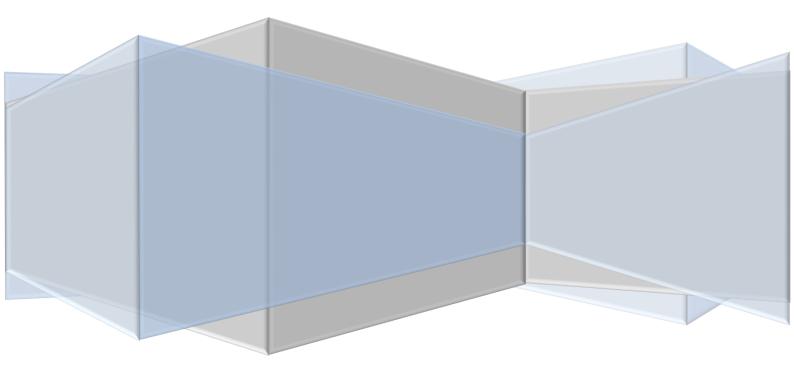
NICE Drug Misuse Prevention:

Economic Modelling Report

Brendan Collins, Simon Leigh, Fatemeh Behzadnejad, Antony P. Martin, Alan Haycox, Harry Sumnall, Geoff Bates.



Contents

1.	Executive Summary & Evidence Statements	. 3
	Results and Evidence Statements	. 3
2.	Introduction	. 8
	2.1 Overall Aims and Objectives	. 9
	2.2 Decision Question	. 9
	2.3 Objectives of this Report	. 9
3.	Summary of Results of Economic Literature Review	. 9
	3.1 Method for selection of effectiveness studies	10
4.	Modelling Methodology	11
	4.1 Model Perspectives	11
	4.2 Model Framework	11
	4.3 Conceptual framework of models	11
	4.4 Population at risk	13
	4.5 Intervention costs	19
	4.6 The cost consequences of drug misuse	25
	4.7 Sensitivity Analysis	27
	4.8 Quality assurance of models	27
	4.9 Limitations of modelling approach	28
5.	Model Description and Results	29
	5.1 Models focussing on cannabis use	29
	5.1.1 Model of Focus on Families intervention based on Catalano et al (1999)	32
	5.1.2 Model of Web-Based Personalized Feedback based on Lee et al. (2010)	
		35
	5.1.3 Model of Familias Unidas based on Prado et al. (2012)	38
	5.2. Model focussing on ecstasy	43
	5.2.1 Model of Brief Intervention for reducing ecstasy consumption amongst those attending nightclubs based on Martin et al. (2010)	49
	5.3 Models focussing on cocaine use	56
	5.3.1 Model of Motivational Interviewing to reduce drug use in young gay and bisexual men, based on Parsons et al., (2014)	60
	5.3.2 Model of Motivational Interviewing intervention to reduce club drug use and HIV risk behaviors among men who have sex with men, based on Morgenstern et al., (2009)	63

	5.3.3 Model of a family intervention to reduce sexual risk behaviour, substance use, and delinquency among newly homeless youth, based on Milburn et al.
	(2012)
6.	6. Discussion and Conclusions72
	6.1 Cost-effectiveness analyses72
	6.2 Evidence Statements75
	6.3 Discussion77
	6.3 Conclusion
7. Se	Appendix 1. Model Assumption Tables & Input Parameters for Univariate ensitivity Analyses
	7.1 Model based on Catalano, et al. "An experimental intervention with families of substance abusers: one-year follow-up of the focus on families project." 82
	7.2 Model based on Lee et al. (2010) "A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial"
	7.3 Model based on Prado et al. (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."
	7.4 Model based on Martin et al. (2010): "Brief intervention for regular ecstasy (MDMA) users: Pilot randomised trial of a Check-up model."
	7.5 Model based on Parsons, et al (2014). A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. Journal of Consulting and Clinical Psychology, 82(1), 9–18 90
	7.6 Model based on Morgenstern et al. (2009) Randomized Trial to Reduce Club Drug Use and HIV Risk Behaviors Among Men Who Have Sex With Men91
	7.7 Model based on Milburn, et al, 2012. A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth. Journal of Adolescent Health, 50(4), pp.358-364
8.	References

NICE Drug Misuse Prevention: Economic Modelling Report

1. Executive Summary & Evidence Statements

Objective: To estimate the likely cost effectiveness of targeted interventions aimed at reducing or preventing drug misuse in pre-defined vulnerable (and at-risk) populations. This is to enable the NICE Public Health Advisory Committee to consider whether interventions are cost effective when making their recommendations.

Method: This model built upon the initial systematic review of studies concerning the 'effectiveness' of such interventions, as undertaken by Liverpool John Moore's University Centre for Public Health and by the NICE team. The modelling involved two stages:

- The selection of relevant studies (and interventions) identified in the effectiveness review, based on the quality of the methodology employed in the studies; and
- The building of a number of economic models, specific to the drug under consideration, the population group being considered, and the intervention identified for such groups. The aim of the models was to estimate the likely impact (and value) of targeted interventions, on the populations in question, and how any intervention may reduce or delay drug use and the harmful consequences that ensue.

This report details the results of the models developed to predict the potential impact of changes in the probability of drug misuse within vulnerable populations. Each model places a value on the expected consequences of drug misuse within a given vulnerable group (as reported by published literature), expressed in terms of the impact on health, healthcare utilisation, and crime. Subsequently, each model compares the economic cost (including on-costs, staff time and equipment costs) of implementing the intervention against the expected costs accrued in the event of 'doing nothing' or treatment as usual, providing an estimate of the return-oninvestment, and in cases where survival and quality-of-life data were available, the cost-effectiveness of such interventions, expressed in terms of the cost per qualityadjusted life year gained (cost utility analysis).

Results and Evidence Statements

Seven studies were modelled. The modelling adopted a broad public sector which included costs of drug treatment and crime, as well as health care costs and quality-adjusted life years (QALYs).

All of the evidence statements from this report, evidence review 1, evidence review 2 and the cost effectiveness review are presented in the paper Evidence statements from all reviews.

Evidence statement 1

An economic model was built based on an experimental intervention with families of substance users by Catalano et al (1999) and a follow-up study by Haggerty et al (2008). The economic and health benefits are limited to 12 months in the model as beyond 12 months of the study, each individual in the intervention or control cohorts had the same probability of using cannabis. The model found that this intervention was unlikely to be cost effective at a willingness to pay threshold of £20,000 per QALY due to the restricted duration of benefits and high intervention costs (£3,367) of 'Focus on Families' for one year. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £99m per QALY gained. The intervention would have to cost less than £4 per person to be considered cost-effective, based on results being limited to 12 months.

Evidence statement 2

An economic model was informed by results from Lee et al (2010) based on a brief, web-based personalized feedback selective intervention for college student cannabis use. Subgroup analysis found promising effects for those with a family history of drug problems and therefore supported selective targeting of the intervention which was applied in the model. Based on a cost of £15 the intervention would not be cost effective but if the intervention could be provided at a low cost of £1 or less then it would be dominant, i.e. less costly and more effective than a 'do nothing' alternative, as it provides resource savings and reductions in cannabis use. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £329,000 per QALY gained.

Evidence statement 3

An economic model was informed by Prado et al (2012) based on an intervention called Familias Unidas to reduce drug use (in particular, cannabis) and alcohol use. Familias Unidas is most effective for adolescents with parents exhibiting high stress and lower levels of social support. Familias Unidas includes eight 2-hour multi-parent group sessions and four 1-hour family visits. The model found that this intervention was unlikely to be cost effective at a willingness to pay threshold of £20,000 per QALY due to restricted benefits of the intervention and the costs of delivery (£154.25 per family). The ICER (incremental cost effectiveness ratio) in the base case scenario was around £241,000 per QALY gained. The intervention would have to cost less than £135 and the effects extrapolated to an additional 12 months to be considered cost-effective.

Evidence statement 4

An economic model based on a study of motivational interviewing to reduce ecstasy use in those attending nightclubs, based on Martin et al. 2010, found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £485,000 per QALY gained. Even if the effect of reducing drug use was maintained for at least two years, the cost halved to £32 and a discount rate of 1.5% applied, the ICER was still £70,000. In fact, the intervention could only be cost effective if delivered at a cost of £4.20 per hour or less in the base case scenario.

Evidence Statement 5

An economic model based on a study of motivational interviewing to reduce drug use in young gay and bisexual men, based on Parsons et al., (2014) found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £301,000 per QALY gained. This intervention would only be cost effective if the effect of reducing drug use was maintained for at least two years, and if the intervention could be provided at a cost of less than £88.

Evidence Statement 6

An economic model based on a study of a motivational interviewing intervention to reduce club drug use and HIV risk behaviours among men who have sex with men by Morgenstern et al. (2009) found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £131,000 per QALY gained. This intervention would only be cost effective if the effect of reducing drug use was maintained for at least two years, and if the intervention could be provided at a cost of less than £190. The intervention was targeted to men with an average age of 38 but if it could be provided to younger men then it would be more likely to be cost effective as younger people are more likely to become drug dependent and to lose more years of life through early death associated with drug use.

Evidence Statement 7

An economic model based on a study of a family intervention called STRIVE (Support to Reunite, Involve and Value Each Other) by Milburn et al (2012) found that this intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £117,000 per QALY gained. If the intervention

cost was less than £500, and the intervention had a longer term effect over two years or more, then it would be cost effective.

Evidence Statement 8

The results of the economic modelling suggest that, to be cost effective, drug use prevention interventions would need to cost less than £100 per person, and would need to reduce drug use by at least five percentage points, maintained over two years (for example to reduce drug use from 20% to 15% of a population). Targeting interventions at individuals who are at high risk of drug use or harmful consequences of drug use, or at individuals who are already drug users, would most likely make interventions more efficient. If interventions can prevent more harmful forms of drug use like opiate use then they will be more likely to be cost effective.

Evidence Statement 9

If drug prevention interventions that are effective over a period of time can be provided as part of multicomponent interventions at an additional cost of less than around £100, then they may represent a cost effective component of these programmes.

2. Introduction

The Department of Health commissioned the National Institute for Health and Care Excellence (NICE) to update and inform public health guidance with respect to community-based interventions aimed at reducing substance misuse among ten distinct populations deemed to be at increased risk of drug misuse. The present report was produced by people from Liverpool Health Economics and LJMU Centre for Public Health. The ten vulnerable groups are as follows;

- 1. people who have mental health problems
- 2. people involved in commercial sex work or are being sexually exploited
- 3. people who are lesbian, gay, bisexual or transgender
- 4. people not in employment, education or training (including children and young people who are excluded from school or are regular truants)
- 5. children and young people whose parents use drugs
- 6. looked after children and young people
- 7. children and young people who are in contact with young offender team but not in secure environments (prisons and young offender institutions)
- 8. people who are considered homeless
- 9. people who attend nightclubs and festivals
- 10. people who are known to use drugs occasionally / recreationally

NICE Guidance PH4 "Substance misuse interventions for vulnerable under 25s" was produced in 2007; this had a different scope than the present piece of work as it included universal interventions but focused on young people only. This guidance recommended that commissioners and practitioners should;

- Develop a local strategy
- Use existing tools to identify children and young people who are misusing, or at risk of misusing, substances.
- Work with parents and carers and other organisations involved with children and young people to provide support and, where necessary, to refer them to other services.
- Offer motivational interviews to those who are misusing substances.
- Offer group-based behavioural therapy to children aged 10–12 years who are persistently aggressive or disruptive and deemed at high risk of misusing substances. Offer their parents or carers group-based parent skills training.
- Offer a family-based programme of structured support to children aged 11–16 years who are disadvantaged and deemed at high risk of substance misuse.

In 2015, the ACMD (Advisory Council on the Misuse of Drugs) published a briefing on the prevention of drug and alcohol dependence; this also had a wider scope than

the present report, and found that some interventions such as 'The Good Behaviour Game' showed promise in preventing drug use (ACMD 2016).

2.1 Overall Aims and Objectives

The economic models were constructed to incorporate data from the prior systematic reviews of clinical and cost effectiveness. The aim was to estimate the cost effectiveness of all interventions which met our pre-defined inclusion criteria. This paper describes the economic models and the resulting estimates of the cost effectiveness of interventions to reduce or prevent drug misuse in vulnerable populations.

2.2 Decision Question

The decision problem under consideration is;

Which targeted interventions are most cost effective in preventing drug misuse among groups of people most at risk?

2.3 Objectives of this Report

The paper builds on a review of effectiveness studies undertaken by NICE and LJMU. The NICE effectiveness review team identified a number of studies demonstrating the effect of relevant interventions on the risk that vulnerable populations will use substances. The objective of this paper is twofold:

- To identify which of the studies identified by the effectiveness team present evidence of sufficient quality to allow estimates of cost-effectiveness of the interventions to be derived; and
- Estimate the cost-effectiveness of the interventions selected.

3. Summary of Results of Economic Literature Review

This economic literature review identified little evidence from English language studies published since 1st January 1995 which estimate the cost-effectiveness of targeted interventions to prevent, delay or minimise the escalation of drug misuse. The only evidence found was from the Washington State Institute for Public Policy (WSIPP 2004), an economic evaluation based on a criminal justice orientated cost-benefit model identified that peer mentoring interventions targeting at-risk students including regular truants (benefit cost ratio 16.42; total benefits \$29,819, total costs \$1,816) were estimated to be cost saving. Not all peer mentoring interventions included within the cost-benefit model were targeted to a specific population. The WSIPP model also found that an intervention targeting looked after children, Multidimensional Treatment Foster Care, (benefit cost ratio 2.11; total benefits \$17,356, total costs \$8,230) was estimated to be cost saving. There was noted to be

potentially serious to minor limitations with the model's applicability outside a criminal justice perspective and uncertainty regarding methodology. There is further uncertainty about its applicability to the UK, as the model is based upon policy options available in Washington State and sources for costs and resources are from the United States and all evaluations of intervention effectiveness included in the model were from the United States. Some of the WSIPP models have been adapted for the UK by Dartington Social Research Unit and estimated to have similar cost benefit ratios. Multidimensional Treatment Foster Care was estimated to have a benefit-cost ratio of £2.64 for every £1 spent in the UK (Investing in Children 2016). This intervention is being implemented in several local authority areas in the UK including Manchester and Salford. One of the peer mentoring interventions (CHANCE) is currently being evaluated in primary schools in London but the study does not include drug-related outcomes (ISRCTN 2016).

The NICE effectiveness evidence review did identify that there has been advances in the drug misuse prevention evidence base since PH4 and found several effective interventions (NICE 2007).

3.1 Method for selection of effectiveness studies

The cost-effectiveness analysis presented in this paper builds upon an effectiveness study review undertaken by NICE. The results of the effectiveness study review were made available to the team undertaking the cost-effectiveness analysis presented in this paper. The task question facing the team was to determine which of the studies identified in the effectiveness study should be included for economic modelling. This section outlines the process undertaken to select the studies to include in the cost-effectiveness analysis, and summarises the results of that process.

The following criteria were applied to the effectiveness studies to determine whether they should be included in the cost-effectiveness analysis:

- The study had to identify a positive impact of the intervention on drug misuse or their risk of drug misuse; (we assumed that, if interventions were not effective, they would not be cost effective);
- The study methodology had to involve the use of a comparator group;
- The study had to clearly define the baseline characteristics of the intervention and comparator groups in quantitative terms that could be translated into an economic model.

It is important to note that studies could be included in the economic analysis even though the effectiveness review concluded that the evidence for the effectiveness of the intervention was inconclusive. This may have happened for one of two reasons:

- A difference in inclusion criteria. The effectiveness study required that a
 positive effect is statistically significant, as measured by appropriate statistical
 techniques. The economic analysis did not apply such restrictions and
 included studies in which there was a positive effect of the intervention,
 regardless of whether that effect is statistically significant or not; and
- The effectiveness study may have concluded that the evidence for the effectiveness of a particular intervention type is not conclusive based on the results of a number of studies. However, the economic analysis only captures the studies that have demonstrated a positive effect.

In practice all of the interventions included in the modelling were also found to be effective in the effectiveness review.

4. Modelling Methodology

4.1 Model Perspectives

The economic models consider a partial societal perspective, in line with the reference case for interventions with health and non-health outcomes in public sector and other settings in the NICE guidelines manual (NICE 2014). In doing so we have primarily relied on a 'bottom up' approach, thereby summing specific social costs, as opposed to a 'top down' approach, identifying the total burden of disease/ social costs attributable to drug use and then reducing in line with the intervention effects.

4.2 Model Framework

The modelling team constructed economic models in MS Excel with VBA (Visual Basic for Applications) software with one-way sensitivity analyses. These models compare a range of published and peer-reviewed interventions for a range of 'at risk' or vulnerable groups. All a-priori assumptions, simplifications and abstractions are made explicit, and in most cases accounted for within sensitivity analyses to minimise parameter-based and structural bias within the model results.

4.3 Conceptual framework of models

Decision models were used to combine data from different sources or to estimate long term outcomes from short term (surrogate) outcomes - to estimate the relationship between drug misuse and long term health, healthcare utilisation, crime and social outcomes. The decision models used decision tree methods. Within each arm, patients are assigned a probability of events occurring based on observed likelihoods within the published literature, whether death, crime or health impairment, in addition to an expected cost of such events, should they occur. The comparative element of the model compares the total costs (and quality-adjusted life years) both with and without intervention.

The preferred methodology was to conduct cost utility analysis, which means that the primary outcome was cost per QALY (quality-adjusted life year) gained through the intervention, a summary measure of longevity and health-related quality of life. This method of analysis is traditionally used for a National Health Service (NHS) and/or local authority perspective but may be insufficient when looking at drug misuse that has an impact on many sectors of the economy

The outcomes considered for the modelling were direct health outcomes such as QALYs, disease incidence and prevalence, hospital admissions, as well as outcomes related to and predictive of harmful drug use, such as crime and social care activity, attitudes and knowledge about drugs, and measures of life skills and self-esteem.

The models were calibrated by searching for information needed to populate the model which came partly from the economic evidence review and the effectiveness review and mainly from sources identified by the modelling team due to shortage of information. Where information could not be found in the evidence we asked the PHAC members for any insights they could share. The information in the models includes;

- The burden of health problems that are caused by substance misuse (within the scope of the guidance). This included searching for evidence on the size of the population for each 'at risk' group, and the prevalence of drug misuse (occasional and harmful) in each group. This evidence came from sources such as ONS, or from charities that work with specific vulnerable groups.
- 2. The cost of interventions to prevent, delay or reduce substance misuse in vulnerable groups. It was difficult to find the cost of interventions that were part of an integrated programme or those which were short, opportunistic interventions and therefore uncertainty was characterised in one-way sensitivity analysis. Where cost data was absent but good quality evidence of effectiveness data was available, a 'break even analysis' may be carried out to determine the maximum price at which an intervention would be cost effective. Costs were based on estimates of practitioner time, matched up to reference costs such as those produced by the PSSRU (Personal Social Services Research Unit). Where interventions are licensed programmes where licenses and training needs to be paid for, some judgement may be required on whether the crucial mechanisms of an intervention could be replicated without licensing or whether the programme would have to be delivered as a licensed product.

- 3. The effectiveness of interventions to prevent, delay or reduce substance misuse in vulnerable groups; measures of effect size such as relative risk reduction (RRR), absolute differences, odds ratios, etc.
- 4. Outcomes associated with drug misuse in vulnerable groups. These outcomes include quality adjusted life expectancy (QALYs experienced); healthcare costs, costs of drug treatment and criminal justice costs.

The information was searched for from September-November 2015 so any information that has been published since then would most likely not have been used in the modelling. Ideally the model parameters would have been populated with data from the economic review and the effectiveness review. However previous reviews on similar topics also highlighted a paucity of effectiveness data for targeted interventions to prevent drug misuse. We have endeavoured to produce a model that can be used in future if and when better evidence and data becomes available. When there was a lack of data on cost and effectiveness of targeted interventions to prevent drug misuse, we used a combination of sources to populate the model.

4.4 Population at risk

Understanding how many people there are in each vulnerable group and what the pattern of drug use is useful for understanding the scale of the opportunity and the optimum size for preventative interventions. For each vulnerable group, data was sought for how many people in the UK were in each group in a year, what the prevalence of drug use was, and any data on the cross over with other groups. This was done in a non-systematic way, mainly with Google searches and searching grey literature, with national surveys or ONS being seen as the best source, and then data from charities and other policy organisations after that. We were aware that charities may be very close to their chosen area so may be subject to more unconscious biases in interpreting data and overstating the size of a problem. Estimates from outside of the UK were not used, although estimates from within the UK were used if whole UK estimates were not available, for instance the Crime Survey for England and Wales (CSEW) was used for several estimates.

A lot of the evidence for drug misuse in particular groups was over ten years old so should be interpreted with caution. We were not able to obtain many estimates of the cross over between different groups, but it is likely that there is a lot of cross over between certain groups such as homeless people, people with mental health problems, and commercial sex workers. The "Hard Edges" Report (Bramley et al., 2015) aimed to estimate the overlap between severe and multiple disadvantage domains of substance use, homelessness and offending in England (Figure 1). Figure 1. Overlap of severe and multiple disadvantage domains in England 2010/11, from Bramley et al. (2015)



Group 1. People with mental health problems

It is estimated that there are around 6 million people aged 16+ in England with a common mental health disorder (IAPT 2015). The England Adult Psychiatric Morbidity Survey 2007 (McManus et al. 2009) estimates that around 36% of people with a mental health problem in the last year used drugs in the last year, which would be around 2.2million people, the majority of whom would be cannabis users. The relationship between drug misuse and mental health problems is likely to be complex and it may be that those individuals with the most severe mental health problems are also likely to be most vulnerable to drug problems. The Adult Psychiatric Morbidity Survey is being repeated from 2014-16 with results expected in 2017.

Group 2. People involved in commercial sex work or are being sexually exploited

There are several different definitions of commercial sex work. Drug misuse is likely to be concentrated in those people who are most vulnerable, for instance on-street sex workers (Jeal et al. 2008). It is estimated that there are between 50,000 and 80,000 commercial sex workers in the UK, 85-90 per cent of whom are women (Balfour & Allen 2014). For female street sex workers it has been estimated that 95% are drug users. Drugs can be used as a means to control people in order to sexually exploit them, as well as a way of trying to cope with the stress of being a sex worker.

Group 3. People who are lesbian, gay, bisexual or transgender

It is estimated that there are between around 65,000 and 300,000 transgender people in the UK (ONS, 2009). The ONS Integrated Household Survey (IHS)

includes a question on sexual identity. This may be different to sexual orientation as it is based on how individuals identify themselves rather than their behaviour or who they are attracted to. Based on IHS data, 1.2% of adults in the UK identified as gay or lesbian, and 0.5% as bisexual. In total this would equate to around 860,000 adults in the UK being gay, lesbian or bisexual. This may be an underestimate.

In a survey of lesbian, gay and bisexual people by Buffin (2012), 35% of respondents had used at least one drug in the last month. In this sample, current (last month) use of all substances, apart from cannabis, was higher for males than for females. While females were equally as likely to have used cannabis in the last month (20% for each), males were four times more likely to have used amyl nitrate ("poppers") (29% compared to 7%), three and a half times more likely to use ketamine (7% compared to 2%), nearly twice as likely to use cocaine powder (10% compared to 6%), ecstasy (9% compared to 5%) and amphetamines (5% compared to 3%) and one a half times more likely to have used non-prescribed benzodiazepines (3% compared to 2%). GHB was almost exclusively used by males. Signs of dependence were highest for users of alcohol (16%), ketamine (13%) and cannabis (8%) (Table 1).

	Respondents with 3 or more indicators of dependency	Total users	%
Alcohol	588	3623	16%
Cannabis	62	798	8%
Poppers	28	686	4%
Cocaine powder	25	300	8%
Ketamine	21	158	13%
Ecstasy	15	268	6%
Amphetamine	8	152	5%

Table 1. Gay and lesbian survey respondents who use drugs, and number and proportion who showed signs of dependence. From Buffin et al (2012).

Group 4. People not in employment, education or training (including children and young people who are excluded from school or are regular truants)

It is estimated that 12.7% of young people aged 16-24 are NEET (not in education, employment or training) which equates to 922,000 people (Delebarre 2015). There is a gap in data for drug use in NEET individuals. There was a paper (Coles et al. 2010) that looked at case studies for young people who were NEET including their drug use, but did not have specific population level data on drug use in NEET young people.

For pupils who had ever truanted or had been excluded from school, it was estimated that 10% had used one or more drug in the last month compared to 1% in pupils who had never truanted or been excluded. Class A drug use in the last year was 9% for this group compared to 1% in those who had never truanted or been excluded (Fuller et al. 2013, p.174).

Group 5. Children and young people whose parents use drugs

ACMD (2003) estimated that drug users in treatment have on average one child each, and estimated 2-3% of children were children of drug users, which equated to 250,000-350,000 children. There was an update to the report in 2007 but no update to the estimated number of children of drug users (ACMD, 2007).

There is a gap around evidence for prevalence of drug use in children of drug users.

Group 6. Looked after children and young people (including care leavers)

There are an estimated 68,840 looked after young people in England, who are generally aged under 21, although in some instances local authorities have responsibilities up until the young person is 25 (DfE 2015). Around 10,000 children a year in England leave care (HM Government, 2013). A survey carried out in 2002 (Meltzer et al. 2003, p.119) found that last month drug use for looked after children was 11% for cannabis, 3% for ecstasy, and 2% for amphetamine. For children in residential care, 29% had used cannabis in the last month. Children with a mental disorder were three times as likely as children with no disorder to have used cannabis in the past month (19% compared with 6%).

A survey of care leavers (see Figure 2) found that drug use was high in care leavers, with 73% having ever used cannabis, and 29% having ever used ecstasy, compared with 36% and 6% of 16-18 year olds in the British Crime Survey respectively(Ward et al., 2003). Care leavers were 15 times as likely to have tried heroin as 16-18 year olds respondents to the British Crime Survey.

These surveys are both from over twelve years ago so it may be that improvements in the care system mean that the difference in drug use between young people in care and other young people is now not the same.

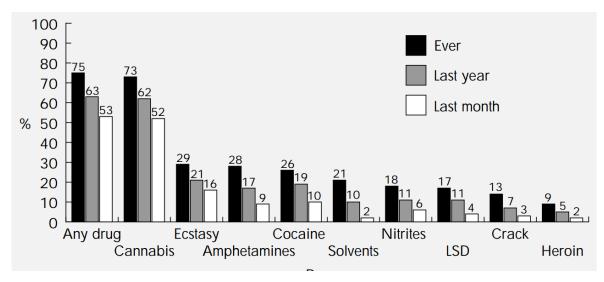


Figure 2. Frequency of Care Leaver Drug Use (from Ward et al., 2003).

Group 7. Children and young people who are in contact with young offender team but not in secure environments (prisons and young offender institutions)

It is estimated that 70,000 young people in England & Wales have been in contact with Youth Justice Services (Ministry of Justice 2015). In the 2001 Youth Lifestyles Survey, based on a sample of nearly 5,000 young people aged 12-30, it was found that 77% of males and 66% of females considered serious or prolific offenders had tried drugs in their lifetime, compared with 26% of non-offenders (Devitt 2011). A study published by Hammersley et al. (2003) found that 15% of young offenders were at a high risk of drug use based on their score on the Assessment of Substance Misuse in Adolescents (ASMA) (Willner 2000). This study found that 86% of offenders had tried cannabis and 11% had tried heroin (see Figure 3). In general offenders were 2-4 times more likely to have used drugs in the past 12 months when compared to the 2001 Youth Lifestyles Survey (YLS). These data are over ten years old.

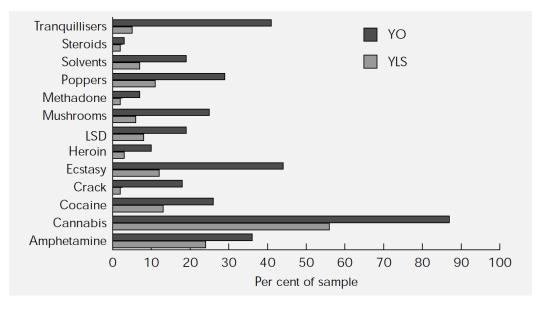


Figure 3. Comparison of drug use prevalence between serious youth offenders and the general youth lifestyle survey. From Hammersley et al (2003).

Group 8. People who are considered homeless

There are different definitions of homelessness, for instance people who are statutory homeless, rough sleepers etc. Evidence suggests that drug use is most prevalent in rough sleepers. In the UK in 2014/15, 161,490 people applied for homelessness assistance (Crisis 2015). Government statistics estimate that 2,744 people slept rough in England on any one night during 2014 (DCLG 2015). A report commissioned by Crisis (Fountain 2002) looked at people with a history of rough sleeping in London and found that 50% of homeless people cited drug use as a reason for becoming homeless. In addition, 83% of people in the sample had used a drug in the last month, with 65% having used cannabis, 47% having used heroin and 47% having used crack cocaine. Bramley et al. (2015) estimated that a total of 92,000 homeless people in England have substance misuse issues. There is significant overlap between prevalence of mental health problems, substance use, crime and homelessness with up to three guarters of rough sleepers having mental health problems, and 10-20% having dual diagnosis; defined as certain serious mental illnesses co-existing with drug or alcohol dependence (Rees 2009; Bramley et al. 2015).

Group 9. People who attend nightclubs and festivals

There is a gap in evidence around drug use and music festivals. There were around 2.5 million attendances at music festivals in 2012 but we could not find data on how many individuals had attended music festivals (Visit Britain 2013). There was a gap around data for drug use in individuals who attend music festivals, although there is some evidence around drug seizures from festivals.

In the Crime Survey for England and Wales 2013/14 (CSEW 2015), 13.5% of adults aged 16-59 had been to a nightclub in the last month. This has fallen from around 21% of adults in 2003/04. Use of any Class A drug in the last year was around 10 times higher among those who had visited a nightclub at least four times in the past month (19.2%) compared with those who had not visited a nightclub in the past month (1.8%). Higher levels of Class A drug use among those who were regular visitors to nightclubs was driven mainly by use of powder cocaine and ecstasy. Last year use of powder cocaine was around eight times higher among those who had visited a nightclub at least four times in the past month (12.2%) compared with those who had not visited a nightclub in the past month (1.4%). Last year use of ecstasy was around 25 times higher among those who had visited a nightclub at least four times in the past month (15.7%) compared with those who had not visited a nightclub in the past month (0.6%). People who had visited a nightclub in the last month were significantly more likely to have used an NPS (new psychoactive substance) in the last year than those who had not. Among young adults aged 16 to 24, 4.9 per cent of those who had visited a nightclub in the last month had used an NPS in the last year, compared with 1.6 per cent of those who had not. New psychoactive substance use was concentrated among 16 to 24 year olds, particularly young men.

Group 10. People who are known to use drugs occasionally / recreationally.

In the Crime Survey for England and Wales 2013/14 (CSEW 2015), of people aged 15-59 who used drugs, 60% used drugs once a month or less frequently. When cannabis is excluded, 88% of people who used drugs used them once a month or less frequently. The survey does not measure dependence so the numbers would depend on the definition of occasional or recreational use.

There is a gap in the evidence around how many occasional users go on to become frequent or dependent users. Most routine data sources like the CSEW are cross sectional rather than longitudinal in nature.

4.5 Intervention costs

The incremental cost of the intervention to the public sector¹ was estimated as the cost per participant of the intervention minus the cost per participant for the alternative used in the studies. The extra resources used per participant in the intervention compared with the control (or no control) were derived from the effectiveness studies.

¹ In addition to the conventional NHS and personal social services (PSS) perspective adopted by NICE, this analysis adopts a public sector perspective, defining relevant costs as any costs incurred by the public sector.

None of the studies selected for inclusion in the modelling reported intervention costs. The modelling team contacted the lead authors of each study to see if the authors could provide any intervention costs. The modelling team also carried out citation and Google searches to find any costs of programmes that were not reported in the studies. Some of the studies were for named programmes which could be searched for.

Costs of recruiting or maintaining participants in the studies or private costs incurred to individuals were not included in costing the interventions. Because the intervention studies were all US or Australia based, any intervention cost per person or family was converted to 2015 GBP (pound sterling). The conversion was done using a tool developed by The Campbell and Cochrane Economics Methods Group and the EPPI-Centre, converting the price-year adjusted cost estimate from the original currency to GBP, using conversion rates based on Purchasing Power Parities (PPP) for GDP (CCEMG 2016). If intervention costs were not reported anywhere, then the practitioner time was matched using PSSRU reference costs and an assumption of 50% additional costs (e.g. travel time, overheads, management, and training) was assumed. PSSRU reference costs do include practitioner training and travel time but we are adding on additional costs for the specific interventions. Any available licensing costs were converted and included. Any costs per family were assumed to be costs per individual person in the model. Where programmes had several objectives, we did not attempt to disaggregate the costs of programmes that had a drug prevention element and other elements for instance, sexual health promotion, but in some cases varied the cost estimates in the sensitivity analysis by a greater amount to account for the fact that adopting the drug use prevention only element may incur a lower cost.

Catalano et al. (1999) An experimental intervention with families of substance abusers: one-year follow-up of the focus on families project

p. 13 of a monograph (Plotnick et al. 1999) on Focus on Families said "The average cost of delivering Focus on Families was \$3,444 per client family."

The average cost was \$3,444 per family in 1996 US dollars which converts to £3,367 in 2015 GBP (see Table 2). This cost is in line with the intervention costs of family interventions reported in the PH4 costing report which reported costs of £490 to £4,398 for family based programmes (NICE 2007). The intervention was targeted at parents who were dependent drug users and their children but for the modelling we are only interested in the preventative outcomes in children. Because of this uncertainty in whether components that focus on drug use could be isolated and delivered at a lower cost, we have varied the average cost down to £842 or 25% of the total intervention cost in the sensitivity analysis.

 Table 2. Focus on Families cost per client family, (Plotnick et al. 1996).

Amount	Total	
Professional and support staff		
Project director	\$ 542	
Case managers	1,998	
Training group leaders	117	
Child care providers	51	
Clerical support	25	
Total staff costs		\$2,733
Operating costs		
Office rent	\$ 144	
Telephone and travel	292	
Photocopying, other consumable		
supplies, depreciation	35	
Participant incentives and		
assistance	213	
Total operating costs		684
Value of donated goods and service	es	27
Total cost per client family		\$3,444

Lee et al. (2010) A Brief, Web-Based Personalized Feedback Selective Intervention for College Student Marijuana Use: A Randomized Clinical Trial

This intervention is a web-based personalised feedback intervention based on brief motivational interviewing techniques. It is difficult to find any costing data but the marginal cost is likely to be low as the intervention is computer-based and not individually tailored. Because most costs are start-up and development costs rather than practitioner costs, unit costs for computer based interventions will reduce significantly as uptake increases. We have assumed a cost of £15 per participant based on information provided to us about a UK-based drug treatment intervention which was more intensive than this intervention, but varied this considerably in the sensitivity analysis between £1 and £30 per participant to account for the high amount of uncertainty in this cost estimate.

Prado et al. (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

This intervention consisted of eight two-hour multi-parent group sessions and four one-hour family visits and seems to be with qualified counselling staff. There is a book online that quotes the cost of Familias Unidas as being around \$200 per family.² If we assume this cost is for 2007 as quoted, then converted to GBP 2015 using the EPPI converter this would equate to £154.25 per family for programme costs in the UK. However this cost intuitively seems quite low given the amount of contact time. We have taken the cost per family to be per individual in the modelling. Due to the uncertainty and possible underestimation of this cost parameter we vary the value up to £300 in deterministic sensitivity analysis.

Training costs

The Familias Unidas website quotes \$50,000 to train 10 staff and says that "Implementation of the intervention requires Spanish-speaking, bicultural facilitators with a minimum of a bachelor's degree in psychology and three years of clinical experience or a master's degree and one year of clinical experience." It also quotes \$3,500 for training one facilitator (Blueprints 2016). This suggests that the upfront costs of commissioning a like for like service may be quite significant. The UK does not have a significant "Hispanic" population so the intervention would most likely need to be adapted in any case. Referring to Blueprints (2016) the costs for a small school (~300 students) for one year is \$100,000 which will be \$333 per family. Assuming that this is for 2012 in the US, the equivalent for UK 2015 will be £238. However, this includes the costs of training guidance counsellors and so the cost is probably less in the following years as the training costs will be reduced if using the same counsellors.

Private costs

There is a study by McCollister et al. (2014) which looked at the opportunity costs for individuals who were enrolled in the Familias Unidas programme but this was concerned with whether the private costs incurred were in line with the payments that were made to families to be involved. This study found that the total opportunity cost per parent/caretaker was under \$40 per group session, under \$30 per family session, and just over \$570 for the duration of the intervention. Participants were compensated between \$40 and \$50 per session which meant that the amount they were compensated was commensurate with the opportunity costs they had incurred.

Martin et al. (2010) Brief intervention for regular ecstasy (MDMA) users: Pilot randomized trial of a Check-up model

² Strategies for Scaling Effective Family-Focused Preventive Interventions to Promote Children's Cognitive, Affective, and Behavioral Health:: Workshop Summary. Forum on Promoting Children's Cognitive, Affective, and Behavioral Health, Board on Children, Youth, and Families, Institute of Medicine, Division on Behavioral and Social Sciences and Education, National Research Council.

This was a single motivational interviewing session delivered by a doctoral level clinician. Cost per hour of contact time for a clinical psychologist from PSSRU reference costs is £138. There is some uncertainty around the costs and the competencies required for this type of intervention, so we have varied the costs significantly in the sensitivity analysis. We have assumed that the costs would be similar to the salary costs of a mental health nurse on around £25,000 p.a. from PSSRU, which would be £67 an hour.

Parsons et al. (2014) A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men

The costs for this programme are likely to be similar to those for Morgenstern et al. (2009) and it may actually be a very similar programme as both authors are on the same study group. The study states that MI sessions were delivered by master'sand PhD- level therapists who had participated in a 3-day MI training and received weekly individual and group supervision throughout the project. But the study also says that "this type of MI intervention can be delivered with fidelity by individuals in community settings, with or without graduate-level training". Cost per hour of contact time for a clinical psychologist is £138, from p. 183 of Curtis L. (2014) Unit Costs of Health and Social Care 2014, PSSRU (Curtis & Burns 2014). There is a 2015 edition of this resource but this does not include specific costs for clinical psychologists. There is some uncertainty around the costs and the competencies required for this type of intervention, so we have varied the costs significantly in the sensitivity analysis. We have assumed that the costs would be similar to the salary costs of a mental health nurse on around £25,000 p.a. from PSSRU, which would be £67 an hour.

Morgenstern et al. (2009) Randomized Trial to Reduce Club Drug Use and HIV Risk Behaviors Among Men Who Have Sex With Men

The study states that the four motivational interviewing interventions were carried out one to one by a PhD level psychologist. Cost per hour of contact time for a clinical psychologist is £138, from p. 183 of Curtis & Burns (2014) Unit Costs of Health and Social Care 2014, PSSRU. There is a more recent 2015 edition of this resource but this does not include specific costs for clinical psychologists. Based on this, the estimated cost for the four one hour sessions of MI would be £552. It was felt by some of the experts we consulted that this type of intervention should be deliverable by a non-clinical drugs worker with the right kind of 'cultural competencies'. We have assumed that the costs would be similar to the salary costs of a mental health nurse on around £25,000 p.a. from PSSRU, which would be £67 an hour, or £268 for four hours. There is some uncertainty around the costs and the competencies required for this type of intervention, so we have varied the costs significantly in the sensitivity analysis.

Milburn et al. (2012) A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth

The STRIVE (Support to Reunite, Involve and Value Each Other) intervention consisted of five * 1.5 - 2 hour sessions with children and parent/carers together which were normally done in the children's own home (STRIVE 2016b). The programme website states that facilitators should have experience working with atrisk adolescents and that the programme requires 3 full days training at a cost of \$2,112 per person. The programme website states that a degree such as a BA or BS in psychology or counselling, or a degree in MFT (Marriage and Family Therapist) is recommended, but not required (STRIVE 2016a).

This has been costed using the hourly costings (£55 per hour) for multi systemic therapy which seems to equate reasonably well to this kind of intervention, from p.89 Unit Costs of Health and Social Care 2015, PSSRU. Based on five, two-hour sessions the cost of the intervention is £550. With an extra 50% for additional overheads and travel the cost is £825. In the modelling we have assumed that family costs equate to individual costs.

(Note: There is also a UK programme for homeless people with the same name (STRIVE), a Government funded homelessness skills and employment support pilot.)

Sensitivity Analysis

Input variables in the model will be subject to some imprecision. Sensitivity analysis is used to translate the imprecision in all input variables into a measure of decision uncertainty in the cost effectiveness of the options being compared. Table 3 provides a summary of intervention cost estimates.

Table 3. Summary – intervention cost estimates

Study	Interventio n cost estimate per client	Low - sensitivity analysis	High - sensitivity analysis
Catalano et al. (1999) Study – Focus on Families Intervention	£3,367	£842	£4,209
Lee et al. (2010) A Brief, Web-Based Personalized Feedback Selective Intervention for College Student Marijuana Use: A Randomized Clinical Trial	£15	£1	£30
Prado et al. (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	£154	£116	£193
Martin et al. (2010) Brief intervention for regular ecstasy (MDMA) users: Pilot randomized trial of a Check-up model	£67	£32	£138
Parsons et al. (2014) A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men	£268	£128	£552
Morgenstern et al. (2009) Randomized Trial to Reduce Club Drug Use and HIV Risk Behaviors Among Men Who Have Sex With Men	£268	£128	£552
Milburn et al. (2012) A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth	£825	£619	£1,031

4.6 The cost consequences of drug misuse

The previous sections have identified the data necessary to predict the impact of the interventions on the risk of an individual becoming a drug misuser. This section reviews the data on the cost of problematic substance use to society.

There have been several Drug Harm Indices produced over the years including for the UK in 2005 (Goodwin 2005). This index had the biggest drivers of drug related harm as crime such as burglary and robbery, drug related deaths, and cases of hepatitis C and HIV caused by drug use.

Problematic substance use is associated with a range of consequences that confer costs to society. Godfrey et al. (2002) wrote "The economic and social costs of Class A drug use in England and Wales, 2000" which estimated the costs of class A drug use. Drug use was estimated to cost society £15.4 billion a year, of which £13.9

billion was related to crime committed by people who are dependent on drugs. This report distinguished between the direct and indirect costs of problematic substance misuse:

- direct costs:
 - \circ costs for users: health, alienation, dependency, poverty; and
 - \circ $\;$ reactive costs: health care, social care, social security, CJS.
- indirect costs:
 - o costs for users: work / productivity, education, driving, crime
 - costs for family and carers: financial, time spent caring, communicable diseases, anxiety and stress, poor parenting, lifestyle transmission; and
 - costs for wider society: property crime, crime against the person, communicable disease, forced lifestyle changes, perceived insecurity.

According to Davies et al. (2012), direct expenditure on drug services was £1.106 billion for the UK in 2010/11 (0.17% of public expenditure), while unlabelled expenditure (expenditure which is in some way related to drug abuse) was estimated as £6.265 billion, the majority of which related to public order and safety, leading to an overall total of drug-related public expenditure amounting to £7.37 billion which was 1.1% of all public sector expenditure.

A lot of the available data on the costs of drug use is around the costs of problematic drug use, or from economic evaluations of drug treatment such as Drug Treatment Outcome Research Study (DTORS) and National Treatment Outcome Research Study (NTORS). The DTORS (Davies et al. 2009) looked at outcomes for drug users and included a cost effectiveness element. It combined cost and activity data from the NDTMS with interview data for around 1,800 people that was used to estimate QALYs gained and resource use (health and social care and cost of offences). The QALYs were calculated using the SF12 survey instrument. There was a lot of variation around the average QALY gains. In the DTORS, the net benefits of drug treatment were positive in 80% of clients. The average net benefit ratio was around £2.50 for every £1 spent. This is much lower than the NTORS ratio of £9.50 for every £1 spent but was measured over a time period of 51 weeks compared to a 4 year time period (2 years before and 2 years after treatment) in the NTORS, as well as there being other differences in measuring costs and benefits between the two studies (Godfrey et al. 2004).

It would be a mistake to apply the costs associated with problematic drug users, or people in drug treatment, to the whole population of drug users, many of whom may not experience these problems with their drug use. The data available to measure the causal relationship between drug misuse and negative consequences, as well as the data available to measure the economic value of these consequences varied between the different cost types. The consequences included in the costeffectiveness analysis were determined by the availability of data to measure the impact of drug misuse on these outcomes and the economic value of these outcomes. The cost of crime associated with drug possession only was included. In reality there may be considerable cross over between people arrested for possession and arrested for supply, and drug users contribute to the maintenance of the drugs market so there would be an argument for including the cost of possession offences.

Two stages were undertaken to determine the availability of data:

- a review of the literature on the economic impact (quality of life and public sector cost impact) of the list of consequences was undertaken. The project did not have the scope to allow a systematic review of the literature. Instead, the following sources were used:
 - the knowledge of the team and members of LJMU team, as well as the expert advisors on the PHAC
 - for those outcomes for which economic values estimates were available, a basic literature search was undertaken to determine the probability that a problematic substance user would experience the consequence.

4.7 Sensitivity Analysis

Scenario analyses are conducted for all interventions except Catalano et al. (1999), varying the duration of effect of the intervention on reducing drug use.

One-way sensitivity analysis was conducted to enable the review to assess the impact that changes in a certain parameter will have on the model's conclusions. Tornado diagrams were used to illustrate the key drivers of the model's results. Sensitivity analyses did not include probabilistic sensitivity analysis (PSA) as it was deemed unlikely to change the direction of the results and would require more time and potentially add unnecessary complexity to the interpretation of results.

The sensitivity analyses within each model are covered in more detail within the results section of the report. In general, each parameter was varied by +/- 25% in the sensitivity analysis to introduce some natural variation into the models. This was in the absence of good quality distributions for many of the model parameters. However intervention costs were varied using a range of values based on different types of staffing time. Discount rates were varied to 0% and 1.5% in line with the NICE guidelines manual. The parameters for the sensitivity analyses are shown in Appendix 2.

4.8 Quality assurance of models

All models, outputs and source code were subject to review by at least two health economists within the Liverpool Health Economics team, the creator and an external reviewer. Following this members of both LJMU and NICE critically appraised each model with respect to the plausibility of assumptions, model structure and results. Then model assumptions were shared with PHAC members and changes were made based on their comments.

4.9 Limitations of modelling approach

Generally, the quality of the studies which were modelled was moderate and several limitations are seen across the studies.

- None of the studies are from the UK, seven are from the USA and one is from Australia. This may limit the applicability of the findings due to differences to healthcare policy, funding and service delivery. Therefore, it is possible that some of the interventions may not be applicable to the UK setting and thus the model is not appropriate. The modelling approach was limited by availability of appropriate local data inputs. The models include parameter estimates from outside of the UK setting and from within the UK; which were used to represent the UK setting. The limitations are that parameter values from different settings and for subsections of the UK may over and underestimate the true value for the UK.
- Some interventions were shown to be efficacious when tested under strict trial conditions; however, it is not necessarily the case that these interventions would prove as effective when delivered in 'real world' settings.
- For many studies, the researcher was also the person who had developed the intervention which can lead to biases (Petrosino & Soydan 2005).
- A particular challenge for each model was to define and determine differing rates
 of drug consumption. The definitions appeared relatively subjective and were
 poorly defined. Another common limitation was that outcomes were poorly
 reported e.g. Lee et al. (2010) reported average frequency of cannabis use in the
 last three months. However, in the model we were interested in a binary
 outcome, cannabis use or not as we did not have sufficient information to
 translate how differing rates of cannabis consumption translates into impact on
 rates of psychosis. Therefore, in modelling we had to make several additional
 assumptions such as an average reduction in the frequency of cannabis use also
 translates to reduction in actual use and that some individuals may stop cannabis
 consumption completely.
- Most studies' findings were based on self-reported drug use; these outcomes were not validated biochemically. In addition, most studies involved relatively small sample sizes thus increasing the risk that they were not powered enough to detect significant effects.

- Another important factor is that there have been changes in the strength, method
 of consumption and quantities of drugs consumed. This applies to all drugs
 evaluated, in particular cannabis as changes in strength of cannabis may be
 associated with differential outcomes (Kirkbride et al. 2012; Hall 2015;
 Degenhardt et al. 2013; Di Forti et al. 2015).
- A key limitation of some models is that a 'do nothing' a 'weak control' comparator was used, whereas in fact this may not be the case in the real world. This may make the intervention appear more cost effective. Whereas a study that is compared to the best alternative would be considered a 'strong control' and more closely represent the real world. However for many preventative interventions there may not be a true 'treatment as usual' comparator.
- Most studies had a short follow-up period; this makes it difficult to assess if the effects of the interventions were sustained over time. The model's results in terms of costs and outcomes were extrapolated over different time horizons. However, several of the differing scenarios were based on assumptions of the length of treatment effect and there was one follow-up study for the Focus on Families intervention with a study by Haggerty et al. (2008). It is notable that this single intervention with long term follow up did not show any evidence of a longer term effect beyond the 12 month follow up of the original (Catalano et al. 1999) study.

5. Model Description and Results

This section describes the models and reports the results of the cost-effectiveness analysis as described in section 4. This section reports the data inputs used, model functionality and limitations, estimates of the cost per outcome of interest and the results of sensitivity analysis.

5.1 Models focussing on cannabis use

Psychosis among cannabis users

Rates of developing psychosis among cannabis users and non-users are widely debated and vary considerably within the literature. There are several case-control studies which attempt to estimate this, however these studies are potentially constrained by differences in unobservable variables (Haggerty et al. 2008; Moore et al. 2006; Hall 2015; Degenhardt et al. 2013; Cooper et al. 2015). In our model we use a value reported by Hall (2015) which suggests a rate of psychosis of 7 in 1000 for non-cannabis users and 14 in 1000 for cannabis users, an effective doubling of a marginal effect (Hall 2015). We have treated with the risk of psychosis as a one off risk as we do not have either intervention or epidemiological data to treat it as a dose-dependent risk. It should be noted that this risk is expected to have only a small effect on psychosis incidence rates, given that not all individuals who develop

psychosis have used cannabis, and given that the absolute incidence of psychotic disorders is low. Therefore, such a risk factor with a high relative risk (e.g. relative risk of 2), may lead to only small changes in incidence, which may be difficult to detect. Cannabis is reported to exacerbate the impact of psychosis development in those who would have developed psychosis in the absence of cannabis use anyway. There is limited data available for the UK and it is difficult to determine whether the rates of substance-induced psychoses reflect a genuine change or is more due to changes in diagnostic practice (Kirkbride et al. 2012).

Costs

All healthcare and crime costs are recorded on a per annum basis.

Figure 4**Error! Reference source not found.** provides a monetary breakdown of the estimated social cost of one year of cannabis use based on Catalano et al. (1999)

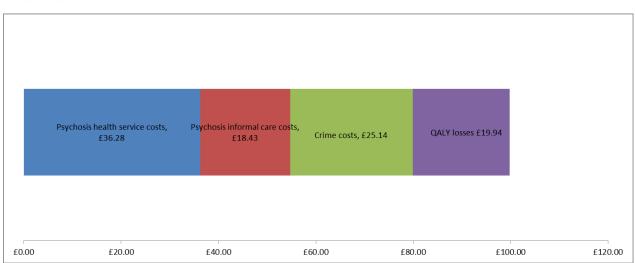


Figure 4. Social costs of one year of cannabis use, from model based on Catalano et al. (1999)./ Total = £99.79

Psychosis-related costs

The model includes data relating to the expected costs of psychosis (relating to health service costs, informal care costs and employment costs) in addition to non-psychosis-related crime costs. We have updated and re-calculated expected annual economic costs of non-affective psychosis in the UK based on a report from the department of health by Kirkbride et al., 2012. UK population and prevalence estimates were updated and cost estimates were subsequently inflated (ONS 2015; CCEMG 2015). Health service costs refer solely to costs borne by the NHS while informal care costs refer to private costs borne by carers who may often be family members.

With a broader societal perspective, the estimated cost of days of employment lost represents the largest potential economic burden associated with non-affective psychosis.

Crime costs

We have used an average cost of criminal arrest of £500 for cannabis-related arrests; however this does not include the private costs associated with arrest, including the longer-term expected consequences of having a criminal record. We have assumed a simplified risk of being arrested for cannabis related crimes being directly proportional to cannabis use; in reality this relationship may be more complex. It may be that people involved in producing and selling cannabis, who may not be users, are those most likely to be encounter a cannabis-related arrest.

Costs related to road traffic accidents (RTA)

Estimates of the increased risk of road traffic accidents for individuals who are under the influence of cannabis ranged from an odds ratio of 1.22 to 18.9. However the studies which suggested these estimates had different criteria for calculating the risk estimate and controlling for potential confounders (Gadegbeku et al 2011; Hartman & Huestis 2013). Drugs are likely to be under-recorded as a contributory factor, since there is no systematic testing for evidence of drug use by those involved in RTAs. The mid-estimate costing for the proportion of all RTAs which were cannabisinduced was taken from Pudney et al (2013) and used in the model. Since the PHAC were not convinced that cannabis associated RTAs were caused by cannabis use, they were included only as a separate scenario in the sensitivity analyses, not in the base case.

QALY loss associated with cannabis use

The impact of interventions on health-related quality of life has been accounted for by a reduction in QALYs, resulting from a utility decrement for psychosis. In doing so we assume that psychosis symptoms cause on average 5 years of QALY decrements and that this quality of life (utility) decrement was on average 0.32 per annum.

Other outcomes that could possibly be included the model but with insufficient evidence or data

It should be noted that the current costs of drug treatment are substantial as the majority of presentations (73%) to drug treatment for young people are for cannabis use. The costs of drug treatment for cannabis in England and Wales were estimated as £53million nationally for 2013/14 in a paper looking at the implications of a regulated cannabis market that was endorsed by a UK Treasury analysis in 2015

(Transform 2015; Pudney et al. 2013). Other outcomes of interest may be productivity costs from IQ deficits associated with cannabis use.

Gateway Theory and Reverse Gateway

If assumptions around cannabis use leading to other more dangerous drug use ("gateway theory"), or on the impact of becoming a tobacco smoker ("reverse gateway") were included, then this may make the intervention more cost effective, but no credible evidence was found to support their inclusion within the model.

Targeting the interventions

If the interventions could be better targeted at groups who have a higher chance of using cannabis or experiencing adverse outcomes resulting from cannabis use, then these too would be likely to render the intervention more cost effective. The interventions may come out as more successful if a broader perspective of outcomes was included, but this analysis has looked only at the outcomes associated with drug use.

5.1.1 Model of Focus on Families intervention based on Catalano et al (1999)

Study

This decision analytic model was informed by results from Catalano et al. (1999); "an experimental intervention with families of substance abusers: one-year follow-up of the focus on families project" and results from Haggerty et al. (2008); "Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment" (Haggerty et al. 2008).

Population

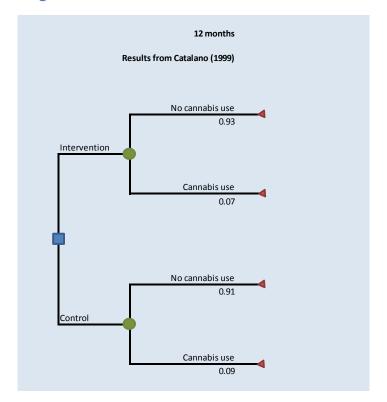
Epidemiological data relating to the proportion of young people whose parents use drugs was informed by ACMD (2007) and the intervention was modelled for this population of 399,339 10-15 year olds whose parents use drugs.

Decision tree

The simple tree, Figure 5 describes the individual pathway with the FOF intervention. There are two arms in the model, those who receive the FOF intervention and those who do not.

Results from Catalano et al. (1999) demonstrate an intervention effect over a period of 12 months. Haggerty et al. (2008) is a follow-up of the Catalano et al. (1999) study and the results show that the beneficial effects of the focus on families (FOF) intervention is restricted to short-term benefits of 12 months. Therefore, the benefits in terms of economic and health are limited to 12 months in the model. The target population of this intervention is group 5 who are children and young people whose parents use drug.

For the each of the first 12 months, those in the FOF intervention arm have differing probabilities of using cannabis versus those in the control arm. Beyond 12 months of the study, each individual in the intervention or control cohorts have the same probability of using cannabis in the future. We have not discounted future values (costs and benefits) as the FOF intervention only has an effect over a 12 month period.



. Figure 5. Decision tree model for Focus on Families intervention.

Results

Table 4. Results of economic model based on Catalano et al. (1999).

Base	Case	Scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs gained	ICER (£) (QALYs)
Intervention	£169,527,975	6.0			
Comparator	£613,343	7.7	£168,914,632	1.7	£99,254,920

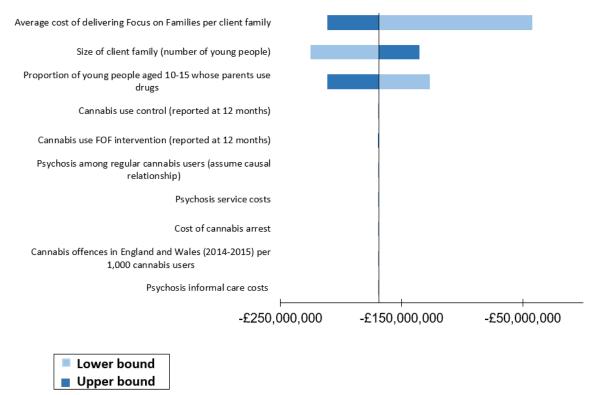
This intervention would not appear to cost-effective based on the subsequent change in drug use outcomes. The intervention would be required to cost less than £4 in order to be cost-effective based on a willingness to pay threshold of £20,000/QALY. This is because the intervention only had a very marginal effect on overall cannabis use in the short-term, and there is a paucity of evidence linking cannabis use to adverse outcomes, with the exception of a marginally increased risk of psychosis and criminal arrest. If assumptions around cannabis use leading to other more dangerous drug use ("Gateway theory"¹³), or on the impact of becoming a tobacco smoker ("reverse gateway"¹⁴) were included, then this may make the intervention more cost effective, but no credible evidence was found to support their inclusion within the model. Finally, if the intervention could be better targeted at groups who have a higher chance of using cannabis or experiencing adverse outcomes resulting from cannabis use, then these too would be likely to render the intervention more cost effective. The intervention may come out as more successful if a broader perspective of outcomes was included, but this analysis has looked only at the outcomes associated with drug use.

One-way sensitivity analysis (Tornado diagram)

As the intervention is a multi-component intervention, we have varied costs substantially in the sensitivity analysis from 25% to 125% to take into account the fact that the drug-specific elements of the intervention could possibly be isolated and replicated at a lower cost. Other input parameters have been varied by +/- 25% (see Figure 6).

The biggest driver of the results is the cost of Focus on Families. Because of the high cost of the intervention and short duration of effect, even if cannabis use was 100% for the control group, and 0% for the intervention group over 12 months, the net cost per QALY would still be around £55,000 so would not be cost effective.

Figure 6. Tornado diagram showing differences in net monetary benefit (NMB) of Focus on Families intervention with changes in model parameters. NMB values each QALY at £20,000.



Discussion and Limitations

Psychosis cases and arrests associated with cannabis use are likely to happen later in an individual's lifetime, but for this model we are assuming a cross-sectional effect. Another limitation is that the literature is still not unanimous about the evidence for a causal link between cannabis use and psychosis.

5.1.2 Model of Web-Based Personalized Feedback based on Lee et al. (2010)

Study

This decision analytic model was informed by results from Lee, et al (2010) "a brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial."

This intervention is a web-based personalised feedback intervention based on brief motivational interviewing techniques. Results from Lee et al. (2010) indicate that although there was no overall intervention effect, subgroup analysis found promising effects for those with a family history of drug problems. The findings imply selective targeting of the intervention which was applied in the model. Group 10 is the target

population for this intervention who are identified as people who are known to use drugs occasionally/recreationally.

Population

Data for the proportion of 17-19 years old that use cannabis are obtained from CSEW 2014-2015. The intervention is modelled for the population of 65,557 17-19 year olds cannabis users that have a family history of drug problem.

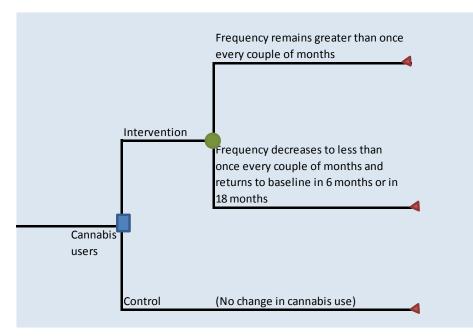
Decision tree

The simple tree, Figure 7 describes the individual pathway with the web-based personalised feedback intervention. There are two arms in the model, those who receive the web-based personalised feedback intervention and those who do not. Those in the web-based personalised feedback intervention arm, have differing probabilities of using cannabis versus those in the control arm for the first 6 months (base case) and 18 months (scenario). Beyond 6 months (base case) and 18 months (scenario) of the study, each individual in the intervention or control cohorts have the same probability of using cannabis in the future. We have not discounted future values (costs and benefits) as the web-based personalised feedback intervention only has an effect over a 6 months (base case) and 18 months (scenario) period.

The outcomes were reported by Lee et al. (2010) as average frequency of cannabis use in the last 3 months. However, differences in costs and outcomes in our model are based on a binary outcome, cannabis use or not. Therefore, in the model we reduce cannabis use by 37% in 2 subgroups only. The first subgroup reports use of cannabis once a month and the second subgroup reports use once every couple of months. We calculated that a 37% reduction of both subgroup populations would achieve abstinence. In extrapolation of the model costs and outcomes, the impact of the intervention was assumed to lead to temporary abstinence over 12 and 24 months.

Under the base case scenario, drug use reduced to the six months level reported in the study and then rebounded back to baseline over the next six months. Under the two year scenario, drug use reduced over six months, and then rebounded back to baseline over the next 18 months. Thus the cost effectiveness was greater in the two year scenario where a reduction in drug use was maintained over a longer period of time.

Figure 7. Decision Tree for model based on Web-Based Personalized Feedback intervention.



Results

Base Case Scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£5,201,640	53.9			
Comparator	£4,520,060	56.0	£681,580	2.1	£328,939

2 Year Reduction Scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£8,817,840	98.0			
Comparator	£8,618,351	94.3	£199,490	3.7	£53,675

This intervention does not appear to cost-effective based on the subsequent change in drug use outcomes. The cost per QALY is around £328,999. The intervention is only expected to have a very marginal effect on overall cannabis use in the shortterm. There is a paucity of evidence linking cannabis use to adverse outcomes, with the exception of a marginally increased risk of psychosis and criminal arrest. Even with the risk of psychosis we have used a lifetime risk which may not be actually be diminished much by reducing cannabis use by 12 or 24 months.

One-way sensitivity analysis (Tornado diagram)

As there is some uncertainty around the potential costs of web-based interventions, we have varied costs in the sensitivity analysis from £1 to £30. Other input

parameters have been varied by +/- 25% (see Figure 8). Road traffic accidents have been included in the sensitivity analysis as a scenario but not in the base case. The key factors for predicting whether or not the intervention was cost effective are programme costs and, if included, costs of road traffic accidents.

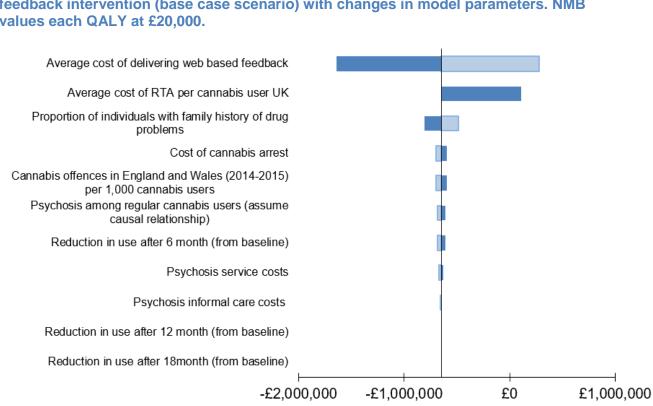


Figure 8. Tornado diagram with differences in net monetary benefit from web-based feedback intervention (base case scenario) with changes in model parameters. NMB values each QALY at £20,000.

Discussion and Limitations

A key limitation of the model is that a 'do nothing' comparator was used, whereas in fact this may not be the case in the real world. In addition, psychosis cases and arrests associated with cannabis use, are likely to happen later in an individual's lifetime, but for this model we are assuming a cross-sectional effect.

A limitation of the cannabis usage is that change in usage is based on self-reported use. In addition, the literature is still not unanimous about the evidence for a causal link between cannabis use, psychosis and crime.

5.1.3 Model of Familias Unidas based on Prado et al. (2012)

Study

This decision analytic model was informed by results from Prado et al. (2012); "The efficacy of Familias Unidas on drug and alcohol outcomes for Hispanic delinquent youth: Main effects and interaction effects by parental stress". The target population of this intervention is group 7 who are children and young people in contact with young offender team but not in secure environments (prisons and young offender institutions.

In the study of Prado et al. (2012) a total of 242 (intervention: N=120, control: N=122) delinquent Hispanic youth aged 12–17 years and their primary caregivers were randomized to either Familias Unidas or community practice and assessed at three time points. Familias Unidas is a family-based preventive intervention that targets multiple adolescent subsystems (including family, school, peers) by intervening through the parent to prevent and reduce problem behaviours, including both substance use and HIV sexual risk behaviours.

Familias Unidas includes eight 2-hour multi-parent group sessions and four 1-hour family visits. The primary goal of the parent groups was to bring parents together in order to establish parental investment, increase parental support, and provide a context for parent participation in a conjoint skills learning process. The primary goal of the family visits was to provide parents with an opportunity to transfer what they learned in the group sessions to their adolescent, foster more nurturing and supportive relationships, and increase parent–child communication, all in the context of family. All intervention sessions were parent-centered, with adolescents' participation in intervention activities limited to the four family visits.

The outcomes in the study are alcohol use, illicit drug use, alcohol dependence and marijuana dependence, and having had sex under the influence of alcohol and drug use. There is no report of the specific drug type in this study. Thus, we consider cannabis as the drug use in this study. If the intervention becomes cost effective with cannabis, it will be cost effective for the combination of cannabis with other types of drugs and alcohol.

Familias Unidas was effective in reducing past 90-day substance use, illicit drug use, and in reducing the proportion of youth with an alcohol dependence diagnosis, relative to community practice. Familias Unidas was most effective for adolescents with parents exhibiting high stress and lower levels of social support. For the adolescents whose parents reported high parental stress the proportion reporting drug use reduced from 27% to 16% and to 10% in 6-months and 12-months follow up respectively. For the control group, however, the proportion initially reduced from 32% to 265 in 6 months follow up, but then increased to 35% in 12 months follow up.

Population

Data for the number of young offenders in England and Wales is from (Ministry of Justice 2015). As the intervention is effective in reducing drug use in adolescent with high parental stress, we model the impact of intervention on this subgroup of young offenders.

Decision tree

The simple tree, Figure 9 describes the individual pathway with the Familias Unidas intervention. There are two arms in the model, those who receive the Familias Unidas intervention and those who do not.

Cannabis use at baseline is 29.5%. The intervention arm showed a reduction in cannabis use at month 6. At 12 months follow up, cannabis use in the control group was 35% which shows an increase in use from baseline. For Familias Unidas arm, however, the proportion of cannabis user continues to decline. For this group, the reduction in cannabis users is less compared with the change from baseline to 6 month follow up.

For this intervention, three different scenarios are modelled.

- 1. The analysis is limited to 12 months. (Base case)
- 2. The proportion reporting drug use returns to baseline 24 months after programme implementation in both groups. (Scenario 2)
- 3. The rate of drug use stays constant at the 12 months level in the control group. (Scenario 3)

Note that we did not consider a scenario in which drug use continues to change over the second year, as further divergence of the two paths seems implausible.

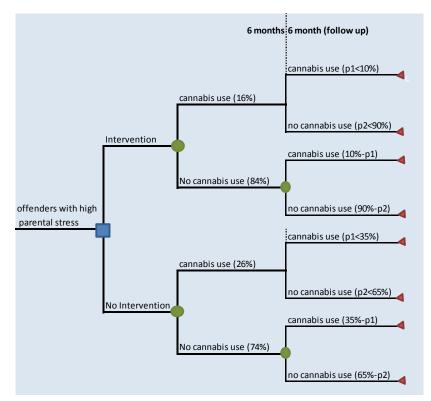


Figure 9. Decision Tree for model based on Familias Unidas intervention

Results

Table 5. Results of economic model based on Prado et al., (2012).

Base Case Scenario.

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£2,188,328	1.5			
Comparator	£1,647,952	3.8	£540,376	2.2	£240,994

Scenario 2. Drug use returns to baseline from 12-24 months.

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£2,410,841	4.2			
Comparator	£1,967,210	7.6	£443,631	3.4	£129,970

Scenario 3.	Drug use	maintained f	from 12-24	1 months.
-------------	----------	--------------	------------	-----------

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£2,410,841	4.2			
Comparator	£1,996,234	8.0	£414,607	3.8	£110,132

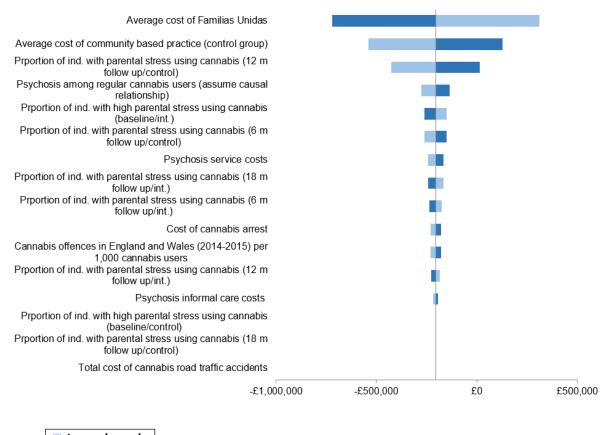
The ICER for Familias Unidas intervention is at least £110,132. Even assuming that the impact of intervention lasts for two years, this intervention would not be cost effective. Incremental cost per young person (12-17) prevented from using cannabis for 12 months is £218. Break-even analysis shows that a reduction in the cost of the intervention will make it cost effective. The cost of the intervention needs to decrease by 24% in the base case or by 16% in scenario 3 for the intervention to be a cost-effective use of NHS resources at a willingness-to-pay threshold of £20,000 per QALY.

RTA costs are not included in the baseline analysis. These costs are limited to individuals at age 17. Including road traffic accidents decreases the ICER in the base case to £205,442.

One-way sensitivity analysis (Tornado diagram)

In a one-way sensitivity analysis the change in the proportion of drug users in the follow up compared with baseline has been varied by +/- 25% (see Figure 10). The intervention is targeted at reducing alcohol use and risky sexual behaviour in addition to drug use. The costs of an intervention targeted at drug use only might be less, so we considered a +/- 25% variation in costs of intervention and comparator. The key factors affecting the cost effectiveness of Familias Unidas are program costs and the costs of community practice (the comparator).

Figure 10. Tornado diagram showing differences in net monetary benefit from Familias Unidas intervention (Scenario 3) with changes in model parameters. NMB values each QALY at £20,000.



Lower bound
 Upper bound

Discussion and Limitations

A key limitation of the model is that a 'do nothing' comparator was used, whereas in fact this may not be the case in the real world. In addition, psychosis cases and arrests associated with cannabis use are likely to happen later in an individual's lifetime, but for this model we are assuming a cross-sectional effect. A limitation of cannabis use reported is that change in use was based on self-reported evidence. In addition, the literature is still not unanimous about the evidence for a causal link between cannabis use, psychosis and crime. It is believed that psychosis cases and arrests associated with cannabis use are likely to happen later in the individual's lifetime, but for this model we are assume a limited impact. Moreover, it is possible that the intervention may have more lasting effects for youths who have committed crimes in the past.

5.2. Model focussing on ecstasy

Assumptions

There is no shortage of literature reporting the difficulties of modelling the harms of ecstasy usage, largely due to the requirement for assumptions with respect to 'dosage' (number of tablets consumed per episode), where tablets are consumed, and to what extent the effects of ecstasy are exacerbated by the use of other drugs. In this model we used as few assumptions as possible in order to express outcomes in terms of an 'expected harms/costs per tablet consumed' as seen in prior analyses (ACMD 2008).ⁱ

Because of reported differences in the prevalence of ecstasy use by age, the model consisted of two sub models focusing on those aged 16-24, and those aged 25-59 (CSEW 2015). It was assumed that 5.4% of those aged 16-24 and 1.7% of those aged 25-59 participated in ecstasy consumption, as reported by the crime survey for England and Wales 2014/15. These estimates were applied to population estimates for their respective age groups. Data from the Office for National Statistics (ONS 2015), gave estimates of 7,419,683 16-24 year olds and 30,105,258 25-59 year olds respectively, which when applying the prevalence rates from the CSEW, gave an estimated 400,663 users in the former and 237,261 users in the latter age group.

In the absence of data to the contrary, it was assumed that 'dosage' i.e. the number of pills per ecstasy consuming episode, was equal between both age groups, suggesting that neither older nor younger users had a propensity/ability to consume more pills than the other at any one time (ACMD 2008).

Due to a paucity of data regarding where ecstasy consumption takes place (how much is at home, how much at festivals, nightclubs etc.) it was assumed for the purpose of the model that all ecstasy consumption occurred in nightclubs/raves/discos. The rationale for this assumption was that at a local level, supply of MDMA is prominently, though not exclusively, based within the night club environment, and the expectation was that demand for, and consumption of ecstasy would mirror supply channels.

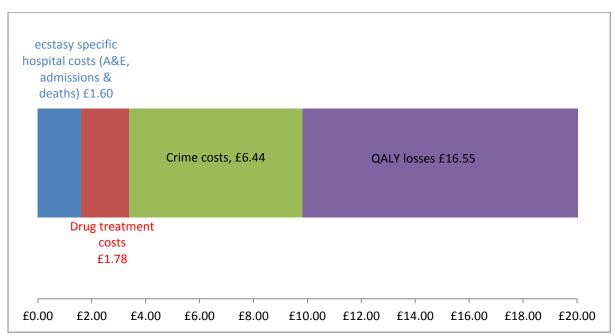
The total number of ecstasy pills consumed for the year, was estimated at 26,000,000 by the association of chief police officers (ACPO). Dividing total consumption per age group (16,329,900 in 16-24 year olds and 9,670,100 in 25-59 year olds) by the estimated number of users based on CWE 2014/5 data, gave an estimate of 40.75 tablets per user per year in across both age groups. Because of a lack of data concerning the distribution/frequency of ecstasy consumption at different points throughout the year, it was further assumed that total ecstasy consumption would be split equally over the course of the year, giving 0.78 tablets per user per weekend, or 314,037 and 185,963 in total per age group per weekend.

The model was built based on outcomes solely attributable to ecstasy use. Ecstasy consumption is often observed as part of a pattern of poly-drug consumption(Croft et al. 2001)(Croft et al. 2001; de Sola Llopis et al. 2008; Rogers et al. 2009; Riley &

Hayward 2004; Milani et al. 2006; Measham F and Moore K. 2009; Schifano et al. 1998), both in the 'up' and 'come-down' phases of ecstasy use. One recent systematic review cautioned the use of estimates where poly-drug use is suspected, due to the significant opportunity for confounding of results.

Costs

A comprehensive literature search provided the basis for data extraction with respect to ecstasy-related outcomes and associated costs. **Error! Reference source not found.** provides an estimate of the social costs of one year of ecstasy use based on Martin et al. (2010).





Crime costs

Our analysis only concerned ecstasy possession. Intent to supply or drug synthesis, were considered less likely to be affected by the intervention in question. A total of 68 persons were referred to immediate custody following ecstasy possession during 2013/14, resulting in a 0.00026% probability of sentencing per tablet consumed. The cost was reported as £8,591 per sentence in 2014, based on the assumption of a 90 day prison stay (ACMD 2008; Minstry of Justice 2014), which was inflated to 2015 prices to give £8,720. Each sentence also attracted an additional cost of £15,618 (£14,603, 2011 prices) accounting for the court episode prior to sentencing, reported by the National Audit Office. Although this is high when compared with the cost of the prison sentence itself, it is likely to be a reflection of the difference in salary

between lawyers, judges and prison warders. Combining the two costs above resulted in a sum total of £24,338 per prison sentence for ecstasy possession, and an average sentencing cost of £0.06 per tablet.

It was estimated that 5% of arrests for ecstasy possession resulted in a prison sentence, so the figure of 68 prison sentences was used to estimate a total of 1,360 arrests over the same period, (a probability of 0.005% per tablet consumed). Each arrest came at an expected cost of £1,346 per arrest (£1,804.7 after inflating to 2015 prices), based on police time, (Godfrey et al. 2004);giving an estimated arrest cost of £0.09 per tablet

Hospital admissions costs

Data from St Thomas' hospital from 2005-6 to 2007-08 reported 382 Ecstasy-related hospital presentations, of which 52 were attributable to ecstasy as a 'sole drug', giving an average of 17.3 hospital admissions per year in this Trust over a three year period.

Data from the most up-to-date available HES statistics (HSCIC 2016) suggested that St Thomas' hospital experienced a total of 134,718 all cause admissions during 2012-13, out of a total 15,145,626 in England that year. Using data from the CSEW 2014/15, the number of ecstasy related admissions observed from 2005-08 were adjusted to reflect the present day prevalence of ecstasy use (CSEW 2015), as this was deemed a suitable predictor of admissions. Subsequently, the 17.3 admissions per year during this period were reduced by 20% to 13.84 per year to reflect the change in ecstasy tablet consumption over time. Combining the HES data and ecstasy poisoning data gave an estimated (13.84/134,718) = 0.0103% of all hospital admissions in this Trust being due to ecstasy poisoning.

Assuming this proportion is representative of the wider population (without any evidence to the contrary) and applying this 0.0103% to the total number of hospital admissions in 2012-13 (15,145,626) gives an estimated 1,556 admissions per year within the NHS, and a probability of hospital admission of 0.006% per tablet consumed.

Australian data (Horyniak et al. 2014), suggest an average hospital stay of 3 hours in the case of ecstasy poisoning, which when combined with NHS reference cost data of £124 per hour of patient contact (all costs are quoted at 2013-14 prices) gave an estimate of £372 per admission (£378 after inflating to 2015 prices) or £0.02 per tablet.

A&E attendances costs

It was assumed that all hospital admissions result from an initial A&E attendance. As such, each of the 1,556 ecstasy-related inpatient admissions per year had an additional cost of £117 per A&E presentation (2015 prices, £109 at 2012 prices), equal to or £0.007 per tablet, based on NHS reference costing, 2011-12.³

Ambulance conveyances costs

Estimates from Horyniak et al. (2014), suggested that approximately 69% of all A&E attendances citing ecstasy poisoning required an ambulance conveyance, resulting in an estimated 1,074 ecstasy-related ambulance conveyances per year in the UK. Using data from NHS Reference Costs 2013-14, we estimated the average cost per call-out for ambulance services where the patient is seen, treated accordingly, and either referred or conveyed to hospital to be £219 at 2015 prices, (£216 in 2014 prices) or £0.009 per tablet consumed.

Death costs

Using data from the ONS Statistical Bulletin: Deaths related to drug poisoning in England and Wales, 2014 registrations, 25 ecstasy-related deaths were observed in 2014, where 'no other drugs' were mentioned in the cause of death. This gave a death rate of 1 in every 520,000 tablets (26,000,000 tablets/25 deaths). For each death, an estimate of £622 was used to reflect hospital costs, (£464 in 2002 prices inflated to 2015) as reported by Godfrey et al. (2002), resulting in a cost of £0.0006 per tablet consumed.

Treatment for dependence costs

Data from the National Drug Treatment Monitoring System (NDTMS) show that there were a total of 433 people in drug treatment with a primary indication of ecstasy use in England during 2014/15: 165 aged 9-17 years old and 268 aged 18-59 years old. Treatment costs from Public Health England were estimated at £2,620 per treatment episode from This value is based on correspondence with Public Health England in 2015 based on their Value for Money Tool methods which considers average numbers of days in drug treatment (NDTMS 2016). Combining the treatment cost with a probability of treatment of 0.00064% and 0.001%, for those aged 16-24 and 25-59, gave an average treatment cost of £0.012 and £0.30 per tablet respectively.

QALY losses associated with premature death

Because ecstasy-related deaths are most likely to occur in those aged 18-59 years old, and in particular, those aged less than 25, the QALY losses associated with premature death can be substantial. In order to account for the QALY losses of

³ N.B. an updated cost is not available from 2013 onwards reference costs publications.

premature death, EQ-5D population norms (Kind et al. 1999) were used to provide an estimate of these losses. Deaths were assumed to occur in the mid-point of any age group such that those aged 16-24 were expected to die aged 20, and for those aged 25-59, deaths were assumed to occur at age 42. For each group discounted values for EQ-5D population norms, as reported by Kind et al. (1999) were summed from the age of death until age 82, when it was assumed that all individuals would have died in absence of an ecstasy-related death.

Other outcomes that could possibly be included the model but with insufficient evidence or data

It is worth noting that had the following outcomes also been included, the intervention may have become more cost-effective, however given the extent of cost-ineffectiveness, this is unlikely to have changed the outcome of the model greatly.

Acquisitive crime

Because it is reported that MDMA/ecstasy users usually fund their drug purchases from their own income rather than from acquisitive crime (ACPO 2013), such costs were not estimated within the model, but we do appreciate that in some, more problematic users, this may be an important consideration.

Psychological morbidity (depression)

An extensive systematic assessment of observational data on the recreational use of MDMA has been examined studies that compared MDMA users versus poly-drug users and MDMA users versus drug-naïve controls with separate analyses for current MDMA users and ex-users (Rogers et al. 2009). The review found that there was a small but consistent negative effect of 'ecstasy' on cognitive and psychomotor function across a large number of controlled observational studies. The authors considered these effects tended to be 'small' in magnitude, noting that the mean scores of 'ecstasy'-exposed cohorts were commonly still in the 'normal range'. Furthermore, the authors noted that reported results should be considered in the context of methodological flaws in studies, which were numerous, including publication bias, selective reporting of outcomes and confounding, particularly with respect to alcohol (Rogers et al. 2009). As such, despite the potential for ecstasy-related depression to be included within the modelling approach, based on the sum of available evidence and variability in results, this outcome was not included.

Acute psychological effects of ecstasy (memory & cognition)

Evidence from self-reporting studies demonstrates that memory problems have been attributed to 'ecstasy' use in mainly 'moderate' and 'heavy' users (Parrott et al. 2002). However, the degree of self-reported psychobiological problems following

MDMA use is to an extent determined by the more extreme the physical exertion of the user, with more exertion leading to more reported problems (Parrott et al. 2006). As such, novice' or short-term users (in terms of lifetime usage) generally remain unimpaired regarding memory or other psychobiological problems which are attributed to 'ecstasy'(Milani et al. 2006).

Despite the consistency within the literature for short term cognitive effects of ecstasy consumption, with no obvious means of monetising such effects, this information was considered of limited use, and as such, was excluded from the model.

It is possible that if these additional outcomes were included, in addition to ecstasy 'poly-drug' deaths and 'poly-drug' hospital admissions, the results of the model may be affected.

5.2.1 Model of Brief Intervention for reducing ecstasy consumption amongst those attending nightclubs based on Martin et al. (2010)

Study

In a randomized controlled trial conducted in Sydney, Australia, 50 adult ecstasy users were assigned to either a single session brief intervention (motivational interviewing) or an assessment-only 3-month delayed treatment control condition. Primary outcome measures were days of ecstasy use and number of DSM-IV dependence symptoms reported, with secondary outcome measures including abstinence and the total number of pills consumed at both baseline and 90 days post intervention.

At 3-month follow-up, significant differences were observed in favour of the intervention group, particularly for measures of DSM-IV dependence symptoms reported, and Severity of Dependence Scale score. Numerically, but not statistically significant differences were detected for quantity and frequency of use, with abstinence rates for intervention and control 16% and 4% respectively, and overall consumption of ecstasy reducing by 32.6% in the intervention group.

Population

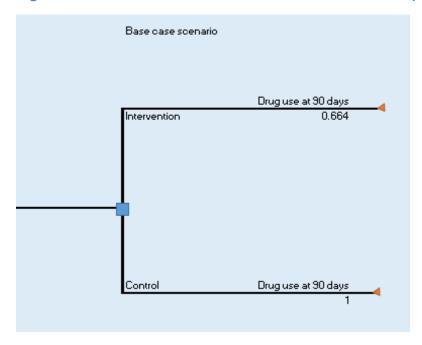
The model considers the 16-24 year old population and 25-59 year old populations separately, and as a whole. (See section Assumptions for detail).

Decision tree

The decision tree (Figure 12) compares intervention to control. Those in the intervention arm experienced a reduction of 32.6% in the number of ecstasy pills consumed compared to the comparator arm. Reduction in ecstasy use for the intervention arm peaks at 90 days (32.6%). Between day 0 and day 90, ecstasy use for the intervention arm decreases linearly.

The base case model has a one year time horizon. Beyond day 90 days, the probability of ecstasy consumption increases linearly back to pre-intervention levels up to a period of 12 months, 9 months post intervention, at which point both groups consume the same amount of ecstasy. Discounting was not considered.

In the scenario the sustainability of the intervention is doubled - the return to preintervention consumption takes twice as long, becoming equal in both groups at month 24 (week 104). The NICE recommended discount rate of 3.5% for both costs and outcomes was applied.





Results

Disaggregated base case results are shown for the 16-24 year old population in Table 6, for the 25-59 year old population in able 7, and for the16-59 year old population in Table 8.

Table 6. Model Results – Ecstasy MI Intervention, 16-24 year olds

16-24 year olds	16-24 year olds					
	Comparator	Intervention	Incremental			
Total annual costs (£'000s)	£11,159	£36,185	£25,026			
Cost per Ecstasy user (£)	£28	£90	£62			
Total healthcare costs (£'000s)	£1,353	£1,133	-£221			
Ambulance costs	£148	£124	-£24			
A&E costs	£114	£95	-£19			
Inpatient admission costs Costs of treating Ecstasy	£369	£309	-£60			
dependence	£713	£596	-£116			
Costs of Ecstasy-related death	£10	£8	-£2			
Total crime costs (£'000s)	£2,580	£2,160	-£421			
Arrest costs	£1,541	£1,290	-£251			
Sentencing costs	£372	£312	-£61			
Court costs	£667	£558	-£109			
Societal costs (£'000s)						
QALY losses attributable to						
early death	£7,226	£6,048	-£1,178			
Number of QALYs	361.3	302.4	58.9			
Motivational interviewing costs (£'000s)		£26,844	£26,844			

Table 7. Model Results – Ecstasy MI Intervention, 25-59 year olds

25-59 year olds					
	Comparator	Intervention	Incremental		
Total annual costs (£'000s)	£5,659	£20,633	£14,974		
Cost per Ecstasy user (£)	£24	£87	£63		
Total healthcare costs (£'000s)	£801	£671	-£131		
Ambulance costs	£88	£73	-£14		
A&E costs	£68	£57	-£11		
Inpatient admission costs	£219	£183	-£36		
Costs of treating Ecstasy					
dependence	£422	£353	-£69		
Costs of Ecstasy-related death	£6	£5	-£1		
Total crime costs (£'000s)	£1,528	£1,279	-£249		
Arrest costs	£913	£764	-£149		
Sentencing costs	£221	£185	-£36		
Court costs	£395	£331	-£64		
Societal costs (£'000s)					
QALY losses attributable to early					
death	£3,330	£2,787	-£543		
Number of QALYs	166.5	139.35	27.15		
Motivational interviewing costs					
(£'000s)		£15,896	£15,896		

Table 8. Model Results – Ecstasy MI Intervention, 16-59 year olds.

16-59 year olds				
	Comparato			
	r	Intervention	Incremental	
Total annual costs (£'000s)	£16,818	£81,943	£65,125	
Cost per Ecstasy user (£)	£24	£126	£102	
Total healthcare costs (£'000s)	£2,154	£1,803	-£351	
Ambulance costs	£235	£197	-£38	
A&E costs	£181	£152	-£30	
Inpatient admission costs	£588	£492	-£96	
Costs of treating Ecstasy				
dependence	£1,135	£950	-£185	
Costs of Ecstasy-related death	£16	£13	-£3	
Total crime costs (£'000s)	£4,109	£3,439	-£670	
Arrest costs	£2,454	£2,054	-£400	
Sentencing costs	£593	£496	-£97	
Court costs	£1,062	£889	-£173	
Societal costs (£'000s)				
QALY losses attributable to				
early death	£10,556	£8,835	-£1,721	
Number of QALYs	527.8	441.8	86	
Motivational interviewing costs				
(£'000s)		£67,866	£67,866	

The cost per QALY for the intervention as a whole (16-59 year olds) is shown in Table 9.

Table 9. Results from economic model based on Martin et al. (2010)

Base-case scenario

	Total Costs (£)	Total QALY losses	Incremental Costs (£)	Incremental QALYs	ICER (£)/QALYs
Intervention					
	£47,982,882	441.8			
Comparator					
	£6,262,813	527.8	£41,720,069	86.03	£484,959

*Total costs excluding societal costs of forgone QALYs as these are accounted for in the denominator

Scenario (2 year reduction)

	Total Costs (£)	Total QALYs lost	Incremental Costs (£)	Incremental QALYs	ICER (£)/QALYs
Intervention	£52,977,610	878.9			
Comparator	£12,313,841	1,055.6	£40,663,769	176.7	£230,097

*Total costs excluding societal costs of forgone QALYs as these are accounted for in the denominator

For the population aged 16-24 and 25-59, the associated ICERs were £444,966 and £571,739 in the base-case scenario, and £211,121 and £271,271 per QALY, in the 2 year reduction scenario respectively.

Regardless of the population modelled this intervention remained cost-ineffective. This is largely because of the relatively minimal harms resulting from ecstasy use in such a wide user base, and the difference between the estimated cost of ecstasy related harms per person per year (£26), and the cost of the intervention (£67).

The model assumes that the intervention is 100% effective at identifying all ecstasy users who may benefit from the intervention with a zero cost of doing so. In reality this is unlikely, given the staffing requirements of locating such individuals and that not all individuals may be willing to undergo the intervention.

Sensitivity analysis

The break-even analysis demonstrated that the cost of the intervention would need to decrease from £67 to £4.20 (less than the UK minimum wage) in order to represent a cost-effective use of NHS resources at a willingness-to-pay of £20,000 per QALY.

If the intervention were able to decrease ecstasy use at 90 days post intervention to a 100% reduction; at the current price, the ICER would be approximately £150,099.

Crime costs for young offenders may be higher than those associated with adult offenders, as suggested by the National Audit Office (2011). Therefore, in an extreme scenario analysis the costs of arrest, sentencing and court appearance for ecstasy related possession offences were doubled. Following the doubling of crime costs, the cost per QALY of the intervention fell from £484,959 to £477,175 per QALY, remaining cost-ineffective.

The effect of modifying the assumptions used within the model, as described in Table 10 is shown in the tornado diagram (Figure 13). The biggest driver is the cost of the intervention, but even at the lowest cost, the intervention is not cost effective.

Table 10. Model assumptions

Parameter	Explanation	Justification
QALY loss (16-24 years old)	Low is assuming all deaths at 24, high is all deaths at 16	Without data as to how death is likely to vary by age, and within age bands, this provided the opportunity to show the full spectrum of the effect of age at death on the results of the model
QALY loss (25-59 years old)	Low is assuming all deaths at 59, high is all deaths at 25	Without data as to how death is likely to vary by age, and within age bands, this provided the opportunity to show the full spectrum of the effect of age at death on the results of the model
Treatment effect	Low is assuming treatment effect is halved, high is doubled (no change on effect sustainability.)	The doubling and halving of effect size was decided upon following deliberation within the health economics team. In the absence of PSA, and only one study demonstrating the effectiveness of this intervention, we had to arbitrarily vary the effect size, and these were the values we chose.
Effect sustainability	Low is assuming it takes 6 months before the effects of the intervention have completely worn off, high is in the event that sustainability is doubled, at every time point, taking twice as long to wear off.	No data were available within the publication demonstrating the duration/sustainability of treatment effect. Much the same as with treatment effect size, the choice of variation of this parameter was arbitrary.
Discount rate	Low is applying a 1.5% discount rate rather than the standard 3.5%	Following best practice.
Cost of intervention	Low is using a cost of £32 and high is using a cost of £128	Recommendations from PHAC

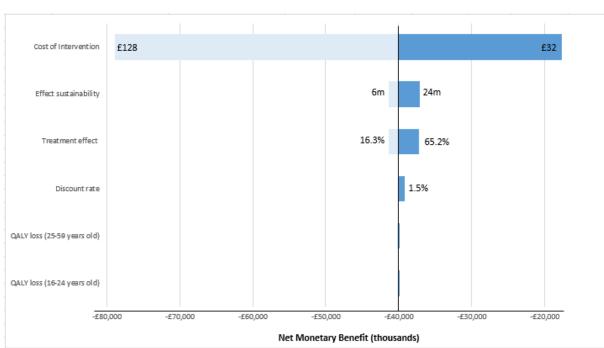


Figure 13. Tornado diagram showing sensitivity of outcome (Net monetary benefit, NMB) to changes in model parameter estimates. NMB values each QALY at £20,000.

Discussion and Limitations

The results of this economic model, based on the results of Martin et al. (2010), show that motivational interviewing to reducing ecstasy use, is a cost-ineffective. A combination of relatively low social harms associated with ecstasy use, a lower degree of dependence than with other drugs, and a low crime cost, show that any intervention, even if successfully delivered to 100% of the effective population would be unlikely to result in sufficient benefit. The cost of delivering any intervention would need to be at a cost no greater than £4.20 (less than the minimum wage of the UK), in order to provide a rational use of NHS resources. While changing the assumptions of the model led to often considerable reductions in the cost per QALY of the intervention, particularly if the effect size and sustainability were increased, these did not affect the overall conclusions of the model.

5.3 Models focussing on cocaine use

Costs

Figure 14 shows an example of the social cost of one year of cocaine use that may be prevented by an intervention.

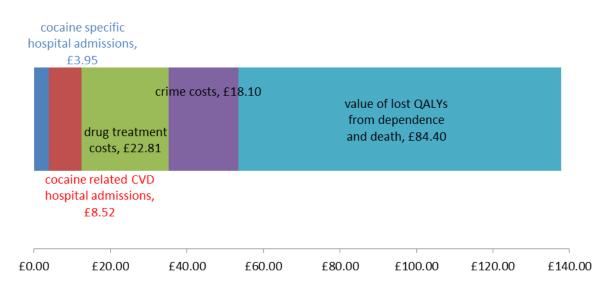


Figure 14. Example social cost of one year of cocaine use based on Morgenstern model. Total cost = £137.78.

Crime costs

We made the assumption that through reducing drug use the intervention did not prevent any acquisitive crime or drug dealing associated with drug use, only that it prevents people being arrested for possession. We have assumed that cocaine use is associated with a risk of arrest for possession offences, but have not assumed any risk around supply offences due to difficulties in estimation. There were 31,962 arrests for possession of controlled drugs (excluding cannabis) in England and Wales between April 2014 and March 2015. If we apply the fact that around 23% of non-cannabis drug use is cocaine use (CSEW 2015) then we have made an assumption that 23% of non-cannabis drug possession arrests are cocaine related. This may not be the case if police do not prioritise policing cocaine over other drugs like heroin. This equates to 9.4 arrests per 1000 cocaine users per year. We have assumed a cost of £1,925 per arrest which is based on costs from Godfrey et al. (2002), inflated to 2015 prices. This equates to a cost of arrest of £18.10 per cocaine user per year.

Hospital admissions costs

There were around 12,000 hospital admissions in England in 2014/15 where cocaine was mentioned in at least one diagnosis field. Of these, 1,624 were cocaine-specific, i.e. mental and behavioural disorders due to cocaine or poisoning by cocaine was the primary diagnosis (HSCIC 2016). A proportion of these might be crack cocaine or polydrug users. This equates to 2.2 admissions per 1000 cocaine users, and an average cost of £3.95 per cocaine user per year.

As mentioned previously, cocaine is also associated with CVD. In the study by Lucena et al. (2010) the main cardiovascular findings relating to cocaine deaths were

for atherosclerosis (blocked arteries) and left ventricular hypertrophy (thickening of the heart muscle), dilated cardiomyopathy (enlarged heart), and myocarditis (inflammation and damage of the heart muscle). The risk of myocardial infarction or stroke increases in the hours after cocaine use. There is evidence that around 1 in 4 myocardial infarctions in 18-44 year olds are cocaine related (Qureshi et al. 2001). Allowing for some admissions to be crack cocaine related, we have assumed that 20% of hospital admissions for myocardial infarction (ICD 10 codes I21 – I23) in 18-44 year olds are powder cocaine related. The cost per myocardial infarction admission was £3,371 based on the NHS hospital tariff cost for 2014/15. The average cost of myocardial infarctions was £4.82 per year. There were 53,355 admissions for other CVD ICD-10 codes ((ICD 10 I10-I79 excluding I21-I23) in 18-44 year old persons in England in 2014/15 financial year which equates to an average of 2.4 CVD admissions per 1000 cocaine users with an average cost of £3.70 per cocaine user per year.

The total cost of hospital admissions (cocaine specific and CVD) was £12.47 per cocaine user per year (made up of £3.95 cocaine specific, plus £4.82 myocardial infarctions, plus £3.70 other CVD admissions).

It is likely that there are a number of A&E attendances that are due to cocaine use as well but A&E attendances are generally not well coded unlike hospital admissions and we did not find any other evidence to estimate this. There may be other cases of temporary cocaine-induced psychosis that are coded under general psychosis rather than 'mental and behavioural disorders due to cocaine'.

Costs of drug treatment

There were 10,610 people in drug treatment with a primary drug of powder cocaine in England based on adult NDTMS data for 2013/14. This was 5% of all people in treatment. The average cost of one year of drug treatment was £6,064 in the NTORS study (Davies et al. 2009) but this is likely to be skewed by high costs for opiate and crack users. We have estimated a total cost of drug treatment of £1,562 based on data supplied by PHE. This leads to a cost of drug treatment of £22.81 per cocaine user per year.

QALY losses associated with premature death

There were 247 drug related deaths registered in England and Wales in 2014 where cocaine was mentioned on the death certificate and 74 where it was the sole drug. This includes crack cocaine as well as powder cocaine. Crack cocaine users are more likely to be disadvantaged and to lead chaotic lifestyles and die from drug use than powder cocaine users, but crack users would also be more likely to have other drugs involved in their death and mentioned on the death certificate as many crack users are also opiate users. We have assumed that 50% of the deaths that

mentioned cocaine only (37) were due to powder cocaine use (we do not have evidence to assess the accuracy of this estimate). Cocaine is a cause of sudden death from cardiovascular disease (CVD), particularly in men aged under 45 where deaths from heart disease are relatively rare. It is unlikely that there is any double counting between CVD causes of death and records showing cocaine poisoning. A study which used urine screening at two London Emergency Departments indicated that 7% of patients presenting with chest pain, and 23% of all patients aged 18 to 30 years, tested positive for cocaine (Maric et al. 2010). A study in Valencia in Spain found that 3% of sudden deaths were cocaine related – this would include crack cocaine (Lucena et al. 2010). Some 62% of these deaths were caused by cardiac disease, and all of the deaths were in men aged between 21 and 45. The deaths were typically in men in their mid-30s, with a high rate of deaths at weekends suggesting recreational users rather than daily dependent users. Many of these cases were heavy smokers which is also a risk factor for heart disease. Cocaine use in Spain is similar to that in the UK, and both countries have high cocaine use when compared to the rest of Europe. It was assumed that deaths happened at an age of 25 on average producing a QALY loss of 20.89 QALYs when discounted at 3.5% or 32.31 QALYs when discounted at 1.5%. Overall the average QALY loss from cocaine related deaths was estimated as 2.64 QALYs per 1000 users per year.

QALY losses associated with Cocaine Dependence

It is estimated that around 15% of cocaine users (according to US data) become dependent (Wagner & Anthony 2002) which was annualised to a risk of 1.2% per year for 18-29 year olds, and that dependence causes a quality of life reduction of around 0.064 over six months where quality of life is measured on a scale of zero to one (Pyne et al. (2011) used SF-6D HRQoL tool). We do not know if this quality of life loss gets better or worse over time. It was assumed that each case of cocaine dependence caused on average five years' worth of QALY decrements, so a QALY loss of 0.64 (undiscounted) or 0.576 (discounted at 3.5%) in total. No evidence was found for HRQoL loss for recreational or non-dependent cocaine use.

Other Health & Social Harms

Cocaine use is associated with an increase in risky sexual behaviour and an increase in risk of sexually transmitted diseases e.g. Leigh & Stall (1993). We have not quantified this or included this in the model. The Parsons study was looking at risky sexual behaviour and drug use but we have only modelled the drug use outcomes.

We have not estimated the cost of other potential social harms caused by cocaine use. But it is worth considering that cocaine use contributes to other social harms like organised crime and violence; drug use and dependence spreading from peer to peer by microdiffusion; debt and associated problems; relationship and family breakdown; and lost productivity and being made unemployed. Cocaine will also be associated with a proportion of drug road traffic accidents.

It may well be that if more consequences were modelled, the intervention would become more cost effective, so the results should be taken as a conservative estimated of cost effectiveness, i.e, the intervention may be more cost effective than these results indicate. However the results are very sensitive to the proportion of CVD risk in young people that can be attributed to cocaine use, which is subject to considerable uncertainty.

5.3.1 Model of Motivational Interviewing to reduce drug use in young gay and bisexual men, based on Parsons et al., (2014)

Study

This study compared four sessions of motivational interviewing in the intervention arm (N=73) with four sessions of content-matched education in the control arm (N=70) in terms of the effect on drug use and unprotected sex measured at 3 month intervals up to 12 months. Men from the New York City metropolitan area, 18-29 years of age, were included in the study if they had a history of drug use and risky sexual behaviour. We estimated the intervention arm cost to be £825 based on clinical psychologist time. Drug use and unprotected sex decreased in both groups, but the decrease was significantly larger in the motivational interview group. The demographics of both groups in the study appear similar. However, the study did not control for observable factors. The outcomes in the study were drug use (broken down into all drug use, cocaine, ecstasy, GHB, ketamine); and number of occasions of unprotected anal intercourse (UAI). The main drug used was cocaine (67.8% at baseline) so the model was based on outcomes associated with cocaine use. It is assumed that because the intervention was aimed at recreational / club drug users that the majority of cocaine use was powder cocaine which is typically insufflated, rather than crack cocaine which is smoked, and is associated with greater social harms and typically with dependent drug use. Cocaine is occasionally injected as well.

Population

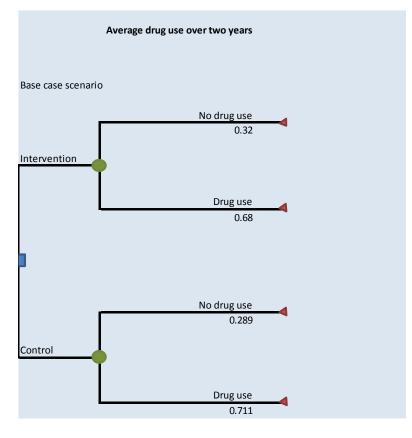
The model was constructed based on an estimated population of 124,791 gay and bisexual men aged 18-29 in the UK (based on the ONS Integrated Household Survey, 2.4% of men). Powder cocaine use was estimated at 10% based on Buffin et al. (2012) so equated to a possible target population of 12,479. The inputs used for the model were ideally for the UK, if not then for England & Wales, and if this data was not available, then for England alone. The inputs were ideally measured for

males as the intervention was targeted at males only. If data was not available for males then data for all persons was used.

Decision tree

The decision tree (Figure 15)) compares intervention to control. The intervention effects were modelled for two years only. Two scenarios were modelled; in the base case scenario the drug use in both the control and intervention groups returned to baseline after 2 years. In the second (maintained reduction) scenario, drug use in both groups continued to decrease in a linear fashion over the two years.





Model Results

Table 11. Results from economic model based on Parsons et al., (2014).

Base case scenario.

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£3,164,427	163			
Comparator	£930,815	170	£2,233,612	7.41	£301,235

2 year reduction scenario.

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£2,364,013	122			
Comparator	£786,807	144	£1,577,206	22.24	£70,903

The intervention was not cost effective under either scenario. Only if the intervention effects were maintained over two years, and the intervention cost less than £88 (£22 per hour of client contact), would it be cost effective at a willingness-to-pay threshold of £20,000/QALY.

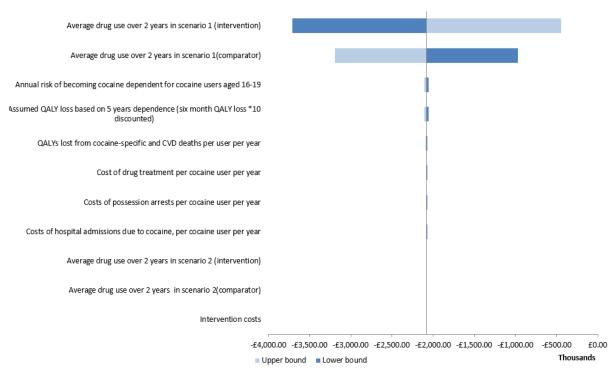
This cost per QALY is from a broad perspective; it includes healthcare costs (which will be mainly borne by the NHS), drug treatment costs (services which are typically commissioned by local authority public health teams in England), and crime costs (which are borne by the criminal justice system).

The cost effectiveness of the intervention is very sensitive to the discount rate as many of the QALYs lost are through early deaths from cocaine use.

One-way sensitivity analysis (Tornado diagram)

A univariate sensitivity analysis was carried out which found that model results were most sensitive to uncertainty in drug use in the intervention and control groups, to the risk of becoming dependent to cocaine and the QALYs lost from dependence, and to the QALYs lost from cocaine and CVD related deaths (see Figure 16). This varied the drug use in the intervention and control groups by +/- 5%, not 25% as in the other models, as if drug use was 25% higher in the intervention group the intervention would no longer be more effective than the comparator.

Figure 16. Tornado diagram showing difference in net monetary benefit (NMB) for motivational interviewing intervention in young gay and bisexual men with changes in model parameters. NMB values each QALY at £20,000.



Discussion and Limitations

The results suggest that this intervention would not be cost effective using a willingness to pay for a QALY of £20,000. However, if the intervention could be shown to have a longer term effect on drug use, then the intervention may be cost effective.

The economic model suggests that the social costs of cocaine use are considerable so an intervention that could prevent cocaine use at a lower cost could be a cost effective use of resources. The main healthcare costs of cocaine were around cardiovascular disease rather than cocaine-specific costs but there is a lack of specific evidence around the UK burden of cardiovascular disease that is caused by cocaine.

5.3.2 Model of Motivational Interviewing intervention to reduce club drug use and HIV risk behaviors among men who have sex with men, based on Morgenstern et al., (2009).

Study

This intervention compared four sessions of motivational interviewing (MI) with educational controls in reducing drug use and HIV risk behaviours in men who have

sex with men in New York. The main drug used was cocaine (12.8%), also methamphetamine (9.8%), and ecstasy (7.1%). Methamphetamine use is rare in the UK, although is reported to be more common in MSM than some other groups (Bourne et al. 2015). The model was based on cocaine use as cocaine was the most harmful drug used in the participants that is commonly used in the UK. Drug use was reported in terms of days of drug use rather than prevalence of drug use. For the purposes of the model, drug use prevalence was assumed to reduce in line with days of drug use.

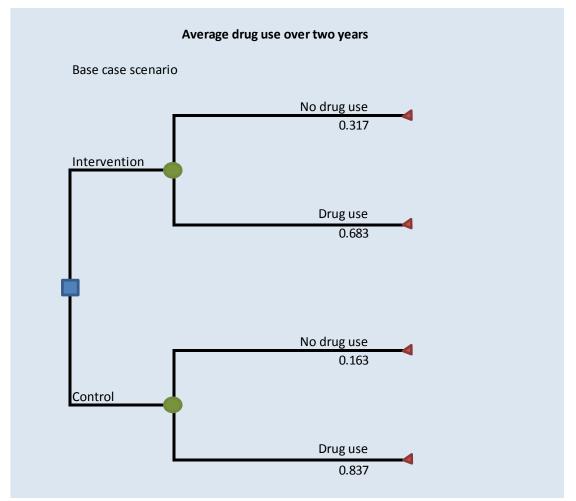
Population

The population for the study was aged 18 to 65 years old with an average age of 37.8 (SD 8.8) years. In this respect the population was older than the populations for other drug use prevention interventions we have modelled. The risk of cocaine dependence was based on 30-40 year olds while the lost QALYs from early deaths associated with cocaine were based on 39 year olds.

Decision tree

The decision tree structure is shown in Figure 17. The intervention effects were modelled for two years only. The study reported days of drug use rather than prevalence. All participants were drug users at baseline and drug use prevalence was assumed to decrease in proportion to days of drug use. In the base case scenario drug use was assumed to rebound back between 12 months and 24 months, whereas in the 2 year reduction scenario, drug use was assumed to continue to decrease in a linear fashion, with drug use in the intervention group reaching zero at 21 months, and drug use in the control group being at 32% in the control group at 24 months. Outcomes were based on the average estimated prevalence of drug use in the two groups over the two year time period.





Results

The model results are shown in Table 12. The intervention does not come out as cost effective in the base case scenario and is not quite cost effective in the 2 year reduction scenario if compared to a willingness to pay for a QALY of £20,000. The intervention had a significant effect in terms of reducing drug use but because the individuals were older on average the opportunity to save QALYs from dependence and early death was lower when applied to the population assumptions.

Table 12. Results from economic model based on Morgenstern et al., (2009)

Base case scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£8,217,791	183	£5,386,242	41.13	£130,971
Comparator	£2,831,549	224]		

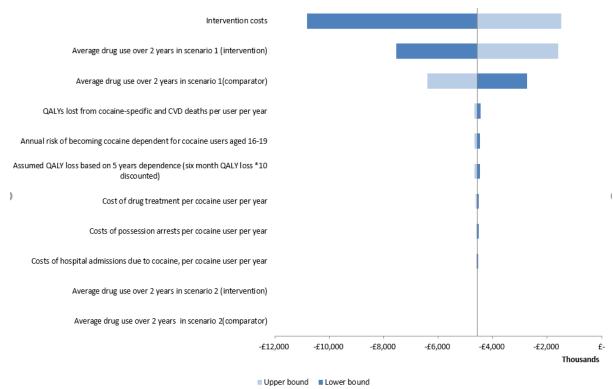
2 year reduction scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£4,568,935	102	£2,378,909	71.58	£33,236
Comparator	£2,190,026	173			

One-way sensitivity analysis (Tornado diagram)

The model results were sensitive to changes in assumptions around drug use in the intervention and comparator groups (see Figure 18) and to intervention costs, but no single change made the intervention cost effective at £20,000 per QALY. This intervention could be potentially cost effective if it was provided at a much lower cost, or was provided at a lower cost with a sustained effect, or if it was provided for younger people who have more potential years of life to lose from early death, and have a higher risk of becoming dependent on cocaine.

Figure 18. Tornado diagram showing differences in net monetary benefit (NMB) for motivational interviewing intervention to reduce club drug use and HIV risk behaviours among men who have sex with men with changes in model parameters. NMB values each QALY at £20,000.



Discussion and Limitations

This intervention was potentially more effective than some other interventions such as in the Parsons study. However because the population in the Morgenstern study were older on average they lost fewer QALYs from early deaths associated with cocaine use which meant that the intervention was less cost effective. The estimated risk of cocaine dependence is lower in older age groups as well at 0.344% of users per year becoming dependent. If the results were maintained over two years, and the intervention cost less than £190, then the cost per QALY would be less than £20,000.

5.3.3 Model of a family intervention to reduce sexual risk behaviour, substance use, and delinquency among newly homeless youth, based on Milburn et al. (2012).

Study

This model looked at a family intervention called STRIVE (Support to Reunite, Involve and Value Each Other) which was compared with standard care (see Figure 19). This intervention was carried out with young people aged 12-17 who had ran away from home for at least two nights in the last six months and returned to their families. The intervention reduced alcohol use, and led to an increase in cannabis use but a decrease in 'hard drug' use. The main 'hard drug' used by the cohort was cocaine (17.2% lifetime use) so this was the drug that outcomes were modelled for. The only other 'hard drug' specifically measured was methamphetamine (12.6% lifetime use), which is relatively rarely used in the UK so may be difficult to model with UK data. The study only reported average number of occasions of drug use over time, not prevalence of drug use, except at baseline (24% using hard drugs in the last three months). To translate the occasions of drug use into other outcomes we assumed a linear relationship between occasions of drug use and prevalence. This is an oversimplification but other ways of estimating prevalence were not available.

Population

The number of young people homeless was based on DCLG data for England, statutory homeless cases aged 16-24, 2014/15. This may be an underestimate or a poor fit for 12-17 year olds who have run away from home. This brought a number of people eligible for the intervention of 3,507. Homeless drug use was based on 26% of young homeless people from Homeless link (2015).

In general, outcomes associated with drug use in 12-17 year olds are difficult to find so the model was populated as the Parsons model but with data for young people where available.

Population-specific data

Cocaine use from the CSEW for 16-19 years olds was combined with NDTMS data for young people in drug treatment used to estimate the risk of being in drug treatment for 16-19 year olds who use cocaine. Annual risk of dependence for 16-19 year old cocaine users was used (1.29% from Wagner & Anthony (2002)). Crime costs were varied in the sensitivity analysis to take account of the fact that youth justice costs are higher than adult criminal justice costs, so the average cost per offence was varied from \pounds 1,925 up to \pounds 5,700.

Apart from this, the costs and outcomes from the Parsons model were used. These were around healthcare costs associated with cocaine use, early death from CVD or cocaine use, and QALY loss from dependence.

It may be that if young people aged 12-17 are using cocaine they are less likely to have the same type of problems as young adults for example in terms of risk of arrest, or cardiovascular disease. But their drug use may still lead to these problems in the future so it is reasonable to include these outcomes in the modelling. The fact that the Wagner & Anthony (2002) suggests that risk of dependence is higher for younger cocaine users suggests that young people who use cocaine and possibly other hard drugs may be more at risk of severe consequences of their drug use.

Decision Tree

The decision tree structure is shown in Figure 19. The intervention effects were modelled for two years only. In the base case scenario, drug use in the intervention and control groups rebounded back between 12 months and 24 months. In the two year reduction scenario, drug use continued to reduce at a linear rate in both groups until 24 months. Because drug use in both groups was on a downward trajectory, this meant that drug use fell to zero in the intervention group at 15 months and in the control group at 24 months. The modelled outcomes were based on average drug use over the 24 month period.

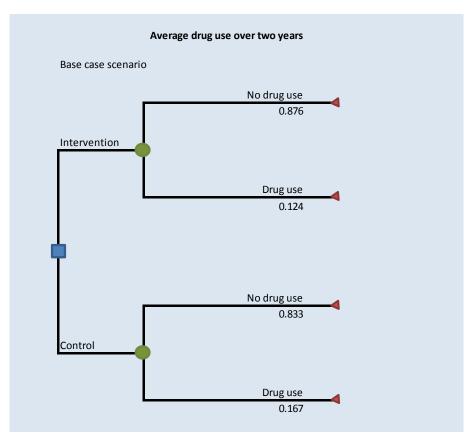


Figure 19. Decision tree for family intervention for newly homeless youth.

Results

The model suggested that in the base case, the intervention would not be considered cost effective using a willingness to pay threshold of £20,000 per QALY. However, if the intervention continued to have an effect and the reduction in drug use continued over two years, the intervention would be approaching cost effectiveness. The intervention cost was varied to 25% lower (£619). If the intervention cost was less than £500, and the intervention had a longer term effect over the two years, then the intervention would have a cost per QALY of less than £20,000.

Table 13. Results from economic model based on Milburn et al., (2012)

Base case scenario

	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£390,528	9			
Comparator	£41,547	12	348,981	2.98	£117,125

2 year reduction scenario

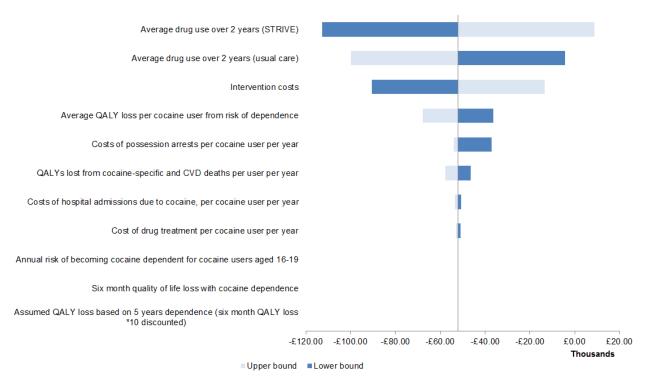
	Total costs (£)	Total QALYs lost	Incremental costs (£)	Incremental QALYs	ICER (£) (QALYs)
Intervention	£167,583	4			
Comparator	£28,527	8	139,056	4.27	£32,560

One-way sensitivity analysis (Tornado diagram)

In the univariate sensitivity analysis, the uncertainty in differences in drug use between the two groups were the biggest drivers of cost effectiveness. Intervention costs and QALY losses from cocaine use were also drivers of uncertainty (see Figure 20).

As average drug use in the control group becomes lower, the difference in drug use between comparator and intervention gets smaller and with everything else being equal the intervention becomes less cost effective so the net monetary benefit reduces. None of the changes in parameter values produced a positive net monetary benefit.

Figure 20. Tornado diagram showing difference in net monetary benefit (NMB) with changes in model parameters for family intervention for newly homeless youth. NMB values each QALY at £20,000. Scenario 2.



Discussion and limitations

This intervention was aimed at young people aged 12-17. In general 'hard drug' use is rare in this age group and those young people who do use drugs may already have multiple types of disadvantage that are exacerbated by drug use. A lot of the outcomes used in the model were for adults (for example, crime and CVD deaths) which may make the model less applicable for young people.

6. 6. Discussion and Conclusions

6.1 Cost-effectiveness analyses

An overall summary of the cost effectiveness of the modelled interventions is described in Table 14. This shows base case scenarios and the 'sustained reduction' scenarios (drug use reduction is sustained over time).

Using the base case analyses:

- The web-based personalised feedback (Lee et al. (2010)) would be costeffective if it could be delivered at a low cost.
- Familias Unidas (Prado et al. (2012)) would be cost-saving, and improve QALY, if it could be delivered at a low cost.

Additionally, using the best case scenarios, with sustained reduction:

 Motivational interviewing for club drug use (Morgenstern et al. 2009) would be considered cost effective at a threshold of £20,000 per QALY if it could be delivered at a lower cost of £128.

The other interventions (Catalano, et al. (1999), Martin et al. (2010), Parsons et al (2014), Milburn et al (2012)) would not be cost effective at a threshold of £20,000 per QALY, even if they could be delivered at a lower cost.

Table 14. Intervention comparison with scenario analyses for lower intervention costs, with effects maintained over a longer period of time.

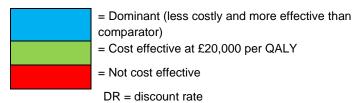
Cost effectiveness - drug use reduction effects diminish over 2 years (base case
scenario)

				ICER (Incremental cost effectiveness ratio) – net cost per			
				QALY gained			
Study	Type of intervention	IC (base case)	IC (low)	Base case	low intervention costs	1.5% DR	low intervention costs & 1.5% DR
Catalano, et al. (1999)	Focus on families project	£3,367	£842	£99,254,921	£24,761,040	£99,254,921	£24,761,040
Lee et al. (2010)	Web-Based Personalized Feedback	£15	£1	£328,939	-£114,004	£326,949	-£115994
Prado et al. (2012)	Familias Unidas	£154	£116	£129,970	-£19,916	£121,692	-£21,627
Martin et al. (2010)	Brief MI amongst those attending nightclubs	£67	£32	£484,959	£225,424	£328,341	£152,663
Parsons et al (2014)	MI for drug use & HIV risk	£268	£128	£301,235	£141,014	£249,754	£116,890
Morgenstern et al. (2009)	MI for club drug use	£268	£128	£130,971	£55,950	£102,658	£43,797
Milburn et al (2012)	Family intervention for youth who had ran away from home	£825	£619	£117,125	£86,986	£110,819	£82,294

- = Dominant (less costly and more effective than comparator)
- = Cost effective at £20,000 per QALY
- = Not cost effective
- DR = discount rate IC = intervention cost

				ICER (Incremental cost effectiveness ratio) – net cost per			
				QALY gained	l		
Study	Type of intervention	IC (base case)	IC (low)	Base case	Low intervention costs	1.5% DR	Low intervention costs & 1.5% DR
Lee et al. (2010)	Web-Based Personalized Feedback	£15	£1	£53,675	-£193,269	£48,314	-£188,620
Prado et al. (2012)	Familias Unidas	£154	£116	£110,132	-£25,767	£102,502	-£27,287
Martin et al. (2010)	Brief MI amongst those attending nightclubs	£67	£32	£230,097	£103,757	£155,786	£70,248
Parsons et al (2014)	MI for drug use & HIV risk	£268	£128	£70,903	£31,005	£58,750	£25,665
Morgenstern et al. (2009)	MI for club drug use	£268	£128	£33,236	£9,271	£25,976	£7,173
Milburn et al (2012)	Family intervention for youth who had ran away from home	£825	£619	£32,560	£23,537	£30,782	£22,243

Note that there is no sustained reduction scenario for Catalano et al (1999) and the base case scenario for Lee is for 12 months only as individuals were only followed up at six months.



IC = intervention cost

6.2 Evidence Statements

Evidence statement 1

An economic model was built based on an experimental intervention with families of substance users by Catalano et al (1999) and a follow-up study by Haggerty et al (2008). The economic and health benefits are limited to 12 months in the model as beyond 12 months of the study, each individual in the intervention or control cohorts had the same probability of using cannabis. The model found that this intervention was unlikely to be cost effective at a willingness to pay threshold of £20,000 per QALY due to the restricted duration of benefits and high intervention costs (£3,367) of 'Focus on Families' for one year. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £99m per QALY gained. The intervention would have to cost less than £4 per person to be considered cost-effective, based on results being limited to 12 months.

Evidence statement 2

An economic model was informed by results from Lee et al (2010) based on a brief, web-based personalized feedback selective intervention for college student cannabis use. Subgroup analysis found promising effects for those with a family history of drug problems and therefore supported selective targeting of the intervention which was applied in the model. Based on a cost of £15 the intervention would not be cost effective but if the intervention could be provided at a low cost of £1 or less then it would be dominant, i.e. less costly and more effective than a 'do nothing' alternative, as it provides resource savings and reductions in cannabis use. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £329,000 per QALY gained.

Evidence statement 3

An economic model was informed by Prado et al (2012) based on an intervention called Familias Unidas to reduce drug use (in particular, cannabis) and alcohol use. Familias Unidas is most effective for adolescents with parents exhibiting high stress and lower levels of social support. Familias Unidas includes eight 2-hour multi-parent group sessions and four 1-hour family visits. The model found that this intervention was unlikely to be cost effective at a willingness to pay threshold of £20,000 per QALY due to restricted benefits of the intervention and the costs of delivery (£154.25 per family). The ICER (incremental cost effectiveness ratio) in the base case scenario was around £241,000 per QALY gained. The intervention would have to cost less than £135 and the effects extrapolated to an additional 12 months to be considered cost-effective.

Evidence statement 4

An economic model based on a study of motivational interviewing to reduce ecstasy use in those attending nightclubs, based on Martin et al. 2010, found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £485,000 per QALY gained. Even if the effect of reducing drug use was maintained for at least two years, the cost halved to £32 and a discount rate of 1.5% applied, the ICER was still £70,000. In fact, the intervention could only be cost effective if delivered at a cost of £4.20 per hour or less in the base case scenario.

Evidence Statement 5

An economic model based on a study of motivational interviewing to reduce drug use in young gay and bisexual men, based on Parsons et al., (2014) found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £301,000 per QALY gained. This intervention would only be cost effective if the effect of reducing drug use was maintained for at least two years, and if the intervention could be provided at a cost of less than £88.

Evidence Statement 6

An economic model based on a study of a motivational interviewing intervention to reduce club drug use and HIV risk behaviours among men who have sex with men by Morgenstern et al. (2009) found that the intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY gained. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £131,000 per QALY gained. This intervention would only be cost effective if the effect of reducing drug use was maintained for at least two years, and if the intervention could be provided at a cost of less than £190. The intervention was targeted to men with an average age of 38 but if it could be provided to younger men then it would be more likely to be cost effective as younger people are more likely to become drug dependent and to lose more years of life through early death associated with drug use.

Evidence Statement 7

An economic model based on a study of a family intervention called STRIVE (Support to Reunite, Involve and Value Each Other) by Milburn et al (2012) found that this intervention was not likely to be cost effective at a willingness to pay threshold of £20,000 per QALY. The ICER (incremental cost effectiveness ratio) in the base case scenario was around £117,000 per QALY gained. If the intervention

cost was less than £500, and the intervention had a longer term effect over two years or more, then it would be cost effective.

Evidence Statement 8

The results of the economic modelling suggest that, to be cost effective, drug use prevention interventions would need to cost less than £100 per person, and would need to reduce drug use by at least five percentage points, maintained over two years (for example to reduce drug use from 20% to 15% of a population). Targeting interventions at individuals who are at high risk of drug use or harmful consequences of drug use, or at individuals who are already drug users, would most likely make interventions more efficient. If interventions can prevent more harmful forms of drug use like opiate use then they will be more likely to be cost effective.

Evidence Statement 9

If drug prevention interventions that are effective over a period of time can be provided as part of multicomponent interventions at an additional cost of less than around £100, then they may represent a cost effective component of these programmes.

6.3 Discussion

The economic modelling results indicate that few of these interventions are likely to be cost effective. This is because:

- some interventions only have a marginal effect on drug use (for example. reducing drug use by 2 percentage points),
- the interventions don't have evidence of having a long term,
- some interventions are relatively high cost for preventative interventions, and
- the social costs per user of cannabis and ecstasy are lower than other more harmful drugs so the opportunity for cost savings is smaller.

It may be that if more outcomes were included, for example productivity, then interventions would become cost effective, but we could not find good quality evidence to quantify other outcomes. Some studies included sexual health outcomes which could increase cost effectiveness; we modelled drug related outcomes only. There are issues with attributing outcomes to drug use or to interventions, so drug use may be associated with a range of negative outcomes but the evidence for causation is not as strong. For example there is some evidence linking ecstasy use with depression but this is not consensus in the literature about this, as people who are prone to depression may also be predisposed to continuing drug use. Also the outcomes associated with drug use may be in part confounded by the fact that the drug used by individuals may not be what they believe they are using, for instance many tablets sold as ecstasy do not actually contain any MDMA, so there may be a lot of uncertainty in estimating outcomes. Some harm may arise from the agents that drugs are cut with rather than the drugs themselves.

The key difference between the results of this economic modelling and the modelling that was carried out for NICE Guidance PH4 is that the PH4 modelling assumed that preventing drug use initiation would prevent more harmful problematic drug use like heroin and crack cocaine use further down the line. In this analysis, on the advice of the committee, the present modelling did not include any of this 'Gateway theory'. If it is the case that using drugs like cannabis or ecstasy does increase the risk of heroin or crack cocaine use and dependence by even a small amount, then the interventions modelled may become much more cost effective.

The results of the economic modelling suggest that based on the information in these studies, drug misuse prevention interventions may not be cost effective unless they:

- Have a long duration of effect on reducing drug use by two years or more
- Reduce drug use by at least 5 percentage points
- Have a low cost less than £100 per participant
- Act on drug use that has more severe consequences, for example crack cocaine use or opiates.

(Some combination of these factors may be required).

The idea of targeting interventions to the most vulnerable groups makes sense as individuals experiencing multiple disadvantages are more likely to become drug users and experience harmful consequences of their drug use; however the evidence base, particularly around cost effectiveness, remains limited for these groups. Drug use prevention interventions do happen in a UK context but the evidence for current practice is not well established and there is a lack of good quality evidence around preventative interventions that can be used to estimate their cost effectiveness.

Several challenges exist in conducting an economic evaluation of public health interventions:

- Multiple outcomes: drug misuse interventions aimed at vulnerable populations have a range of outcomes and outcome measures. It is difficult to determine which intervention is the most efficient when each intervention is measured using a different parameter.
- Natural units: it is difficult to conclude whether a policy is value for money using natural units, such as the number of young people at risk of using cannabis, as it is difficult to know how much money we can justify spending in achieving this outcome.

- Intermediate outcomes: the timeframe of evaluations are generally much shorter than the timeframe over which the impact of policies are felt. For instance, a drug misuse prevention programme may reduce the risk of cannabis use in the timeframe of the effectiveness study. This impact will in turn reduce the chance that the young person will experience negative health outcomes, commit crimes and be unemployed. However, this longer-term impact will not be measured in the timeframe of the effectiveness study as many public health interventions have a long payback time.
- Many public health interventions have cross sector effects where investment in one sector of the economy produces savings in other sectors.

From the analysis undertaken it is possible to make only limited recommendations regarding the cost-effectiveness of interventions to prevent or reduce drug misuse in vulnerable populations. We were unable to find conclusive evidence regarding the cost-effectiveness of the interventions because of the following issues:

- **Modelling of the long-term impacts of the interventions**: the complexity of the relationship between people's risk factors and longer-term drug misuse, the limited scope of the analysis, and the limited availability of data combined to require the modelling of longer-terms effects to make to a number of important assumptions. These are summarised in the box below. Two features of these assumptions result in uncertainty regarding the conclusions drawn by the model:
 - $\circ\;$ it is difficult to determine the combined impact of these assumptions on the outcome of the model; and
 - the sensitivity analysis suggests that relatively small changes in these assumptions will impact the conclusions drawn by the model.
- **Quality of studies:** they were not sufficiently powered as an insufficient number of participants were included in the control and intervention arms to for significant treatment effect size to be determined. Studies were largely single centre and sometimes of limited quality.
- **Generalising to the UK context** from the studies identified. Public health interventions face a number of factors that can confound the impact of the intervention. Interventions effects will vary with socio-demographic context, with programme fidelity and with the baseline characteristics of participants. It is difficult to generalise to the UK context from the specific populations and locations from the studies identified.

Assumptions that cause the models to **underestimate** the cost per QALY gained (i.e. make interventions seem more cost effective than they are)

It is assumed that the effects of the interventions on the vulnerable population risk factors identified by the effectiveness studies are maintained. As it is likely that some of these effects will not be maintained, this will overestimate the impact of the intervention and underestimate the cost per QALY gained.

Assumptions that cause the model to **overestimate** the cost per QALY gained (i.e. make interventions seem less cost effective than they are)

Only the impact of the interventions on drug use have been included in the model. Intervention impacts on educational attainment, family relationship, alcohol use, peer relationships, attitudes and other behavioural measures have not been modelled.

It is assumed that the participants in the interventions have the same baseline risk of drug use as the general population. As the risk of drug use may be higher among the participants, this assumption underestimates the impact of the intervention and thus overestimate the cost per QALY gained.

The models generally assume that individuals have the same risk of harmful consequences resulting from drug use as the general population, and that these risks are uniformly distributed in the population of drug users. It may be more likely that people from disadvantaged groups are more likely to have harmful consequences of their drug use.

Data is only available to measure and value the impact of drug use on a number of the consequences associated with it. This will cause the model to underestimate the value of the impact of the intervention and thus overestimate the cost per QALY gained. So for many people, drug use may cause family, financial, social and relationship problems that may cause a QALY loss but we have not found evidence to quantify this.

The crime costs were for possession offences only; in reality there will be an overlap between individuals arrested for possession and individuals arrested for supply offences which have a higher cost. In addition, drug users contribute to the maintenance of the drugs market so there is an argument for including the cost of possession offences.

Assumptions that cause the model to have an **indeterminate impact** on the cost per QALY gained

The analysis uses estimates of the average change in risk factors for the people in the effectiveness studies. It is not known who among the young people receiving the intervention experienced a change in these risk factors. Furthermore, it is difficult to say how an effect concentrated in the less or more at risk groups of young people would impact the longer-term benefits of the intervention.

Because people from disadvantaged backgrounds are more likely to use drugs, they may be more likely to have harmful outcomes associated with drug use, but it is difficult to unpick which outcomes are caused by drug use along, and which outcomes are caused by other types of disadvantage or other risk factors. Drug use will be associated with negative outcomes but association is not causation.

6.3 Conclusion

This modelling report has reinforced the lack of economic evidence around targeted interventions to prevent drug use in vulnerable groups. The only intervention that had a reasonable chance of being cost effective was a brief web-based intervention that had a very low cost. More long term follow up of interventions, testing lower cost interventions that use new technologies, and demonstrating the effectiveness of interventions in preventing the most harmful types of drug use, would increase the chance that future evidence reviews and models could identify cost effective interventions. The social cost of drug use is considerable so there is an opportunity for preventative interventions to be cost effective.

7. Appendix 1. Model Assumption Tables & Input Parameters for Univariate Sensitivity Analyses

These tables present the assumptions used in each of the economic models. Each of the models has a two year time horizon.

7.1 Model based on Catalano, et al. "An experimental intervention with families of substance abusers: one-year follow-up of the focus on families project."

Input/Outcome	Assumption	Data source
Target population	85,354	Based on proportion of young people aged 10-
		15 whose parents use drugs from Hidden Harm (2003).
Intervention cost	£3,367	 p. 13 of a monograph on Focus on Families said "The average cost of delivering Focus on Families was \$3,444 per client family." (Plotnick et al. 1996) The average cost was \$3,444 per family in 1996 US dollars which converts to £3,367 in 2015 GBP.
Proportion of young people aged 10-15 whose parents use drugs	2.0%	Based on data from ACMD (2003). Hidden harm: Responding to the needs of children of problem drug users. London: Home Office.
Drug use - base case model	7%	Catalano paper reports the prevalence of cannabis use among the children of drug user parents.
Drug use - maintained reduction scenario	2%,7% (intervention) and 9%,9% (control) in 6 months and 12 months follow up	The model is restricted to available data for 6 months and 12 months follow ups.
Risk of psychosis in cannabis users	0.014	Based on Hall (2015) risk of psychosis is 7 in 1000 for non cannabis users and 14 in 1000 for cannabis users.
Psychosis service costs	£13,136 per year	Based on data on prevalence of psychosis for different age groups and annual costs for non- affective psychoses from Kirkbride et al (2012)
Psychosis informal care	£4,424 per year	Based on data on average informal care costs
costs Utility scores of patients	0.68	reported by Kirkbride et al. (2012) Based on EQ-5D scores for patients with
with psychosis	0.00	schizophrenia (which were similar to SF-6D) reported in McCrone et al. (2012)
Cannabis arrest cost	£500 per cannabis offence	Based on officers' time spent on investigating cannabis cases from May et al. (2002) Sensitivity analysis was used to adjust crime

		cost to account for average yearly cost per young offender who did not receive any custodial sentence to £5,677 from National Audit Office (2011) (figure 15)
Number of cannabis offences per 1000 cannabis users in the UK	50.27	Based on data for all drug offences in England and Wales (2014-2015) and possession of cannabis offences of all police recorded drug offences from Office for National Statistics
Total social costs per user per year	£103	Summed from above
Total QALYs lost per user per year	0.0013	Summed from above

Variable description	Parameters	Low	High
Proportion of young people aged 10-15 whose parents use drugs	2.00%	1.50%	2.50%
Psychosis among regular cannabis users (assume causal relationship)	0.014	0.011	0.018
Cannabis use control (reported at 12 months)	9%	7%	11%
Cannabis use FOF intervention (reported at 12 months)	7%	5%	9%
Average cost of delivering Focus on Families per client family	£3,367	£842	£4,209
Size of client family (number of young people)	1.70	1.28	2.13
Psychosis service costs	13,136	9,852	16,420
Psychosis informal care costs	4,424	3,318	5,530
Cost of cannabis arrest	£500	£375	£625
Cannabis offences in England and Wales (2014- 2015) per 1,000 cannabis users	50.27	37.70	62.84

7.2 Model based on Lee et al. (2010) "A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial"

Input/Outcome	Assumption	Data source
Target population	66,236	Based on the proportion of cannabis users aged 17-19 with a family history of drug problems. Number of cannabis users are from Office for National Statistics Tables for drug misuse: Findings from 2014-2015 CSEW
Intervention cost	£15	We have assumed a cost of £15 per participant based on

		information provided to us about a UK-based drug treatment intervention which was more intensive than this intervention.
Proportion of cannabis users with family history of drug problem	29%	Lee paper found promising effects of intervention for those with a family history of drug problems. It is assumed that the proportion of 17-19 cannabis users with family history of drug problem is similar to the proportion in the Lee paper.
Drug use - base case model	12 days (intervention) ; 9 days (control) - Number of days with drug use in the last 3 months	Lee paper reports the number of days of drug use in the last 90 days.
Drug use - maintained reduction scenario	Number of days with drug use decreases to 7 (intervention) and increases to 12 (control) in 6 months	It is assumed that the frequency of drug use returns to baseline either in 6 months (scenario 1) or in 18 months (scenario 2).
Risk of psychosis in cannabis users	0.014	Based on Hall (2015) risk of psychosis is 7 in 1000 for non cannabis users and 14 in 1000 for cannabis users.
Psychosis service costs	£13,136 per year	Based on data on prevalence of psychosis for different age groups and annual costs for non-affective psychoses from Kirkbride et al (2012)
Psychosis informal care costs	£4,424 per year	Based on data on average informal care costs reported by Kirkbride et al. (2012)
Utility scores of patients with psychosis	0.68	Based on EQ-5D scores for patients with schizophrenia (which were similar to SF-6D) reported in McCrone et al. (2012)
Cannabis arrest cost	£500 per cannabis offence	Based on officers' time spent on investigating cannabis cases from May et al. (2002) Sensitivity analysis was used to adjust crime cost to account for average yearly cost per young offender who did not receive any custodial sentence to £5,677 from National Audit Office (2011) (figure 15)
Number of cannabis offences per 1000 cannabis users in the UK	50.27	Based on data for all drug offences in England and Wales (2014-2015) and possession of cannabis offences of all police recorded drug offences from Office for National Statistics
Total costs of cannabis road traffic accidents (Not included in base case scenario, only as a separate scenario)	£95.98 per cannabis user	Based on total cost of cannabis road traffic accidents from Bryan et al. Licensing and regulation of the cannabis market in England and Wales: Towards a cost-benefit analysis. 2013.

Total social costs per user per year	£69	Summed from above
Total QALYs lost per user per year	0.0009	Summed from above

Variable description	Parameters	Low	High
Proportion of individuals with family history of drug problems	29.30%	21.98%	36.63%
Psychosis among regular cannabis users (assume causal relationship)	0.014	0.011	0.018
Average cost of delivering web based feedback	£15	£1	£30
Reduction in use after 6 month (from baseline)	37%	28%	46%
Reduction in use after 12 month (from baseline)	25%	19%	31%
Reduction in use after 18month (from baseline)	13%	9%	16%
Psychosis service costs	13,136	9,852	16,420
Psychosis informal care costs	4,424	3,318	5,530
Cost of cannabis arrest	£500	£375	£5,677
Cannabis offences in England and Wales (2014- 2015) per 1,000 cannabis users	50.27	37.70	62.84

7.3 Model based on Prado et al. (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."

Input/Outcome	Assumption	Data source
Target population	41,029	Based on data of age and ethnicity of young people convicted of an offence from Youth Justice Statistic 2013/14
Intervention cost	£154	This intervention consisted of eight two-hour multi-parent group sessions and four one-hour family visits and seems to be with qualified counselling staff. There is a book online that quotes the cost of Familias Unidas as being around \$200 per family. If we assume this cost is for 2007 as quoted, then converted to GBP 2015 using the EPPI converter this would equate to £154.25 per family for programme costs in the UK. We have taken the cost per family to be per individual in the modelling. In sensitivity analysis this cost was varied up to an estimate of

		£238, the costs for a small school (~300 students) for one year is \$100,000 which will be \$333 per family. Assuming that this is for 2012 in the US, the equivalent for UK 2015 will be £238. However, this includes the costs of training guidance counsellors and so the cost is probably less in the following years as the training costs will be reduced if using the same counsellors (Blueprints 2016).
Proportion of delinquent youth with high parental stress	32.6%	The intervention in Prado paper is effective for 32.6% of delinquent youth who have low social support and high parental stress
Drug use - base case model	27% (intervention), 32% (control)	Prado paper reports the proportion of delinquent youth who have used drugs in the last 90 days.
Drug use - maintained reduction scenario	15%,10% (intervention) and 26%,36% (control) in 6 months and 12 months follow up	The model is restricted to available data for 1 year in scenario 1. In scenario 2 it is assumed that the proportion of drug users returns to baseline in 2 years. In scenario 3 the proportion of drug users increases to baseline for intervention group and stays constant for the control group in the second year.
Risk of psychosis in cannabis users	0.014	Based on Hall (2015) risk of psychosis is 7 in 1000 for non cannabis users and 14 in 1000 for cannabis users.
Psychosis service costs	£13,136 per year	Based on data on prevalence of psychosis for different age groups and annual costs for non-affective psychoses from Kirkbride et al (2012)
Psychosis informal care costs	£4,424 per year	Based on data on average informal care costs reported by Kirkbride et al. (2012)
Utility scores of patients with psychosis	0.68	Based on EQ-5D scores for patients with schizophrenia (which were similar to SF-6D) reported in McCrone et al. (2012)
Cannabis arrest cost	£500 per cannabis offence	Based on officers' time spent on investigating cannabis cases from May et al. (2002) Sensitivity analysis was used to adjust crime cost to account for average yearly cost per young offender who did not receive any custodial sentence to £5,677 from National Audit Office (2011)(figure 15)
Number of cannabis offences per 1000 cannabis users in the UK	50.27	Based on data for all drug offences in England and Wales (2014- 2015) and possession of cannabis offences of all police recorded drug offences from Office for National Statistics
Total costs of cannabis road traffic accidents (Not included in base case scenario, only as	£95.98 per cannabis user	Based on total cost of cannabis road traffic accidents from Bryan et al. Licensing and regulation of the cannabis market in England and Wales: Towards a cost-benefit analysis. 2013.

a separate scenario)		
Total social costs per user per year	£452	Summed from above
Total QALYs lost per user per year	0.0010	Summed from above

Variable description	Parameters	Low	High
Psychosis among regular cannabis users (assume causal relationship)	0.014	0.011	0.018
Average cost of Familias Unidas	£154	£116	£193
Average cost of community based practice (control group)	£100	£75.00	£125.00
Proportion of individuals with high parental stress using cannabis (baseline/intervention)	0.27	0.20	0.34
Proportion of individuals with high parental stress using cannabis (baseline/control)	0.32	0.24	0.40
Proportion of individuals with parental stress using cannabis (6 m follow up/intervention)	0.15	0.11	0.19
Proportion of individuals with parental stress using cannabis (6 m follow up/control)	0.26	0.20	0.33
Proportion of individuals with parental stress using cannabis (12 m follow up/intervention)	0.10	0.08	0.13
Proportion of individuals with parental stress using cannabis (12 m follow up/control)	0.36	0.27	0.45
Proportion of individuals with parental stress using cannabis (18 m follow up/intervention)	0.19	0.14	0.24
Proportion of individuals with parental stress using cannabis (18 m follow up/control)	0.34	0.26	0.43
Psychosis service costs	13136	9852	16420
Psychosis informal care costs	4424	3318	5530
Cost of cannabis arrest	500	375	5677
Total cost of cannabis road traffic accidents	£96	£0	£120
Cannabis offences in England and Wales (2014- 2015) per 1,000 cannabis users	50.27	37.70	62.84

7.4 Model based on Martin et al. (2010): "Brief intervention for regular ecstasy (MDMA) users: Pilot randomised trial of a Check-up model."

Input/Outco me	Assumption	Data source
Target	637,261	It was assumed that 5.4% of those aged 16-24 and 1.7% of those aged
-	037,201	25-59 participated in ecstasy consumption (CSEW 2014/15). Applying
population		
		these to population estimates from the ONS, gave estimates of
		400,663 users (16-24) and 237,261 users (25-59).
Intervention	£67	Based on salary costs of a mental health nurse from PSSRU, which are
cost		£67 an hour for face to face contact.
Drug use -	Interventio	Number of ecstasy pills consumed (90 days):
base case	n: 0.674 (3	Intervention: 16.48 (baseline)> 11.11 (3 months) Reduction of
model	months)	<u>32.6%.</u>
	>1.0 (12	Control: 20.14 (baseline)>20.95 (3 months) Martin et al. (2010)
	months)	
	Control: 1.0	
	(3 months)	
	> 1.0	
	(12months)	
Drug use -	Interventio	
maintained	n: Linear	
reduction	increase	
scenario	from 0.674	
	(3months) to	
	1.0 (24	
	months)	
	Control: 1.0	
	(3 months)	
	>1.0 (24	
	months)	
Ecstasy	£0.02 per	Based on an estimated 1,556 annual admissions for ecstasy poisoning
specific	tablet	out of an estimated 26m tablets consumed annually (ACPO 2008).
hospital		Assumption of 3 hour stay in the case of ecstasy poisoning, (Horyniak
(inpatient)		2013) at a cost of £124 per hour of patient contact (NHS reference
costs		costs), giving an estimate of £372 per admission or £0.02 per tablet.
Ecstasy	£0.15 per	Assumed that all inpatient admissions citing ecstasy poisoning resulted
specific	tablet	from an initial A&E admission, at a cost of £109 per A&E visit (NHS
A&E costs		reference costs). Estimated that 69% of all A&E admissions received
		ambulance conveyance (Horyniak 2013), at a cost of £216. (NHS
		reference costs)
Costs of	£0.0006 per	25 ecstasy-related deaths were observed in 2014 (ONS Statistical
Ecstasy-	tablet	Bulletin), giving a mortality rate of 1/520,000 tablets consumed. For
related	laviel	each death, an estimate of £464 was used to reflect hospital costs, as
death		
uean		reported in McDougall et al. (2002), resulting in a cost of £0.0006 per tablet consumed.
Trootmost	Arred 10	
Treatment	Aged 16-	NDTMS data, show a total of 433 people in drug treatment with a
for ecstasy	24: £0.012	primary indication of ecstasy use in England during 2014/15, consisting
dependence	per tablet	of 165 aged 9-17 years old and 268 aged 18-59 years old. Treatment
		costs from Public Health England were estimated at £2,620 per
	Aged 25-	treatment episode.
	59: £0.30	
	per tablet	

Input/Outco	Assumption	Data source
me		
QALY losses from premature death	16-24: 0.0009 per user per year 25-59: 0.0007 per user per year	Deaths were assumed to occur in the mid-point of any age group. Those aged 16-24 were expected to die aged 20, and for those aged 25-59, deaths were assumed to occur at age 42. For each group discounted values for EQ-5D population norms, as reported by Kind et al. (1996) were summed from the age of death until age 82, the expected age of an otherwise natural death. This yielded losses of 23 and 17.9 QALYs for those aged 16-24 and 25-59 respectively. If valued at £20,000 per quality-adjusted life year, these would result in estimated losses of £460,173 and £358,137 per life lost respectively.
Crime (Court appearance and sentencing) costs	£0.06 per tablet	68 persons were referred to immediate custody following ecstasy possession during 2013/14 (Advisory council on the misuse of drugs), at a cost of £8,591 per sentence (90day stay) and £14,603 per court episode (NAO), giving a combined cost of £23,194 per sentence.
Crime (Arrest) costs	£0.09 per tablet	It is estimated that just 5% of arrests for ecstasy possession result in a prison sentence (ACMD). The figure of 68 prison sentences was used to estimate a total of 1,360 arrests over the same period, at a cost 0f \pounds 1,346 per arrest, based on police time (Godfrey 2002).
Total social costs per user per year	£23.85	Summed from above
Total QALYs lost per user per year	0.00080	Summed from above

Parameter	Cost per QALY	Cost per QALY	Explanation
	(low)	(high)	
QALY loss	£129,660,232	£129,199,178	Low is assuming all deaths at 24, high is all
(16-24 years			deaths at 16
old)			
QALY loss	£129,585,088	£129,144,220	Low is assuming all deaths at 59, high is all
(25-59 years			deaths at 25
old)			
Treatment	£130,747,904	£126,840,814	Low is assuming treatment effect is halved,
effect			high is doubled (no change on effect
			sustainability.)
Effect	£130,747,904	£128,300,606	Low is assuming it takes 24 months before
sustainability			the efffects of the intervention have
			completely worn off, high is in the event that
			pre-treatment consumption is seen at 6
			months post intervention, rather than the 12
			months assumed in the base-case

7.5 Model based on Parsons, et al (2014). A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. Journal of Consulting and Clinical Psychology, 82(1), 9–18.

Input/Outcome	Assumption	Data source
Target population	12,479	Based on 10% of gay men from Buffin et al (2012), gay/bisexual men aged 18-29 based on ONS Integrated Household Survey
Intervention cost	£268	Based on salary costs of a mental health nurse from PSSRU, which are £67 an hour, or £268 for four hours.
Drug use - base case model	0.680 (intervention); 0.711 (control)	Prevalence of all drug use of which cocaine was the most prevalent drug.
Drug use - maintained reduction scenario	0.508 (intervention); 0.601 (control)	Prevalence of all drug use of which cocaine was the most prevalent drug.
Cocaine specific hospital costs	£3.95 per cocaine user per year	Based on 1624 admissions for cocaine poisoning or mental & behavioural disorders due to cocaine (each costing £1,590) divided by 726,559 cocaine users aged 18-59, assuming 80% conveyed by ambulance.
Cocaine related CVD hospital costs	£8.52 per cocaine user per year	Based on 20% of 5,067 myocardial infarction admissions in 18-44 year olds (Qureshi et al 2001 estimated 1 in 4), plus 3% of 53,355 non-myocardial infarction CVD admissions in 18-44 year olds (based on Lucena et al.)
QALY loss from risk of future cocaine dependence	7.56 QALYs per 1000 cocaine users per year	Based on risk of dependence of 1.2% per year for 18-29 year olds from Wagner et al (2002) multiplied by 10 * 0.064 QALYs lost every six month from Pyne et al (2011).
QALYs lost from cocaine related deaths	4.082 per 1000 cocaine users per year	Based on 32.3 discounted QALYs lost per death (assume age 25 on average) and 3% of CVD deaths (1586 deaths in men in 2014) aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. In reality young people may be unlikely to die from cocaine use but use may lead to deaths after age 25.
Drug treatment costs	£22.81 per user per year	Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment

		from PHE.
Crime costs	£18.10 per cocaine user per year	Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from Godfrey (2002 inflated to 2015 prices) divided by 766,402 cocaine users in England & Wales
Total social costs per cocaine user per year	£53.38	Summed from above
Total QALYs lost per cocaine user per year	0.01164	Summed from above

Variable description	Parameters	Low	High
Average drug use over 2 years in scenario 1 (intervention)	0.68	0.646	0.714
Average drug use over 2 years in scenario 1(comparator)	0.71	0.67545	0.74655
Average drug use over 2 years (intervention)	0.51	0.4826	0.5334
Average drug use over 2 years in scenario 2(comparator)	0.60	0.57095	0.63105
Intervention costs	£268	£128	£552
Costs of hospital admissions due to cocaine, per cocaine user per year	£12	£9	£16
Costs of possession arrests per cocaine user per year	£18	£14	£23
Cost of drug treatment per cocaine user per year	£23	£17	£29
QALYs lost from cocaine-specific and CVD deaths per user per year	0.003	0.002	0.003
Annual risk of becoming cocaine dependent for cocaine users aged 16-19	0.0129	0.010	0.016
Assumed QALY loss based on 5 years dependence (six month QALY loss *10 discounted)	0.58	0.43	0.72

7.6 Model based on Morgenstern et al. (2009) Randomized Trial to Reduce Club Drug Use and HIV Risk Behaviors Among Men Who Have Sex With Men.

Input/Outcome	Assumption	Data source
Target population	32,266	Based on 10% of gay men from Buffin et al (2012), gay men based on ONS Integrated Household Survey
Intervention cost	£268	Based on salary costs of a mental health nurse from PSSRU, which are £67 an hour, or £268 for four hours.

Drug use - base case model	0.683 (intervention);	Morgenstern paper reported days of drug use, which is assumed to be in
	0.837 (control)	line with prevalence. So as days of
	- average	drug use change from 17 days to 6
	drug use over	days in the intervention, prevalence is
	two years	assumed to change from 100% to
Drug use - maintained reduction scenario	0.380	65%. Morgenstern paper reported days of
Drug use - maintaineu reduction scenario	(intervention);	drug use, which is assumed to be in
	0.647 (control)	line with prevalence. So as days of
	- average	drug use change from 17 days to 6
	drug use over	days in the intervention, prevalence is
	two years	assumed to change from 100% to
	the years	65%.
Cocaine specific hospital costs	£3.95 per	Based on 1624 admissions for cocaine
	cocaine user	poisoning or mental & behavioural
	per year	disorders due to cocaine (each costing
		£1,590) divided by 726,559 cocaine
		users aged 18-59, assuming 80%
		conveyed by ambulance.
Cocaine related CVD hospital costs	£8.52 per	Based on 20% of 5,067 myocardial
	cocaine user	infarction admissions in 18-44 year
	per year	olds (Qureshi et al 2001 estimated 1 in
		4), plus 3% of 53,355 non-myocardial
		infarction CVD admissions in 18-44
		year olds (based on Lucena et al.)
QALY loss from risk of future cocaine	1.98 QALYs	Based on risk of dependence of
dependence	per 1000	0.344% for 30-40 year olds from
	users per year	Wagner et al (2002) multiplied by 10 *
		0.064 QALYs lost every six month
		from Pyne et al 2011).
QALYs lost from cocaine related deaths	2.24 QALYs	Based on 17.7 discounted QALYs lost
	per 1000	per death and 3% of CVD deaths
	users per year	(1596 dootho in mon in 2014)
		(1586 deaths in men in 2014)
		aged<45 being cocaine related , and
		aged<45 being cocaine related , and 50% of cocaine specific deaths (74
		aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to
		aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine.
Drug treatment costs	£22.81 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug
Drug treatment costs		aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug
Drug treatment costs	£22.81 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by
Drug treatment costs	£22.81 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in
Drug treatment costs	£22.81 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated
Drug treatment costs	£22.81 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment
	£22.81 per user per year	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE.
Drug treatment costs Crime costs	£22.81 per user per year £18.10 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non-
	£22.81 per user per year £18.10 per cocaine user	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non- cannabis drug possession arrests =
	£22.81 per user per year £18.10 per	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from
	£22.81 per user per year £18.10 per cocaine user	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from Godfrey (2002 inflated to 2015 prices)
	£22.81 per user per year £18.10 per cocaine user	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from Godfrey (2002 inflated to 2015 prices) divided by 766,402 cocaine users in
	£22.81 per user per year £18.10 per cocaine user	aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. Based on 10,610 people in drug treatment in England with primary drug of cocaine in 2013/14 divided by estimated 726,559 cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE. Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from Godfrey (2002 inflated to 2015 prices)

Total QALYs lost per cocaine user per	er y	year	0.004223107	Summed from above

Variable description	Parameters	Low	High
Average drug use over 2 years in scenario 1 (intervention)	0.68	0.51	0.85
Average drug use over 2 years in scenario 1(comparator)	0.84	0.63	1.05
Average drug use over 2 years in scenario 2 (intervention)	0.38	0.28	0.47
Average drug use over 2 years in scenario 2(comparator)	0.65	0.49	0.81
Intervention costs	£268	£128	£552
Costs of hospital admissions due to cocaine, per cocaine user per year	£12	£9	£16
Costs of possession arrests per cocaine user per year	£18	£14	£23
Cost of drug treatment per cocaine user per year	£23	£17	£29
QALYs lost from cocaine-specific and CVD deaths per user per year	0.002	0.002	0.003
Annual risk of becoming cocaine dependent for cocaine users aged 16-19	0.003	0.003	0.004
Assumed QALY loss based on 5 years dependence (six month QALY loss *10 discounted)	0.58	0.43	0.72

7.7 Model based on Milburn, et al, 2012. A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth. Journal of Adolescent Health, 50(4), pp.358-364.

Input/Outcome	Assumption	Data source
Target population	3,507	Based on an estimated 26% of young homeless people being drug users, from a base of 13,490 young homeless people aged 16-24 (DCLG data for England, statutory homeless cases aged 16-24 2014/15)
Intervention cost	£825	This has been costed using the hourly costings (£55 per hour) for multi systemic therapy which seems to equate reasonably well to this kind of intervention, from p.89 Unit Costs of Health and Social Care 2015, PSSRU. Based on five, two-hour sessions the cost of the intervention is £550. With an extra 50% for additional overheads and travel the cost is £825
Drug use - base case model	0.124 (intervention); 0.167 (control) - average drug use over two years	Paper reported prevalence of drug use at baseline only. Assumes that days of drug use is in line with prevalence of drug use.

Input/Outcome	Assumption	Data source
3507Drug use - maintained reduction scenario	0.053 (intervention); 0.115 (control) - average drug use over two years	Paper reported prevalence of drug use at baseline only. Assumes that days of drug use is in line with prevalence of drug use.
Cocaine specific hospital costs	£3.95 per cocaine user per year	Based on 1624 admissions for cocaine poisoning or mental & behavioural disorders due to cocaine (each costing £1,590) divided by 726,559 cocaine users aged 18-59, assuming 80% conveyed by ambulance.
Cocaine related CVD hospital costs	£8.52 per cocaine user per year	Based on 20% of 5,067 myocardial infarction admissions in 18-44 year olds (Qureshi et al 2001 estimated 1 in 4), plus 3% of 53,355 non-myocardial infarction CVD admissions in 18-44 year olds (based on Lucena et al.)
QALY loss from risk of future cocaine dependence	7.89 QALYs per 1000 users per year	Based on risk of dependence of 1.3% per year for 16-19 year olds from Wagner et al (2002) multiplied by 10 * 0.064 QALYs lost every six month from Pyne et al (2011).
QALYs lost from cocaine related deaths	2.66 QALYs per 1000 users per year	Based on 32.3 discounted QALYs lost per death and 3% of CVD deaths (2334 deaths in persons 2014) aged<45 being cocaine related , and 50% of cocaine specific deaths (74 deaths in 2014) being related to powder cocaine. In reality young people may be unlikely to die from cocaine use but use may lead to deaths after age 25.
Drug treatment costs	£5.49 per user per year	Based on 250 young people in drug treatment in England with primary drug of cocaine in 2014/15 divided by estimated 71,156 sixteen year old cocaine users in England, multiplied by estimated £1,562 per cocaine user in treatment from PHE.
Crime costs	£18.10 per cocaine user per year	Based on 22.6% of 31,915 non- cannabis drug possession arrests = 7,207, multiplied by £1,925 from Godfrey (2002 inflated to 2015 prices) divided by 766,402 cocaine users in England & Wales
Total social costs per cocaine user per year	£36.06	Summed from above
Total QALYs lost per cocaine user per year	0.01009	Summed from above

Variable description	Parameters	Low	High
Intervention costs	825	618.750	1031.250
Costs of hospital admissions due to cocaine, per cocaine user per year	12.46622411	9.350	15.583
Costs of possession arrests per cocaine user per year	18.10241576	13.58	53.6
Cost of drug treatment per cocaine user per year	9.205189688	6.904	11.506
Average QALY loss per cocaine user from risk of dependence	0.007428527	0.006	0.009
QALYs lost from cocaine-specific and CVD deaths per user per year	0.002658946	0.002	0.003
Annual risk of becoming cocaine dependent for cocaine users aged 16-19	0.0129	0.010	0.016
Average drug use over 2 years (STRIVE)	0.124285714	0.093	0.155
Average drug use over 2 years (usual care)	0.167142857	0.125	0.209
Six month quality of life loss with cocaine dependence	0.064	0.05	0.08
Assumed QALY loss based on 5 years dependence (six month QALY loss *10 discounted)	0.58	0.43	0.72

8. References

ACMD, 2008. *MDMA ('ecstasy'): A review of its harms and classification under the Misuse of Drugs Act 1971*, Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/1 19088/mdma-report.pdf.

- ACMD, 2016. *Prevention of drug and alcohol dependence*, Available at: https://www.gov.uk/government/organisations/advisory-council-on-the-misuseof-drugs/about/membership.
- ACMD (Advisory Council on the Misuse of Drugs)., 2007. *Hidden Harm Three Years On: Realities, Challenges and Opportunities.*, Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/1 19104/HiddenHarm1.pdf.
- ACMD (Advisory Council on the Misuse of Drugs)., 2003. *Hidden harm: Responding to the needs of children of problem drug users.*, Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/1 20620/hidden-harm-full.pdf.
- ACPO, 2013. Written evidence submitted to the ACMD. Association of Chief Police Officers. Available at:

http://www.publications.parliament.uk/pa/cm201314/cmselect/cmhaff/819/819we

04.htm.

Balfour, R. & Allen, J., 2014. *A Review of the Literature on Sex Workers and Social Exclusion.*, Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/3 03927/A_Review_of_the_Literature_on_sex_workers_and_social_exclusion.pdf. Blueprints, 2016. Familias Unidas. Available at:

http://www.blueprintsprograms.com/program-costs/familias-unidas.

Bourne, A. et al., 2015. Illicit drug use in sexual settings ('chemsex') and HIV/STI transmission risk behaviour among gay men in South London: findings from a qualitative study. *Sexually transmitted infections*, 91(8), pp.564–568. Available at:

http://apps.webofknowledge.com/full_record.do?product=WOS&search_mode= CitingArticles&qid=1&SID=W1HnFq71TOmNoSHorBF&page=1&doc=1&cacheu rlFromRightClick=no.

- Bramley, G. et al., 2015. *Hard Edges: Mapping severe and multiple disadvantage*, Available at: http://lankellychase.org.uk/wp-content/uploads/2015/07/Hard-Edges-Mapping-SMD-2015.pdf.
- Buffin, J. et al., 2012. *Part of the Picture: Lesbian, gay, and bisexual people's alcohol and drug use in England (2009–2011).*, Available at: http://lgbt.foundation/policyresearch/part-of-the-picture/.
- Catalano, R.F. et al., 1999. An experimental intervention with families of substance abusers: one-year follow-up of the focus on families project. *International Journal of Conflict Management*, 10(2), pp.130–153.
- CCEMG, 2015. CCEMG EPPI-Centre Cost Converter v.1.4. Available at: http://eppi.ioe.ac.uk/costconversion/Default.aspx [Accessed January 6, 2016].
- CCEMG, 2016. EPPI-Centre Cost Converter. Available at: http://eppi.ioe.ac.uk/costconversion/Default.aspx.
- Coles, B. et al., 2010. Estimating the life-time cost of NEET: 16-18 year olds not in Education, Employment or Training,

Cooper, K. et al., 2015. Psychological and psychosocial interventions for cannabis cessation in adults: a systematic review short report. *Health Technology Assessment*, 19(56), pp.1–130. Available at:

http://www.journalslibrary.nihr.ac.uk/hta/volume-19/issue-56.

Crisis, 2015. Definition and numbers: homeless across the UK. Available at: http://www.crisis.org.uk/pages/homeless-def-numbers.html [Accessed January 1, 2015].

Croft, R.J. et al., 2001. The relative contributions of ecstasy and cannabis to cognitive impairment. *Psychopharmacology*, 153(3), pp.373–379.

CSEW, 2015. Drug misuse: Findings from the 2014/15 Crime Survey for England and Wales, Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/4 62885/drug-misuse-1415.pdf.

- Curtis, L. & Burns, A., 2014. PSSRU | Unit Costs of Health and Social Care 2015. Available at: http://www.pssru.ac.uk/project-pages/unit-costs/2015/.
- Davies, C. et al., 2012. United Kingdom drug situation: annual report on the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Available at: http://www.nta.nhs.uk/uploads/2012.pdf.
- Davies, L. et al., 2009. The Drug Treatment Outcomes Research Study (DTORS): Cost effectiveness analysis. , (December), p.18.
- DCLG, 2015. Rough Sleeping Statistics England Autumn 2014 Official Statistics,

Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/4 07030/Rough_Sleeping_Statistics_England_-_Autumn_2014.pdf.

- Degenhardt, L. et al., 2013. The Global Epidemiology and Contribution of Cannabis Use and Dependence to the Global Burden of Disease: Results from the GBD 2010 Study. *PLoS ONE*, 8(10), p.e76635. Available at: http://dx.plos.org/10.1371/journal.pone.0076635.
- Delebarre, J., 2015. *NEET: Young people not in Education, Employment or Training,* Available at: http://80.75.66.219/sqa/files_ccc/David Raffe - Young People Not in Education, Employment or Training.pdf.
- Devitt, K., 2011. Young adults today: substance misuse and young adults in the criminal justice system, Available at: http://www.t2a.org.uk/wp-content/uploads/2011/09/Young-Adults-in-Focus-Substance-Misuse-Factfile-2011.pdf.
- DfE, 2015. Children looked after in England, including adoption. *Department for Education, National Statistics*. Available at: https://www.gov.uk/government/statistics/children-looked-after-in-england-including-adoption--2.
- Di Forti, M. et al., 2015. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *The Lancet Psychiatry*, 2(3), pp.233–238. Available at: http://linkinghub.elsevier.com/retrieve/pii/S2215036614001175.
- Fountain, J. & Howes, S., 2002. *Home and dry? Homelessness and substance use*, Available at: http://www.drugsandhousing.co.uk/homeanddrycrisis.pdf.
- Fuller, E. et al., 2013. Smoking, Drinking and Drug use among young people in England in 2012, Available at:

http://www.hscic.gov.uk/catalogue/PUB11334/smok-drin-drug-youn-peop-eng-2012-repo.pdf.

Gadegbeku, B., Amoros, E. & Laumon, B., 2011. Responsibility study: main illicit psychoactive substances among car drivers involved in fatal road crashes. *Annals of advances in automotive medicine / Annual Scientific Conference ... Association for the Advancement of Automotive Medicine. Association for the Advancement of Automotive Medicine. Scientific Conference*, 55(October), pp.293–300. Available at:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3256820&tool=pmcen trez&rendertype=abstract.

- Godfrey, C. et al., 2002. *The economic and social costs of Class A drug use in England and Wales*, Available at: http://webarchive.nationalarchives.gov.uk/20110218135832/rds.homeoffice.gov. uk/rds/pdfs2/hors249.pdf.
- Godfrey, C., Stewart, D. & Gossop, M., 2004. Economic analysis of costs and consequences of the treatment of drug misuse: 2-Year outcome data from the National Treatment Outcome Research Study (NTORS). *Addiction*, 99(6), pp.697–707.
- Goodwin, A., 2005. *Measuring the harm from illegal drugs : the Drug Harm Index 2005 Drug Harm Index 2005*,
- Haggerty, K.P. et al., 2008. Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment. *Addiction (Abingdon, England)*, 103(12), pp.2008–16. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2728465&tool=pmcen

trez&rendertype=abstract [Accessed December 26, 2015].

- Hall, W., 2015. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? *Addiction*, 110(1), pp.19–35. Available at: http://doi.wiley.com/10.1111/add.12703.
- Hammersley, R., Marsland, L. & Reid, M., 2003. Substance use by young offenders: the impact of the normalisation of drug use in the early years of the 21st century., Available at:

http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.470.2614&rep=rep1&t ype=pdf.

- Hartman, R.L. & Huestis, M. a., 2013. Cannabis effects on driving skills. *Clinical Chemistry*, 59(3), pp.478–492.
- Homeless link, 2015. Young and Homeless. Available at: http://www.homeless.org.uk/facts/our-research/young-and-homeless-research.

Horyniak, D. et al., 2014. Pattern and characteristics of ecstasy and related drug (ERD) presentations at two hospital emergency departments, Melbourne, Australia, 2008-2010. *Emergency medicine journal : EMJ*, 31(4), pp.317–22. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23404807.

HSCIC, 2016. Hospital episode statistics 2014/15. *Health & Social Care Information Centre*. Available at: http://www.hscic.gov.uk/.

IAPT, 2015. Estimate of prevalence of Common Mental Disorders at CCG level, Available at: https://www.england.nhs.uk/wpcontent/uploads/2014/03/prevalence-cmd.pdf.

Investing in Children, 2016. Multidimensional Treatment Foster Care. Available at: http://investinginchildren.eu/interventions/multidimensional-treatment-fostercare.

ISRCTN, 2016. An evaluation of the Chance UK mentoring programme. Available at: http://www.isrctn.com/ISRCTN47154925?q=ECHO chance uk&filters=&sort=&offset=1&totalResults=2&page=1&pageSize=10&searchType =basic-search.

Jeal, N., Salisbury, C. & Turner, K., 2008. The multiplicity and interdependency of factors influencing the health of street-based sex workers: a qualitative study. *Sexually transmitted infections*, 84(5), pp.381–5. Available at: http://sti.bmj.com/content/84/5/381.long.

Kind, P., Hardman, G. & Macran, S., 1999. *UK population norms for EQ-5D*, Available at: http://www.york.ac.uk/che/pdf/DP172.pdf.

Kirkbride, J. et al., 2012. Systematic Review of the Incidence and Prevalence of Schizophrenia and Other Psychoses in England, Available at: http://www.psychiatry.cam.ac.uk/files/2014/05/Final-report-v1.05-Jan-12.pdf.

Lee, C.M. et al., 2010. A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors*, 24(2), pp.265–73. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-77954166069&partnerID=tZOtx3y1.

Leigh, B.C. & Stall, R., 1993. Substance use and risky sexual behavior for exposure to HIV. Issues in methodology, interpretation, and prevention. *The American psychologist*, 48(10), pp.1035–45.

Lucena, J. et al., 2010. Cocaine-related sudden death: A prospective investigation in south-west Spain. *European Heart Journal*, 31(3), pp.318–329.

Maric, T. et al., 2010. Prevalence of cocaine use among patients attending the

emergency department with chest pain. *Emergency medicine journal : EMJ*, 27(7), pp.548–50.

- Martin, G. & Copeland, J., 2010. Brief intervention for regular ecstasy (MDMA) users: Pilot randomized trial of a check-up model. *Journal of Substance Use*, 15(2), pp.131–142. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-77952485836&partnerID=40&md5=a0c5c0610a0d0c8947aad937a7bf8b69.
- May, T. et al., 2002. Times they are a-changing Policing of cannabis,
- McCollister, K.E. et al., 2014. Opportunity costs and financial incentives for Hispanic youth participating in a family-based HIV and substance use preventive intervention. *Journal of Primary Prevention*, 35(1), pp.13–20.
- McManus, S. et al., 2009. Adult psychiatric morbidity in England, 2007: Results of a household survey, Available at: http://discovery.ucl.ac.uk/164862/.
- Measham F and Moore K., 2009. Weekend poly drug repertoires across the night time economy: Exploring the relationship between patterns of illicit drug use, entertainment type and venue type by customers in licensed leisure venues in an English city. *submitted*.
- Meltzer, H. et al., 2003. The mental health of young people looked after by local authorities in England,
- Milani, R. et al., 2006. MDMA in humans: factors which affect the neuropsychobiological profiles of recreational ecstasy users, the integrative role of bioenergetic stress. *Journal of psychopharmacology (Oxford, England)*, 20(2), pp.147–163.
- Milburn, N.G. et al., 2012. A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth. *Journal of Adolescent Health*, 50(4), pp.358–364. Available at: http://dx.doi.org/10.1016/j.jadohealth.2011.08.009.
- Ministry of Justice, 2015. Youth Justice Statistics 2013/14: England and Wales, Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/2 78549/youth-justice-stats-2013.pdf.

- Minstry of Justice, 2014. Costs per place and costs per prisoner National Offender Management Service Annual Report and Accounts 2013-14 Management Information Addendum Ministry of Justice Information Release, Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/3 67551/cost-per-place-and-prisoner-2013-14-summary.pdf.
- Moore, T.H.M. et al., 2006. Cannabis use and risk of psychotic or affective mental health outcomes : a systematic review. *The Lancet*, pp.319–328.
- Morgenstern, J. et al., 2009. Randomized trial to reduce club drug use and HIV risk behaviors among men who have sex with men. *Journal of consulting and clinical psychology*, 77(4), pp.645–56. Available at:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2758623&tool=pmcen trez&rendertype=abstract.

National Audit Office, 2011. The cost of a cohort of young offenders to the criminal justice system, Available at: https://www.nao.org.uk/wp-

content/uploads/2010/12/1011663_technical_paper.pdf.

- NDTMS, 2016. Value for Money tool. Available at: https://www.ndtms.net/ValueForMoney.aspx.
- NICE, 2007. Substance misuse interventions for vulnerable under 25s, Available at: https://www.nice.org.uk/guidance/ph4.
- ONS, 2015. UK Statistics Population and migration. Available at:

http://www.ons.gov.uk/ons/guide-method/compendiums/compendium-of-uk-statistics/population-and-migration/index.html [Accessed January 6, 2016].

- Parrott, A.C. et al., 2006. Dancing hot on Ecstasy: Physical activity and thermal comfort ratings are associated with the memory and other psychobiological problems reported by recreational MDMA users. *Human Psychopharmacology*, 21(5), pp.285–298.
- Parrott, A.C. et al., 2002. Ecstacy/MDMA attributed problems reported by novice, moderate and heavy recretional users. *Human Psychopharmacology*, 17(6), pp.309–312.
- Parsons, J.T. et al., 2014. A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. *Journal of consulting and clinical psychology*, 82(1), pp.9–18. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3935799&tool=pmcen trez&rendertype=abstract.
- Parsons, J.T.. et al., 2014. A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. *Journal of consulting and clinical psychology*, 82(1), pp.9–18. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3935799&tool=pmcen trez&rendertype=abstract.
- Petrosino, A. & Soydan, H., 2005. The impact of program developers as evaluators on criminal recidivism: Results from meta-analyses of experimental and quasiexperimental research. *Journal of Experimental Criminology*, 1(4), pp.435–450.
- Plotnick, R.D. et al., 1996. Benefits and Costs of a Family- Focused Methadone Treatment and Drug Abuse Prevention Program : Preliminary Findings, Available at:

https://archives.drugabuse.gov/pdf/monographs/monograph176/161-183_Plotnick.pdf.

- Prado, G. et al., 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 and Alcohol Dependence*, 125(SUPPL.1), pp.S18–S25. Available at: http://dx.doi.org/10.1016/j.drugalcdep.2012.06.011.
- Pudney, S., Bryan, M. & DelBono, E., 2013. *Licensing and regulation of the cannabis* market in England and Wales: Towards a cost-benefit analysis, Available at: https://www.iser.essex.ac.uk/d/153.
- Pyne, J.M. et al., 2011. Longitudinal association of preference-weighted healthrelated quality of life measures and substance use disorder outcomes. *Addiction*, 106(3), pp.507–515.
- Qureshi, A.I. et al., 2001. Cocaine Use and the Likelihood of Nonfatal Myocardial. *World Wide Web Internet And Web Information Systems*, (Mi), pp.502–506.
- Rees, S., 2009. *Mental ill health in the adult single homeless population: a review of the literature.*, Available at: http://www.crisis.org.uk/data/files/publications/Mental health literature review.pdf.
- Riley, S.C.E. & Hayward, E., 2004. Patterns, trends, and meanings of drug use by dance-drug users in Edinburgh, Scotland. *Drugs: Education, Prevention* {&} *Policy*, 11(3), pp.243–262. Available at:

http://ovidsp.ovid.com/ovidweb.cgi?T=JS{&}CSC=Y{&}NEWS=N{&}PAGE=fullte xt{&}D=psyc4{&}AN=2004-15730-008\nhttp://res.cisti-icist.nrc-

cnrc.gc.ca/sfxhclcl3/?sid=OVID:psycdb{&}id=pmid:{&}id=doi:10.1080/096876303 10001643111{&}issn=0968-7637{&}isbn={&}volume=11{. Rogers, G. et al., 2009. The harmful health effects of recreational ecstasy The harmful health effects of recreational ecstasy: a systematic review of observational evidence, Available at: http://www.drugsandalcohol.ie/11867/.

- Schifano, F. et al., 1998. MDMA ('ecstasy') consumption in the context of polydrug abuse: A report on 150 patients. *Drug and Alcohol Dependence*, 52(1), pp.85–90.
- de Sola Llopis, S. et al., 2008. Cognitive performance in recreational ecstasy polydrug users: a two-year follow-up study. *Journal of psychopharmacology* (*Oxford, England*), 22(5), pp.498–510.
- STRIVE, 2016a. Interviews with Developers of Evidence-Based Programs for Teen Pregnancy Prevention. Available at: http://www.hhs.gov/ash/oah/oahinitiatives/tpp_program/db/programs/webinars/strive-webinarslides.pdf.
- STRIVE, 2016b. Teen Pregnancy Prevention Evidence Review. Available at: http://tppevidencereview.aspe.hhs.gov/ProgramDetails.aspx?rid=3&sid=221.
- Transform, 2015. *Potential fiscal impacts of introducing a regulated cannabis market in the UK*, Available at: http://www.tdpf.org.uk/sites/default/files/Treasury-cannabis-regulation-CBA.pdf.
- Visit Britain, 2013. *Wish you were here: Music tourism's contribution to the UK economy.*, Available at:

http://www.ukmusic.org/assets/general/LOWRESFORHOMEPRINTING.pdf.

- Wagner, F.A. & Anthony, J.C., 2002. From first drug use to drug dependence: Developmental periods of risk for dependence upon marijuana, cocaine, and alcohol. *Neuropsychopharmacology*, 26(4), pp.479–488.
- Ward, J., Henderson, Z., & Pearson, G., 2003. One problem among many: drug use among care leavers in transition to independent living., Available at: https://lemosandcrane.co.uk/resources/Home Office - One problem among many.pdf.
- Willner, P., 2000. Further validation and development of a screening instrument for the assessment of substance misuse in adolescents. *Addiction (Abingdon, England)*, 95, pp.1691–1698.
- WSIPP, 2004. Benefits and costs of prevention and early intervention programs for youth, Available at: http://www.wsipp.wa.gov/ReportFile/881.