Article:

Pennington, R.M., Collins, B., Leigh, S. et al. (5 more authors) (2018) The cost-effectiveness of seven behavioural interventions to prevent drug misuse in vulnerable populations. International Journal of Drug Policy, 57. pp. 42-50. ISSN 0955-3959

https://doi.org/10.1016/j.drugpo.2018.03.028

Second page

Title: The cost-effectiveness of seven behavioural interventions to prevent drug misuse in vulnerable populations

Keywords: cost-effectiveness, economic evaluation, prevention, NICE

Structured Abstract

Background The National Institute for Health and Care Excellence (NICE) developed a guideline on drug misuse prevention in vulnerable populations. Part of the guideline development process involved evaluating cost-effectiveness and determining which interventions represented good value for money.

Methods Economic models were developed for seven interventions which aimed to prevent drug use in vulnerable populations. The models compared the costs (to the health and crime sectors) and health benefits (in quality-adjusted life years (QALYs)) of each intervention and its comparator. Sensitivity analysis explored the uncertainty associated with the cost of each intervention and duration of its effect.

Results The reduction in drug use for each intervention partly offset the costs of the intervention, and improved health outcomes (QALYs). However, with high intervention costs and low QALY gains, none of the interventions were estimated to be cost-effective in the base case. Sensitivity analysis found that some of the interventions could be cost-effective if they could be delivered at a lower cost, or if the effect could be sustained for more than two years.

Conclusions For drug misuse prevention to be prioritised by funders, the consequences of drug misuse need to be understood, and interventions need to be shown to be effective and cost-effective. Quantifying the wider harms of drug misuse

and wider benefits of prevention interventions poses challenges in evaluating the cost-effectiveness of drug misuse prevention interventions. A greater understanding of the consequences of drug misuse and causal factors could facilitate development of cost-effective interventions to prevent drug misuse.

1. Introduction

In 2015, the Department of Health in England asked the National Institute for Health and Care Excellence (NICE) to develop guidance on drug misuse prevention (National Institute for Health and Care Excellence, 2017). The guideline scope focussed on interventions targeted at populations who were already using drugs occasionally, or were considered at most risk of starting to use drugs. The scope considered groups including (but not limited to) those with co-occurring mental health problems, those not in education, and children and young people whose parents used drugs. The guideline focussed on interventions that aimed to prevent or delay drug use and excluded interventions related to the supply of drugs, treatment of drug misuse or dependence and interventions to promote safer injecting (National Institute for Health and Care Excellence, 2015).

NICE follows a defined process in developing guidelines that considers evidence for the effectiveness and cost-effectiveness of interventions when making recommendations (National Institute for Health and Care Excellence, 2016). In considering cost-effectiveness evidence, NICE's preference is usually to conduct cost-utility analysis, using quality-adjusted life years (QALYs) as the outcome metric. QALYs combine quality of life with length of life, and therefore allow comparison of outcomes across different health areas. An incremental cost-effectiveness ratio (ICER) can be calculated by dividing the difference in costs of an intervention and its comparator by the difference in QALYs. Judging the size of ICERs assists decision makers in determining whether an intervention represents good value for money. (It should be noted that cost-effectiveness is not the sole factor considered in NICE's decision making, and that other elements such as the fair distribution of resources should also be considered (National Institute for Health and Care Excellence, 2008a)).

A systematic review of the literature did not identify any articles that reported relevant cost-effectiveness evidence (Bates et al., 2016). Three reports summarising findings from a US-based cost-benefit model for interventions targeting relevant populations were identified from additional sources, but these were considered to have limited applicability to the UK setting. Given the absence of relevant cost-utility analysis from the literature, the development of new economic models was considered important in understanding which interventions aimed at drug misuse prevention represent good value for money. The economic models considered behavioural interventions identified in a systematic review of the literature. None of the interventions considered in the economic models were considered cost-effective using NICE's standard approach.

This article aims to explore why these interventions were not cost-effective and how future economic evaluations should consider interventions to prevent drug misuse. We do this by:

- providing an overview of the modelling approach and inputs and reporting the results of the analysis,
- providing sensitivity analysis to understand which parameters would need to change for interventions to be cost-effective, and
- discussing the challenges of economic evaluation of drug misuse prevention.

We draw comparison with alcohol and smoking, and refer to established challenges in economic evaluation in public health. We discuss the limitations of our analysis and suggest alternative approaches which could be used in future analyses, and areas in which further research would be particularly valuable.

2. Material and methods

2.1 General modelling approach

Economic modelling compares the costs and consequences of two alternative courses of action. Models combine data from multiple sources to estimate the total costs and benefits that would occur if each of the two courses of action were implemented. Decision tree models use ‘branches’ to represent the different pathways patients can follow or events that can happen, and multiply the probabilities of these events by the costs and consequences of the events (Brennan et al, 2006; Briggs et al, 2006; Drummond et al, 2005; Morris et al, 2012). Decision trees are commonly used in evaluating the cost-effectiveness of health interventions for drug or alcohol problems (Hoang et al., 2016). We developed decision tree models to compare the costs and QALYs associated with the change in drug use for each intervention and its comparator in the study. We performed literature searches to identify the events, costs and consequences which would be included in the models. These required numerical data comparing outcomes between drug use and non-drug use such as relative risks or odds ratios. Outcomes for which quantifiable effects could not be identified were excluded from the models. Included events were discussed and agreed with an advisory committee.

We adopted a partial public sector perspective, including costs to healthcare and criminal justice sectors. We did not include costs relating to employment, education or out-of-pocket expenses incurred by individuals. We considered health effects to the individuals at risk of drug misuse, using QALY losses to capture the impact of both reductions in quality-of-life, and of premature death. The costs and opportunity for QALY gains for each intervention were specific to the drug in question, as the potential consequences of cannabis, ecstasy and cocaine usage differ and no single source was identified which reported data for all drugs. Costs and QALYs were discounted at 3.5% per annum (National Institute for Health and Care Excellence, 2016). All costs were expressed in 2015 prices (GBP). The modelled time horizon (time period over which events, costs and consequences are considered) depended upon the duration of the study and evidence base for drug-related consequences, and was varied in scenario analyses. Details of all the models and inputs are available elsewhere (Collins et al., 2016).

2.2 Interventions

Interventions identified in a systematic literature review of the effectiveness of targeted prevention programmes (Novakovic et al., 2016) were included in the models if they reduced drug misuse, the source study included a comparator group, and the baseline characteristics of the population in the study were defined. A total of seven interventions met these criteria. These were:

1. Focus on Families: a multicomponent intervention with families of substance abusers (Catalano et al., 1999).
2. A web-based personalised feedback intervention based on brief motivational interviewing techniques, for college student cannabis users (Lee et al., 2010).
3. Familias Unidas: a group based multi-parent intervention for families of delinquent youth (Pradoet al., 2012).

4. A single brief motivational interviewing session for regular ecstasy users (Martin and Copeland, 2010).

5. A brief motivational interviewing intervention to reduce both risky sex and drug use in young gay and bisexual men (Parsons et al.,2014).

6. A motivational interviewing intervention to reduce club drug and HIV risk behaviours use among men who have sex with men (Morgenstern et al.,2009).

7. STRIVE (SupporT to Reunite, Involve and Value Each other): A family-based intervention to reduce substance use among newly homeless youth (Milburn et al.,2012).

The effectiveness of the interventions was derived from the effectiveness studies identified in the systematic review (Novakovic et al., 2016). Population, intervention, comparator and effectiveness data are presented in Table 1.

None of the studies provided UK costs for the interventions, so we estimated intervention costs by converting costs from other currencies to GBP, or by applying UK unit costs to reported resource use. UK practice may differ from the source studies, and there may be local variation in the implementation of the interventions, so the intervention costs were varied in sensitivity analysis. Estimates including lower and upper bounds are provided in Table 2.

[Table 1 to go here]

[Table 2 to go here]

2.3 Models focussing on cannabis use

Cannabis use was associated with an increased risk of psychotic disorders and of being arrested. The models assumed that cannabis use increased the rate of psychotic disorders from seven in 1,000 to 14 in 1,000 (Hall, 2015). Annual psychotic disorder-related costs included service costs (£13,136) and informal care costs (£4,242). Psychotic disorders were assumed to reduce health related quality of life from 1 to 0.68 (McCrone et al., 2009) (where 1 is equivalent to full health and 0 is equivalent to being dead). It was estimated that there are 50.27 cannabis possession arrests per 1,000 cannabis users based on police recorded data from 2014-15, costing £500 per arrest. The cost of £500 is based on the average time it takes an officer to deal with an offence, noting that that this cost is low as most cannabis possessions are assumed not to result in court activity (May et al., 2007).The literature indicated that cannabis use may be associated with an increased risk of road traffic accidents (Gadegbeku et al., 2011; Harman and Huestis 2013) but the advisory committee which developed the guideline was not convinced of the robustness of these estimates, and so they were included in sensitivity analysis only. Cannabis-related lung cancer was excluded from the models as robust UK data were not identified. Our modelled social costs for one year of cannabis use are shown in Figure 1.

Three interventions reported changes in cannabis use: Focus on Families, the web-based personalised feedback intervention, and Familias Unidas.

2.3.1 Focus on Families

Seven percent of children receiving the intervention had used cannabis 12 months after receiving Focus on Families, compared nine percent of children in the comparator group (Catalano et al., 1999). The model did not assume any continued effect beyond the 12 month time horizon because a follow-up study demonstrated that the intervention effect was restricted to 12 months (Haggerty et al., 2008).

2.3.2 Web-based Feedback

The study duration was six months (Lee et al., 2010), and we did not identify evidence that the duration of effect would be sustained beyond the study period. Therefore the base case (most plausible scenario) considered a one year time horizon, assuming that cannabis use was reduced at month six and then rebounded to baseline at month 12. To explore the sensitivity of the model to this assumption, we considered a scenario with a two year time horizon, assuming that cannabis use was reduced at month six, and returned to baseline at 24 months.

2.3.2 Familias Unidas

The base case considered the 12 month study duration only. Two scenarios considered a 24 month time horizon, using the trial data for drug use at baseline, month six, 12 and extrapolating for month 18: one scenario assumed drug use returned to baseline at month 24, while the other assumed drug use remained constant beyond the extrapolated value for month 18.

2.4 Models focussing on ecstasy use

Ecstasy use was associated with an increased risk of arrest, hospital admission, accident and emergency attendance, ambulance conveyance, death, and drug dependence. The models assumed that each ecstasy user consumed 40.75 tablets per year, which was calculated from estimates of the number of tablets consumed per year, UK population data, and the prevalence of ecstasy use (Collins et al., 2016). The model assumed that there are 0.11 sentences per 1,000 ecstasy users, costing £23,194 per sentence, and 2.13 arrests per 1,000 ecstasy users, costing £1,346 per arrest (Advisory Council on the Misuse of Drugs 2008; Ministry of Justice 2014). Rates of hospital admission, A&E attendance and ambulance conveyance were 2.43, 2.43, and 1.68 per 1,000 users, with unit costs of £372, £109 and £216 respectively (Department of Health, 2014). Ecstasy use also carries a risk of death, estimated at 0.039 per 1,000 users (Office for National Statistics, 2014) which has a cost of £464 to the National Health Service and (discounted) QALY loss of 22.3 for 16-24 year olds and 17.9 for 25-59 year olds. The risk of ecstasy dependence is 0.68 per 1,000 users with a cost of £2,620 (Collins et al., 2016). Our modelled social costs for one year of ecstasy use are shown in Figure 1.

Only the brief motivational intervention studied by Martin and Copeland (2010) focussed on ecstasy use.

2.4.1 Brief intervention

The study (Martin and Copeland, 2010) reported ecstasy use at baseline and month three. In the model for the intervention group, we assumed that ecstasy use decreased linearly over the first three months for the intervention group, and then increased linearly to baseline at 12 months (base case) or 24 months (scenario analysis). The model assumed no change in ecstasy use in the comparator group.

2.5 Models focussing on cocaine use

Cocaine use was associated with an increased risk of arrest, hospital admission, death, and drug dependence. The models assumed that the risk of cocaine-related arrest was 9.4 per 1,000 users at a cost of £1,925 per arrest (Godfrey et al., 2002). Hospital admissions included cocaine-specific diagnoses with a probability of 2.24

per 1,000 users and cost per admission of £1,765, cocaine-related cardiovascular admissions with probability 2.20 per 1,000 users and cost per admission of £1,678, and cocaine-related myocardial infarctions with probability of 1.39 per 1,000 users and cost per event of £3,459 (Godfrey et al., 2002). The probability of being in treatment for dependence on cocaine use varies by age – for people aged 16-19 this was 12.9 per 1,000 users and for people aged 30-40 this was 3.44 per 1,000 users. Drug dependence was assumed to lead to a QALY loss of 0.576 per person (Pyne et al., 2011) and a cost of £1,562 for treatment. Cocaine use carries an annual excess risk of death of 0.048 per 1,000 users. The QALY loss for premature death depends on age and is 20.9 (discounted) for someone who dies at age 25 and 17.7 (discounted) for someone who dies at age 39 (Collins et al., 2016). Our modelled social costs for one year of cocaine use are shown in Figure 1.

Three interventions reported change in cocaine use: motivational interviewing in young gay and bisexual men, motivational interviewing in men who have sex with men, and STRIVE.

2.5.1 Motivational interviewing to reduce drug use in young gay and bisexual men

The model assumed that drug use changed between the levels reported in the study (Table 1) until 12 months (the study duration). Between months 12 and 24, the base case assumed that drug use returned linearly to baseline, and a scenario analysis extrapolated data from the first 12 months.

2.5.2 Motivational interviewing to reduce club drug use among men who have sex with men

The model assumed that the prevalence of drug use changed in line with the days of drug use from the study (Table 1) until month 12 (the study duration). Between months 12 and 24, the base case assumed that drug use returned linearly to baseline, and a scenario analysis extrapolated data from the first 12 months.

2.5.3 STRIVE

The model assumed that prevalence of drug use changed in line with days of drug use from the study (Table 1), until month 12 (the study duration). Between months 12 and 24, the base case assumed that drug use returned linearly to baseline, and a scenario analysis extrapolated data from the first 12 months.

[Figure 1 to go here]

For all of the models, we performed threshold analyses to explore the duration of intervention effect needed for each intervention to be cost-effective.

Results

The base case costs, QALYs and incremental cost-effectiveness ratios (ICERs) for each intervention are reported in Table 3. 'Costs' refers to both the cost of the intervention (or the comparator) and social costs associated with drug misuse. 'QALYs' refers to the QALY losses associated with drug misuse only. For all interventions, the base case ICERs are estimated to be above £100,000/QALY, and well above the £20,000/QALY level that NICE generally considers for cost-effectiveness (National Institute for Health and Care Excellence, 2016). This is because the cost savings and QALY gains from reducing drug use are not large enough to offset the costs of the interventions.

The QALY losses for each intervention and comparator are small – in context, a QALY loss of 0.00011 equates to losing one hour of life in full health. The QALY losses are small because the risk of a person who misuses a drug experiencing an event which leads to QALY loss is very low, even though in some cases the QALY loss per event (such as premature death) can be substantial. Furthermore, three of the interventions (Catalano et al., 1999; Milburn et al., 2012; Prado et al., 2012) are delivered to a population where not all recipients at baseline are misusing drugs – and so the number of people experiencing a QALY loss is very small indeed. Therefore, there is limited potential for interventions to reduce this QALY loss and the resulting incremental QALY gain is very small.

With low incremental QALYs, ICERs are very sensitive to intervention costs, and so sensitivity analysis for low and high intervention costs as well as sustained duration of effect is presented in Table 4. The web-based feedback intervention, which targeted a population who were all occasional drug users at baseline, becomes dominant (providing more benefit than comparator at a lower cost) when the cost is reduced to £1. At this price, the cost saving from avoiding drug use is sufficient to offset the intervention cost. It may be feasible for an online intervention to be delivered at such a low cost per person when provided to a sufficiently large population. Changing the cost of the Focus on Families intervention does not sufficiently decrease the ICER for the intervention to be cost-effective. This is because only a small proportion of the study population uses drugs and the intervention effect is small. Like Focus on Families, Familias Unidas targets people at risk of drug use, but has a lower intervention cost and higher incremental effect than Focus on Families. Familias Unidas would be dominant if the duration of effect was sustained and the intervention cost was £116, but the feasibility of delivering an intensive intervention with the same effectiveness for such a low cost is unknown. The interventions for ecstasy and cocaine use are estimated to be not cost-effective even with a low cost and sustained duration of effect.

The ICERs for Focus on Families and STRIVE remain above £30,000/QALY even in a scenario where drug use took over 60 years to return to baseline. The other interventions become cost-effective at £20,000 - £30,000/QALY when the duration of effect increases. For motivational interviewing among men who have sex with men the duration of effect needs to be 25-45 years, for motivational interviewing in young gay and bisexual men and the brief intervention for ecstasy, the duration needs to be 10-20 years. Familias Unidas and the web-based feedback are cost-effective with durations of 4-8 years, and actually become cost-saving if the effect is sustained for 11 and 6 years respectively.

[Table 3 to go here]

[Table 4 to go here]

Discussion

Although interventions may well exist that are cost-effective in preventing drug misuse in vulnerable populations, these were not included in the NICE scope and none of the interventions considered in our analyses were estimated to be cost effective in the base case. This is at least partially due to the relatively low effectiveness of the interventions – more robust evidence of larger intervention effect sizes would translate into more favourable cost-effectiveness estimates. However, the analyses were additionally subject to a number of limitations, many of which are common challenges in the economic evaluation of public health interventions (Weatherly et al, 2009).

Duration of intervention effect

NICE has found interventions to prevent smoking and alcohol misuse to be cost-effective (National Institute for Health and Care Excellence, 2010; National Institute for Health and Care Excellence, 2008b; National Institute for Health and Care Excellence, 2007). However, interventions with similar costs in drug misuse prevention and alcohol consumption or smoking have very different cost-effectiveness results. Interventions that cost £15 per head and prevented smoking prevalence by 0.5% were estimated to be cost-effective, with ICERs much lower than those for the web-based intervention included in the current analysis, which also cost £15 per head (Raikou and McGuire, 2008). Screening to identify people at increased risk followed by brief advice costing £80 was estimated to reduce alcohol use by 12.3%, and the ICERs varied between being dominant and £6,000/QALY (Purshouse et al., 2009). In comparison, the brief intervention to reduce ecstasy use had a similar cost and reduced drug use by 32% but had ICERs above £200,000/QALY.

The effect of the screening followed by brief advice for alcohol consumption was assumed to return to baseline over seven years (Purshouse et al., 2009), a longer duration than the ecstasy brief intervention model (12 months). The cost-effectiveness of any intervention is sensitive to the duration of effect, and Purshouse et al., (2013) found that assuming that the effect returned to baseline over three years halved the QALY gain and increased the ICER to £39,000/QALY. We did not identify any evidence to support conducting analyses with longer duration of effect for the included interventions and the single study that included longer term follow up found no effects beyond 12 months (Haggarty et al., 2008). However, sensitivity analysis demonstrated that with duration of effect comparable to that of the brief intervention for alcohol, four of the seven interventions could be cost-effective or even cost-saving.

Long-term consequences of drug misuse

Most interventions to prevent alcohol misuse or smoking are cost-effective partially because the long term consequences of smoking and alcohol are well understood and avoidable costs are high (Allender et al., 2009; Balakrishnan et al., 2009; Ekpu and Brown, 2015; Nutt et al., 2010; Scarborough et al., 2011; Wadd and Papadopoulos, 2014). There is high quality evidence linking alcohol and smoking to a range of health outcomes such as high blood pressure, heart disease, respiratory disease, cancers, digestive disease and road traffic accidents, whereas the evidence for the association between illicit drug use and these types of outcomes is much weaker. We note that including cannabis-related road traffic accidents in sensitivity analyses decreases the ICERs for interventions, for example from £240,994 to £205,442 for Familias Unidas.

The social costs associated with each drug in our analysis are limited by the data available, although we note that all were validated through discussion with a committee of experts. This relative paucity of data is likely a feature of the comparatively lower drug usage rates in the general population: 2.2% of adults are frequent illicit drug users (Home Office, 2015) compared with 19% of adults who smoke cigarettes (Office for National Statistics, 2014a) and 79% who drink alcohol

(Office for National Statistics, 2014b). The illicit status of drugs may also lead to underreporting and further limit the accuracy of estimates. Changes in drug purity, potency, and the use of substitute and excipient compounds in some drug preparations also presents additional challenges in understanding their long-term consequences (Cole et al., 2011). For example, there has been a change in the ratio of cannabinoids in analysed samples of cannabis over the last two decades, which may have implications for assessments of psychosis risk (Elsohly et al., 2016).

Our models did not consider the ‘gateway theory’ that early adolescent use of cannabis, ecstasy or cocaine can lead to later use of drugs such as opiates which have much greater social costs. Evidence for gateway effects are weak (Degenhardt et al., 2010; Nkansah-Amankra and Minelli, 2016), but if a causal link does exist then our models would underestimate the benefits and cost-effectiveness of drug misuse prevention programmes. In addition, our models considered illicit drug use in isolation of alcohol and tobacco use. Unhealthy behaviours often cluster together and have a magnified combined effect, so drug use may increase the liver damage seen with alcohol use (Degenhardt and Hall, 2012), or cannabis use may increase the lung damage seen with tobacco use, and may lead to nicotine dependence (Lee and Hancox, 2011).

Appropriateness of the QALY as an outcome

There are harmful effects of drug misuse which our economic models have not captured. Although we include costs related to crime, drug misuse may also have (indirect) impact upon attendance and attainment in education and employment, and an effect on family and social problems (Lynskey and Hall, 2000; Chatterji 2006; Fergusson et al., 2003; Zhang et al., 2006). These would all impact quality of life in a way that health-focussed QALYs do not capture. We considered the harms and costs associated with the individual using drugs, but there are also economic, health, and social consequences of involvement in illicit drug market and criminal justice system (United Nations Office on Drugs and Crime, 1998). Although presentation of a cost-utility analysis facilitates comparison with interventions in other health-related areas, and allows NICE to apply decision making criteria for recommending interventions, this approach may not always capture the full range of relevant outcomes in a particular domain. This may be why so few studies were identified in the literature review of cost-effectiveness evidence.

Perspective of analyses and inclusion of wider outcomes

Our analysis considered only costs to the healthcare and criminal justice systems and health effects to the individual. Drug misuse may additionally impact productivity, through difficulty in finding or maintaining employment, absenteeism and presenteeism, or through premature death. We considered a scenario in the models focussing on ecstasy and cocaine use where premature death was associated with a loss of earnings, assuming that people would otherwise work until age 65, using mean annual salaries by age band (Office for National Statistics, 2016). In this scenario, the ICERs decreased to £445,274 for the brief intervention, £442,324 for motivational interviewing in young gay and bisexual men, £178,805 for motivational interviewing in men who have sex with men and £959,695 for STRIVE. These small changes to the ICER demonstrate that the inclusion of lost productivity due to death would not change the conclusions of the economic models. This is because although the cost of lost productivity for one death is relatively high (£617,966 for a 25-year-old), it is only incurred by a very small proportion of the population receiving the intervention. Quantifying and including suffering of family and friends would have increased the negative outcomes associated with drug misuse for a greater proportion of the population, but if the per-person impact was relatively low, this would also have little impact on the ICERs.The interventions included in our analyses did not all focus solely on reducing drug use. Arguably, in calculating whether an intervention is cost-effective, we should consider the potential costs and benefits of its effect on all reported outcomes. Five studies additionally measured changes in risky sexual behaviour (Martin and Copeland, 2010; Milburn et al, 2012; Parsons et al., 2014; Prado et al., 2012). Decreases in risky sexual behaviour may lead to reductions in sexually transmitted infections and unwanted pregnancies. Incorporating such additional outcomes would be likely to increase the cost offsets and QALY gains for the interventions and hence decrease the ICERs, possibly to such a level that the interventions become cost-effective. Furthermore, the interventions may have reduced use of more than one drug, which would deliver additional QALY gains and cost offsets for the same intervention cost, therefore decreasing the ICER. Interventions which additionally reduced use of injectable drugs such as heroin may lead to reductions in needle-sharing and hence avoid transmission of disease such as hepatitis, which would have further benefits.

Our study focussed on interventions which targeted high-risk populations. There are strong associations between problematic drug use, socioeconomic disadvantage, co-morbidities, and other vulnerabilities (e.g. homelessness) (Daniel et al., 2009; PHE, 2016). It is difficult to disaggregate the effect of an individual’s drug use from other risk factors in contributing to harmful outcomes and so primordial prevention of risk factors, as well as actions to reduce the influence of these risk factors, may impact upon multiple outcomes (Wilkinson and Pickett, 2010). The models we developed considered the differential distribution of drug use in study populations, but there was not sufficient evidence in primary studies to consider differential outcomes in detail. So, for example, the modelling took into account the increased likelihood that someone who was homeless was more likely to use drugs, but not that they might be more likely to be arrested than a drug user who was not homeless, or that intervention participation also increased the (unmeasured) likelihood that the individual would find stable housing.

There is little high-quality review-level evidence on the effectiveness of selective drug prevention programmes (Novakovic et al., 2016) However, there are multiple levels of influence that might potentially reduce the propensity to use drugs (Griffin and Botvin, 2010) in higher risk groups. These include psychobiological, social, family, and socioecological factors, and so programmes designed to improve outcomes in these domains, although not specified as drug prevention programmes, may have indirect effects on drug use. For example, the Good Behaviour Game is a universal elementary school classroom behaviour management intervention, and participation has been found to be associated with lower rates of drug and alcohol use disorders, regular smoking, antisocial personality disorder, criminal justice involvement and suicide ideation in late adolescence (Kellam et al., 2011). Secondary analysis suggested that intervention impact might be more pronounced in those participants rated at higher risk at baseline (Kellam et al., 2014). Inclusion of data from some universal programmes and including a wider range of outcomes in economic evaluation may lead to further cost savings and health benefits, and therefore improve the cost-effectiveness of the intervention.

Targeting interventions

The interventions considered here, as with many public health interventions, are aimed at prevention rather than treatment. This means that costs are incurred by a whole population, but only a proportion of that population is actually affected as not all would experience long term drug-related harms. Better targeted interventions at those sub-populations most at risk of experiencing drug related harms could increase the proportion of recipients who benefit from the interventions studied, and therefore increase the cost-effectiveness of interventions. However, this requires that the interventions under review have differential effectiveness for higher risk sub-groups. Whilst analysis of other prevention programmes has shown this to be the case (Conduct Problems Prevention Research Group, 2007; Kellam et al., 2008; McKay et al., 2014), others have not (Botvin et al.,1998; Elliott and Mihalic, 2004; Komro and Toomey, 2008; Spoth et al., 2006), and without secondary analysis of the programmes included in the current review, differential effects cannot be assumed.

Conclusion

Our analysis estimated that none of the seven drug misuse prevention interventions were cost-effective in the base case, because the cost savings and health benefits from preventing drug use did not sufficiently offset the intervention costs. Sensitivity analyses demonstrated that some interventions were cost-effective when a longer duration of intervention effect was assumed, demonstrating the importance of long-term follow up. Similarly, intervention cost was a key driver of cost-effectiveness, indicating that consideration should be given to the resources required to deliver the interventions in specific settings.

The ICERs for some interventions remained high even under more optimistic assumptions about duration of effect and intervention cost. This may be because in these cases, the intervention effect size was not sufficiently large to generate benefits to outweigh the cost. Inclusion of a broader range of benefits has the potential to reduce the ICERs somewhat, but may not have a substantial impact because only a fraction of people receiving the intervention are affected by serious consequences. A greater understanding of the consequences of drug misuse and the causal factors may facilitate the targeting of interventions to the most vulnerable populations and lead to more favourable cost-effectiveness results.

References

Allender S, Balakrishnan R, Scarborough P, Webster P, Rayner M. 2009. The burden of smoking-related ill health in the UK. Tob Control. 18(4): 262-7.

Advisory Council on the Misuse of Drugs. 2008. MDMA: A review of its harms and classification under the misuse of drugs act 1971. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119088/mdma-report.pdf Accessed 31 March 2017

Balakrishnan R, Allender S, Scarborough P, Webster P, Rayner M. 2009. The burden of alcohol-related ill health in the United Kingdom. J Public Health. 31(3):366-73.

Bates G, Jones L, Maden M, Collins B, Pendlebury M, McCoy E, Cochrane M, Sumnall H. NICE guidance on drug misuse prevention: targeted interventions. Review of economic evidence. December 2015. Available from: https://www.nice.org.uk/guidance/GID-PHG90/documents/economic-report-2 Accessed 2 November 2016

Botvin, G., Mihalic, S., & Grotpeter, J. K. (Eds.). (1998). Life skills training (Vol. 5). Boulder, CO: Center for the Study and Prevention of Violence, Institute of Behavioral Science, University of Colorado

Brennan A, Chick SE, Davies R. 2006. A taxonomy of model structures for economic evaluation of health technologies. 15:1295-1310.

Briggs AH, Claxton K, Sculpher MJ. 2006. Decision modelling for health economic evaluation. Oxford.

Catalano RF, Gainey RR, Fleming CB, Haggerty KP, Johnson NO. 1999. An experimental intervention with families of substance abusers: one-year follow-up of the Focus on Families project. Addiction. 94(2):241-54.

Chatterji P. 2006. Illicit drug use and educational attainment. Health Econ. 15(5):489-511.

Cole C, Jones L, McVeigh J, Kicman A, Syed Q, Bellis M. 2011. Adulterants in illicit drugs: a review of empirical evidence. Drug Test Anal. 3(2):89-96.

Collins B, Leigh S, Behzadnejad F, Martin AP, Haycox A, Sumnall H, Bates G. NICE Drug Misuse Prevention: Economic Modelling Report. May 2016. Available from https://www.nice.org.uk/guidance/GID-PHG90/documents/economic-report Accessed 2 Nov 2016

Conduct Problems Prevention Research Group. 2007. Fast track randomized controlled trial to prevent externalizing psychiatric disorders: findings from grades 3 to 9. J Am Acad Child Adolesc Psychiatry. 46(10):1250-62.

Daniel JZ, Hickman M, Macleod J, Wiles N, Lingford-Hughes A, Farrell M, Araya R, Skapinakis P, Haynes J, Lewis G. 2009. Is socioeconomic status in early life associated with drug use? A systematic review of the evidence. Drug Alcohol Rev. 28(2):142-53.

Degenhardt L, Wall H. 2012. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet. 379 (9810): 55-70.

Degenhardt L, Dierker L, Chiu WT, Medina-Mora ME, Neumark Y, Sampson N, Alonso J, Angermeyer M, Anthony JC, Bruffaerts R, de Girolamo G, de Graaf R, Gureje O, Karam AN, Kostyuchenko S, Lee S, Lépine JP, Levinson D, Nakamura Y, Posada-Villa J, Stein D, Wells JE, Kessler RC. 2010. Evaluating the drug use "gateway" theory using cross-national data: consistency and associations of the order of initiation of drug use among participants in the WHO World Mental Health Surveys. Drug Alcohol Depend. 108(1-2):84-97.

Department of Health. 2014. NHS reference costs 2013 to 2014. Available from: https://www.gov.uk/government/publications/nhs-reference-costs-2013-to-2014 Accessed November 2015.

Drummond MF, Sculpher MJ, Torrance GW, O’Brien BJ, Stoddart GL. 2015. Methods for the Economic Evaluation of Health Care Programmes. 4th ed. Oxford.

Edkpu VU, Brown AK. 2015. The Economic Impact of Smoking and of Reducing Smoking Prevalence: Review of Evidence. Tob Use Insights. 14;8:1-35.

Education Endowment Foundation. Good Behaviour Game evaluation protocol. Available from: https://v1.educationendowmentfoundation.org.uk/uploads/pdf/Good_Behaviour_Game_-_protocol.pdf Accessed 25 Nov 2011

Elliot DS and Mihalic S. 2004. Issues in disseminating and replicating effective prevention programs. Prev Sci. 5(1):47-53.

Elsohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC. 2016. Changes in Cannabis Potency Over the Last 2 Decades (1995-2014): Analysis of Current Data in the United States. Biol Pyschiatry. 79(1):613-9.

European Monitoring Centre for Drugs and Drug Addiction. 2016. Health responses to new psychoactive substances. Available from: http://www.emcdda.europa.eu/system/files/publications/2812/TD0216555ENN.pdf Accessed 15 Dec 2016

Fergusson DM, Horwood LJ, Beautrais AL. 2003. Cannabis and educational achievement. Addiction. 98(12):1681-92.

Fernandez-Hermida JR, Calafat A, Becoña E, Tsertsvadze A, Foxcroft DR. 2012. Assessment of generalizability, applicability and predictability (GAP) for evaluating external validity in studies of universal family-based prevention of alcohol misuse in young people: systematic methodological review of randomized controlled trials. Addiction. 107(9):1570-9

Flay BR, Biglan A, Boruch RF, Castro FG, Gottfredson D, Kellam S, Mościcki EK, Schinke S, Valentine JC, Ji P. 2005. Standards of evidence: criteria for efficacy, effectiveness and dissemination. Prev Sci. 6(3):151-75.

Gadegbeku B, Amoros E, Laumon B. 2011. Responsibility study: main illicit psychoactive substances among car drivers involved in fatal road crashes. Ann Adv Automot Med. 55: 293-300.

Godfrey C, Eaton G, McDougall C, Culyer A. 2002. The economic and social costs of Class A drug use in England and Wales, 2000. Available from: http://webarchive.nationalarchives.gov.uk/20110218135832/rds.homeoffice.gov.uk/rds/pdfs2/hors249.pdf Accessed 31 March 2017

Griffin KW, Botvin GJ. 2010. Evidence-Based Interventions for Preventing Substance Use Disorders in Adolescents. Child Adolesc Psychiatr Clin N Am. (3): 505–526.

Haggerty KP, Skinner M, Fleming CB, Gainey RR, Catalano RF. 2008. Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment. Addiction. 103(12):2008-16.

Hall W, 2015. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? Addiction. 110(1): 19-35.

Hartman RL, Huestis MA. 2013. Cannabis effects on driving skills. Clin Chem. 59(3): 478-92.

Hoang VP, Shanahan M, Shukla N, Perez P, Farrell M, Ritter A. 2016. A systematic review of modelling approaches in economic evaluations of health interventions for drug and alcohol problems. BMC Health Serv Res. 16:127.

Kellam SG, Wang W, Mackenzie AC, Brown CH, Ompad DC, Or F, Ialongo NS, Poduska JM, Windham A. 2014. The impact of the Good Behavior Game, a universal classroom-based preventive intervention in first and second grades, on high-risk sexual behaviors and drug abuse and dependence disorders into young adulthood. Prev Sci. 15 (S1): S6-18.

Kellam SG, Mackenzie AC, Brown CH, Poduska JM, Wang W, Petras H, Wilcox HC. 2011. The good behavior game and the future of prevention and treatment. Addict Sci Clin Pract. 6(1): 73-84.

Kellam SG, Brown CH, Poduska JM, Ialongo NS, Wang W, Toyinbo P, Petras H, Ford C, Windham A, Wilcox HC. 2008. Effects of a universal classroom behavior management program in first and second grades on young adult behavioral, psychiatric, and social outcomes. Drug Alcohol Depend.95 Suppl 1:S5-S28.

Komro KA, Toomey TL. 2002. Strategies to prevent underage drinking. Alcohol Res Health. 26(1):5-14.

Lee CM, Neighbors C, Kilmer JR, Larimer ME. 2010. A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial. Psychol Addict Behav. 24(2):265-73.

Lee MH, Hancox RJ. 2011. Effects of smoking cannabis on lung function. Expert Rev Respir Med. 5(4):537-46.

Lynskey M, Hall W, 2000. The effects of adolescent cannabis use on educational attainment: a review. Addiction. 95, 1621-1630.

Martin G, Copeland J. 2010. Brief intervention for regular ecstasy (MDMA) users: Pilot randomization trial of a Check-up model. J Subst Use. 2:131-42.

May T, Duffy M, Warburton H, Hough M. 2007. Policing cannabis as a Class C drug: an arresting change? Available from: https://www.jrf.org.uk/report/policing-cannabis-class-c-drug Accessed 31 March 2017

McCrone P, Patel A, Knapp M, Schene A, Koeter M, Amaddeo F, Ruggeri M, Giessler A, Puschner B, Thornicroft G. 2009. A comparison of SF-6D and EQ-5D utility scores in a study of patients with schizophrenia. J Ment Health Policy Econ. 12(1): 27-31.

McKay M, Sumnall H, McBride N, Harvey S. 2014. The differential impact of a classroom-based, alcohol harm reduction intervention, on adolescents with different alcohol use experiences: a multi-level growth modelling analysis. J Adolesc. 37(7):1057-67

Milburn NG, Iribarren FJ, Lightfoot M, Solorio R, Rotheram-Borus MK, Desmond K, Lee A, Alexander K, Maresca K, Eastmen K, Arnold EM, Duan N. 2012. A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth. J Adolesc Health. 50(4): 358-64.

Ministry of Justice 2014. Youth justice statistics 2012/13. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/278549/youth-justice-stats-2013.pdf Accessed 31 march 2017

Morgenstern J, Bux DA Jr, Parsons J, Hagman BT, Wainberg M, Irwin T. 2009. Randomized trial to reduce club drug use and HIV risk behaviors among men who have sex with men. J Consult Clin Psychol. 77(4): 645-56.

Morris S, Devlin N, Parkin D. 2007. Economic Analysis in Healthcare. John Wiley & Sons.

National Institute for Health and Care Excellence. Drug misuse prevention: targeted interventions. 2017. Available from: https://www.nice.org.uk/guidance/ng64 Accessed 12 April 2017

National Institute for Health and Care Excellence, Developing NICE guidelines: the manual. 2016 Available from: https://www.nice.org.uk/process/pmg20/chapter/introduction-and-overview Accessed 2 Nov 2016

National Institute for Health and Care Excellence, Final Scope, 2015. Available from: https://www.nice.org.uk/guidance/GID-PHG90/documents/drug-misuse-prevention-final-scope2 Accessed 2 Nov 2016

National Institute for Health and Care Excellence, Alcohol-use disorders: prevention. 2010. Available from: https://www.nice.org.uk/guidance/ph24 Accessed 2 Nov 2016

National Institute for Health and Care Excellence, Social Value Judgements. 2008a. Available from: https://www.nice.org.uk/Media/Default/About/what-we-do/Research-and-development/Social-Value-Judgements-principles-for-the-development-of-NICE-guidance.pdf Accessed 01 September 2016

National Institute for Health and Care Excellence, Smoking: preventing uptake in children and young people. 2008b. Available from: https://www.nice.org.uk/guidance/ph14 Accessed 2 Nov 2016

National Institute for Health and Care Excellence, Alcohol-use disorders: school-based interventions. 2007. Available from: https://www.nice.org.uk/guidance/ph27 Accessed 2 Nov 2016

Nkansah-Amankra S, Minelli M. 2016. "Gateway hypothesis" and early drug use: Additional findings from tracking a population-based sample of adolescents to adulthood. Prev Med Rep. 4:134-41.

Novakovic E, Rutter L, Ainsworth N, Hudson T, Cullum A, Canning U, McSloy A. Drug misuse prevention: targeted interventions. Evidence review 1. July 2016. Available from: https://www.nice.org.uk/guidance/GID-PHG90/documents/evidence-review Accessed 2 Nov 2016

Nutt DJ, King LA, Phillips LD. 2010. Drug harms in the UK: a multicriteria decision analysis. The Lancet. 376 (9752):1558-65.

Office for National Statistics: Annual Survey of Hours and Earnings 2015, 2016. Available from: https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/datasets/agegroupashetable6 Accessed September 2016.

Office for National Statistics: deaths related to drug poisoning in England and Wales: 2014 registrations. 2015. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2015-09-03 Accessed November 2015

Office for National Statistics. Cigarette smoking prevalence, in Scotland and England and Wales (combined), by sex 2007 to 2014. 2014a. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/drugusealcoholandsmoking/adhocs/005495cigarettesmokingprevalenceinscotlandandenglandandwalescombinedbysex2007to2014 Accessed 8 Nov 2016

Office for National Statistics. Adult drinking habits. 2014b. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/drugusealcoholandsmoking/datasets/adultdrinkinghabits Accessed 8 Nov 2016

Parsons JT, Lelutiu-Weinberger C, Botsko M, Golub SA. 2014. A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. 82(1):9-18.

Poduska JM, Kellam SG, Wang W, Brown CH, Ialongo NS, Toyinbo P. 2008. Impact of the Good Behavior Game, a universal classroom-based behavior intervention, on young adult service use for problems with emotions, behavior, or drugs or alcohol. Drug Alcohol Depend. 95 (S1): S29-44.

Prado G, Cordova D, Huang S, Estrada Y, Rosen A, Bacio GA, Leon Jimenez G, Pantin H, Brown CH, Velazguez MR, Villamar J, Freitas D, Tapia MI, McCollister K. 2012. The efficacy of Familias Unidas on drug and alcohol outcomes for Hispanic delinquent youth: main effects and interaction effects by parental stress and social support. Drug Alcohol Depend. 125 Suppl 1:S18-25.

Purshouse RC, Brennan A, Rafia R, Latimer NR, Archer RJ, Angus CR, Preston LR, Meier PS. 2013. Modelling the cost-effectiveness of alcohol screening and brief interventions in primary care in England. Alcohol Alcohol. 48(2):180-8.

Purshouse R, Brennan A, Latimer N, Meng Y, Rafia R, Jackson R, Meier P. 2009. Modelling to assess the effectiveness and cost-effectiveness of public health related strategies and interventions to reduce alcohol attributable harm in England using the Sheffield Alcohol Policy Model version 2.0. Available from: https://www.nice.org.uk/guidance/ph24/evidence/economic-modelling-report-371533357 Accessed 2 Nov 2016

Pyne JM, Tripathi S, French M, McCollister K, Rapp RC, Booth BM. 2011. Longitudinal Association of Preference-Weighted Health-Related Quality of Life Measures and Substance Use Disorder Outcomes. Addiction. 106(3): 507-515.

Raikou M, McGuire A. 2008. Cost-effectiveness of a mass media campaign and a point of sale intervention to prevent the uptake of smoking in children and young people: Economic modelling report. Available from:

https://www.nice.org.uk/guidance/ph14/evidence/economic-modelling-report-369943165 Accessed 2 Nov 2016

Scarborough P, Bhatnagar P, Wickramasinghe KK, Allender S, Foster C, Rayner M. 2011. The economic burden of ill health due to diet, physical inactivity, smoking, alcohol and obesity in the UK: an update to 2006-07 NHS costs. 33(4):527-35.

Spoth R, Shin C, Guyll M, Redmond C, Azevedo K. 2006. Universality of effects: an examination of the comparability of long-term family intervention effects on substance use across risk-related subgroups. Prev Sci. 7(2):209-24.

United Nations Office on Drugs and Crime. 2016. World Drug Report. Available from: https://www.unodc.org/doc/wdr2016/WORLD_DRUG_REPORT_2016_web.pdf Accessed 13 December 2016

Wadd S, Papadopoulos C. 2014. Drinking behaviour and alcohol-related harm amongst older adults: analysis of existing UK datasets. BMC Res Notes. 20;7:741.

Weatherly H, Drummond M, Claxton K, Cookson R, Ferguson B, Godfrey C, Rice N, Sculpher M, Sowden A. 2009. Methods for assessing the cost-effectiveness of public health interventions: Key challenges and recommendations. Health Policy. 93: 85-92.

Wilkinson R & Pickett K (2010). The spirit level: why equality is better for everyone. London: Penguin.

Zhang C, Brook JS, Leukefeld CG, Brook DW. Trajectories of marijuana use from adolescence to adulthood as predictors of unemployment status in the early forties. Am J Addict. 25(3):203-9.