 3$	1.32–2.2%	1.63*HIV transmission probability	Ratio of epidemiological data (see Appendix)
				1.32%	For hollow-bore deep injections [3]
				2.2%	Meta analysis of needle-stick risk [38]
				1.8%	Centre for Disease Control reviews
Ratio of initial peak of viraemia to viraemia in chronic phase		$\beta 1/\beta 3$	1–10	No difference in viraemia	[17]
				~3 times higher	[13]
				>10 times higher	[14]
Ratio of initial viraemia peak to viraemia in chronic phase for self-curers		$\beta 2/\beta 3$	0.1–1	~10 times lower	[17]
				~23% lower	[13]
				No difference	[18]
Duration of acute phase among non-self-curers (initial peak of virus)		$1/\sigma 1$	8–16 weeks	8–16 weeks	[13]
				~8 weeks	[14]
Duration of acute phase among self-curers		$1/\sigma 2$	6–24 weeks	8 weeks	[13]
				12 weeks	[18]
				6 weeks	[19]
				16 weeks	[39]
				12 weeks	[40]
				11 weeks	[20]
				~8 weeks	[41]
				8–24 weeks	[15]
				8–22 weeks	[16]
Proportion of those infected who self-cure	Transfusion data	δ	18–66%	45%	[21]
				20%	[19]
	HCV infections with symptoms			29%	[41]
				66%	[20]
				30%	[40]
				52%	[18]
	IDUs with no symptoms			33%	[13]
				18%	[17]

Model parameter definition	Parameter notation	Parameter range used	Specific estimates	References
Duration till sero-convert		2–14 weeks	7 weeks	[42]
			2–9 weeks	[43]
			12–14 weeks	[39]
			~8 weeks	[14]
			Later than acute phase	[44]
Duration till sero-revert	$1/\eta$	7–15 years for serum test. Less for oral tests	~9 years	[39]
			>8 years	[35, 36]
			>20% in 7 years	[37]
			10–18 years	[26]
			>3 years	[17]

3.2.4 Methods for modelling the transmission of HCV in London

The mathematical model in Equation 1 was modified to simulate the transmission of HCV in London. Firstly, the time variable was redefined as the duration of injecting, to enable the model to simulate the transmission of HCV within IDU cohorts who have been injecting for the same duration. Secondly, it was also adapted to allow for some IDUs not sharing syringes or injection equipment. Lastly, because of the high incidence of HCV observed among new injectors in London[33], the model was modified to enable new injectors to have a higher frequency of syringe sharing, and to allow them to share partly with older injectors (with a higher prevalence of HCV).

Because of the modified structure of the model, it could now be fit to epidemiological data on the overall HCV prevalence, and the HCV prevalence against duration of injecting. This was done for data from IDUs in London for 2001/2002 (see Figure 4). However, because of uncertainty in the model's biological and behavioural parameters, an uncertainty analysis was undertaken. Five thousand parameter sets were randomly sampled from the uncertainty ranges of the model parameters (Table 7), and any model simulation that lay within the confidence intervals of the HCV prevalence data was selected. These model simulations were ranked with respect to the total squared difference between the model's projected HCV prevalence and the observed HCV prevalence for different durations since starting injecting. The simulation with the smallest difference was defined as the best-fit simulation. The model simulations that fit the data were used to estimate the proportion of IDUs who are either chronically infected with HCV or have self-cured and are 'immune' to reinfection, and the likely impact of decreasing syringe sharing on the HCV sero-prevalence for different durations of injecting.

3.3 Results

3.3.1 General model projections for London

Among the model simulations from the uncertainty analysis, 134 of them fit all the HCV prevalence data. The best-fit simulation and observed HCV prevalence data is shown in Figure 3. The model simulation shows a reasonable fit to data, except it does not accurately simulate the observed decreases in HCV prevalence among IDUs injecting for 30 months or longer than 70 months. However, the significance of these two decreases in HCV prevalence is ambiguous because data from other years in London do not show the same trends.

Figure 3: Observed and model 'best fit' HCV prevalence among IDUs for different durations of injecting
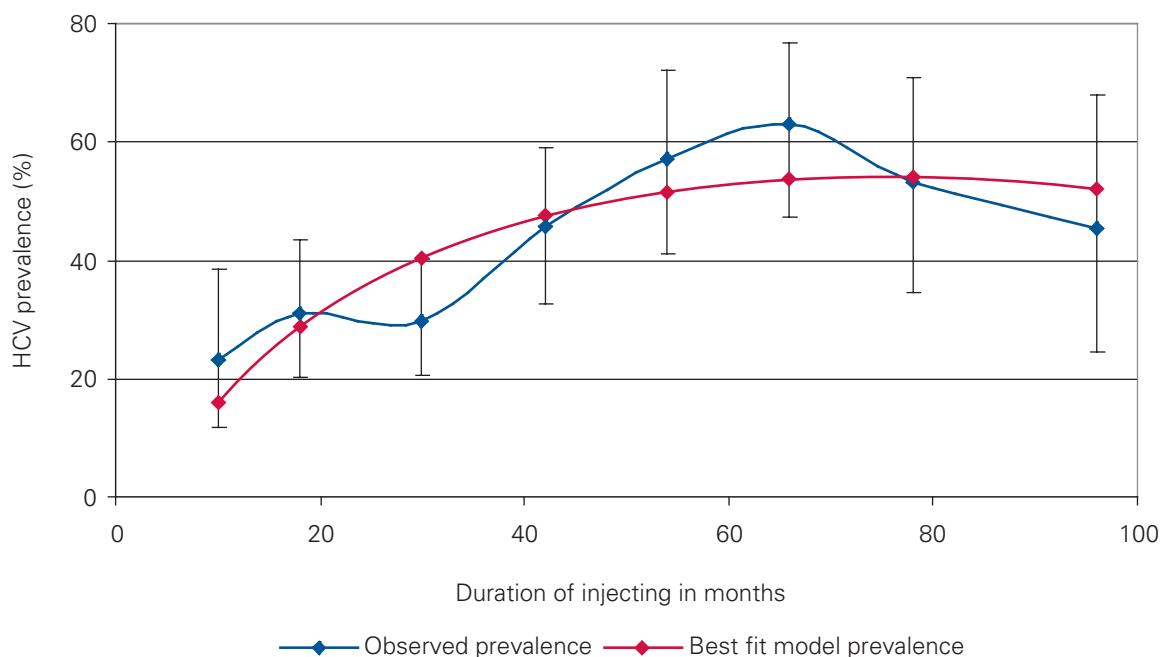
The different model simulations that fit the HCV prevalence data project that among IDUs who have injected for 8 years or less, 31% (18%-43%) are infected with HCV, 24% (7-38%) have had a self-cured HCV infection (and are assumed to be immune), and 45% (33-58%) are susceptible. This is in a population with an estimated HCV sero-prevalence of 44% (37-46%). Among IDUs who have been injecting for longer, the prevalence of infection and self-curers is higher. For example, among IDUs who have been injecting for 16 years, 37% (23-50%) and 31% (9-54%) of them are infected and self-cured respectively. Interestingly, the model projects that the proportion of sero-positive IDUs who are infected varies considerably with the duration of injecting (see Figure 4 for the projections using the best-fit simulation). This is due to some self-curers sero-reverting, and is likely to be more pronounced in our projections because the sero-reversion rate was assumed to be higher

(average duration till sero-reversion was five years in the best-fit simulation) because antibodies were tested in oral fluids, not serum[45]. This result implies that care should be taken in estimating the proportion of HCV infections that self-cure from the proportion of sero-positive individuals who are not HCV RNA positive.

Figure 4: Percentage of antibody-positive IDUs who are infected
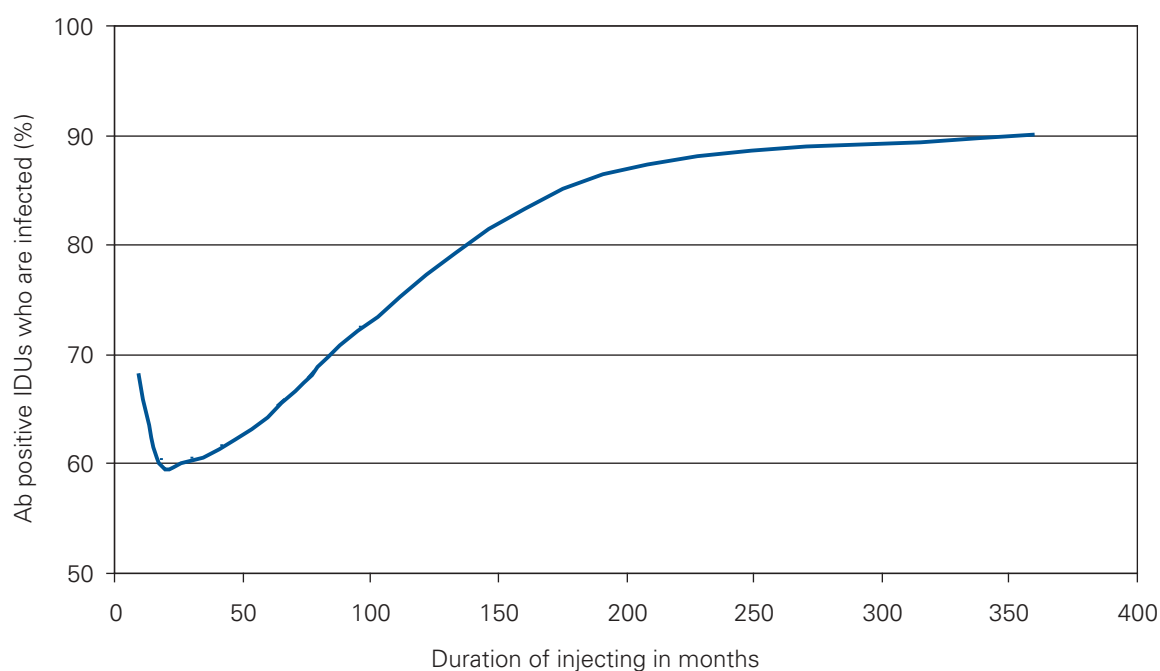
3.3.2 Uncertainty analysis

Although only a small proportion of the model simulations fit the HCV prevalence data, they fit the data over a wide range of parameter values, with most parameters varying across their full uncertainty range. However, from analysing the behavioural parameter values for the simulations that fit the epidemiological data, they seem to suggest that IDUs have a greater frequency of syringe sharing when they start injecting (2.5 times greater in first six months), and some new injectors are likely to share with older IDUs. The reason for the constraints on these behavioural parameters is due to the rapid increase in HCV prevalence observed shortly after IDUs initiate injecting (Figure 3). Both these phenomena have been observed in other IDU populations[6]. However, care should be taken in drawing strong conclusions from this result because the high incidence of HCV among new injectors could be due to other factors not included in the model. These are likely to include the attribute that some IDUs may have a much higher frequency of syringe sharing resulting in them becoming infected soon after starting to inject. This and other possible factors will be analysed in future studies, and highlight the importance of collecting better data on the risk behaviour of IDUs as they progress through their injecting career. This will reduce the current uncertainty about the risk

behaviour of new injectors and the reason for the high incidence of HCV among new injectors. This would be an important step forward because, as will be seen later, it has grave implications for the impact of interventions attempting to prevent HCV transmission.

Conversely, all the biological parameters vary across their full uncertainty ranges for the different model fits. This means that, currently, the model simulations that fit the data have widely different parameter sets. This highlights the importance of further studies to obtain more precise values for the different biological and behavioural parameters in Table 6. The importance of this is further highlighted by noting that, among the model fits, four of the model parameters are heavily correlated with each other. These correlations include a strong negative correlation between the proportion of new injectors who share with older injectors and the increase in syringe sharing among new injectors, so, if one of these parameters is high, the other has to be low for the model to fit the data, and a positive correlation between the proportion of IDUs who share and the proportion of acute infections that self-cure. If one of these parameters is low, the other has to be high for the model to fit the data.

If better estimates are obtained for some of these behavioural and biological parameters, improved estimates for other parameters can be made.

3.3.3 Impact of decreasing syringe sharing in all IDUs

When the best-fit simulation is used to project the impact on the endemic HCV prevalence of decreasing syringe sharing in all IDUs, the predictions in Figure 6 are obtained for IDUs who have been injecting for different durations.

Figure 5 suggests that a modest decrease in syringe sharing will result in a noticeable decrease in the HCV prevalence among IDUs who have been injecting for less than eight years. However, among IDUs who have been injecting for longer than this, syringe sharing has to decrease by at least 50% to result in a 20% relative decrease in HCV prevalence. For example, among IDUs who have been injecting for 16 years, syringe sharing has to decrease by nearly 75%, from 16 to 4 receptive syringe shares per month, to result in a decrease in HCV prevalence from 45% to 32%. To reduce the HCV prevalence to a very low level, say less than 5% among all IDUs who have been injecting for 16 years or less, the rate of receptive syringe sharing has to decrease to a very low level – less than once a month. It is important to note that these projected reductions in HCV prevalence (Figure 5) assume that the average syringe-sharing rate was at this reduced level when the individuals started injecting. For example, the reduction in syringe sharing will have to have been sustained for at least eight years to get the reduction in HCV prevalence predicted for IDUs injecting for eight years.

Figure 5: Projected endemic HCV prevalence for different syringe-sharing rates among IDUs who have been injecting for different durations

The initial level of syringe sharing is 16 per IDU per month in London.

Duration since initiating injecting:

- prevalence over first 8 yrs
- prevalence after 8 yrs
- prevalence after 16 yrs
- prevalence after 30 yrs
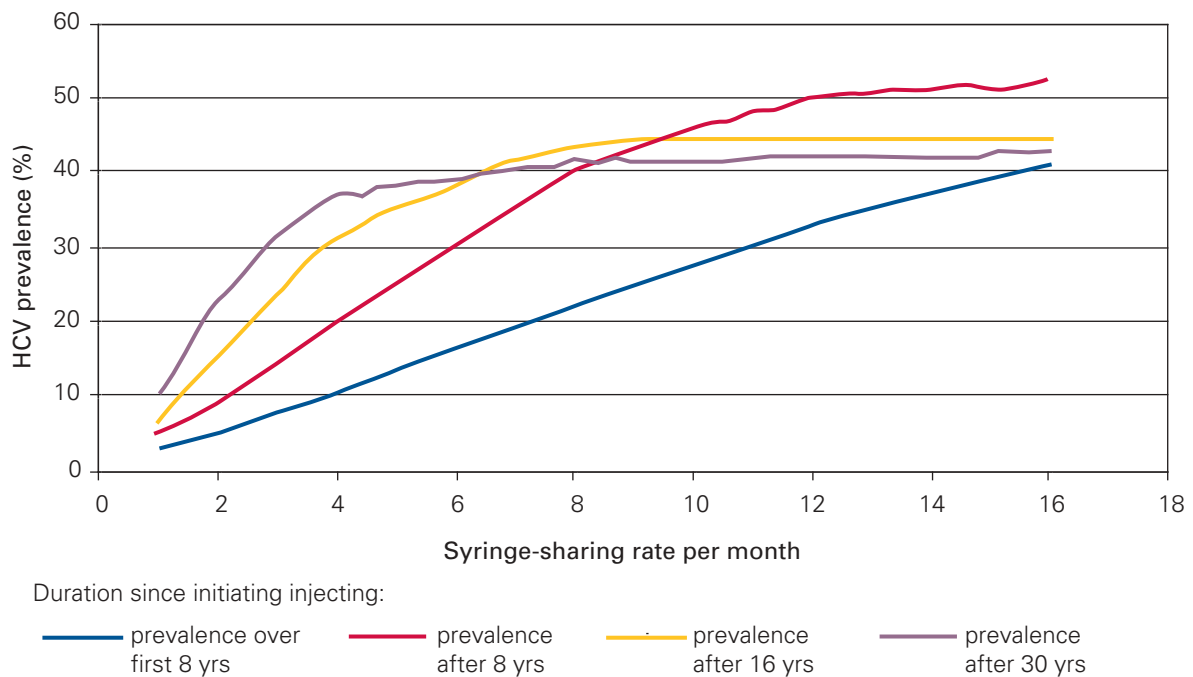
Similar trends to those seen in Figure 5 are found for the effect of reducing syringe sharing on the proportion of IDUs infected with HCV or self-cured. This shows that care should be taken in maintaining any reduction in syringe sharing, because any reduction in HCV prevalence will coincide with a reduction in the prevalence of self-cured 'immune' IDUs. If there was an increase in syringe sharing, HCV could quickly spread through the population again.

For the other model fits from the uncertainty analysis, similar predictions are found, with receptive syringe sharing having to decrease to less than two per month to result in the HCV prevalence decreasing below 5% in all IDUs who have been injecting for 16 years or less.

3.3.4 Impact of decreasing syringe sharing in all IDUs except new injectors

One of the difficulties for IDU harm-reduction interventions is trying to reach new injectors. This is of great importance for HCV transmission because many IDUs become infected with HCV soon after starting to inject (see Figure 3). The importance of reaching these new injectors is emphasised in Figure 6, which compares the impact of reducing syringe sharing (from 16 receptive syringe shares per month) among all IDUs with the impact of only reducing sharing among IDUs

who have been injecting for greater than 6 months or one year. Figure 6 uses the best-fit simulation.

Figure 6: Impact on the endemic HCV prevalence of reducing syringe sharing among all IDUs, or IDUs who have been injecting for longer than six months or one year

The HCV prevalence is the average over all IDUs who have been injecting for eight years or less.
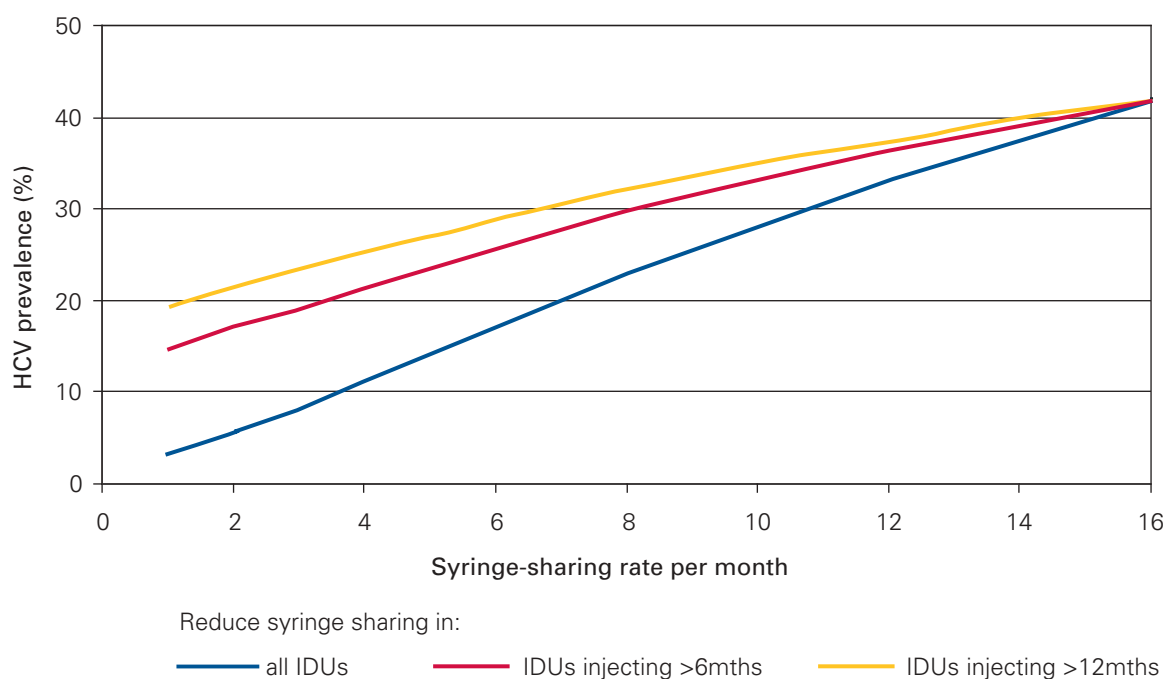

Figure 6 shows that the impact of the intervention is substantially reduced if it is unable to reduce syringe sharing among new injectors. For example, if it manages to reduce syringe sharing by 50%, to eight sharing events per month, among IDUs who have been injecting for more than six months, HCV prevalence will reduce to 30% among IDUs who have been injecting for eight years or less, whereas it would have reduced to 22% if it had reduced sharing in all IDUs. The effect is most profound at low syringe-sharing rates. For example, if syringe sharing is reduced to once per month among all IDUs, the HCV prevalence reduces to 2.8%, whereas it only reduces to 15% if syringe sharing is not reduced among IDUs who have been injecting for less than six months.

3.4 Discussion

Following a review of the literature, a model was developed that incorporated the main features of the natural history of HCV infection. The initial form of the model assumed a homogeneous IDU population. This meant the model could be solved to produce analytical solutions for the basic reproduction rate and the endemic HCV

prevalence. Using basic IDU behavioural data from London, this model was used to explore the nature of HCV transmission in this setting. However, the model was too simple to replicate certain aspects of HCV transmission in London.

For the model to portray the observed trends in HCV prevalence against duration of injecting, we had to assume that new injectors were more susceptible to infection. Two possible ways this can occur is by either assuming new IDUs share syringes more than older IDUs, or that there is a core group of higher-frequency syringe sharers who become infected soon after initiating injecting. In this initial analysis, we adapted the model to incorporate the first of these possibilities and assumed that IDUs share more when they have been injecting for less than six months. This adaptation of the model could fit the observed HCV prevalence data, but because of uncertainty in many of the model parameters, numerous model fits were possible.

These model fits were used to explore the relationship between the HCV antibody prevalence of an IDU population and the likely prevalence of those currently infected with HCV and of IDUs who have self-cured. The findings suggested that the prevalence of those infected will be much lower than the HCV antibody prevalence because many infected IDUs self-cure, but remain sero-positive for a long time after. Indeed, the percentage of sero-positive IDUs who are infected is likely to vary with the duration of injecting. This is due to a higher proportion of those infected being sero-negative among new injectors (in an acute phase of infection), whereas, later, some self-curers sero-revert, increasing the proportion of sero-positive IDUs who are infected. This has implications for estimating the proportion of self-curers from the proportion of sero-positive IDUs who do not have the infection, and may partly explain why there is so much heterogeneity in different estimates for this parameter (see Table 6). Indeed, for IDUs who have injected for eight years or less, the model predicts that 43.6% of those infected self-cure, but only 30% of sero-positive IDUs are not infected. Depending on what test is used, many self-curers may not be sero-positive.

The model was also used to explore the impact of increasing the coverage of current syringe distribution by reducing syringe sharing from its current estimated level of 16 receptive syringe shares per month. If we assume that all IDUs reduce their syringe sharing, the model suggested that modest reductions in syringe sharing will reduce the HCV prevalence in IDUs who have injected for about eight years. However, among longer-term IDUs (over ten years of injecting), syringe sharing has to be reduced substantially before their HCV prevalence reduces noticeably. In addition, syringe sharing has to become very low for the HCV prevalence to be reduced to 5% or less. This highlights the difficulty in effectively controlling HCV transmission among IDUs.

These results also give insights into how increases in syringe distribution may affect HCV prevalence in London. At best, an increase in syringe distribution will decrease the frequency of sharing by the number of times that each syringe is safely re-used

before disposal. If so, a similar relationship should exist between endemic HCV prevalence and the frequency of syringe distribution, with modest increases having little effect except among newer injectors, and substantial increases being required before HCV prevalence reduces noticeably among long-standing injectors. However, it is likely that an increase in syringe distribution will also decrease the number of times that each syringe is safely re-used[46], and so a smaller reduction in syringe sharing will result. The implications of this depend on the complex, and largely unknown, relationship between the level of syringe distribution and the frequency of syringe sharing and syringe re-use[46, 47]. More data needs to be collected on this relationship to better determine the impact of increases in syringe distribution.

The predictions above assumed that new injectors would reduce their risk behaviour to the same extent as older injectors in response to an increase in syringe distribution. However, it is likely that new injectors will not be reached by outreach services and so may not reduce their syringe sharing. When this factor was incorporated into the model simulations, they predicted a much smaller decrease in HCV prevalence for the same decrease in syringe sharing, and suggested that syringe sharing would have to be even lower to reduce the HCV prevalence to below 5%. This highlights the importance of outreach services reaching all new injectors, which is not an easy undertaking. However, there is uncertainty over whether the high HCV incidence among new injectors is due to them having higher syringe-sharing frequencies. If, for example, it is mainly due to a subsection of the IDU population having much higher rates of syringe sharing, outreach services would only have to reach these new injectors to attain nearly the same impact as if all IDUs were reached. This again highlights the importance of collecting better data on the risk behaviour of IDUs in London, especially among new injectors and how their syringe-sharing patterns change during their injecting career.

3.5 Conclusions

Although the work undertaken so far is preliminary, it gives an idea of the insights that this type of modelling can give. It can be used to simulate the transmission of different diseases associated with drug taking, and estimate the impact of different intervention strategies. These estimates can be combined with health-treatment cost data or intervention costs to determine the cost-effectiveness or cost-benefit of different strategies. However, as was the case with this analysis, the insights of possible modelling analyses are often limited by data weaknesses, resulting in uncertainty as to the best model structure and the value of some model parameters.

3.5.1 Dealing with uncertainty in IDU behavioural data

There was uncertainty in the structure of the model because of a lack of data on the patterns and frequency of syringe sharing, and how it varies within the population

and with duration of injecting. It was also difficult to estimate the impact of increases in syringe distribution because there is no data on the relationship between the level of syringe distribution among different IDUs and the rate of syringe sharing and re-use. It is important that other relevant data sources be compiled and reviewed in order to collate more data on IDU risk behaviour, specifically on the level of syringe sharing. In addition, specific behavioural surveys should be designed and undertaken to obtain better data on these aspects of IDU risk behaviour. If this was done, more accurate and deeper insights could be obtained.

3.5.2 Dealing with uncertainty in HCV biological data

There were uncertainties in many HCV biological parameters. This resulted in a large number of different parameter combinations that produced model fits to the HCV epidemiological data. Some of these will not be valid and so will result in increased uncertainty in the model predictions. Specific data uncertainties include:

- HCV transmission probability for syringe sharing and equipment sharing

- the effectiveness of syringe cleaning for HCV

- the proportion of acutely infected IDUs who self-cure

- the status of protective immunity among IDUs after self-cure.

Better estimates for some of these parameters would improve our model projections and indeed our estimation of other parameters, because some of them are highly correlated.

3.5.3 Possible directions for future modelling work

Despite uncertainty in the model structure and the input parameters, the wealth of epidemiological data available for London and for other cities in the UK means that mathematical modelling could be used to gain many insights into the factors affecting the transmission of HCV among IDUs in the UK. These analyses could improve intervention design by helping us understand what factors are important in determining why some IDU populations have much lower levels of HCV transmission than others.

The modelling undertaken so far could be extended and improved in a number of ways:

1. Review other data sources to obtain more data on IDU risk behaviour, specifically on the level of syringe sharing. This would improve the way that syringe sharing is represented in the model, and so improve the model's impact estimates for reductions in syringe sharing and enable it to estimate the impact of interventions focusing on IDUs with different syringe-sharing behaviour.

2.   Incorporate a core group of higher-frequency syringe sharers into the model. This is done for similar reasons to those above, but also to explore whether the high incidence among new injectors could be due to a core group becoming quickly infected.

3.   Extend the analysis to explore the impact of changes in other IDU behavioural parameters to understand the impact of other types of intervention. Specifically, it would be interesting to estimate the possible impact of:

   ● increases in the cessation of injecting due to methadone treatment programmes

   ● decreases in the recruitment of new IDUs due to active anti-drug publicity campaigns

   ● increases in the frequency and/or effectiveness of syringe cleaning.

4.   Modify the model to incorporate IDUs who have been injecting for different durations. This will enable the model to be used to accurately explore the effect of new IDUs sharing syringes with older IDUs, and to estimate the impact of interventions targeting new and old injectors.

5.   Adapt the model so that it can simulate changes in the cessation or recruitment rate over time.

6.   Fit the model to other HCV prevalence/incidence data for London, such as from other years, to obtain better estimates for parameter values and to understand the dynamics of HCV infection over time.

7.   Use the model to explore what factors determine the differences between HCV epidemics in other cities in the UK. This could help us understand what factors are protective for HCV infection, giving insights into what to focus on in intervention strategies.

These additional analyses would give important insights and should be given a high priority.

3.5.4 Recommendations for further data collection

Detailed surveys on the risk behaviour of IDUs need to be undertaken, specifically focusing on:

● syringe-sharing practices – who people share with and the nature of their sharing networks

- the impact of syringe distribution and increases in syringe-distribution coverage on syringe sharing:

  - What are the syringe-sharing patterns of IDUs who exchange many syringes compared to those who do not?

  - If IDUs are given more syringes, do they just reduce their sharing, or do they start restricting their sharing to people they know and trust?

  - Why do some people exchange fewer syringes than others? What methods could be used to increase the syringe-exchange rate of these IDUs?

It is also important to emphasise that different data sets need to be comparable. If they are not, it is much harder to discern trends in the data and to use different data sets in a modelling analysis. This is important not just over different years for the same survey, but also for data collected by different institutions.

To fully understand the transmission dynamics of HCV, and to accurately estimate their impact on the UK health service and the effectiveness (or cost-effectiveness) of different intervention strategies, in-depth research on specific aspects of HCV epidemiology needs to be undertaken among IDUs:

- HCV transmission between IDUs through syringe sharing and equipment sharing. At present, the only HCV transmission estimates are for needle-stick injuries. These are likely to underestimate the HCV transmission probability from needle sharing because greater quantities are frequently involved.

- The nature of HCV immunity following self-curing acute HCV infection. Do most self-cured individuals remain immune to infection, or is the protection partial, short-term, or only for some strains of HCV?

- The effectiveness of different methods of syringe cleaning for disinfecting against HCV. At present, there is only data on the effectiveness of syringe cleaning in disinfecting syringes infected with HIV. These studies need to be replicated for HCV to determine the effectiveness of this possible intervention strategy.

- The proportion of those acutely infected who self-cure following HCV infection from syringe and equipment sharing. Our study illustrates the huge uncertainty in this parameter, and the potential problems in estimating it. Despite this, the estimation of this parameter and the determination of the factors that affect it should be given a high priority.

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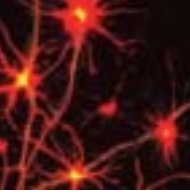
4 Agent-based model: DrugChat case study

In this section an agent-based model is developed that uses insights from ethnographic research to investigate the role of social networks, choice and social influence on drug use and on transitions from use to dependence or addiction. Instead of fitting model results to observed data, the agent-based model creates hypotheses to be tested against further research in order to take forward our understanding of how drug use may spread within communities.

The model starts with a population of agents connected through social networks. Agents are either non-users, users, or addicts – non-users and users choose to use drugs if offered on the basis of their attitudes to risk and to taking drugs, which are influenced by members of their social network and prior experience. The simulation follows the evolution of a simulated population and measures the number in the population who remain non-users, use drugs and become addicts, as well as changes in attitude to drugs. It can also illustrate types of individual histories of drug use that may be compared with existing or future ethnographic work to validate the model. The model could be developed with additional data to explore other mechanisms. These include changing the probability of having a good experience from using drugs with increased use or facing potential harms associated with use, adding dealing and a drug market, and allowing the dynamic formation of deviant networks based on shared attitudes to risk and drug taking. The priority given to these different developments (or others) could reflect policy interest, synthesis and collection of ethnographic knowledge, and our ability to generate sensible agent biographies and aggregate-use statistics that validated the model.

4.1 Description of the DrugChat model

This is an enhanced re-implementation of the DrugTalk model[1] written in the LISP programming language.[ii] It is intended to investigate the role of social networks, choice and social influence on drug transitions. It is important to be clear about what this model does and does not do and thus how it should be judged. It does not present 'best belief' from the literature in all its assumptions. In the time available,

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ii   The original was in the NetLogo language. Replicating a simulation from the published description using a different programming language is a very good way both to test the robustness of results and understand the programme. More details of the parameter settings used (following Agar's discussion wherever possible) can be found in the Appendix.

calibrating the model in such a way was not feasible.[iii] So the model cannot be regarded as empirically plausible and its results should not be treated as policy advice. Instead it makes a complete set of explicit behavioural assumptions about how drug use works and shows the dynamic consequences of those assumptions. This is something, for reasons discussed above, that statistical and dynamic models do not, and possibly cannot, do. In some cases, as discussed later, it is necessary to make untested assumptions because only this modelling technique has been in a position to draw attention to gaps in our knowledge of the drug-use process, particularly at the behavioural level. However, unlike what happens with statistical and dynamic models, these untested assumptions are not built in to the approach and could easily be replaced by others established empirically. Gaps in our knowledge brought to light by the agent-based approach can legitimately be seen as an opportunity rather than a problem.

The model begins with an empirically plausible social network in which a few agents have many associates but most have a much smaller number. Agents exist in three 'types', non-users, users, and addicts. However, unlike statistical and 'stocks/flows' modelling the distinctions between these types are not attributes or transition probabilities but distinctive behaviours and interactions. For example, users and addicts differ in their drug-sharing behaviour while users and non-users differ in the kind of information they transmit about drugs and the amount of credibility it has with other agents.

Each cycle of the simulation begins with some 'doses' of the drug being introduced into the social system by street dealing.[iv] Addicts will actively seek out such deals and thus have a high probability of obtaining drugs in each period, but in rather low quantities, measured in doses.[v] Users will have some probability (through the kind of company they keep and the places they keep it) to obtain drugs but in somewhat larger quantities. Non-users have a fairly low chance of encountering street deals. For those still able to choose (users and non-users), the decision about whether to take a drug depends on two cognitive factors, attitude to risk and attitude to drugs. When the value of the 'parameter' for attitude to risk exceeds the 'parameter' for attitude to drugs, the agent will take drugs if they are made available. The interpretation of this comparison is that when an agent is badly disposed towards drugs, they would have to seem exceedingly safe before they might be taken. By contrast, when the agent is well disposed towards drugs, they are prepared to tolerate a greater degree of risk without curtailing drug use. The value of the attitude to risk, based on research in innovation diffusion, is normally distributed around 50, implying that most people have a 'middling' belief about the risks of drugs, while rather fewer have significantly higher or lower perceptions of drugs'

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iii   At the same time, it is based on a model built by someone with many years of ethnographic experience so it is unlikely that the assumptions chosen are too outlandish.

iv   Following Agar, typical populations involve about 500 agents.

v   This reflects poverty and other factors such as apparent neediness, appearance and so on.

'riskiness'.[vi] Attitude to risk is assumed, following the Agar model, to be a fixed characteristic of individuals (like a standard statistical attribute). By contrast, attitude to drugs can change through social interaction. It is initialised at 50 for all agents in the network reflecting the 'societal view' of a drug prior to widespread experience of it. This means that initially the population is neither particularly well nor particularly badly disposed to the drug. Each agent has a stock of drugs (the stash) from which they will, in each period, use themselves or share.

In the simplest version of the model, users and addicts are also distinguished by their drug-use behaviour. Users will share their stash with individuals they know who are willing to try, but keep back at least one dose for personal use in case nobody reciprocates.[vii] Addicts, by contrast, will not share but use some or all of their own stash 'privately' in each period.[viii] The sharing of drugs by users ('partying') is the main way in which non-users are initiated into use. After drugs have been shared around, each agent uses some number of doses and evaluates their experience. For each dose ingested, there is a probability that the drug will lead to a good experience and another probability that it will lead to bad experience[ix] Both can occur from the same dose, or neither, reflecting the ambiguous nature of the drug experience. Agents 'keep count' of all the good and bad experiences they have had and it is assumed that it makes sense to treat the drug – for now at least – as having the same range of effects on everyone. The system also keeps count of doses ingested because, after five doses, a user becomes an addict.[x] In addition, each good and bad experience updates the attitude an agent has to drugs. The formula for this updating involves adding (1/number of good experiences)×20 and (2/number of bad experiences)×20 to the current attitude. Early experiences with drugs change attitudes more than later ones and bad experiences make more impression than good ones. Both of these insights are borne out in social psychology and experimental economics, with the concept of 'loss aversion'.[xi]

vi   Both of these parameters have values in the range 0-100.

vii   A user is assumed to give out as many doses as they have – keeping one back – as long as they can find associates willing to use at that moment.

viii   In practice, addicts may well share with other addicts but rather seldom with non-addicts. However, this refinement will be deferred for reasons discussed later.

ix   Following Agar, who is thinking of heroin, the changes for good and bad experiences are 70% and 30% respectively.

x   This is Agar's assumption and seems rather deterministic and strong even for heroin. We have also experimented with a fixed probability (10%) per dose of addiction. The analysis presented in Figure 10 below suggests that it is the assumption of deterministic addiction that has more impact on outcomes than the specific number of uses after which it is assumed to have taken place.

xi   It might reasonably be thought that all this discussion of numerical attitudes and updating equations refutes the earlier claim that agent-based models deal with behaviour rather than parameters. However, the limited choice of agent-based drug-use simulations available as case studies gives a false impression. Agar[2] discusses the distinctive role and legitimacy of such parameterisations in his papers and an example of an agent-based model based almost entirely on decision rules rather than parameters (though not unfortunately in the field of drug use) can be found in Moss[3]. Thus, we see that even when an agent-based model uses parameters (and it need not), they do not have the same problematic 'exogenous' interpretation found in other types of models.

Now agents communicate with each other through their networks. This communication is divided into three classes. Addicts have no communicative credibility (as in labelling theory within the sociology of deviance).[xii] It is their status as addicts that 'speaks to' those they know and has a strong negative effect on the drug attitudes of their associates (20 points on the 100-point scale) making these associates less willing to consider using.[xiii] By contrast, the other two modes of communication involve users and non-users saying what they know. Users who have used in the current period have a direct influence (positive or negative) on the attitudes of associates by 'turning on' or 'turning off'. They are credible by direct experience and possible observation. Thus, the new attitude of the user's associate is the average of the user's attitude and the old attitude of the user's associate: increased congruence of attitude occurs. By contrast, non-users and users who have not used in this period can only 'gossip' with much lower credibility. In this communication mechanism, agents simply transmit their current counts of good and bad experiences and recipients 'total' all the good and bad experiences of drugs they hear about through their networks (double-counting the bad experiences as before) and then adjust their attitude directly by the net amount. In the Agar model, the fact that gossip has a smaller influence than experience and encounters with users, using is ensured by a spatial element in the model. In this version, it is assumed that gossip of this kind is less prevalent than the more 'sensational' details of use and tends to be driven out by it. By these different and simultaneous interaction processes, the horrible example of addicts, the credible information of users and the wash of less-credible gossip, users and non-users adjust their drug attitudes. However, just as addicts have no credibility, they also have no reason to adjust their attitudes in the light of outside information. They hardly need gossip to tell them what they should think about drugs!

For each agent, the programme goes through the list of associates and decides (with a probability) whether the agent will communicate with that associate in that period. If communication occurs, then the effects are, as described above, based on transmitter status (has used this period or not, is an addict or not) and receiver status (is an addict or not).

4.2 Results and discussion

The agent-based approach is quite capable of generating exactly the same kind of aggregate time-series data produced by other dynamic modelling techniques. Figure 7 shows a typical evolution for the number of users and addicts for the entire simulated population. The number of users grows rapidly, stabilising at 20% of the population. The number of addicts grows slowly at first, then more rapidly and finally slowly again (displaying the characteristic S-shaped curve of innovation

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xii   The classic statement is found in Becker[4].

xiii   This mechanism is commonly associated with the work of Musto[5] but Agar developed it independently on the basis of direct ethnographic evidence.

diffusion by word of mouth) and stabilises at about 17% of the population.[xiv] In addition, however, the graph displays the simulated 'at risk' population. These are agents whose attitude to drugs and risk attitudes are such they would be prepared to use if exposed to street deals or drug offers from friends. It is clear that this population of susceptible individuals chokes off rather rapidly for reasons that will be discussed below.

Figure 7: Agent drug-use status totals (whole population)
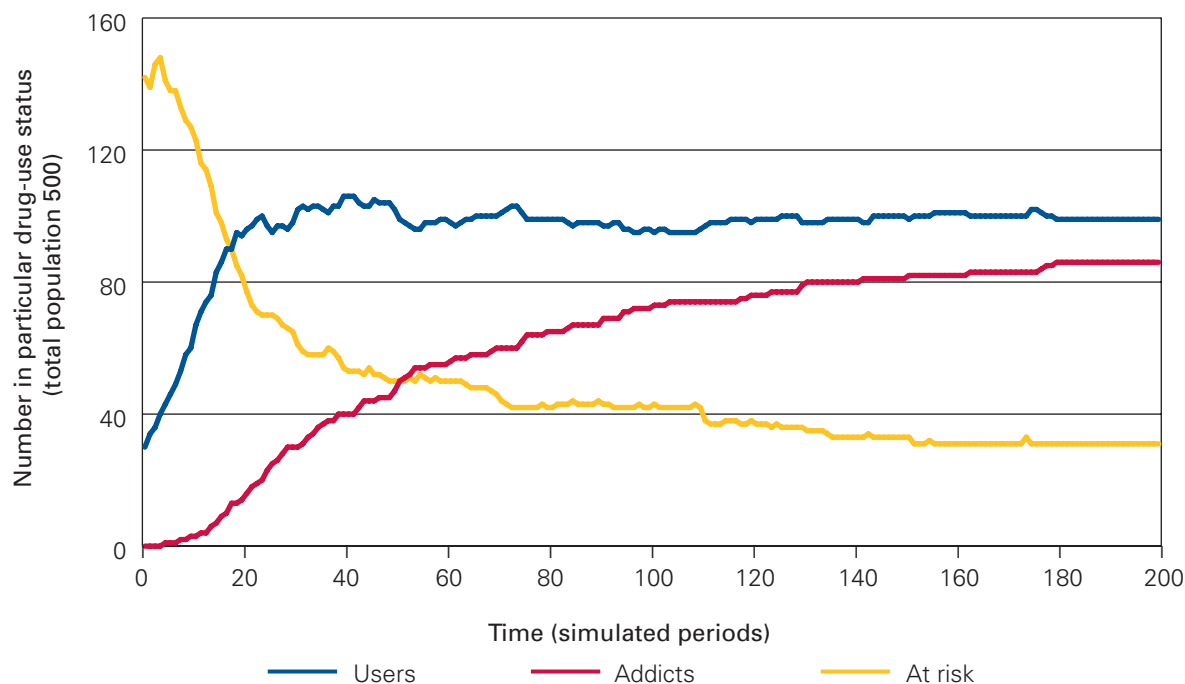
However, because agent-based models are based on explicit behavioural interaction, they can be 'interrogated' to produce aggregate summary data in different ways. For example, it is possible to plot the final drug-use status of individual agents against their initial (and unchanging) risk attitude. In other words, given the agent's risk attitude at the start of the simulation, can we predict their drug-use status at the end? The results are shown in Figure 8. The absence of a correlation is surprising *prima facie*, but actually illustrates the earlier concern about the quest for 'early-life' predisposing factors in the statistical approach. Given the assumptions of DrugChat (and particularly the assumption that risk attitude is fixed), it would be reasonable to expect risk attitude to predict final drug-use status. However, the fact that it doesn't illustrates how the dynamics of behavioural interaction may undermine the presumptions on which the search for statistical regularities is based. In this case, the dynamic evolution of attitudes to drugs appears to render risk attitude largely non-explanatory. It is important to stress that this is not an empirical result but an illustration of an earlier methodological point. We are not claiming that risk attitude isn't important to drug-use

xiv   The relatively similar population sizes for users and addicts are determined by the highly addictive nature of the simulated drug.

status in the real world. To do that, we would have to show that the DrugChat model assumptions were largely accurate. What we have shown, however, is why the search for robust statistical regularities based on individual attributes may be problematic if systems are behaviourally dynamic. For all the possible weaknesses in its specific assumptions, DrugChat represents a class of models with a certain level of complexity and it is likely that the dynamics of other models in this class will also undermine the search for statistical regularities in the same way.

Figure 8: Correlation between initial risk attitude and final drug-use status (whole population)
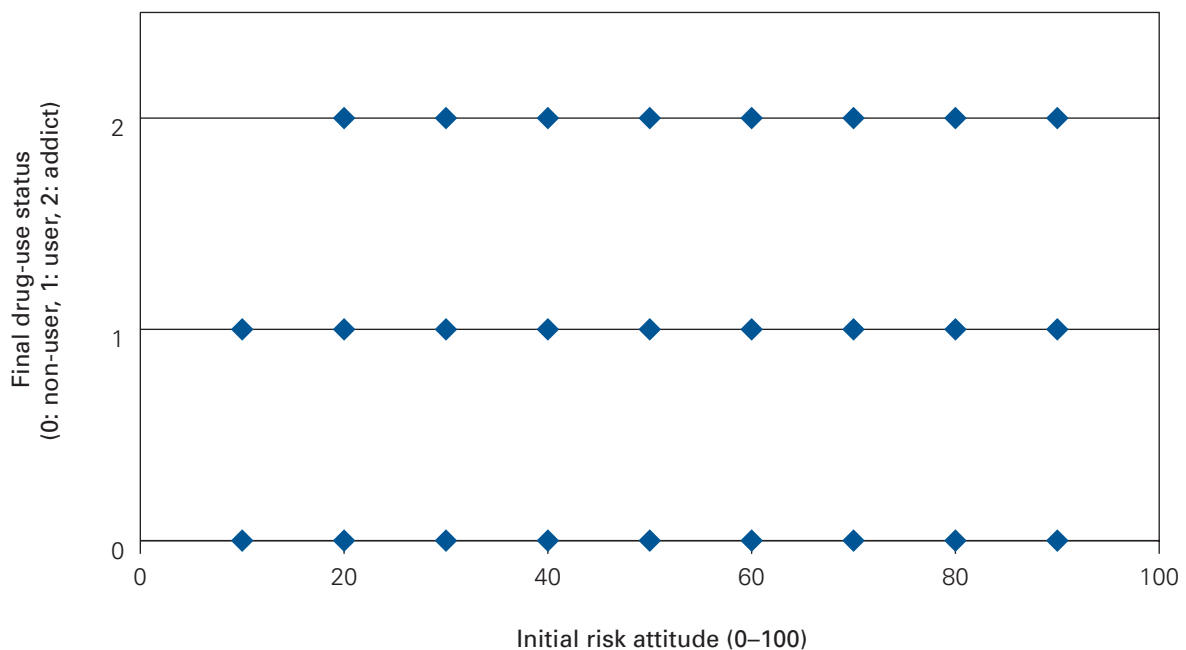
The same kind of analysis can be carried out for the assumption of fixed transition parameters on which the Caulkins *et al*. models referred to by Agar are based.[xv] The results are shown in Figure 9. The parameter for a particular drug-use-status transition in each period is given by the number of agents making that transition during the period, divided by the number of agents in the 'origin' status at the start of the period.[xvi] Not only are the transition parameters far from constant (except in the trivial case where the simulation has reached a steady state) but they regularly change sign, the worst possible situation for any model based on the assumption of stable transition parameters. As before, this result must be interpreted carefully. It does not show that the DrugChat model is 'right' or that the Caulkins et al. model

xv These parameters can be interpreted either as flow rates (the fraction of any given population that will change state in any period) or as individual probabilities (that each member of the population will change state in any period). In either case, the model relies on their being fixed.

xvi To show that this parameter mirrors the fixed elements of the Caulkins et al. model, consider 100 agents and a flow rate of 0.1. In the first period, 10 agents should make the transition and (110 – 100/100) = 0.1. In the second period, starting now with 110 agents, 11 should make the transition and (121 – 110/100) = 0.1 also.

is 'wrong'. That would involve demonstrating the relative empirical adequacy of the assumptions in each model. What is does show is how agent-based modelling can illustrate the potential weaknesses of the statistical and dynamic approaches previously described. Given DrugChat's behavioural assumptions, it appears that constant transition parameters are not generated by the system and thus a traditional dynamic model would not be a good approximation of that system. It may be that there are other agent-based models (or other real systems) for which constant transition parameters are a good approximation. But the agent-based approach ought to diminish our optimism on that score. If something as behaviourally naïve and simplistic as DrugChat cannot be well approximated by constant transition parameters, what hope for the subtleties of a population of real agents in a social system?

Figure 9: Flow rates between drug-user statuses (whole population)
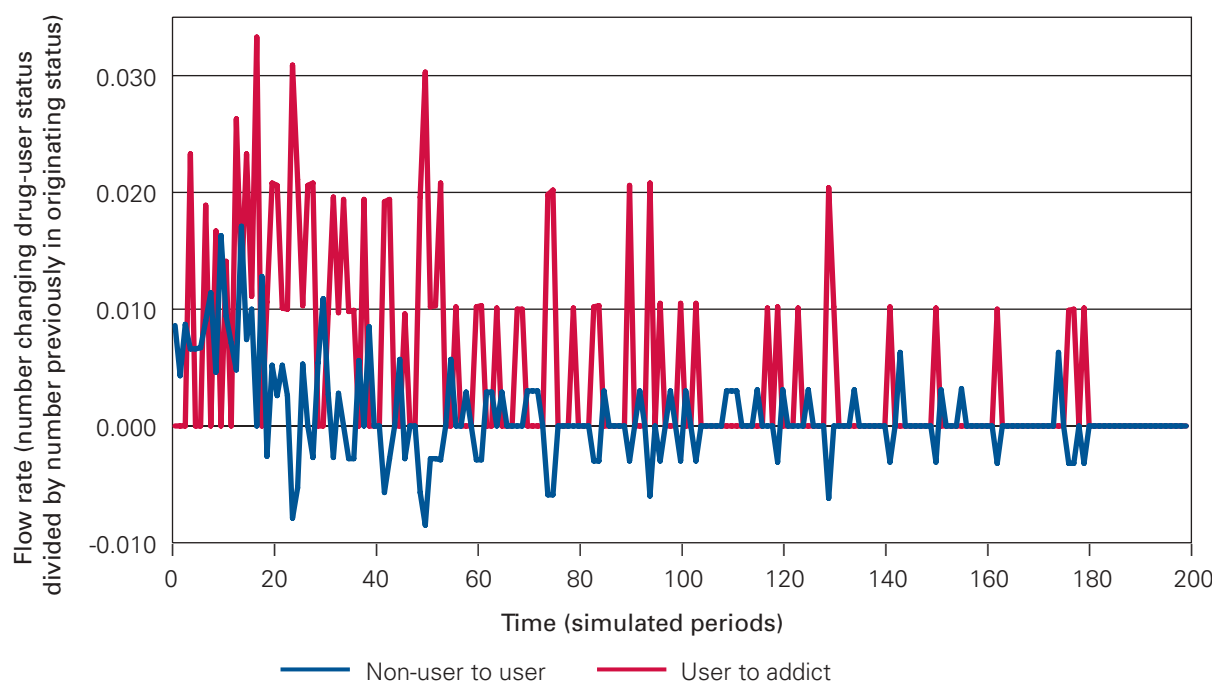
Finally, the simulation can be used to explore the mapping between the way that agents would respond to different survey questions and their actual drug-use status. Figure 10 shows what happens if people are surveyed in every period – clearly an unrealistic assumption – about whether they have ever used drugs, whether they have used in the last six periods and in the last period. Even under the extremely strong assumption that all survey responses are honest and that a 100% survey is carried out in every period, it can be seen that none of the survey measures tracks user and addict status particularly well. (The 'never used' question does track non-users but only under the strong model assumption that anyone who has ever used drugs counts as a user thereafter. Thus, this tracking is a matter of definition, not a substantive result.) Figure 11 shows what happens under the reasonable

assumption that people are more prepared to own up to ever having used than having used recently and are rather unwilling to report having used very recently.[xvii] Under these circumstances, tracking of the actual situation is poorer still, with estimates of the addict population particularly inaccurate.[xviii] As with the two previous examples, this is not an empirical finding because DrugChat is not (yet) an empirically calibrated model. What is does show is how agent-based models can be 'interrogated' to deliver different kinds of data that can be compared to real data and how the approach can explore concerns about the implicit assumptions of alternative modelling (or, in this case, data collection) techniques.

These analyses suggest a first substantive use for this modelling approach, an examination of different survey sampling strategies and the plausibility of simplified modelling approaches in capturing the dynamics of social interaction. However, different summary data can also be used to provide a more stringent test (and additional understanding) of the agent-based model itself. We have already argued both that curve-fitting models are hard to falsify because of low information content in relatively short and inaccurate drug-use time series, and that more matching of independent data sources against simulation output improves the chance that simulation has captured features of a social process. We now illustrate this claim by looking at the 'biographies' of simulated agents.

Figure 10: Comparison of reported and actual drug-use status assuming honest response (whole population)
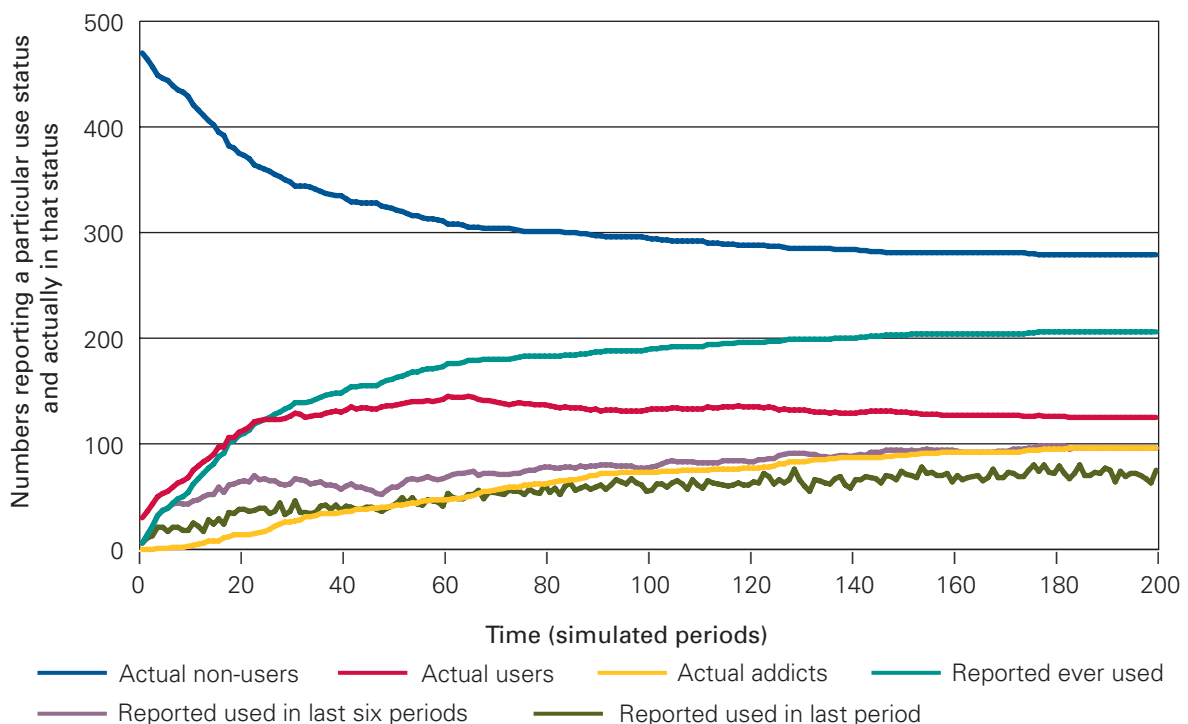
xvii   The probabilities for honest reporting are then assumed to be 100%, 80% and 50% respectively. These are only indicative figures.

xviii   In a more advanced version of the simulation that incorporated criminal activity and medical harms, it would also be possible to explore the accuracy of arrest and hospitalisation records in tracking the hidden population.

Figure 11: Comparison of reported and actual drug-use status assuming differential response (whole population)
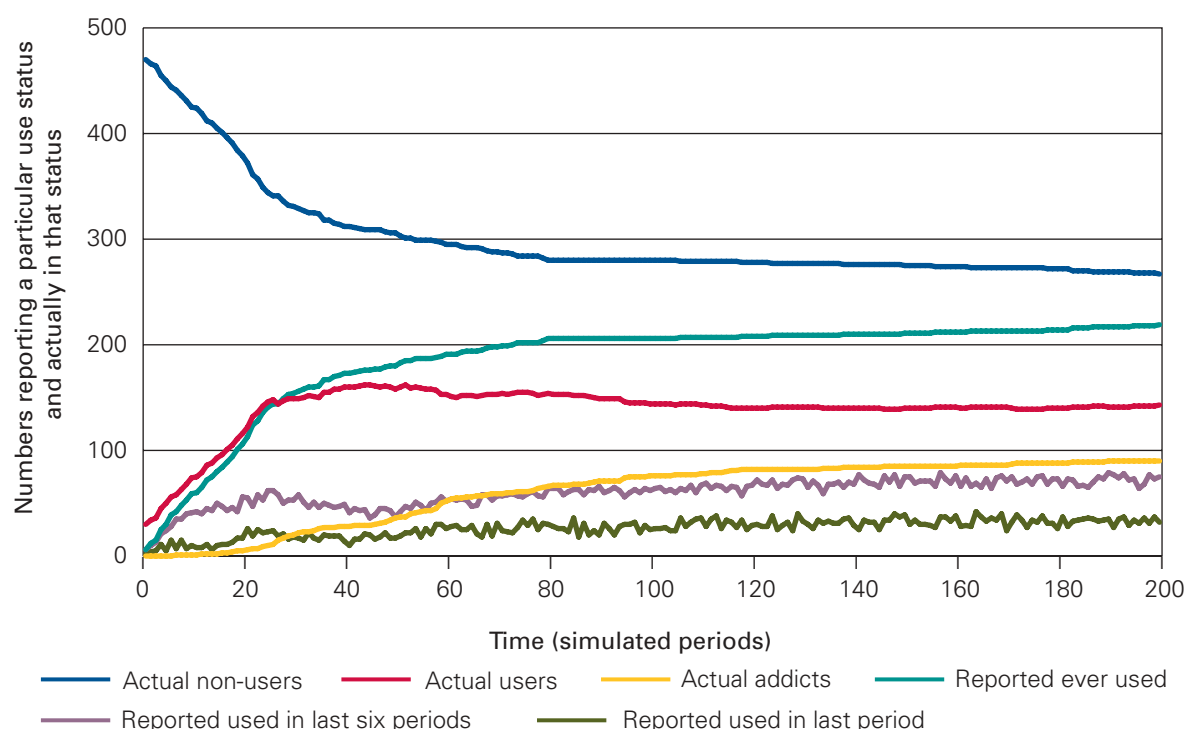

Figure 12 shows the evolution of a single randomly selected agent over time in terms of drug-use status and number of doses consumed in each period. By contrast to the first five figures, which dealt with whole populations, this figure is a 'simulated biography'. This agent became a user almost immediately and only survived a relatively short time before using five doses and thus becoming an addict. This pattern can be explained by the dynamics of the drug attitude shown in Figure 13. Repeated good experiences early on left this user very positively disposed to drugs. The existence of level plateaux between these uses implies that this was a relatively socially isolated agent not receiving anything significant in the way of gossip or other drug experiences. Once the user became an addict, however, usage increased and, with it, both good and bad experiences. The 'toothed saturation' pattern of drug attitude is distinctive to a simulated addict. Because bad experiences are rarer and have more effect, each takes the addict nearer to the most-negative-possible attitude to drugs, while repeated 'good trips' have increasingly little effect, despite their frequency. This can be seen as another illustration of a counterintuitive finding. Although addicts are very negative about drugs, this attitude can be driven by satiation rather than by the assumption that addicts experience more negative effects from drug use.

Figure 12: Drug-use status and use levels (first randomly selected single agent)
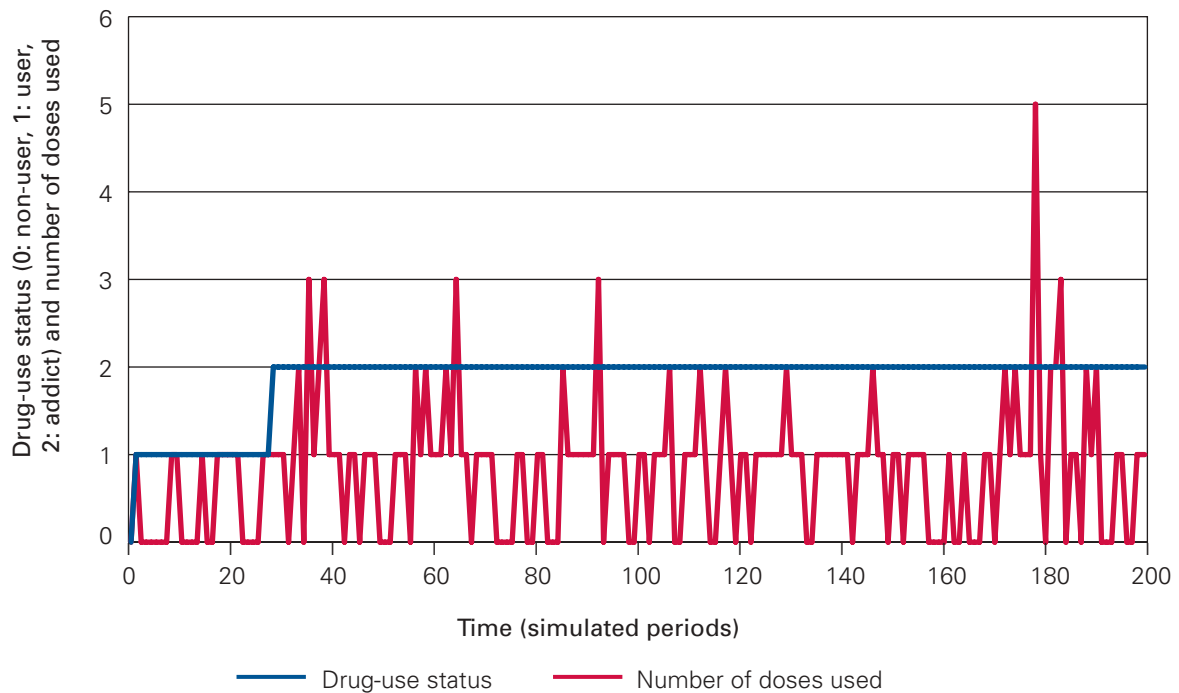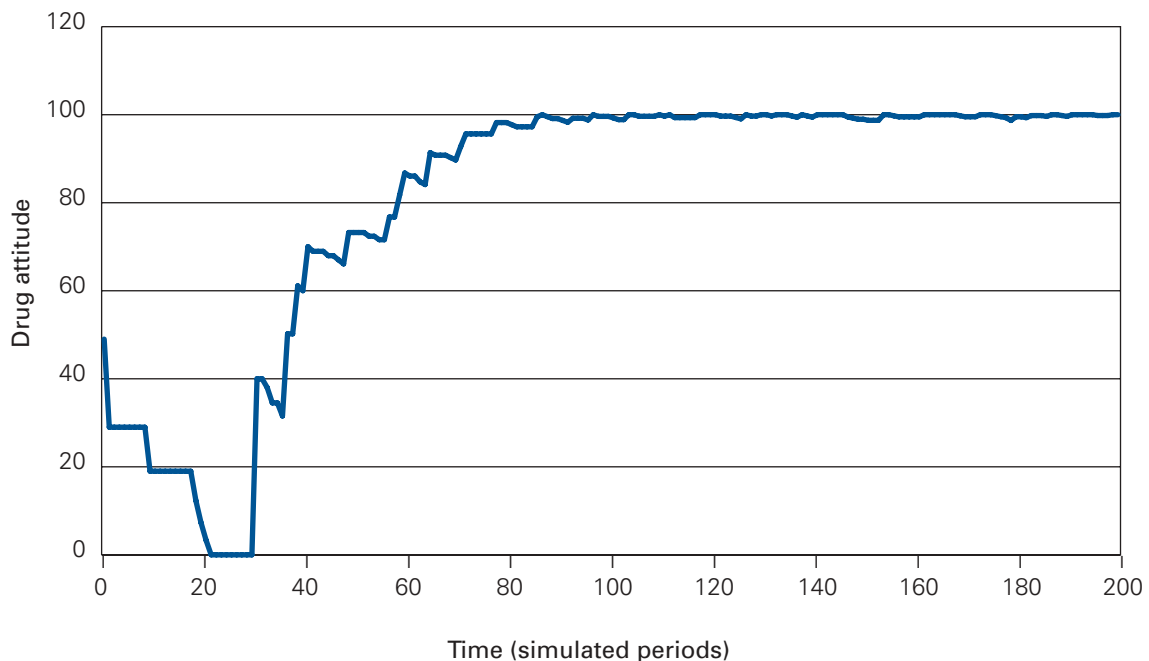

Figure 13: Drug attitude (first randomly selected single agent)

Figures 14 and 15 show the corresponding biographical information for a different simulated agent also selected at random. This agent remained a non-user for a far longer period and also survived longer as a user before becoming an addict. This difference can be explained by examining the attitude dynamics in Figure 15. Unlike

the previous agent, this one was clearly better socially connected and had two 'warnings' from contact with addicts at an early stage, the spikes observed in the plot. Against this, gossip and 'turning on' gradually made this agent more favourable to drug use. However, its first use had both good and bad outcomes, offsetting this information. This process of gradual improvement of attitude followed by negative experience was repeated again when the agent appeared to have good and bad experiences in quick succession in its second and third 'hits'. By now, however, addiction was imminent and no further bad experiences arose until the agent was addicted and it was too late.

Figure 14: Drug-use status and use levels (second randomly selected single agent)
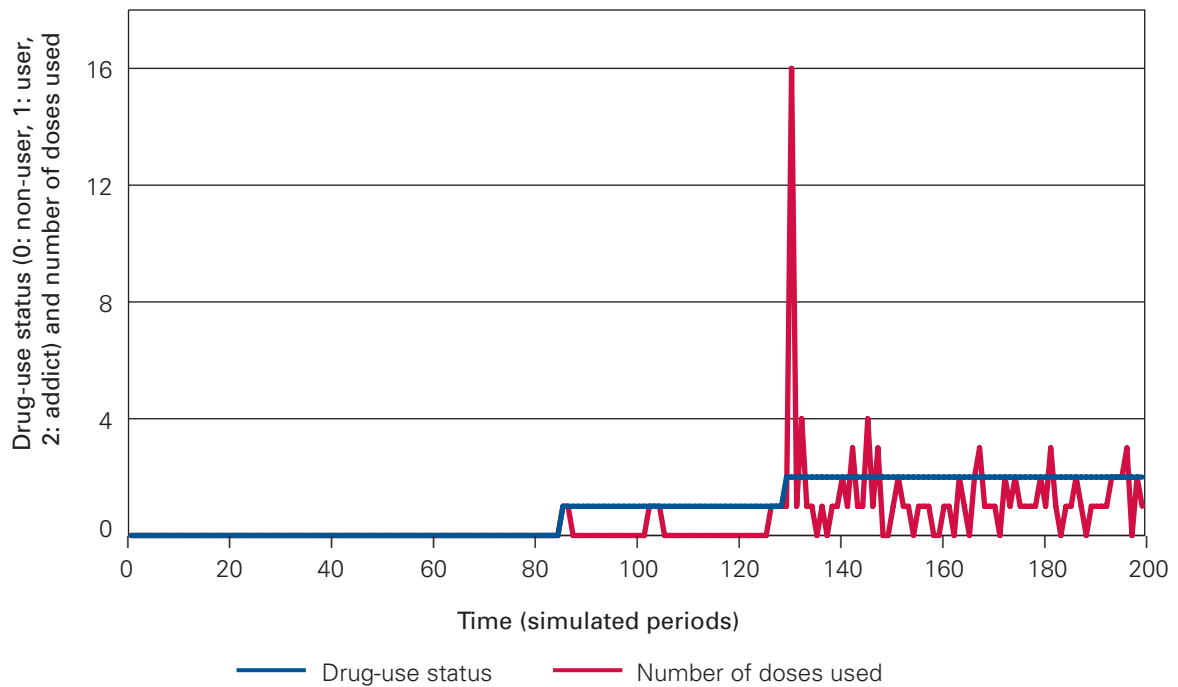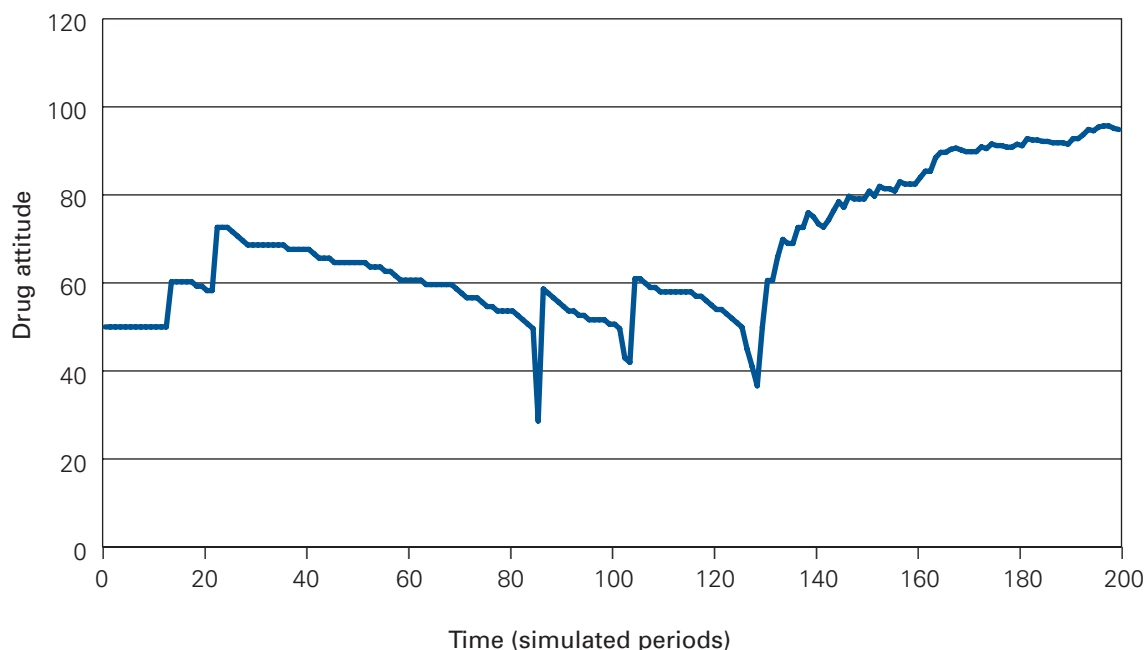
Figure 15: Drug attitude (second randomly selected single agent)

Two lessons can be drawn from this style of analysis. Firstly, diverse agent
interactions through networks give rise to the unique circumstances and pattern of
each individual's use status. This contingency and context-dependency goes some
considerable way to illustrating the earlier claim that static statistical and
'stock/flow' models are unlikely to be good approximations except in special cases.
Secondly, the simulated biographies generated by this method can be compared, for
example, with real qualitative data from biographical interviews[6] to see whether
they capture the broad behavioural patterns of entry into use and addiction.
Compare the sociable individual who was protected from use by a bad initial
experience with the social isolate who had the misfortune to have a succession of
good experiences and no countervailing influence. Thus, having calibrated the model
on ethnographic data about the behaviours and interactions of drug users, we can
test its ability to generate both plausible aggregate trends and individual
biographies.[xix] This ability to test a model against diverse data is a second
substantive advantage of the agent-based approach with policy implications. Many
data-fitting models merely do just that, fit the data. It soon becomes clear with new
data that they have failed to capture any underlying truth about the social process.[xx]
By contrast, at least in the cases where data are available, agent-based models can

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xix   In fact, independent data outputs do not stop there. Comparison of real and simulated social networks is
        an additional possibility but some technical difficulties with social network analysis software have
        prevented this analysis being presented here.

xx   It is surprising how many of the existing models do not use simple tests for these issues developed in
        economics, such as prediction on 'held-back' data and tests for parameter stability performed by re-
        estimating the model on random data subsets. There is simply not enough UK data for these tests but
        there is (barely) US data on which most of the models are fitted.

be forced to face far stronger tests before they are trusted for policy analysis, and those that pass the test should be correspondingly more robust and insightful.

The third substantive use of agent-based simulation is one it shares with the other modelling techniques – the ability to perform 'thought experiments' at low cost, both as an aid to the understanding of complex systems and to investigate the effects of different policies on drug use trends. Figure 16 shows one such simple experiment, comparing the steady-state number of addicts and users in the population under different assumptions about the addictiveness of the drug. Two interesting observations are suggested by this figure. Firstly, for the case where addiction definitely occurs after a fixed number of doses, the numbers of users and addicts is relatively insensitive to the actual number of doses involved. (The addictiveness is reduced by a factor of four between the extreme conditions shown.) By contrast, the number of users and addicts under the assumption of probabilistic addiction track the corresponding values for deterministic addiction in the early stages but then diverge quite sharply in the steady state. This implies that the early and late addicts (absent in the fixed-period model) are more influential than the 'average' addicts in determining the dynamics of the system. This kind of parameter adjustment (called sensitivity analysis) both provides insight into how the system works and allows data gathering and further research to focus on the areas of the model that have the greatest impact on the outputs. A number of these experiments suggest how the dynamics of the system unfold and this can be confirmed by Figure 17. This shows that there is a rapid trend towards a negative drug attitude in the population as a whole based on gossip, negative experiences and contact with addicts. This explains the rapid choking-off for the population of susceptible agents shown in Figure 7.

Figure 16: The effect of different drug addictiveness assumptions on numbers of users and addicts (whole population)
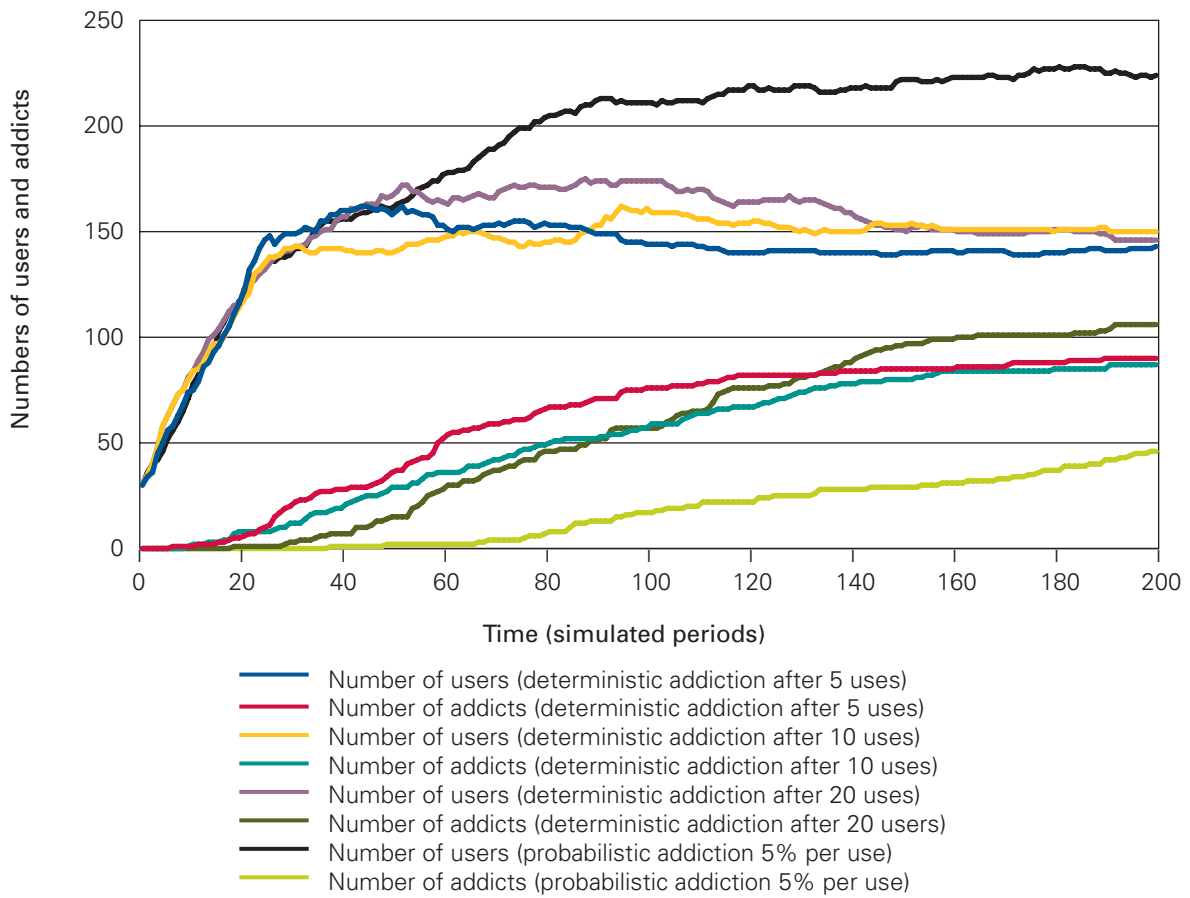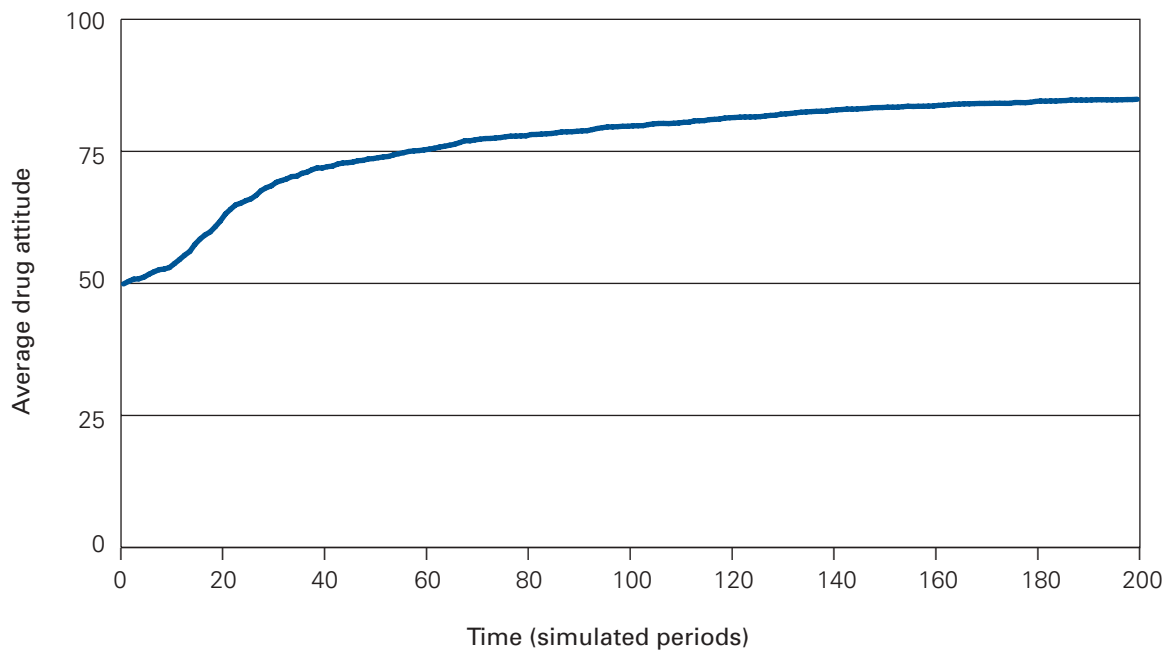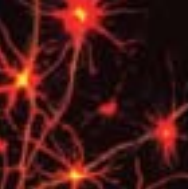

— Number of users (deterministic addiction after 5 uses)
— Number of addicts (deterministic addiction after 5 uses)
— Number of users (deterministic addiction after 10 uses)
— Number of addicts (deterministic addiction after 10 uses)
— Number of users (deterministic addiction after 20 uses)
— Number of addicts (deterministic addiction after 20 users)
— Number of users (probabilistic addiction 5% per use)
— Number of addicts (probabilistic addiction 5% per use)

Figure 17: Average drug attitude (whole population)

Some parameters in the model are susceptible to policy control. Drug education might make initial attitudes to new drugs less favourable among non-users. This effect is shown in Figure 18. As might be expected, increasing the drug attitude (and thus decreasing the extent to which agents are well disposed to drugs) has a significant effect on reducing levels of use and addiction.[xxi]

Figure 18: Effect of initial drug attitude increase (decreased agent enthusiasm) on user and addict numbers (whole population)
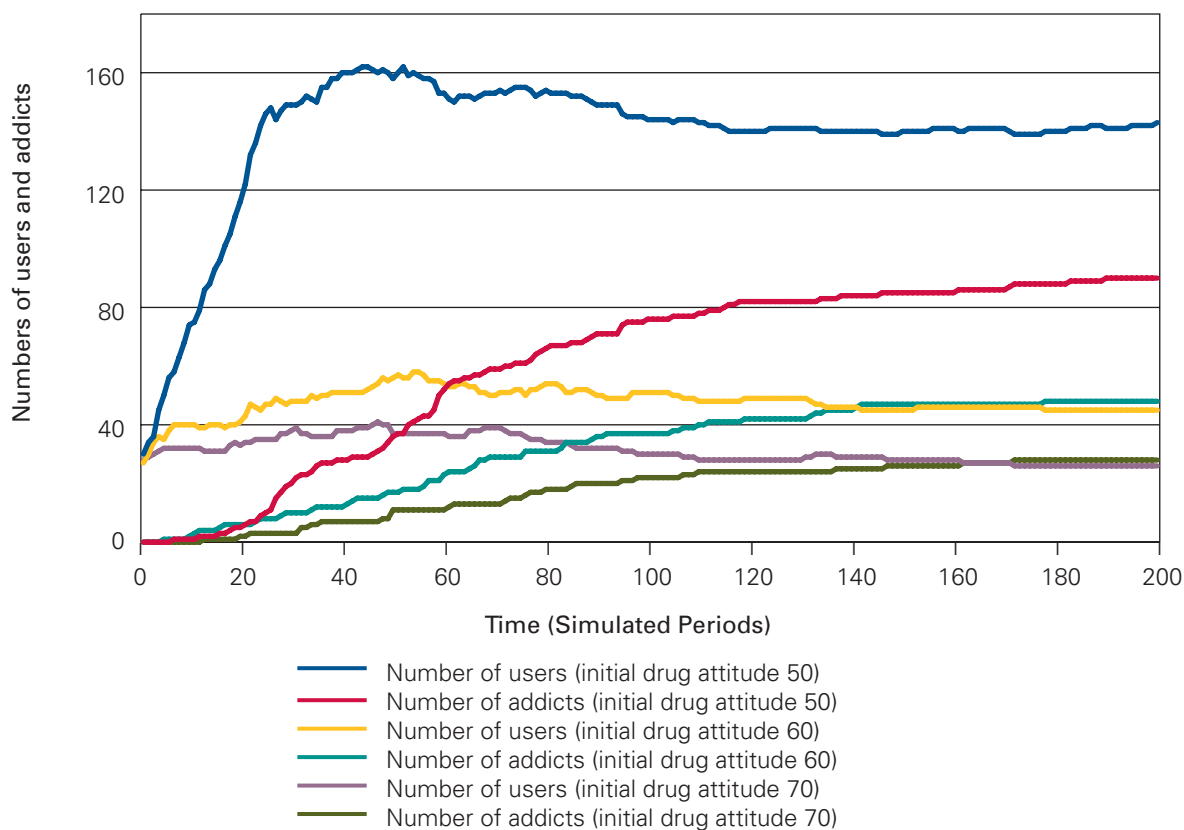
In this section, we have illustrated three different uses for agent-based simulation: understanding sampling efficacy and investigating the plausibility of simpler modelling techniques, building more robust models by comparison with multiple independent data sources, and using sensitivity analysis to understand complex systems and explore the effects of policies. In each case, it was possible to use data from the simulation to make the points directly. In the next section, we illustrate and discuss a more programmatic advantage to the agent-based approach: the ability to synthesise existing knowledge and specify clear questions for future research.

xxi   Although this parameter has a significant impact, there is still a major challenge in designing an advertising campaign of sufficient credibility to actually produce this scale of effect. Fortunately, measurement of attitudes is relatively straightforward, though measuring exposure to the campaign is harder.

4.3 Developing the model

Whatever the merits of the specific assumptions presented in the DrugChat model (chosen mainly for its relative simplicity), it has at least presented them all within a single framework. This allows for the possibility of an academic division of labour in further investigation of the subject. Economists and psychologists might contribute to a better understanding of use decisions; public health experts and medical researchers to the likely harms of use; sociologists to patterns of drug sharing and social interaction, and so on. In addition, discussion around a model can be used as an elicitation technique to establish how experts, policy makers and stakeholders differ in their mental maps of social processes, allowing competing views to be compared or combined. At the same time, any model is only provisional, a stepping stone to new data, more plausible models and better policy advice. In the case of the Agar model, understanding it also involves understanding its inevitable limitations.[xxii] Exploration of the model shows that the bad example of addicts has a significant impact in driving the system towards a steady state. Early enthusiasm for a drug rapidly turns to widespread disdain, with those who were 'caught' as early addicts ending up as the victims and agents who survive the initial fad without using being safe thereafter. Thus, any drug epidemic will tend to be choked off by the growing 'mass' of addicts it produces: a straightforward negative feedback loop.[xxiii] However, this outcome is predicated on two assumptions. Firstly, that the social networks do not change as a result of changes in use status and, secondly, that addiction leads to no medical harms that might remove addicts from the population, death being the limiting case. It is easy to see how the increasing social isolation of addicts (ultimately as a deviant subculture) might reduce their impact among non-users, some of whom may be uncomfortable about associating with recreational users.[xxiv] Changes in social networks resulting from use and addiction would be measurable using standard social network analysis techniques, though research in this domain would be particularly challenging in terms of ethics and access. In the remainder of this section, we discuss three possible extensions to the model and the issues of data collection that they raise. There are clear parallels here with the interdisciplinary aspirations of Foresight.

4.3.1 Economics

So far, the model ignores the economic constraints on drug use. Agents are assumed to be able to buy whatever they are offered and to share it freely. At most, poverty is represented by the assumption that addicts tend to access fewer doses than users in each buy. It would be straightforward to add per-period disposable

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xxii   All models are simplifications of reality. The trick is to provide adequate simplifications. There would be nowhere to unroll a 1:1 scale map of the UK and, even if there were, it would be useless.

xxiii   In addition, the fact that users share and addicts don't (under the assumption that street deals for non-users are rare) also reduces the supply of initiates.

xxiv   A countervailing force may be the role of the less-discerning media in broadcasting the worst possible 'horror stories' they can find. This can also have undesirable consequences, however[7].

income to the attributes of agents. This would have several interesting consequences. Firstly, agents (particularly addicts) could 'bid' for drugs held by others, a preliminary representation of the process of small-scale dealing through networks. These network markets (contrasted with standard public legal markets) have interesting properties,[xxv] as well as policy implications through the 'don't waste time arresting small dealers' debate. Secondly, dealing might emerge (again, particularly among addicts) as a deliberate way of increasing income. Thirdly, although the processes by which users 'turn to crime' are highly complex, the number of users whose costs exceeded disposable income would give an indicative measure of those most likely to offend or suffer other harms. These might include breakdown of family relations through deception, loss of jobs through pilfering or inattention, and so on.

4.3.2 Physiology

So far it has been assumed that the drug affects all agents in the same way and for any use status. Furthermore, the concept of addiction has been represented in terms of properties such as sharing behaviour, communication and sizes of deals. In practice, drugs clearly affect different people in different ways and, furthermore, there are reasons to believe that a combination of need and escalating use might increase the number of bad experiences through administering drugs carelessly or being less discerning about sources. It would be relatively straightforward to augment the feedback on good and bad effects so that agents required bigger doses to achieve good effects and, at the same time, started to receive bad effects from failing to take the drug. At present, binges (multiple doses consumed in a single period) carry no additional harms such as overdose (which would remove addicts from the system) or increased chances that later doses will have more bad effects than good. The introduction of physiological need is also highly likely to 'drive' the kinds of behaviour that lead to drug use becoming problematic: escalating use, excessive spending, dealing, breaking of work and family ties through selfish and dishonest actions and so on.

4.3.3 Technology

Since one of the aims of the current Foresight project is to explore the uptake of new drugs, another obvious development to the model would be to incorporate multiple drugs with different properties in terms of good and bad effects and addictiveness. This would also lead to preliminary modelling of polydrug use. A highly topical example would be the crack epidemic and its domination of powder cocaine use via the introduction of a drug which is often cheaper (or at least offers more 'bang per buck') and easier to make but is also considerably more addictive. So far, the model assumes there is only a single kind of 'goodness' and 'badness'

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xxv   Prices are likely to vary far more widely and inventory is stored in the system in a way that may smooth demand and supply.

but in practice some drugs become substitutes for those that are currently unavailable in the network market.[xxvi] In addition, certain patterns of drug use result from the different physiological effects of drugs: mood management using alternating 'uppers' and 'downers', for example. These interplay factors may be responsible for a number of the most serious harms associated with drug use (mixing unfamiliar drugs, dangerous administration methods, increasingly unstable mental state, and so on).

Many of these developments can be added straightforwardly (from a technical perspective) to the model presented. However, the priority given to each should depend on their policy interest, available data and our ability to test the resulting model against real data on networks, aggregate statistics, agent biographies, and so on. The final substantive use of agent-based simulation is therefore a heuristic one. Building models and understanding them helps us to synthesise what we know, identify what we don't know and envision the research that would need to be carried out to enhance existing models in the light of emerging policy concerns. These research questions would also be interesting from the perspective of social science. Using the cases above, the following questions suggest themselves. Which drugs do users see as substitutes and why? What motivates polydrug use: availability, disinhibition of use generally, desirable physiological effects, management of undesirable effects or some combination of these? How does network dealing actually take place? What are the social practices associated with sharing, helping and dealing? Which combination of properties makes a drug particularly likely to constitute an epidemic hazard? Partial answers to all these questions already exist in the literature but the modelling process can sharpen the focus on both our knowledge and our ignorance.

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xxvi   This is also the insight behind methadone maintenance.

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Appendix

Default parameters for the *DrugChat* model

Some of these parameters are adjusted to different values in individual simulation runs. These changes are shown in the relevant figures.

- Population size: 500.

- Distribution of associate numbers: 36% of the population have 2 associates, 20% have 3, 12% have 4, 10% have 5, 6% have 6, 6% have 7, 4% have 8, 4% have 9 and 2% have 10.

- Initial distribution of use status in the population: 95% non-users, 5% users and 0% addicts.

- Initial drug attitude for all agents: 50.

- Initial risk attitude: Selected from an approximated normal distribution that has a 2%-each chance of producing a risk attitude of 10 and 90, 4% each of 20 and 80, 8% each of 30 and 70, 16% each of 40 and 60 and 40% of 50.

- Maximum number of doses an agent, initialised as a user, is assumed to have taken 'historically' i.e. before the simulation starts: 5.[xxvii]

- Maximum number of doses an agent, initialised as an addict, is assumed to have taken 'historically' i.e. before the simulation starts: 25.

- Chance of non-users getting 'street' drugs per period: 0%.

- Deal size for non-users: 80% chance of 1 dose and 20% chance of 2 doses.

- Chance of users getting 'street' drugs per period: 25%.

- Deal size for users: 20% chance of 1 dose, 40% chance of 2 doses, 20% chance of 3 doses, 10% chance of 4 doses and 10% chance of 5 doses. (If non-users don't buy on the street then only partying will get them using.)

- Chance of addicts getting 'street' drugs per period: 70%. (Because they search.)

- Deal size for addicts: 70% chance of 1 dose, 20% chance of 2 doses and 10% chance of 3 doses. (Addicts will be typically poorer and less desirable customers.)

- Probability that addict will talk to each of their associates per period and thus act as a horrible example: 50%.

- Probability that user who has used will 'turn on' each associate per period and thus significantly influence them: 50%.

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xxvii   This parameter avoids a 'step' in the initialisation process since agents recorded as users or addicts from the outset will be at different points in their history of drug use when the simulation starts.

- Probability that users who have not used and non-users will 'gossip' to each associate per period and thus influence them weakly: 50%.

- Probability of addiction: 100% on the fifth dose.

Agent attributes for the *DrugChat* model

- **Number of positive drug experiences (0-n)**: Based on past drug use.

- **Number of negative drug experiences (0-n)**: Based on past drug use.

- **Risk attitude (1-100)**: Normally distributed at the start of the simulation and fixed. Some individuals are just more willing to take drug risks than others are.

- **Drug attitude (1-100)**: The same for all agents at the start of the simulation (reflecting the 'prevailing view') on a drug, but changing over time based on network contacts with different kinds of user and personal experience with drug use.

- **Stash (0-n)**: The number of drug doses the agent currently holds for the future.

- **Dose (0-n)**: The number of drug doses the agent intends to consume in the present period.

- **Drug status (0-2)**: Whether the agent is a non-user, a user or an addict.

- **Associate list:** The list of all the other agents that the agent knows in the simulated world.

In addition, the (single) drug in the current version of the model has a constant chance to cause good (70%) and bad (30%) drug experiences each time a dose is taken.

System parameters for the *DrugChat* model

- The simulation collects a random sample (10%) of the agent population and records their 'biographies'.

5 Conclusions

The three models – statistical, system-dynamic, and agent-based – were intended to illustrate the potential utility and benefits of modelling for understanding the dynamics of drug use and to support policy making. In no way are the examples exhaustive. Each has limitations and each generates specific recommendations. But in general they show that useful insights may be generated even within a very short timetable. Policy makers will benefit from investing in modelling, and we anticipate that the Australian Drug Policy Modelling Project*, conducted over a longer period, will provide more detail and other useful examples of models and insights of relevance to policy makers in England and Wales.

We have shown that statistical models can enhance routine data sets to estimate the prevalence and incidence of drug use, but these models could be improved and could potentially address new drugs, given a co-ordinated surveillance effort. We recommended that policy makers consider initiating a review across government departments and with multidisciplinary scientific input to identify key gaps in our information, and opportunities for greater integration of current information systems.

In the example of a system-dynamic model, we developed an initial model of the transmission of Hepatitis C (HCV), which is pertinent given the growing public failure to prevent HCV transmission among IDUs. The model implied that early intervention is critical to the success of prevention, and can be extended to assess whether the most effective intervention is achieved by targeting all IDUs or a core subgroup. Though the model was limited by uncertainty in key behavioural and biological parameters, it has provided a base for taking research forward to improve the evidence base and give policy makers greater assurance on the level and types of intervention required to reduce HCV infections. Recommendations were also made for improving data collection in order to aid the accuracy and power of these modelling techniques.

In the example of the agent-based simulation, we showed how comparatively simple rules that could be obtained from ethnographic data can provide a deeper understanding of a complex system, and suggested ways in which the model could be extended to incorporate additional information so that we understand better how individuals interact and how drug-use patterns may emerge.

* http://www.turningpoint.org.au/research/dm_proj/res_dm_proj.htm
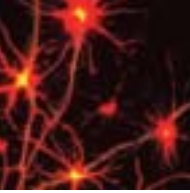
List of publications:
Drugs Futures 2025?

All publications are available in hard copy and/or can be downloaded from the Foresight website except those marked *** which are available only from the website (www.foresight.gov.uk).

1. Executive summary and project overview

2. State-of-science reviews ***
    I.   Cognition Enhancers
    II.   Drug Testing
    III.   Economics of Addiction and Drugs
    IV.   Ethical Aspects of Developments in Neuroscience and Addiction
    V.   Experimental Psychology and Research into Brain Science and Drugs
    VI.   Problem Gambling and other Behavioural Addictions
    VII.   Genomics
    VIII.   History and the Future of Psychoactive Substances
    IX.   Life Histories and Narratives of Addiction
    X.   Neuroimaging
    XI.   Neuroscience of Drugs and Addiction
    XII.   Sociology and Substance Use
    XIII.   Social Policy and Psychoactive Substances
    XIV.   Psychological Treatment of Substance Abuse and Dependence
    XV.   Pharmacology and Treatments

3. State-of-science reviews (2 page summaries)

4. Ethical issues and addiction overview ***

5. Horizon scan

6. The scenarios

7. Public perspective

8. Perspective of the pharmaceutical industry

9. Modelling drug use