APPENDIX 1
REVIEW OF LITERATURE PERTINENT TO THIS REPORT

This review examines three areas concerning opioid dependence: (A) epidemiological methods for determining population prevalence of drug dependence, (B) international trends in opioid dependence prevalence and innovations for opioid substitution waitlists; and (C) the influence of the "methamphetamine epidemic" on the prevalence, presentation and treatment of opioid dependence.

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1.0 EPIDEMIOLOGICAL METHODS FOR DETERMINING POPULATION PREVALENCE OF DRUG DEPENDENCE

It has long been recognised that drug use can cause and exacerbate physical, psychological, social, and economic harm at both an individual level and a societal level. The overarching goal of the New Zealand Drug Policy is to prevent and reduce harm linked with drug use (Ministerial Committee on Drug Policy, 2007). The policy outlines a clear commitment to being evidence-based which requires careful analysis of the most up-to-date and reliable information. Knowledge of the prevalence of drug use and related problems, and how this has changed over time helps health care managers and policy makers set political agendas, allocate resources, monitor performance of services, and evaluate outcomes of preventative interventions (Hickman & Taylor, 2005; Smit, Toet, van Oers, and Wiessing, 2003). However, there is still a large degree of uncertainty around reliability and validity of the current methods that measure epidemiology particularly for illicit drug use.

1.1 Direct Methods

Direct methods such as population or general household surveys are usually considered the "gold standard" for estimating population prevalence (Hickman & Taylor, 2005). However, these direct methods are very expensive and time-consuming. In the case of substance use, they are more effective for measuring the use of some substances (e.g. nicotine and alcohol) compared with others (e.g. illicit substances; Hickman & Taylor, 2005). Direct methods are particularly unreliable for estimating injecting drug users and opioid or crack-cocaine users which is partially attributed to these types of drug users being relatively rare and difficult to reach because they are a largely "hidden" population (e.g. some do not have phones[1] or are homeless, and many are concentrated in a small geographical regions; Degenhardt, Rendle, Hall, Gilmore, & Law, 2004). Furthermore, if these illicit drug users are contacted, refusal to participate and underreporting of use and related problems is likely because of the high degree of stigmatisation and the legal implications of using drugs of these kinds in many countries (Degenhardt et al., 2004; Makkai & McAllister, 1998). Another disadvantage of these surveys is that they rarely attempt to estimate whether the individual uses opioids daily or whether the criteria of dependency is met, often only gathering information as to whether the individual has ever used the illicit drug or whether the drug was used within the last year or month (Degenhardt et al., 2004).

Smit and colleagues (2003) argue that school surveys offer a more reliable method for studying illicit drug prevalence rates in comparison to household surveys, because refusal rates upon contact are lower and during the interview disclosure rates are higher. However, school surveys are limited to the school aged population and will miss out individuals who are truant or have dropped out (Smit et al, 2003). Given that drug use and dependence tends to increase over adolescent (Boden, Fergussion, Harwood, 2006; Lynskey et al., 1999), and is associated with school non-attendance (Henry & Huizinga, 2007; Patrick & Martin, 1999) and leaving school without any qualifications (Fergussion,

[1] A recent New Zealand sample of frequent methamphetamine users recruited via the snowball technique found that 17% percent of the sample did not have connected landline telephones and thus would not have been included in the National Drug Survey sampling (Wilkinss, Reilly, Roy, Pledger, &Lee, 2004).

Horwood, Beautrais, 2003; Boden et al., 2007), these school surveys do not target those who are most likely to be heavy users or substance dependent (Degenhardt, 2004).

Therefore, direct methods (i.e. household and school surveys) are likely to underestimate the true population prevalence for many illicit drugs. For opioids and other illicit drugs direct methods typically yield estimates significantly lower that those estimated from indirect methods (e.g. Frischer et al., 2001) and sometimes produce implausible results. For example, based on the results of the British Crime Survey (n > 30 000), Aust, Sharp, and Goulden (2002) estimated that 32 000 16-59 year olds had tried heroin in Britain in the last month; however, this was lower that the number of heroin users known to present at treatment (Hickman & Taylor, 2005).

1.2 Indirect Methods

In comparison to direct methods, indirect methods are based on more objective secondary data, which typically do not constitute random samples of the target population, and are less expensive and time consuming (Kraus et al., 2003). In the context of estimating drug use, indirect methods utilise routinely collected data from data sources that the drugs users have had contact with. Potential data sources include special drug treatment (e.g. methadone maintenance), low threshold drug agencies (e.g. drop-in services), needle exchanges, laboratory, police/prison (i.e. arrests or imprisonment), probation, social service assessments, hostels for drug users, addict registers, and overdose casualties and deaths (Hickman & Taylor, 2005). The basic format of indirect methods is having information on a sample of drug users ("observed" data set) which includes some key characteristics and the number of drug users. Hickman and Taylor (2005, p.117) state that 'the aim of the indirect estimation method is to analyze the observed data set or combine it with other information to estimate the "proportion of the [problem drug use] target population sample within the observed dataset", and thereby to arrive at an estimation, some of which may be available locally or could be generated'. Indirect methods usually require using two or more data sources (where there is enough information to ascertain a match i.e. whether individuals appear in multiple data sources); or information on how one data source relates to the overall population of drug users (Hickman & Taylor, 2005).

A major disadvantage of indirect methods is that there are a number of assumptions that need to be met regarding the relationship between the observed sample/s and the target population, and violations of these assumptions reduce the reliability and validity of the estimate (Hickman & Taylor, 2005). According to Hickman and Taylor there are up to four basic assumptions that may apply to specific indirect methods: having a stable population; equal probabilities that a single individual will be observed in a given data source; matching of individual characteristics across data sources; and that appearing on one data source is independent of appearing on another.

1.2.1 Lag Distribution

Early approaches to estimation of population include that used by Hunt (1974) whom at the time offered a novel statistical approach that challenged the interpretation of routine data collections which had suggested that heroin use in the United States had peaked and was declining (Law et al., 2006). Hunt agreed that heroin use had peaked in larger cities but proposed that heroin use was still increasing in smaller cities. Hunt used data collected from treatment units to estimate the 'lag' distribution. This approach relies on a good

estimate of the number of new heroin users who had entered treatment and assumes that all new heroin users will enter treatment within 6-7 years (Law et al., 2006). This assumption is problematic because research has demonstrated that a small but significant number of heroin users will have either died or become abstinent within 6-7 years without receiving treatment for their use (e.g. Hser et al., 2001). Even heroin users who do seek treatment often do not do so within 7 years. For example, a study by Kessler and colleagues (2001) that looked at samples of substance users from United States, Canada, and Mexico showed that while most people with substance use disorders eventually seek treatment (50-85% across samples) this usually occurs at least a decade (median across the samples ranged between 10-15years) after onset of the symptoms of the disorder[2].

Hunt's (1974) analyses also assumed that the 'lag' distribution did not change over time which has since been challenged by cohort studies. For example, Kessler and colleagues (2001) research showed that lag varies by age of first use and also varies within different birth cohorts[3]. Research has shown that treatment seeking is also likely to differ between cities due to differences in local demographics, ethnicity and other social factors, and the availability of treatment services (Law et al., 2006). Despite a number of limitations Hunt's method is particularly notable for the use of what amounts to a simplified version of the analytic approach that is currently referred to as back-projection or back-calculation (see below).

1.2.2 Registers of Drug Users

An alternative method is to compile a register of known drug users, similar to that which is used to monitor diseases such as cancer (Hickman & Taylor, 2005). Even if a number of data sources were used (e.g. treatment, police and hospital records) simply counting the number of individuals who contact these services would underestimate prevalence because not all users come into contact with these services (Hickman & Taylor, 2005).

1.2.3 Back-projection

Back-projection has been used most widely to provide estimates and projections of the HIV/AIDS epidemic and has been adapted to estimate the incidence and prevalence of heroin dependence in Australia (Law, Lynskey, Ross and Hall, 2001; also see Degendart et al., 2004). In the case of heroin, this method uses estimates of the average time it takes for individuals to progress from regular heroin use to first entry treatment, and uses that information to back project the number of people who become regular heroin users in any one year (Degendarht et al.; Law et al.). The level of uncertainty (with upper and lower limits) needs to also be determined, which is the rate at which new heroin users progress to treatment. Law and colleagues based estimates of progression rates on information obtained in cohort studies and community surveys to account for individuals who never entered treatment or died before ceasing heroin use. In addition to using methadone management data, Law and colleagues used opioid overdose deaths, and conducted two separate back-calculations of the number of people who became dependent on heroin (defined as daily or nearly daily users) in any one year and obtained very similar results.

[2] Note that Kessler and colleagues (2001) also found that cocaine and heroin users are more likely to seek treatment than users of other substances with comparable symptoms.

[3] More specifically, Kessler and colleagues (2001) found that individuals who were between the ages of 30 to 54 years when they first used the drug were more likely to seek treatment and younger cohorts were more likely to seek treatment)

Their results were also similar to results obtained via multiplier methods using different data sources (Law et al.).

Back-calculation assumes that progression rates from dependence to treatment or from treatment to overdose are constant. In an attempt to assess the sensitivity of the results to this assumption, Law and colleagues (2001) performed sensitivity analyses to estimate the upper and lower limits of their estimates and these were used to reflect the level of uncertainty. However, the large range between the upper and lower limits of uncertainty indicated that their results needed to be interpreted with caution. While this technique can be useful for estimating changes in trends over time, the records (i.e. treatment and overdose) need to be complete and consistent throughout the period that is being projected back from. A further limitation is that back-calculation is less useful for detecting recent changes in heroin dependence because estimates based on this method are most uncertain in the recent past (Law et al., 2006).

1.2.4 Multiplier Method

The multiplier method (also called the ratio-estimation) is a relatively simple and commonly used method for determining the prevalence of problematic drug use. This method has been employed in a number of countries including Australia (e.g. Degenhardt et al., 2004), Russia (e.g. Hickman et al., 2006), countries within the European Union, and Norway (e.g. Kraus et al., 1999; 2003; Hickman et al., 2006). This method involves two components: a benchmark and a multiplier. The benchmark (B) is the observed number (i.e. of drug users) that have experienced a particular event (e.g. treatment, arrests, overdose/death, or HIV/AIDS). The second element is an estimation of the proportion (p) of all the target population (i.e. number of problematic drug users) that have been observed by the benchmark. The reciprocal of the proportion is the multiplier (1/p). The unknown population prevalence of the target population (N) is estimated by multiplying the benchmark by the multiplier (i.e. $N=B \times 1/p = B/p$).

In theory this method can be applied to a large variety of data sources where an estimate of the proportion of the target population observed in the benchmark (p) can be determined by either a sample of drug users or from the literature. The most common data sources include: treatment, police, mortality, and HIV/AIDS. Below is a description of how the multiplier method can be applied using each of these data sources.

1.2.4.1 Multiplier Method Based on Treatment Data

This method typically uses the total number of problematic opioid users who underwent treatment in a given time frame (benchmark) and this is divided by the estimated proportion of problematic opioid users in-treatment which is often estimated based on surveys in drug using populations. For example, a study by Hickman and colleagues (2006) assumed (based on historical multipliers) that the proportion of injecting drug users in treatment in England was 33-50% (multiplier between 2 and 3), and 10-25% in Russia (multiplier between 4 and 10). Kraus and colleagues (1999) commented on two issues which need to be considered when using treatment data. Firstly, typically not all treatment services are covered by national monitoring systems and thus the estimated number of treated individuals needs to take the estimated treatment coverage rate into account. The second issue pertains to how the in-treatment rate is estimated. Estimation techniques include snowball sampling and other nomination techniques (these are described in detail by Taylor and Griffiths, 2005). For example, Kraus and colleagues (2003) describe a

procedure whereby opioid users were interviewed and asked to 'nominate' individuals that they knew who were regular opioid users and indicate whether they had been in treatment. Then the ratio of the treated to non treated regular opioid users was used as the multiplier.

1.2.4.2 Multiplier Method Based on Police Data

Studies have incorporated data from police sources in a number of ways. For example, in a study of problem drug use prevalence in the European Union, Kraus and colleagues employed a prevalence-based and an incidence-based approach (Kraus 1999; Kraus et al., 2003). The prevalence based approach estimated the total current problematic opioid users in a given year. This was done by dividing the number of opioid users registered by the police in a year (benchmark) by the proportion of opioid users who had come into contact with the police. The incidence approach estimated the total problematic opioid users by using the number of opioid users who made contact with the police for the first time in the past ten years (benchmark). The multiplier was the number of drug-related deaths in the past ten years divided by the number of drug-related deaths in the past ten years of people previously known to the police as drug users. A weakness of police data identified by Kraus and colleagues (1999) is that many police do not differentiate between occasional and regular users which can lead to over estimation of the benchmark. Furthermore, differences in law enforcement can make comparisons across locations unreliable (Kraus and colleagues, 1999). A third weakness is that the method relies on the assumption that the probability of police contact and the probability of overdose are independent.

1.2.4.3 Multiplier Method Based on Mortality Data

Multiplier methods based on mortality data include information on both drug-related deaths and the mortality rate of drug users. Estimation of current problematic opioid users is calculated by dividing the number of registered drug-related deaths by the mortality rate of drug users (Kraus et al., 1999; 2003). Kraus and colleagues (1999) point out a number of issues which need to be considered when using mortality data including the fact that the mortality rate is not constant due to changes in circumstances (e.g. improvement of HIV/AIDS and substance dependency treatment) and thus mortality estimates need to be up-to-date and relevant to the location. Mortality rates are typically estimated based on treatment records but rates for individuals who do not receive treatment are likely to be different. Also, many mortality registers do not include forms of drug related deaths other than drug overdose (such as fatal accidents under the influence of drugs) which may lead to unreliable results. Nevertheless, some research suggests that multiplier methods based on mortality data provide the most reliable information in comparison to other data sources. For example, Hickman and colleagues (2006) found that the mortality multiplier estimates were the closest to estimates based on the capture-recapture, which they considered to be the 'preferred/ gold standard'.

1.2.4.4 Multiplier Methods Based on HIV/AIDS Data

Multiplier methods based on HIV or AIDS data, divides the number of drug users that are HIV/AIDS positive by the proportion of drug users who have HIV/AIDS in order to estimate the prevalence of lifetime drug users (Kraus et al., 2002). Because the number of HIV positive drug users is not known in many countries it is often estimated using back-calculation techniques (Kraus et al., 2003).

1.2.4.5 Strengths and Limitations of the Multiplier Method

The strength of this technique is its simplicity and ability to be applied to recent data. The weaknesses of this method include the difficulty to which the accuracy of the estimation can be verified (Law et al., 2006). It is critical that the sample used to estimate the multiplier is representative of the overall population of drug users. A number of methods have been derived which attempt to approximate a random sample in order to estimate the multiplier. These methods include site sampling (sampling at representative geographical sites), 'community sampling' (which include chain referral or snowball techniques, and other nomination techniques that aim to gather a representative sample of all drug users; Hickman & Taylor, 2005; Taylor and Griffiths, 2005). Nevertheless, it is difficult to verify how representative the sample is, which is complicated further by knowing that multipliers can vary over time and location (Law et al., 2006). Furthermore, the definition of the benchmark needs to be specific and it needs to be the parallel of that used for estimating the multiplier. For example, if arrests are used for the benchmark then the multiplier needs to be the proportion of target population (i.e. drugs users) arrested rather than those charged or sentenced (Hickman and Taylor, 2005). The population of drug users also needs to be stable and the same during both the benchmark observation and during the multiplier estimation (Hickman and Taylor, 2005). Furthermore, the accuracy of the benchmark (e.g. the number of arrests) depends of on the accuracy of recording practices which can also vary across time and location, which along with inaccuracies in the multiplier; make the multiplier method susceptible to systematic bias.

The aforementioned limitations notwithstanding, multiplier estimates (especially those based on mortality and treatment data) have produced results consistent with other analytical approaches (such as capture-recapture), which supports its validity (Degenhardt et al., 2004). The multiplier method has the advantage that it is able to reflect the immediacy of the data on which it is based. For example, a recent study conducted by Degenhardt and colleagues (2004) used multiple analytic methods and data sources to make annual estimates of the active, regular heroin users after a marked reduction in heroin supply. Their analyses consisted of multiplier methods (data sources consisted of opioid overdose fatalities, entrants to opioid pharmacotherapy, arrests and ambulance callouts suspected to be overdosed), capture-recapture (data sources consisted of methadone and police arrests), and back-calculation (data sources consisted of fatal opioid overdose and treatment). They found that in periods where there are dramatic and sudden changes to the supply of heroin that multiplier methods were best suited to estimate the population during these periods because of their relatively straightforward use of the sources of data and ability to capture changes in the short-term. Whereas, capture-recapture methods require information over a longer window period, tending to "average" changes across time, and therefore making this method less sensitive to recent changes. While back-calculating was found to be more sensitive to changes across time it was limited in its ability to model changes that had occurred most recently.

1.2.4.6 Enhanced/event-based Multipliers

Simeone and colleagues (1997) piloted a modified multiplier method for estimating the number of "hardcore" drug users in the United States. Instead of basing their estimate on a single data source they used multiple data sources (booking facilities, drug treatment programmes, and residential homeless shelters) to generate the rate at which "hardcore" drug users made contact with these services, and the total use of contacts. In essence the total number of contacts was divided by the estimated rate of contact to give an estimate of the size of the "hardcore" drug using population. The use of multiple data sources theoretically accounts for the inherent biases in any one data source (Hickman and Taylor,

2005) and this method offers a feasible and alternative approach that requires continued investigation and validation (Simeone et al., 1997).

1.2.5 Multivariate Indicator Method

In contrast to the multiplier method, the multivariate indicator method (also referred to as the multiple indicator, or synthetic estimation) involves a more complicated statistical procedure and has been proposed to provide a more valid way of estimating the prevalence of drug use (Frischer et al., 2003). It has been used to estimate the prevalence of drug use in a number of countries including the United States, France, Italy, UK (e.g. Kraus et al., 1999; 2003; Frischer et al., 2001), and the Netherlands (Smit et al., 2003). It is a method which uses several variables that are associated with drug use (drug related indicators) in areas where the prevalence has already been estimated (called the anchor points or calibration samples) to predict the prevalence in other areas that have the same drug-related indicators (Frischer et al; Kraus., 1999; 2003). The functional relationship between the drug-related indicators and the prevalence in the anchor points is determined and is used to estimate the prevalence in the target populations. For example, Frischer et al., (2001; also described in Kraus et al., 2002) used the multivariate indicator method to estimate the prevalence of problematic drug use in the United Kingdom. They combined information on drug-related indicators (convictions for drug offences, people in treatment for drug misuse, HIV related to IDU, and drug related deaths) that were available in all regions in the United Kingdom with the prevalence of problematic drug use which was available in North Thames, West Midlands, Wales, and Strathclyde (anchor points). A single latent variable which was assumed to underlie all drug-related indicators was determined via principal component analyses. The following steps were taken: indicator values were standardised and least square regression was employed to determine the relationship between the values of the main factor (which explains most of the variation in the original variables and the anchors). Prevalence of problematic drug use in regions where only drug-related indicators were available was then estimated via linear regression. Lastly, the total prevalence for the United Kingdom was estimated by summing together all of the regions.

Smit and colleagues (2003) investigated the use of the multivariate indicator method for estimating population prevalence of problem drug use in the Netherlands. They came across a number of practical obstacles which included having to use demographic indicators (e.g. population density and housing density) because of a lack of drug-related indicators across regions. They also found that their principal component analysis resulted in the extraction of a single component which was not as helpful for estimating prevalence as a regression model based on two factors. Nevertheless, Smit and colleagues were able to obtain new estimates for previously understudied regions and generate a national estimate by employing this technique. Even with their adaptation they found that the estimate of national prevalence based on the multivariate indicator method was very similar to a treatment multiplier estimate which provides some validity for the use of multivariate indicators methods and related regression imputation techniques.

The assumed linear relationship between the unknown prevalence and the known indicators has been criticised (Kraus et al., 2003). For example, it is assumed that the number of drug users in treatment has a linear relationship with the prevalence of drug use in the population but in practice the number of individuals in treatment is restricted by the capacity and availability of services, and this is likely to vary across regions within a nation. Furthermore, the reliability and validity of this method depends on the reliability and validity

of the anchor points which can make the national estimate difficult to evaluate. Ideally the anchor points are obtained through a variety of techniques (Kraus et al., 2003).

1.2.6 Capture-recapture

Capture-recapture is a method that has been used for over a century to estimate the size of populations of fish and other wild animals (Kraus et al., 2003; Dengerhardt et al., 2004). Even though this method has only relatively recently been used for the estimation of drug use it has become very widespread (Law et al., 2006) and has been used in a number of countries such as Russia (e.g. Hickman et al., 2006), Australia (e.g. Degenhardt et al., 2004) and a number of countries in the European Union (e.g. Kraus et al., 1999; 2003) including England (e.g. Hickman et al., 2006). This method requires at least two samples of the population of interest. As the name suggests in order to estimate the size of the population of wild animals, a random sample of that animal is captured, tagged and released. Later a second random sample is captured and the number of already tagged animals is identified (i.e. recapture). The ratio of animals already tagged to the second sample size is assumed to be the same as the ratio of first sample to the total population (Stimson, Hickman, Quirk, Frischer, Taylor, 1996).

In the drug field, the capture-recapture method randomly selects at least two samples of drug users, each sample must contain enough information so that individuals that occur in multiple samples can be identified as a match (Hickman & Taylor, 2005; Kraus et al, 1999; 2003). Also, the capture period must be long enough to allow for all the drug users in the first sample to be released (as may occur for arrest and treatment sampling) and be given enough time to be recaptured. However, longer capture periods increase the analysis period, which in turn reduces the ability to detect rapid changes in the sample (Dengerhardt et al., 2004). Capture-recapture methods usually involve sampling from multiple data sources but it is possible to use a single data source (e.g., McKeganey, Barnard, Leyland, Coote, & Follet, 1992). The use of a single data source is rare because it is very hard to find a single data source that is representative of the target population (Hickman & Taylor, 2005).

Assumptions of the capture-recapture method include (Stimson et al., 1996): (1) samples are representative of the population and the population is closed (i.e. individuals do not enter or leave the population during the study period). (2) Homogeneous samples (probability of selection is constant for all individuals). (3) Samples are mutually independent (i.e. being captured should not affect an individuals chances of being recaptured). Consequences of violating these assumptions are outlined in detail by Stimson and colleagues (1997). Population heterogeneity, for example, has been shown to underestimate prevalence rates; however, this can be avoided or limited by stratifying the data into more homogeneous subsets. To overcome violations that result in severe biases in a two-sample model such as the causal relationship (i.e. lack of independence) between samples, more sophisticated models have been developed which involve three or more data sets and are analysed using log-linear modelling with dependencies/interactions between data sources to generate an adjusted prevalence estimate (Hickman & Taylor, 2005).

The strengths of capture-recapture models are that they are a relatively simple application using available data sources, where the estimate is based on data and does not rely on parameters derived from other sources, as is the case for the multiplier method or rates of progression as is needed for back-projection estimates (Kraus et al., 2003). Research has suggested that the capture-recapture method (with three or more data sets) is more

suitable for estimating prevalence of drug users in cities rather than for nations. For example, in the United Kingdom the capture-recapture method has become the pre-eminent method for estimating prevalence in UK cities but because of regional heterogeneity within lists this method was found to be problematic for estimating the prevalence of drug injecting users for the UK as a whole (Frisher et al., 2001).

1.2.7 Truncated Poisson

Truncated poisson methods use information about repeat events (i.e. number of times a drug user has contact with a service) within an observation period to estimate the population with no events (i.e. no contact with a service). There are many assumptions that need to be considered when applying the truncated poisson method, which include a 'closed' and homogeneous population, individuals must be able to be uniquely identified as a match, and probability that an individual will be observed and then re-observed will remain constant over time (Hay and Smith, 2003). Hickman and Taylor (2005) point out that several of the assumptions of this model limit its use, and in particular the assumption that repeat events are independent which in this instance means that a drug user who has been arrested is as likely to be arrested again as a drug user who has not been arrested before. Also, like mentioned above for capture-recapture methods using a single data source, it is very hard to get one data source which is representative of all problem drug users, and Hickman and Taylor (2005) state that criminal justice and specialist treatment data would not be sufficient.

Nevertheless, a study conducted by Hay and Smith (2003) illustrates how the truncated poisson method can be calculated and be used to estimate drug injecting populations, and how some of its underlying assumptions can be checked. Hay and Smith used data from a needle exchange to estimate the size of the population of drug injectors (N) based on a following formula proposed by Zelterman (1988): $N = S / [1 - \exp(-2f_2 / f_1)]$; where f_1 equals the number who had only visited the needle exchange once, f_2 equals the number who had only visited the needle exchange twice, S is the total number of clients, and exp is the exponential. They estimated that the total number of drug injectors was 1041 (95% confidence interval of 960-1137) and this estimate was based on the information of 647 individuals that attended the needle exchange (175 attended once and 85 attended twice) in 1997. Hay and Smith (2003, p. 235) argue that "the truncated Poisson estimator can be an easy and quick method of providing a prevalence estimate of drug injecting and may produce valid estimates of relative changes in prevalence rates over time". Clearly this method warrants further research into its application (i.e. could be used on other sources of data like opioid substitution treatment) and validity which could be achieved by comparing it to other estimation methods.

1.3 Data Sources and Data Collection

Each data source is also subject to a number of limitations when it is applied for the purpose of estimating prevalence. For example, the following weaknesses for each of the following data sources were outlined by Law (2006, p 156):

Fatal opioid overdose data

- Changes in coding causes of death over time
- Delays in reporting data, leading to unavailability of data in most recent time periods

Pharmacotherapy maintenance treatment

- Entry may depend on treatment availability and palatability in an area rather than demand
- Treatment option increases with introduction of buprenorphine in addition to methadone in 2001 (in Australia), and with increased treatment places from this time

Heroin arrests

- Uncertain levels of data duplication
- Number of arrests for heroin offences may reflect short-term policing objectives at certain periods

Ambulance callouts at suspected drug overdoses

- Uncertain levels of data duplication
- Naloxone may be administered for non-opioid drugs

Given the numerous limitations to the sources of data to which analytic methods are then applied, an important aspect to improving estimates on the prevalence of drug users relies on improving routine data collections and record keeping, and for this to be done in a way that has prevalence estimation as one of its goals (Hickman & Taylor, 2005). Kraus and colleagues (1999; 2003) used the same methodology (i.e. same data source and same analytical approach) with the aim of improving the comparability of prevalence estimates between countries in the European Union. However, they found that differences in national collection procedures, case definitions, and availability of this data limited the comparability. Kraus and colleagues found that even a theoretically simple task of recording drug-related deaths or treatment was confounded by differences in definitions, laws, and reporting regulations. Furthermore, these variables (e.g. definitions and laws) can vary over time within a region/country as well as between countries. Thus, even when using the same method and the same data source, differences in data collection can confound prevalence estimates.

An additional limitation is that data sources often do not allow for a definition of harmful use or dependence according to international classification criterion, such as the DSM-IV or ICD-10 (Kraus et al., 2003). For example, police data may record individuals who have been caught for possession of illegal drugs but we cannot assume that all offenders are substance dependent and equally police often do not have the means to investigate an individual's behaviours and experiences related to drug use needed to constitute a diagnosis, nor are many offenders willing to reveal that information to the police. Thus, often alternative definitions are employed such as injecting drug use or regular user of opioids (Kraus et al.). This means that the generalisability of prevalence studies needs to be done cautiously, and the comparability of the results needs to be considered in terms of the target population (Kraus et al.).

1.4 Summary

Household surveys and other direct methods have been criticised as being unreliable for the estimation of the prevalence of illicit drug use. As a result a variety of analytical methods have been developed which can utilise routinely collected data from a number of sources (such as treatment, police, mortality, and HIV data) to indirectly estimate the prevalence of illicit drug use. Indirect methods include back-projection, multiplier methods, multivariate indicator methods, capture-recapture, and the truncated Poisson methods. However, each data source is subject to a number of limitations and analytical methods rely on a number of assumptions which are often related to a large amount of uncertainty.

Thus, “it is being increasingly recognised that there simply is not a single data source or analytical method which will give you the best estimate in areas of such great uncertainty like illicit drug use” (Law et al., 2006, p. 156). In the absence of a ‘gold standard’ for estimating the prevalence of illicit drug users, applying different analytical methods to a variety of data sources and providing a honest assessment of the uncertainties involved is considered the best approach. Then the multiple estimates need to be examined in order to determine the level of convergence between estimates, where higher convergence is indicative of more robust results (Degerhardt et al., 2004; Law et al., 2006).

2.0 INTERNATIONAL TRENDS IN OPIOID DEPENDENCE PREVALENCE

The terms *opiates* and *opioids* are not infrequently used interchangeably in the literature to refer to drugs which are derived from opium. Some authors reserve the term *opioids* to refer to endogenous chemicals, a class of peptides secreted by the brain that act like on opioid receptors Carlson (2001, p 125), and use the term *opiates* to refer to opium based drugs themselves (Carlson, 2001) such as morphine, codeine, opium, heroin and a wide range of pharmaceutical drugs such as methadone and buprenorphine" (National Drug Policy, 2007). Other authors use the term opioids more broadly as an overarching term to refer to any substance, endogenous or exogenous that acts on opioid receptors (eg Young et al 2002), reserving the term opiate to refer to any naturally occurring exogenous opioid. This latter use of the terms is how they are used in this report.

These drugs are used because of their ability to reduce pain (analgesic properties) and increase feelings of euphoria. Opioids have a number of personal and financial costs (Carlson, 2001). Firstly, the illegal nature of most of these drugs, which by definition makes those who use them criminals. Secondly, neurotransmitter adaptation to opioids occurs very rapidly which means that people need to use more and more to achieve the same high, and often people turn to crime to support their opioid use (Adamson & Sellman, 1998). Thirdly, the majority of people who use opioids inject them and because such equipment needed for injecting is not always sterile there is a high risk of developing infections and contracting diseases such as hepatitis C and HIV. Fourth, because opioids easily cross the placental wall, babies are often born physiologically dependent on opioids if their mother has used opioids during her pregnancy. Another important concern relevant to non-pharmaceutical opioid use is that the strength and purity of different 'batches' varies, and unusually strong batches or those diluted with dangerous ingredients can lead to fatal overdoses (Carlson, 2001).

It is important to acknowledge that not all those who use opioids become dependent but research suggests that the type of person who is likely to take the risk and seek out opportunities to use opioids, combined with the quick development of tolerance and physical dependence characteristic of opioids, increases the likelihood that an individual will develop opioid dependence (Schuckit 1995; Sellman, 1996). Unfortunately, the majority of the epidemiological research in both New Zealand and internationally typically estimate the proportion of individuals who have tried opioids either within their lifetime, or during the last year or month. This means that less is known about the frequency of use and the prevalence of opioid abuse or dependence. Furthermore, most of the estimations are based on population surveys which are likely to underestimate the prevalence of opioid use.

2.1 Worldwide

According to the 2007 World Drug Report (United Nations Office on Drugs and Crime [UNODC], 2007) opioids continue to be a primary problem drug worldwide. The annual prevalence of opioid use[4] in 2005 was estimated as being 0.4% (71% of whom primarily use heroin) of the world's population between the ages of 15 and 64 (UNODC, 2007) and

[4] The 2007 World Drug Report uses the term *abuse*; however, this does not appear to refer to substance abuse as defined by the DSM-IV (American Psychiatric Association, 2000) or ICD-10 rather it appears to be a term used to describe those who use substances.

this has remained stable since 2000/2001 but represents an increase from the 1990s. The annual prevalence of opioid use rose during the 1990s, estimated at 0.1% in the early 1990s (United Nations International Drug Control Programme, 1997) and 0.3% in the late 1990s (United Nations Office for Drug Control and Crime Prevention, 2002).

2.1.1 Asia

According to the 2007 World Drug Report (UNODC, 2007) more than half of the world's opioid abusing population live in Asia and opioids account for two-thirds of the treatment demand in Asia. Even so, the prevalence of opioid use in 2005 was estimated to be 0.3% of the population in Asia which was around the global average (UNODC, 2007). In 2005, China, Malaysia and Vietnam ranked heroin as the number one problematic drug of abuse and Myanmar ranked opium as number one problematic drug of abuse[5] (UNODC, 2006b).

Opioid use in Asia followed the global trend from 1992 but by 2004 it was clearly increasing at a significantly higher rate (UNODC, 2006a). The rise in opioid use in Asia primarily reflects the increase in opioid use in countries close to Afghanistan which is the country with the highest source of illicit opium in the world[6] (UNODC, 2007). Afghanistan has seen continued increase of production since the 2001 overthrow of Taliban rule (Chossudovosky, 2005; Jelsma, Kramer, River, 2006)

2.1.2 Africa

The 2007 World Drug Report indicated that prevalence of opioid use in Africa was 0.2% which was below the global average. However, this represents an increase of opioid use in the African states between 1992 and 2004 which was marginally larger than the global trend (UNODC, 2006a). A study by Parry, Plüddemann, and Myers (2001) analysed data from 41 specialist alcohol and drug services in Cape Town and Gauteng Province in South Africa between 1997 and 2003. They found that the proportion of individuals treated for heroin related problems has increased significantly from 0.7% in the first half of 1997 to 7.1% in the second half of 2003. These analyses also indicated that most heroin users in treatment were most likely to be European, male, between the ages of 21 and 24 and tend to smoke rather than inject the substance. However, the percentage of injecting as the primary route of administration tended to increase over the time period, particularly in Gauteng. Even though Parry and colleagues suggest that these results indicate a substantial increase in heroin use over time, it is also likely that this increase is influenced by other factors such as the availability of opioid substitution treatment.

[5] The UNDOC (2006b) report was based on information submitted by drug abuse control officials and other institutions and agencies in Australia, Brunei, Cambodia, China, Indonesia, Japan, Lao PDR, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Viet Nam.

[6] The World Drug Report (UNODC, 2006a) indicated that there are currently three distinct production centres which supply three distinct markets. The identified routes are: (1) from Afghanistan to neighbouring countries, the Middle East, and Europe; (2) from Myanmar/Laos to neighbouring countries of South-East Asia, (notably China) and to the Oceania region (mainly Australia); (3) from Latin America (Mexico, Colombia and Peru) to North America (notably USA).

2.1.3 Americas

The 2007 World Drug Report indicated that 0.4% of individuals in the Americas (0.5% in North America and 0.3% in South America) used opioids. This represented a sharp decline since 2000/2001 (UNODC, 2007).

2.1.3.1 United States of America

Consistent with the UNODC (2007) other studies indicated a stable or declining trend in the United States while non-medical use of opioid based pain relievers may have increased since the late 1990s (e.g. Newmeyer, 2003; Substance Abuse and Mental Health Services Administration [SAMHSA], 2002, 2006a & 2006b).

Newmeyer (2003) conducted a comprehensive review of indicators of illicit substance use (e.g. emergency department, treatment, and police data) in the San Francisco Bay Area between 1996 and 2002. Newmeyer found that heroin indicators consistently show a peak in 1999 followed by a significant decline and the street price of heroin rose in 2001. Ethnographic observers and emergency department data alluded to a strong increase in the use of oxycodone. However, data based on medical examinations revealed no discernable trends between 1996 and 2000 (Newmeyer, 2003).

The annual United States national survey on drug use and health[7] found that the percentage of individuals estimated to have used heroin in their lifetime, in the past year, and in the past month was not significantly different in 2005 compared with the previous three years (SAMHSA, 2006a) and are very similar to those reported in 2001 (SAMHSA, 2002).

Table 1 displays the prevalence rates for 2001 and 2005. The percentage of lifetime non-medical use of pain relievers was estimated at 13.4% in 2005 which was a significant increase since 2002 (12.6%), and 2001 (9.8%) (SAMHSA, 2002). Non-medical use of pain relievers within the past year and in the past month was estimated as not being significantly different in 2005 compared with the three years prior (SAMHSA, 2006a) but both had increased since 2001. Across the years surveyed, past month opioid use peaked in the 18-25 age group, with this also being the only age group to register a significant increase in prevalence across the reporting period.

[7] This survey is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) and surveys civilian, noninstitutionalised population of the United States aged 12 years old or older, and interviews approximately 67,500 persons each year.

Table 1:

Comparison of prevalence of opioid use based on the most recent household surveys (and in 2001) in New Zealand, Australia, Unites States of America, and Britain[8].

	New Zealand	**Australia**	**United States of America**	**Britain[9]**
Author (year)	Wilkins et al., (2002)	AIHW (2005)	SAMHSA (2006a)	Roe & Man (2006)
Year of estimate	2001	2004 (2001)	2005 (2001)	2005/2006 (2001)
Age range of sample	15-45	14+	12+	16-59
Current/ Past Month				
Any Opioids	0.6	0.1		0.1 (0.1)
Heroin	0.03		0.1 (0.1)	0.1 (0.1)
Other Opioids	0.3= homebake; 0.06= morphine; 0.1= poppies; 0.1= other opioids		1.9= pain relievers (1.6)	0.1= methadone (0.1)
Past year use				
Any Opioids	1.0	0.3 (0.5)		0.1 (0.2)
Heroin	0.03	0.2 (0.2)	0.2 (0.2)	0.1 (0.1)
Other Opioids	0.5= homebake; 0.2= morphine; 0.3= poppies; 0.3= other opioids	0.1= methadone (0.1); 0.2=other opioids (0.3)	4.9= pain relievers (3.7)	0.1= methadone (0.1)
Lifetime use				
Any Opioids	4.3	2.3		0.9 (0.7)
Heroin	0.7	1.4	1.5 (1.4)	0.6 (0.6)
Other Opioids	1.5= homebake; 1.0= morphine; 2.4= poppies; 1.0= other opioids	0.3= methadone; 1.4=other opioids	13.4= pain relievers (9.8)	0.5= methadone (0.4)

It was estimated that 0.1% of the US population aged 12+ met the DSM-IV criteria for heroin dependence or abuse in the past year for each of the years between 2002 and 2005 (SAMSHSA, 2006a). In regards to non-medical use of pain relievers, 0.6% were estimated to met the criteria for substance dependence or abuse for each of the years between 2002 to 2005 (SAMSHSA, 2006a).

Analyses of substance treatment episode data[10] in the United States of America (SAMHSA, 2006b) indicated that heroin (as the primary substance) admissions had been fairly stable between 1995 and 2005, accounting for 14% at each of those times and peaked at 16% in 2000[11]. For opioids other than heroin (as primary substance) the

[8] So that the estimates are more comparable to the most recent estimate in New Zealand which was in 2001, the 2001 estimates for other countries are also listed in the addition to the most recent estimate for that country.

[9] For this British survey any opioids includes the use of heroin and/or methadone but does not include other types of opioids.

[10] Note their analyses only included those admissions to facilities that are licensed or certified by the state.

[11] In 2005, two-thirds of clients for which heroin was the primary substance were male, 50% were non-Hispanic White, 24% Hispanic, and 23% non-Hispanic Black. Average age was 36 years. 63% reported that that their primary route of heroin administration was injecting, 33% inhalation, 2% smoking (SAMHSA, 2006b).

percentage of all admissions increased from 1% to 4% from 1995-2005[12](SAMHSA, 2006b).

2.1.4 Europe

In the 2007 World Drug Report, Europe was the only major region[13] that was above the global average of 0.4%, with 0.7% of individuals in Europe being estimated to use opioids (UNODC, 2007). This prevalence rate was pushed up by the prevalence in Eastern Europe which was estimated at 1.6% (compared with 0.5% in Central and Western Europe, and 0.2% in South-East of Europe). Between 1992 and 2002 there has been a stable to declining trend in opioid abuse in West and Central Europe but there have been rising levels in the east (UNODC 2006a). Also, in Europe opioids account for over half of the treatment demand (UNODC, 2006a).

In regards to specific countries within the European Union a study by Kraus and colleagues (2003) reported national prevalence rates based on multiple indirect methods and multiple data sources[14]. Kraus and colleagues found that problem opioid use varied from 0.3% of the population (between 15-64 years of age) in Austria, Germany[15], Ireland, and the Netherlands; to 0.6% in the United Kingdom; 0.7% in Spain; estimates of 0.7% and 0.8% in Italy[16]; and estimates between 0.7% and 0.9% in Luxemburg. Analyses of past year injecting drug prevalence produced estimates of 0.2% and 0.3% for Ireland; 0.3% for Austria, Finland, Germany, and Spain; 0.4% for Denmark, Norway, Portugal, and the United Kingdom; and estimates of 0.5% and 0.8% for Luxemburg (Kraus and colleagues, 2003).

2.1.4.1 Britain

The 2005/2006 and the 2001 prevalence estimates from the National British Crime Survey (Roe & Man, 2006) are summarised in Table 1. The proportion of 16 to 59 year olds estimated to have used opioids (heroin and/or methadone) and specifically heroin, in the last year has been stable over the 1998 - 2005/2006 period[17]. The prevalence rates for overall use of opioids (both methadone and heroin in the last year for individuals aged between 16 and 24 years of age has decreased significantly between 1998 and 2005/2006, from 0.8% to 0.2%. This was primarily attributable to the decrease in the use

[12] In 2005, of the group admitted for opioids other than heroin, 54% were male, 89% were non-Hispanic white, and the average age was 33 years old. Most people for which non-heroin was their primary substance reported administrating it orally (72%), 13% inhalation, 12% by injection (SAMHSA, 2006b).

[13] Other major regions consisted of the Americas, Asia, Oceania, and Africa.

[14] "Data were generally selected on a 12 month basis. In the case of injecting we distinguished between current (12 months) and lifetime events. Not so clear, however, are the time definitions of the respective multipliers. The time frame depends very much on the methods used and may vary between estimates." (L. Kraus, personal communication, September 7, 2007).

[15] An earlier study which estimated of the prevalence of problem opioid use in Germany based on the multiplier method using three different types of data (treatment, police, and mortality) suggested that the numbers of problem opioid users has increased between 1990, 1995 and 2000 (Augustin & Kraus, 2004). For example, estimates based on mortality multiplier (1.5-2 was the multiplier) estimated the current injecting drug population during 1990 was between 71 000 and 94 600, between 78 300 and 104 3000 in 1995, and between 101 500 and 135 300 in 2000.

[16] Similarly, another study looking at Italian 18 year old males found that 0.8% had used heroin in their lifetime. This study consisted of a sample (*n*=3169) of men 18-year old when they attended the compulsory conscription medical examination which all 18 year Italian men have to undergo (Siliquini et al., 2001).

[17] It must be noted that the authors suggested prevalence rates and changes need to be interpreted with care because prevalence figures for rare activities such as taking opioids are subject to big percentage change swings from year to year (Roe & Man, 2006).

of methadone from 0.6% in 1998 to 0.1% in 2005/2006[18] for that age bracket. Those aged between 25 and 29 years reported the highest lifetime use of opioids of 1.9% in 2005/2006. Roe and Man also found that while a higher proportion of men used opioids, this gender imbalance was reduced amongst younger age groups. That is, a similar proportion of males and females between the age of 16 and 24 years old reported using opioids in their lifetime (0.8 and 0.7, respectively), while for those aged between 16-59 years old the proportion of men was twice that of women (1.2 compared with 0.6).

A study by Hay and colleagues (2006) used capture-recapture methods, the multiple indicator method, and four data sources (drug treatment, probation, police and prison) to estimate national prevalence of opioid use, yielding results similar to Roe and Man (2006). Their national estimate of the prevalence of opioid use (2004/05) was 8.53 per 1000 (95% confidence intervals between 8.48-8.88) 15 – 64 year old individuals. Hay and colleagues also found that opioid use was most common in men and those aged between 25 and 35 years. Specifically, they found that approximately a quarter of those who had used opioids were female, and that 21% of individuals who used opioids were between the age of 15-24, 44% between 25-34, and 35% between 35-65 years old.

2.1.5 Oceania

The 2007 World Drug Report (UNODC, 2007) suggested that in Oceania there was a strong increase in opioid use over the 1990's but the trend has declined since 2000.

2.1.5.1 Australia

Law and colleagues (2001) used back calculation methods to estimate the number of total opioid dependent users and the number of current dependent users between 1960 and 1997 in Australia. These estimates were based on data from overdose deaths and new entrants into methadone treatment in New South Wales. Both of these analyses indicated that the number of opioid dependent individuals was very low before the 1970s and substantially increased from the 1970s onwards. Between 1960 and 1997 it was estimated 104 000 (lower limit of 72 000 and upper limit of 157 000) and 108 000 (82 000 -141 000) were dependent on opioids based on estimates derived from overdose deaths and new entrants in methadone treatment, respectively. In 1997, 67 000 (39 000 -120 000) were estimated to still be dependent on opioids based on the overdose deaths and 71 000 (47 000 – 109 000) based on new entrants into methadone treatment. Similar estimates were obtained by another study that estimated the prevalence of heroin dependent Australians (1997-1998) which used multiple methods (back-calculation, capture-recapture, and multiple) and multiple data sources (overdose, treatment, arrests; Hall, Ross, Lynskey, Law, & Degenhardt, 2000). Hall and colleagues yielded a median estimate of 74 000 (range 67 000- 92 000;) which was equivalent to 6.9 per 1000 adults (age 15-54) and was similar to estimates in Britain and European Union.

[18] Use of drugs in the last year is considered by Roe and Man (2006) as the best indicator available to measure trends in recent drug use because lifetime use tells little about recent use, and use within the last month is less reliable due to smaller number of users. Nevertheless they reported the following trends: prevalence of lifetime overall opioid use for individuals aged between 16 and 24 years of age has decreased significantly between 1998 and 2005/2006 from 1.7% to 0.8%, which again is primarily attributable to the decrease in the in the use of methadone from 1.2% in 1998 to 0.4% in 2005/2006. Lifetime use of heroin has not changed significantly since 1998 for this age bracket. The proportion of 16 and 24 year olds reporting having used opioids in the last month has also decreased significantly from 1998 to 2005/2006, from 0.7% to 0.1%.

Analyses based on household surveys demonstrated that use of opioids has increased over the 1990s (Law and colleagues, 2001). From 1991 to 1998 it was estimated that there was an increase in prevalence of heroin used within the last year from 0.4% to 0.8%. In 2001, this dropped to 0.2% and remained stable in 2004 (Australian Institute of Health and Welfare, 2005). This sharp decline was also evident in estimates of current regular users of opioids estimated via multiplier methods (using multiple data sources conducted by Degenhardt and colleagues, 2004). Degenhardt and colleagues estimated the number of current regular users in New South Wales increased over the later half of the 1990's (from 35 300 in 1997 to 48 200 in 1999), and sharply declined in 2001 (22 100) and 2002 (19 900). The sharp decline was a result of a major shortage in supply of heroin in 2001 when a major trafficking network from South-East Asia was dismantled (UNODC, 2006a). This so called 'heroin drought' resulted in large decrease in purity and increase in price which forced some users out of the market and the number of drug users declined substantially (UNODC, 2006a). The World Drug Report indicated that up until the 'heroin drought' in 2001, Australia had some of the highest opioid prevalence rates in the world.

The 2004 (and 2001) estimates of the proportion of the Australian population (aged 14 years and over) that have used opioids based on the National Drug Strategy Household survey (Australian Institute of Health and Welfare, 2005) are summarised in Table 1. Almost twice as many men as women were estimated to have used opioids in their lifetime (3.1% verses 1.7%) but for recent use this discrepancy was greatly reduced (e.g. within the last month 0.1% of both females and males). People under the age of 19 and over the age of 40 were less likely to have used opioids recently or during their lifetime. Of those who had used heroin or methadone within the year, 45% had used at least once a week. The mean age of initiation was 21 years for heroin and 25 years for methadone.

2.1.5.2 New Zealand

In New Zealand, drug surveys have been conducted in 1990 (Black & Casswell, 1993), 1998 (Field & Casswell, 1999a & b), and 2001 (Wilkins, Casswell, Bhatta, & Pledger, 2002). Each of these surveys obtained information from over 5000 New Zealanders. Table 1 summarises the 2001 estimates. As can seen in Table 1, New Zealand appears to have higher rates of opioid use in general in 2001, compared with Australia and Britain; however, it must be noted that both of these studies include a larger age range (where younger and older ranges are less likely to use opioids) and in the British survey *any opioid* only included the use of heroin and/or methadone. As can be seen in Table 1, the use of heroin is less common in New Zealand compared with many other countries. The Ministerial Committee on Drug Policy (2007) propose that New Zealand's low rate of heroin use is due to its geographic isolation which limits the bulk importation of heroin and raw opium. As a result the majority of opioids abused in New Zealand have been prescription medications (such as morphine sulphate and methadone), poppies and 'home bake' (produced from products containing codeine).

Estimates based on the New Zealand national drug surveys indicated that the percentage of people who currently used opioids remained the same in both 1998 and 2001 (0.6%; Wilkins et al., 2002). However; there are some differences in the particular type of opioids being used. For example, a decrease in current use of heroin occurred between 1998 and 2001 (0.1% vs. 0.03%). This decrease is consistent with the aforementioned sudden and

dramatic decrease in heroin availability that occurred throughout Australia early in 2001 (Degenhardt et al., 2005)[19].

The regional drug surveys (Black & Casswell, 1993; Field & Casswell 1999a) and the national surveys (Field & Casswell 1999b, Wilkins et al., 2002) showed that around 1 percent of New Zealanders had used opioids in the last year for each of the years surveyed (1990, 1998, and 2001). There was a slight increase in those who had ever tried opioids from 1990 (3%; New Health Information Service) to 1998 and 2001 (4%; Wilkins, Casswell, Bhatta, & Pledger, 2002). As can be seen in Table 2 and Table 3, men are more likely to have tried opioids and used within the last year for both 1998 and 2001. Also, men and women between the ages of 18-24 were generally more likely to have used opioids in the last year in 1998 and 2001, compared with other age ranges.

Table 2:

Proportion of Men and Women who reported ever trying Opioids in 1998 and 2001

	1998		2001	
Age range	Men (*n*=2860)	Women (*n*=2615)	Men (*n*=2942)	Women (*n*=2562)
15-17	2.5	2.3	2.4	0.3
18-19	5.6	3.9	3.6	4.3
20-24	6.1	4.5	8.3	4.9
25-29	5.2	1.9	6.3	3.7
30-34	4.6	3.0	4.2	2.1
35-39	3.2	3.1	4.1	3.3
40-45	3.5	2.7	6.9	2.2
15-45	4.3	3.0	5.4	3.2
		3.7		4.3

Note: this table was produced based on raw data reported in *Drug Use in New Zealand: National Surveys Comparison 1998 and 2001* (Wilkinss et al., 2002)

Table 3:

Proportion of Men and Women who reported last year use of Opioids in 1998 and 2001

	1998		2001	
Age range	Men (*n*=2860)	Women (*n*=2615)	Men (*n*=2942)	Women (*n*=2562)
15-17	2.5	1.7	1.9	*
18-19	3.9	2.2	3.1	1.6
20-24	2.6	3.4	3.0	0.9
25-29	1.2	0.3	1.5	0.0
30-34	1.3	0.0	0.7	0.2
35-39	0.2	0.0	0.6	0.2
40-45	0.2	0.0	0.5	0
15-45	1.4	1.0	1.4	0.6
		1.2		1.0

Note: this table was produced based on raw data reported in *Drug Use in New Zealand: National Surveys Comparison 1998 and 2001* (Wilkinss et al., 2002)

* could not be calculated because sample size was not reported

While only a small proportion of New Zealanders use opioids the associated health and social harm is serious (Ministerial Committee on Drug Policy, 2007). The number of hospitalisations and poisoning related to opioid use is high relative to use of other drugs

[19] New Zealand's main supply of heroin and opium is from Myanmar/Laos, either directly from there or indirectly via Australia (UNODC, 2006a).

(New Zealand Health Information Service, 2001). During the three years between 1996 to 1998 there was a rise in the number of hospitalisations which involved opioid related conditions or poisoning from 940 in 1996, 1350 in 1997, and 1665 in 1998 (New Zealand Health Information Service). This rise was thought to be due to the increasing number of individuals reporting using opioids rather than increases in opioid related harm within this period (New Zealand Health Information Service). Of those opioid related hospitalisations between 1996 and 1998, 56% were female and 10% were Maori (New Zealand Health Information Service). The highest hospitalisation rate for Maori and non-Maori males was between the ages 30-34 years (48 per 100 000 and 73 per 100 000, respectively) and for Maori and non-Maori females it was between the ages of 25 to 29 (67 per 100 000 and 84 per 100 000, respectively; New Zealand Health Information Service). Between 1990 and 1996 the number of deaths attributed to opioid related conditions has increase for both males and females, from 11 registered deaths in 1990 to 29 in 1996 for men and from 1 in 1990 to 11 in 1996 for females (New Zealand Health Information Service).

Estimations of the prevalence of opioid dependence in New Zealand are limited. In 1996, Sellman and colleagues (1996) estimated the prevalence of opioid dependence using the treatment multiplier method. This calculation yielded an estimate of 13 500 opioid dependent New Zealanders in 1996[20]. Another calculation conducted by Sellman and colleagues assumed that 0.5% of the population were regular users of opioids, and that 50-80% of regular users were dependent. Based on these assumptions they estimated that between 0.3%- 0.5% of New Zealanders were opioid dependent in 1990. Sellman and colleagues then assumed that the prevalence grows 15% per year (as was found in Australia) which inferred that between 0.6% and 0.9% were dependent in 1996 (the mean of which estimated that 26 600 were opioid dependent). Thus, based upon these two methods Sellman and colleagues (1996) suggested that in 1996 there were between 13 500- 26 600 opioid dependent individuals. However, Sellman and colleagues noted that neither of these estimates were based on quality New Zealand data.

Studies of clients presenting at alcohol and drug services in New Zealand indicated that opioid dependence was not uncommon in these settings. Telephone surveys in 1998 and 2004 of randomly selected alcohol and other drug treatment workers (*n*= 217 and 288, respectively) found that 17% and 15% (respectively) of individuals who presented to these services did so mainly because of their opioid use (Adamson et al., 2000; Adamson, Sellman, Deering, Robertson & de Zwart, 2007). Similarly, another study (*n*=105) found that 15% (95% confidence interval between 8% and 22%) of people in an alcohol and other drug outpatient sample had a current diagnosis of opioid dependence and 24% (95% confidence interval between 16%-32%) had met the criteria for opioid dependence within their lifetime (Adamson, Todd, Sellman, Huriwai, and Porter; 2006). In the 2004 telephone survey, a higher proportion of clients who mainly used opioids attended follow-up appointments (20%) compared with assessments (7.5%), which could be explained by the long-term nature of opioid substitution treatment (Adamson, Sellman and colleagues, 2007).

[20] Sellman and colleagues (1996) used the 2700 individuals known to be either on methadone treatment programme or on the waitlist in 1996 as the benchmark and the lower multiplier of 5 suggested by the World Health Organisation in 1990 was employed. Sellman and colleagues use of a multiplier that was not specific to New Zealand means that the validity of the estimate is questionable.

2.2 Prison Population

Opioid dependence is much more common in prison populations compared with non prison populations[21] and is among the most prevalent psychiatric disorders in prisons around the world. For example, studies of prison populations in Iran (Assadi et al., 2006) and Denmark (Andersen, Sestost, Lillebaek, Gabrielsen, & Hemmingsen, 1999) found opioid dependence to be the most common psychiatric disorder. In Denmark 32% of prisoners meet the criteria for heroin dependence (Andersen et al., 1999)[22], in Iran 73% of prisoners meet the criteria for lifetime opioid dependence and 9.5% of current dependence or abuse[23] (Assadi et al., 2006). In a Canadian sample (*n*=267) of prisoners (Brink, Doherty, & Boer, 2001), opioid dependence was found to be the second most prevalent substance use disorder (as measured by a computer-assisted version of the SCID) after cocaine dependence, with 11% meeting the criteria for either current or lifetime opioid dependence.

In sample of men serving a sentence in Britain (*n*=1751), 11% met the criteria for drug dependence, and opioid dependence was the most common with 7% of the sample meeting the criteria (Maden, et al., 1992). In a similar study of a sample of women prisoners (*n*=272), 18% reported being dependent of opioids prior to arrest (Maden, Swinton, & Gunn, 1990). While opioid dependence maybe more prevalent in women prisoners, Maden and colleagues (1992) point out that the female prison population is only a one-thirtieth the size of the male prison population which means that only 6% of all sentenced inmates who were dependent on drugs were women. A later study looking at self-reported levels of opioid use before arrest among randomly selected remanded prisoners across England and Wales (*n*=995) suggests an increase in opioid dependence during the 90s, with 11.3% of men and 20.8% of women reported daily or almost daily use during the 6 months prior to being remanded (Brooke, Taylor, Gunn, & Maden, 1998).

Opioid use disorders have also been found to be common in female prisoners in New Zealand (Hurley & Dunne, 1991; Andersen, 2004). For example, in a small sample of female prisoners (*n*=92) 28% met the criteria (based on the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders-III—Revised) for a substance use disorder based on their lifetime use of heroin (Hurley & Dunne, 1991).

2.3 Summary

Worldwide use of opioids increased over the 1990s and has remained stable since 2000. New Zealand appears to have a high rate of opioid use in general relative to many other countries but has a lower rate of heroin use. Internationally, it appears that men are more likely to use opioids than females but gender differences reduce with younger age groups and more recent use. People between the ages of 18-29 appear to be more likely to use opioids than individuals in lower or higher age ranges. Most of the literature reports estimates on the prevalence of opioid use rather than opioid dependence. More research focusing specifically on prevalence of opioid dependence is needed.

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[21] It is important to note that drug use in custodial settings (similar to non custodial settings) are likely to underestimate true levels of use due to under-reporting (Brooke, Taylor, Gunn, & Maden, 1998).

[22] The Danish study consisted of a sample of remanded Danish prisoners (*n*=228). In addition to finding that heroin dependence was the most common psychiatric disorder they found that the majority (61%) of prisoners had tried illegal opioids (Andersen et al., 1999). They found opioid dependence had lasted an average of 8 years. Also, injection as the primary route of administration outnumbered smoking 3:1 (Andersen, Sestost, Lillebaek, Gabrielsen, & Hemmingsen, 1999).

[23] Based on a stratified random sample of prisons (*n*=351) interviewed using the Structured Clinical Interview for DSM-IV Axis 1 Disorders.

3.0 INNOVATIONS FOR OPIOID SUBSTITUTION TREATMENT WAITLISTS

The number of opioid dependent individuals on waitlists for comprehensive opioid substitution treatment and the time on waitlists has been a significant problem both in New Zealand (Adamson & Sellman, 1998; Ministry of Health, 2007; Sellman, Harvey, & Deering, 2001) and overseas (e.g., Donmall, Watson, Millar, & Dunn, 2005; Schwart et al., 2006; Schwart, Jaffe, Highfield, Callaman & O'Grady, 2007; Stewart, Gossop, & Arsden, 2004; Vancovitz et al., 1991). Opioid dependent individuals on waitlists for treatment are likely to continue engaging in substance misuse, associated crime, and other risk taking behaviours (Adamson & Sellman, 1998). Thus, "long wait lists are contrary to the intention and spirit of opioid substitution as a harm minimisation strategy" (Ministry of Health, 2003, p.16).

Greater use of General Practitioners (G.Ps) appears to be the primary strategy for reducing waiting lists. In New Zealand the use of G.Ps has been suggested while waiting for comprehensive treatment ("interim prescribing"). Interim prescribing of methadone is a strategy outlined by the Ministry of Health (2003; 2007) who recommend that those who are opioid dependent who have to wait longer than two-weeks for opioid substitution treatment should be given the option of being prescribed methadone by an 'authorised prescriber' (i.e. client's G.P) while waiting. The purpose of interim prescribing is to reduce withdrawal and cravings for opioids, and minimise harm to the client's health and social environment. Another strategy is that once a client has been stabilised on methadone they could then be transferred to G.P prescribing upon authority of specialist treatment service; thus freeing up specialist services for those who require them the most (Ministry of Health, 2007; Sellman et al., 2001).

In the United States, even though interim methadone treatment had been approved by the Food and Drug Administration since 1993, restrictions on its implementation have meant that its use has been largely limited to clinical trials (Schwartz et al., 2007). The randomised controlled trials of interim prescribing of methadone compared with waitlist controls have demonstrated that interim prescribing is related to a reduction in heroin use and criminal behaviour, and more clients entering comprehensive treatment (Vancovitz et al., 1991; Schwart et al., 2006; Schwart, Jaffe, Highfield, Callaman & O'Grady, 2007). Such studies provide strong support for the use of interim prescribing rather than leaving the opioid dependent individual on waiting lists. It is important to note that these studies do not infer that interim prescribing be a substitute for more comprehensive treatment. Indeed research has demonstrated that methadone treatment in conjunction with counselling has been shown to be more effective than methadone alone, and the addition of other on-site professional services (i.e. medical, psychiatric, employment, and family therapy) is associated with even better outcomes (McLellan, Arndt, Metzger, Woody, & O'Brien, 1993).

Australia's response to the demand of methadone outstripping the publicly funded agencies in the mid 1980s was to make methadone (and more recently, buprenorphine) widely available by shaping a "medical" approach which provided little provision for counselling and welfare services (Bell, Burrell, Indig, & Gilmour, 2006). In order for opioid substitution treatment to be able to take place in private settings as well as public, efforts were undertaken to encourage G.Ps to provide opioid substitution treatment for opioid dependent individuals (Bell et al., 2006; Hotham, Roche, Skinner, & Dollman, 2005).

Furthermore, universal health insurance allowed for G.Ps and psychiatrists to be reimbursed for consultation which meant that clients only had to then pay for the methadone to be dispensed (Bell et al., 2006). Little difference with regard to treatment retention between private and public settings has been found in Australia (Bell et al., 2006). In order to expand access to opioid substitution a similar trend towards G.P care has occurred in many European countries including England, Scotland, Ireland, France and Belgium (Hotham, Roche, Skinner, & Dollman, 2005; Winrich & Stuart, 2000).

While not directly related to reducing wait list times there are some suggestions about how to best manage individuals while they are on wait lists. Maintaining contact with clients on wait lists and providing them information about the expected length of time is critical. Additional support should also be provided which could include drop-in facilities (Donmall et al., 2005).

In summary, it appears the increased utilisation of G.Ps is currently the primary strategy for reducing wait-list for comprehensive opioid substitution treatment. This appears to be taking two main forms: (1) interim prescribing of an opioid substitute until the client is in a comprehensive treatment or (2) for individuals to engage in private treatment via their G.Ps rather than engaging public comprehensive opioid substitution treatment.

4.0 THE INFLUENCE OF THE "METHAMPHETAMINE EPIDEMIC" ON THE PREVALENCE, PRESENTATION AND TREATMENT OF OPIOID DEPENDENCE

Methamphetamine has been being increasingly recognised "as the major 'hard drug' problem facing New Zealand" (Ministerial Action Group on Drugs, 2003, p 5). It is a drug that is commonly associated with violence, crime, and mental health problems (Ministerial Committee on Drug Policy, 2007; Wilkinss, Reilly et al., 2004). Manufacture and use has surged over the last two decades and is posing new challenges to social, treatment, and law enforcement agencies (Adams & Hodges, 2005). Exactly how this 'methamphetamine epidemic' will affect the prevalence, presentation and treatment of people with opioid dependence is yet to be fully determined.

4.1 Methamphetamine

Methamphetamine is a synthetic drug derived from pseudoephedrine which acts as a central nervous system stimulant, and is classed as an amphetamine[24]. In New Zealand there are a variety of colloquial terms for methamphetamine (Ministerial Action Group on Drugs, 2003), such as 'meth', 'crank', 'goey', 'speed'[25]. The terms 'P', 'Burn', or 'Pure' refer to a high purity of methamphetamine that is one step removed from the virtually pure form of methamphetamine, crystal methamphetamine ("ice", crystal meth). Methamphetamine can be snorted, smoked, injected or taken orally. Crystal methamphetamine is usually smoked but because of its crystallised form it enters the blood stream very quickly which increases the intensity of the effects. The immediate effects of methamphetamine include euphoria, increased energy and confidence, and decreased appetite which last between 4-12 hours depending on the dose[26]. High doses are associated with irritability, hostility, paranoia, hallucinations and violent behaviour. People sometimes use it in a binge fashion, where it is taken continuously for a few days without sleep. Long binges have been characterised by panic and terror, and sometimes induce a psychosis that is similar to paranoid schizophrenia even in individuals who have never experienced mental health problems before. The "crash" occurs at the end of a binge and can include depression, fatigue, insomnia, headaches, and strong cravings to continue to use. Upon regular use dependence is easily formed and relapse is common. Long term use is associated with physiological harm including damage to the cardiovascular systems, and dopamine systems within the brain which could be linked to mood and motor disorders later in life (Wilkinss et al., 2002).

[24] The DSM-IV-TR (APA, 2000) grouped amphetamines and amphetamine-like substances together. They included all substances with a substituted-phenylethamine structure such as amphetamine, dextroamphetamine, methamphetamine, and crystal methamphetamine. This class also included other substances which have an amphetamine-like action but are structurally different, such as methylphenidate or agents used as appetite suppressants ('diet pills"); and plant derived stimulants (such as khat). While the DSM-IV-TR included amphetamine analogues (such as 3,4-methylenedioxymethamphetamine/ "ecstasy") as a hallucinogen rather than an amphetamine, research in both New Zealand (e.g. Wilkinss et al., 2002; 2004) and internationally (e.g. UNODC, 2006) often extends the Amphetamine-Type Stimulants category to include these analogues. Thus, the term amphetamine in this document refers to this broader definition. In addition to amphetamines, cocaine and crack are also stimulants (Ministerial Committee on Drug Policy, 2007).

[25] The term "speed" is also sometimes used to refer to amphetamine sulphate (Ministerial Action Group on Drugs, 2003)

[26] Methamphetamine and crystal methamphetamine have effects more similar to cocaine than some of the amphetamines particularly diet pills and other prescription drugs (Wilkinss et al., 2002).

4.2 Prevalence of Amphetamine Use

The use and manufacture of powerful amphetamines (such as methamphetamine) has increased rapidly in New Zealand (Wilkinss, Bhatta, & Casswell, 2002; Wilkinss, Reilly et al., 2004) and worldwide (Australian Bureau of Criminal Intelligence, 2001, Baker et al., 2004; Copeland, Howard, Keogh, & Seideler, 2003; Hao et al., 2002; Mazlan, Schottenfeld, & Chawarski, 2006)[27]. Research suggests that this trend is likely to continue even though there is more awareness about adverse consequences (Rawson, Anglin, & Lin, 2002). Wilkinss and colleagues' (2002) comparison between the 1998 and 2001 New Zealand National Drug Surveys revealed that stimulants had moved from being the third most commonly used illicit drug (after cannabis and LSD) to the second in 2001. For New Zealanders (aged between 15-45), last year use of amphetamine or methamphetamine increased from 2.9% in 1998 to 5.0% in 2001 and the use of crystal methamphetamine increased from 0.1% to 0.9%, whereas, use of LSD and cannabis remained stable. Approximately one in ten New Zealanders 18-29 years old had used amphetamines in the last year, and a third of them used them at least once a month (Wilkinss, Pledger et al., 2004). In an Auckland sample of frequent methamphetamine users (at least monthly use) recruited via snowballing techniques (Wilkinss, Reilly et al., 2004), two-thirds reported using methamphetamine continuously for at least 48hours ('bingeing') in the last six months, with the average bingeing frequency being once a fortnight. The majority of methamphetamine users either used it weekly (60%) or daily (14%). Consistent with increased amphetamine use in the community there was a significant increase in the number of clients seen for treatment at dedicated alcohol and drug treatment services whose main substance of use was amphetamine between 1998 and 2004 (0.3% and 9.7%, respectively; Adamson et al., 2006).

Use of amphetamines in New Zealand is higher than other countries, including Australia (3.4% used in the last year; AIHW, 2002); with only Thailand reporting a higher prevalence of last year use (5.9%; ODCCP, 2002). The estimate of the global average is 0.6% of adults (UNODC, 2006).

4.3 Amphetamine Injection and Possible Precursor to 'Harder' Drugs

Injection is a common route of administration of amphetamines, particularly for more pure forms (Wilkinss, Reilly, et al., 2004). One-fifth of frequent methamphetamine users (at least monthly use) had injected methamphetamine in the last six months. Other countries have found that injection of amphetamines has become increasingly common (e.g. Baker, Boggs, & Lewin, 2001; Baker et al., 2004: Kaye and Darke, 2000; Klee, 1992; McAllister & Makkai, 2001; Peters, Davies, & Richardson, 1997). Wilkinss, Reilly and colleagues (2004) propose that the increase in popularity of injecting amphetamines in New Zealand is likely to be fuelled by increased tolerance of current heavy users and/or traditional injecting opioid users responding to the greater availability of amphetamines within New Zealand relative to the traditional supply of opioids. When Australia experienced a sudden and dramatic decrease in heroin availability throughout the country in 2001 heroin was substituted with other more readily available drugs, most commonly cocaine,

[27] Interestingly, large numbers of seizures of methamphetamine in Southeast Asia indicate that heroin producers in that region continue to diversify into methamphetamine manufacturing (Australian Bureau of Criminal Intelligence, 2001). A higher profit is able to be made from methamphetamine compared with heroin because it is not tied up having to grow the key ingredient (i.e. poppies; Australian Bureau of Criminal Intelligence, 2001).

methamphetamine, and benzodiazepines (Dengenhardt et al., 2004; 2005; Weatherburn, Jones, Freeman, & Makkai, 2003).

There is concern that the growing prevalence of injection of amphetamines might lead to people to being introduced to 'harder' drugs (i.e. opioids) who may not have ordinarily used that drug (Australian Bureau of Criminal Intelligence, 2001). There is some evidence to support that concern. For example, in a prospective study (*n*=3657), amphetamine use was the single best predictor of non-medical use of opioids[28] five years later (87% sensitivity and 79% specificity; Pletcher, Kertesz, Sidney, Kiefe, & Hulley, 2006).

4.4 Demographics of Amphetamine Use

Until the mid-1990s the amphetamine scene was restricted to 'white' motor cycle gangs but following international trends in youth culture, amphetamine and related compounds have become the drug of choice in the 'dance party' scene in New Zealand (Wilkinss, Reilly et al., 2004). Similar to the demographics of other drug using populations, the majority of amphetamine users are males, with the highest use being amongst 20-24 year olds (Wilkinss, Pledger et al., 2004). Less characteristic of other drug using populations, most amphetamine users were in full time employment (65%), came from a range of occupational backgrounds including professional and managers (18%), earned mid-level incomes, and had a relatively high level of educational achievement. These demographics were very similar to that found for frequent methamphetamine users (Wilkinss, Reilly et al., 2004). It appears that the demographics of individuals using amphetamines in New Zealand are somewhat different to that found overseas. For example, in an Australian sample of regular amphetamine users, twice as many were unemployed compared with the New Zealand statistics (Baker et al., 2004).

Based on information obtained from drug enforcement, drug treatment, and regular methamphetamine informants, the use of methamphetamine is continuing to rise in New Zealand particularly among teenagers and business people (Wilkinss, Reilly et al., 2004). Those who have attended alcohol and drug treatment with amphetamine as their main substance were more likely to be younger and majority lived in the north island (Adamson et al., 2006).

4.5 Supply of Methamphetamine

Methamphetamine is of particular concern because it is the only illegal stimulant that is commonly manufactured in New Zealand. Domestic manufacture and sale of methamphetamine are closely linked to gang members and associates. The manufacture has increased rapidly which is partially attributed to the wider use and awareness of 'recipes' of methamphetamine in the internet (Wilkinss, 2002). The process of manufacture is relatively simple and the principle precursor, pseudoephedrine, can be extracted from over-the-counter flu medicines (Wilkinss, 2002). The availability of methamphetamine appears to be becoming easier and price has remained stable which indicates that large profits are likely to be being obtained by the suppliers (Wilkinss et al., 2002; Wilkinss, Reilly et al., 2004). The manufacture of methamphetamine continues to grow with more laboratories being detected by the police each year and more seizures at customs (Wilkinss, Reilly et al., 2004).

[28] These included Dilaudid, morphine, Demerol, hydrocodone, oxycodone, and methadone.

4.6 Prevalence of Amphetamine/Stimulant and Opioid Co-use

Internationally, the use of multiple drugs is considered to be the norm in regular amphetamine and opioid using populations (Darke & Hal, 1995, Gossop, Marsden, Stewart, Treacy, 2002; Leri, 2002). A study by Darke and Hall (1995) revealed that none of the regular amphetamine and 1% of the heroin user sample reported using less than three other drugs in the last six months. Thus, to simply "characterise drug users as 'heroin' or 'amphetamine' users misses the context in which these drugs are used" (Darke and Hall, 1995, p. 235).

In New Zealand, Wilkinss, Pledger, and colleagues (2004) found that in individuals who had used amphetamines in the last year only a minority had also used opioids within the last year (0.5% heroin, 6.8% homebake, 3.1% morphine, 3.5% poppies). Of the 0.2% of the whole sample who had used a needle in the last year to inject a drug, 77% had also used opioids in the last year and 67% had also used stimulants. Thus, most needle using amphetamine users also used opioids and Wilkinss, Pledger, and colleagues (2004) suggested that those individuals might primarily be opioid users. The use of other drugs in addition to amphetamines varies depending on the type of amphetamine (Wilkinss, Reilly et al., 2004). Crystal methamphetamine users reported the highest levels of other drug use including opioid use. For example, of those who used crystal methamphetamine in the last year 3% had used heroin, 25% homebake, 9% morphine, 21% poppies, and 10% had used other opioids in the last year. It is also likely that more regular amphetamine users may use opioids more often. For example, Hando, Topp, and Hall (1997), found that among an Australian sample of regular amphetamine users (n=200; at least monthly for the last six months) 44% had used heroin, 12% methadone, and 27% other opioids in the last six months. Interestingly, Darke and Hall (1995) found that regular amphetamine users were heavier multiple drug users than regular heroin users and a higher rate had used opioids within the last six months (61%) compared with the use of amphetamine by regular heroin users (42%).

Similarly, stimulant use in opioid dependent individuals is not uncommon and is not restricted to particular regions or countries (Leri, 2002). For example, Leri et al., (2005) found that in a sample of regular opioid users over half had used cocaine within one week of the interview (n=304). It appears that high proportions of individuals who are in treatment for opioids also use stimulants. For example, a study by Beswick, Best, Rees, Coomber, Gossop, and Strang (2001) of individuals who were attending treatment for opioid use (n=116) found 60% had used crack cocaine during the month prior to the interview and 52% had used heroin and crack in the same drug using episode. They found that those who also used crack were more likely to be younger and female, whereas men were more likely to use benzodiazepines.

4.7 Patterns of Stimulant and Opioid Co-use

Wilkinss, Pledger, and colleagues (2004) suggested opioids (and tranquillisers) were used to self-medicate against the side effects rather than in conjunction with amphetamines. However, based on the literature on the use of stimulants (predominantly cocaine) and opioids it is likely to the two are used for many purposes in addition to self-medication.

Patterns of co-use can either be simultaneous or sequential[29,30] (Leri et al., 2002; 2003). For example, Leri et al., (2005) found that in a sample of regular opioid and cocaine users (*n*=304) that while opioid use was fairly constant throughout the day, cocaine use was more variable with a peak at the 21st hour. They found three different patterns of cocaine and opioid use within a day: 30% used both of the drugs in a sequential fashion, 35% took them in the same hour, and 35% reported taking them at the same time or mixing them. The latter two groups consumed greater amounts of both drugs compared with those who used them sequentially (Leri et al., 2005).

Studies which have looked at the subjective effects of opioids and cocaine have indicated that when used separately these drugs have distinct subjective effects; opioids are 'sedating' and cocaine is 'stimulating' (e.g. Foltin & Fischman, 1992; Walsh, Sullivan, Preston, Garner, and Bigelow, 1996; see Leri et al., 2002 for a review). However, there is no one single answer as to why individuals would use stimulants in addition to opioids. Research generally suggests that simultaneous administration of these drugs do not induce a novel set of subjective effects, instead, produce effects similar to both drugs (Leri et al., 2003). For example, the study by Foltin & Fischman (1992) found that simultaneous IV administration of cocaine and morphine in nondependent males (*n*=9) produced cardiovascular effects best predicted by cocaine alone. The subjective effects induced by both drugs were typical of each of these drugs alone, in addition to some effects common to both drugs. Similarly, Walsh and colleagues (1996) found that the injection of hydromorphone and cocaine at the same time produced subjective effects similar to both drugs but the magnitude of these effects were greater than produced by either drug alone (*n*=8). These studies suggest that it is not that the combination of opioids and cocaine 'feels different' rather they may simply 'feel better' than administration of each of these drugs alone and thus attract individuals to use them simultaneously (Leri et al., 2003). While there is some support for this from anecdotal research, experimental research suggests that this may only be the case when low doses of either drug are used (Leri et al., 2003).

In addition to the ideas that people may use cocaine simultaneously with opioids because the effects are unique or more reinforcing, another suggestion is that the combination is used for self-medication (Leri et al., 2003). For example, Hunt, Lipton, Goldsmith, and Strung (1984) reviewed interviews of men dependent on heroin (*n*=10) who successfully detoxified by injecting decreasing amounts of heroin and gradually increasing amounts of cocaine until they were they were no longer injecting any heroin. The men reported that cocaine interacts with heroin in a way that masks the physiological withdrawal.

There is also evidence that the two drugs are used in sequential fashion in order to reduce the side-effects of the other. Leri and colleagues (2003) suggest that there are two distinct groups of opioid and stimulant users that depends on which is their primary drug. Research suggests that heavy stimulant users may use opioids to alleviate the "crash" or to take the "edge" (over-excitability) off the stimulant use (Foltin and Fischman, 1992; Leri et al., 2003). The second group consists of those who use opioids regularly and stimulants are used to alleviate unpleasant side-effects and opioid withdrawal. The mechanism by which stimulants can alleviate dysphoria associated with opioid withdrawal is not

[29] The simultaneous administration of opioids and cocaine is often referred to as 'snowballing', 'dynamite', or 'whizbang' and in the case of simultaneous use of opioids and amphetamines, 'goofball' or 'bombitas' (Leri, 2002).

[30] The neurobiology of opioids and cocaine is discussed in detail in Leri and colleagues' (2003) review of opioid and cocaine co-use and suggests that there may be multiple pharmacological explanations for cocaine use in opioid dependent individuals.

completely known. However, stimulants ability to increase the activity in the mesolimbic dopaminergic system or the endogenous opioid system have been implicated, along with the possibility of reducing the activity of the noradrenergic system (Leri et al., 2003). Also, use of amphetamines in regular opioid users may develop out of personal circumstances where amphetamines might be used to sustain the activity needed to generate the money to support their opioid use (Ellinwood, Eibergen, & Kilbey, 1976).

In regards to sequential use of cocaine and opioids, Leri and colleagues' (2003) review of the literature indicated mixed results in regards to whether the subjective effect of cocaine is enhanced in individuals maintained on methadone. Nevertheless, it is known that cocaine continues to induce its subjective effects in clients maintained on methadone, buprenorhine (Leri et al., 2003), or Naltrexone (Walsh et al., 1996).

The fact that stimulant use may be highly related to opioid use needs to be taken into consideration when formulating treatment.

4.8 Harm Related to Amphetamine

Use of amphetamines in New Zealand has been associated with increases in mental health problems, violence, and other crime (Wilkinss, 2002; Ministerial Action Group on Drugs, 2003).

4.8.1 Mental Health

In New Zealand, over a third of those who had used amphetamine in the last year and a half of frequent methamphetamine users identified experiencing harm in one or more areas of their life as a result of their use (Wilkinss, Reilly et al., 2004). Psychological rather than physical harm was more closely associated with frequent methamphetamine use. Many (40%) identified having mental health problems prior to using methamphetamine. However, mental health problems after the use of methamphetamine was even more common, with two-thirds endorsing 'anxiety', 'mood swings', 'short-temper', 'paranoia', and 'depression' since they had begun using methamphetamine. Higher frequencies of use were associated with greater levels of harm. Suicidal ideation was also more common after methamphetamine use compared with prior (21% vs. 13%), as was suicide attempts (13% vs. 8%).

The association between use of amphetamines and a significant increase of mental health problems is consistent with overseas research (e.g. Baker et al., 2004; Domier, Simon, Rawson, Huber, & Ling, 2000; Hall & Hando, 1994; Hall, Hando, Darke, & Ross, 1997; Longo et al., 2004; Vincent, Shoobridge, Ask, Allsop, & Ali, 1999). For example, a study by Baker and colleagues found that approximately half of a sample of at least weekly amphetamine users (n=214) had been previously diagnosed or treated for a mental health condition and this had occurred on average two years after onset of regular amphetamine use. A quarter of those with a mental health problem had received a diagnosis of psychosis, and among them just under three quarters received this diagnosis after onset of regular amphetamine use. Similar to others (e.g. Domier et al., 2000;Vincent et al., 1998), Hall, Hando, Darke, and Ross' (1997) analyses involving amphetamine users (n=301) revealed that injection as the usual route, frequency of use, and psychological symptoms prior to amphetamine use, were all significant independent predictors of psychological severity after using amphetamines for the first time. Interestingly, multiple drug use was not a significant independent predictor of psychological severity which indicated that the

relationship between psychological symptoms and amphetamine drug use is unlikely to be due to multiple drug use. Their findings indicated that individuals should be recommended against injecting amphetamines, using amphetamines weekly or more, and use by those with pre-existing psychological problems.

4.8.2 Violence and Other Crime

Fifteen percent of the New Zealand frequent methamphetamine users reported experiencing violent behaviour after methamphetamine use (Wilkinss, Reilly, et al., 2004). Overseas research has reported higher levels of aggression associated with amphetamine use for those who are dependent on amphetamines and who are seeking treatment. For example, in a sample of very heavy amphetamine users, 72% reported having episodes of aggression and this was higher among these who felt they were dependent and those who found abstaining more difficult (Wright and Klee, 2001). In a study conducted by Vincent and colleagues (2001), they found that all of those seeking treatment had experienced aggressive outbursts since they began using amphetamines compared with 54% in the non-treatment seeking amphetamine dependent group. In fact the development of aggression since using amphetamine was one of the strongest independent predictors for seeking treatment for amphetamine use[31].

Amphetamine use has also been associated with crime. For example, in a New Zealand sample of arrestees 21% had used amphetamines within the last year and 9% just prior to committing their offence. Amongst those who had used amphetamines within the 48 hours prior to committing an offence a quarter of them attributed their offence entirely to their use. Along with alcohol, amphetamines were the drugs considered by arrestees most likely to make them feel angry (Wilkinss, Reilly et al., 2004).

The relationship between amphetamine use, violence, and crime is a complicated issue (Wright & Klee, 2001). Research suggests that the reason that amphetamine users commit crimes has less to do with economic factors than is often the case with opioid users. Instead, violence may result from the psychoactive affects of amphetamines by enhancing an individual's level of aggression associated with either increased confidence or disinhibition of behaviour, or amphetamines may induce paranoia and defensive behaviour. Exacerbation of pre-existing mental health conditions could also increase the risk of violence, as well as irritability associated with withdrawal or lack of sleep. There also appear to be sub-cultural norms among some groups of amphetamine users where excitement is sought from committing the crime (Klee and Morris, 1994; Wright and Klee, 2001). A greater degree of violence is associated with those involved with the dealing of amphetamine which may be related to ensuring reputation and hierarchy (Wilkinss, Reilly et al., 2004; Wright & Klee, 2001)

The association between aggression or violence and paranoia related to amphetamine use has been implicated by researchers in both New Zealand (Wilkinss, Reilly et al., 2004) and overseas (Wright and Klee, 2001). Delusions revolving around the potential threat from others are likely to result in defensive violence. Amphetamine (and methamphetamine in particular) induced psychosis is reported to be very similar to paranoid schizophrenia in presentation (Wilkinss, Reilly et al., 2004). Furthermore, Wright and Klee found that among the amphetamine users in their study, paranoia, hostility, and associated defensive behaviour was most likely in strange environments. Aggression and suspicious behaviour towards people in positions of authority including health professionals has also been

[31] Other strong independent predictors were greater time spent unemployed and poor general health.

noted. Wilkinss, Reilly and colleagues (2004, p. 85) suggested that individuals who use amphetamines regularly "should be approached with caution and a reassuring manner, to avoid triggering any violent defensive response."

4.9 Harm Related to the Use of Stimulants and Opioids

It appears that for individuals who use opioids the level of harm is increased by the additional use of stimulants. For example, for individuals in methadone management treatment stimulant use has been associated with increased risk of blood-borne diseases; and increased crime, violence, and work in the sex industry (Australian Bureau of Criminal Intelligence, 2001; Bux, Lamb, & Iguchia, 1995; Joe & Simpson, 1995; Leri, 2002; Strung, 1985); and higher levels of anxiety, depression, and physical health problems (Beswick, Best, Rees, Coomber, Gossop, & Strang, 2001).

Research looking at overdose death rates suggests that the use of stimulants and opioids may be a lethal cocktail (Australian Bureau of Criminal Intelligence, 2001; Davidson at el., 2003; and Ochoa, Davidson, Evans, Hahn, Page-Shafer, and Moss, 2005). Davidson and colleagues' (2003) study of heroin-related overdose deaths (*n*=333) revealed that 55% had cocaine and 12% amphetamine or methamphetamine present (Davidson et al., 2003). Ochoa and colleagues (2005) found that heroin mixed with cocaine and heroin mixed with amphetamine were significant predictors of recent overdose[32]. The authors suggested the following three explanations for these results. Firstly, co-use may act as a marker of heroin dependence. Secondly, the impulsivity typical of stimulant users may place co-users at greater risk (Moeller et al., 2001). Thirdly, chronic use of stimulants may make individuals more vulnerable to opioid overdose possibly by reducing the ability of the brain to take up oxygen.

4.10 Stimulants and Opioid Dependence Treatment

Stimulant use has been associated with worse treatment outcomes for people who are in treatment for opioid dependence (e.g. Peres, Trujols, Ribalta, & Casas, 1997; Downney, Helmus & Schuster, 2000); however, most of the research is based on cocaine use rather than amphetamines. Baseline levels of cocaine use and heroin use were found to be the most robust predictors of contingency management and buprenorphine maintenance outcome (Downey et al., 2000). Another study showed that the presence of the cocaine metabolite (benzoylecgonine) in the urine of clients at the beginning of a heroin detoxification program is strong a predictor of clients withdrawing from this treatment against medical advice (Peres et al., 1997). Also, a study conducted by Hartel and colleagues (1995) which looked at heroin use during methadone treatment (*n*=652) found that cocaine use was associated with heroin use during treatment (odds ratio 4.9), and this association was independent of the methadone dose. Hartel and colleagues suggested that it is possible that methadone clients who use cocaine do not experience the opioid cravings and blockage in the same way as those who do not use cocaine. It is likely that stimulant-opioid interactions do occur such as that indicated in a study conducted by Stine, Satel, & Kosten (1993) who found that cocaine use precipitated early and more severe opioid withdrawal among opioid dependent heroin users.

[32] The other four significant predictors were years since first injection, having been tested for hepatitis, extensive incarceration history and witnessing the overdose of others.

4.11 Treatment of the Co-use of Stimulants and Opioids

Many people in treatment for opioid dependence also have problems related to stimulant misuse, and more attention needs to be paid to the multidimensional nature of drug use patterns (Gossop et al., 2002; Strang et al., 2006). Many services are primarily geared toward opioid and alcohol dependence, and the treatments of stimulants have lagged behind (Foer, Mathers, Glenning, & Keen, 2004; Gossop, Marsden, and Stewart, 2000; Mazlan et al., 2006; Peters et al., 1997). It has been recognised in New Zealand (Ministerial Action Group on Drugs, 2003) and overseas, both by the clients (Foer, et al., 2004) and service providers (Keen, Gossop et al., 2000; Longo et al., 2004; Vincent et al., 1999), that there is a substantial gap in knowledge about amphetamine misuse and appropriate management. More resources need to be put into training of individuals who work in this area and into the development of improved treatment protocols for both methamphetamine use and treatment of multiple substances. At the same time it has been argued that core skills for successfully treating amphetamine misusers already exist in alcohol and other drug treatment services (Ritter, 2007).

Opioid substitution and residential rehabilitation are efficacious in terms of reducing opioid use (e.g., Degenhardt et al., 2005; Gossop, Marsden, Stewart, and Treacy, 2002; Mazlan et al., 2006). Gossop and colleagues analyses of the National Treatment Outcome Research Study revealed that while the frequency of heroin use more than halved in both methadone maintenance and residential rehabilitation over the two-year follow-up period, only residential rehabilitation was related to significant reductions in amphetamine use as well.

Similar results were found in the Australian Treatment Outcome Study with regard to stimulants (Darke, Williamson, Ross, & Teesson, 2006; follow-up of 24 months; n = 615). They found that weekly heroin use declined significantly at 3, 12, and 24 months across treatments and use of other drugs did not increase as had been found in non-treatment populations (e.g., Degenhardt et al. 2005; Longo, Henry-Edwards, Humeniuk, Christie, & Ali, 2004). Reductions in use of other opioids, cocaine, amphetamine, cannabis, and benzodiazepines were associated with less use of heroin, whereas alcohol and cannabis use was unrelated to heroin use (Darke, et al.,). Longer periods spent in residential rehabilitation was associated with reductions of all drugs, whereas, longer periods in methadone maintenance was associated with reductions of only heroin and alcohol, and longer periods of detoxification was not related to reductions of any drug use. Darke and colleagues suggested that the difference in drug reductions between residential rehabilitation and methadone maintenance reflect the focus of each of these treatments with methadone maintenance focusing on stabilisation through opioid substitution and residential rehabilitation adopting a global approach toward abstinence of all drugs. Rawson, Huber and colleagues (2002) also found that methadone maintenance was not effective in reducing cocaine use. Their analyses supported the efficacy of cognitive behavioural therapy and contingency management, but found no benefit in combining the two treatments.

While the abstinence-focused treatment may be appropriate for some clients, harm reduction strategies may be indicated for clients who are at an earlier stage of change (Baker and colleagues, 2001). Because many of the regular amphetamine users were also engaged in methadone maintenance, Baker and colleagues suggested that interventions could be provided in that context, along with primary care and community settings.

4.12 Summary

How exactly the “methamphetamine epidemic” affects the prevalence, presentation, and treatment of individuals with opioid dependences is yet to be determined. However, it appears that many opioid users also use amphetamines; and for some, amphetamines may be a gateway into opioid use. While crime, blood-borne disease, and overdose have been implicated in opioid use for a long time, it appears the use of amphetamines further increases the risk. In addition, a greater degree of psychopathology has been related to amphetamine use which may complicate the management of individuals who use both drugs. Stimulant use has been associated with worse outcome for those in treatment for opioid use. Additional or alternative treatment strategies may need to be adopted for individuals who present with problematic use of both opioids and amphetamines, particularly given the recognition that methadone maintenance treatment does not, in itself, treat other substance use problems. With the increased prevalence of amphetamine use and treatment presentations in New Zealand there is a clear demand for services to be able to address this need. The best treatment for amphetamine dependence, in the context of methadone maintenance treatment, remains as yet unclear and is an area requiring further research.

5.0 CONCLUSION

Opioid dependence is related to personal and social harm. The ability to prevent and reduce harm associated with opioid use relies on valid methodology and up-to-date information on the prevalence of opioid use and related problems. Direct methods of estimating prevalence such as those based on population surveys are likely to underestimate the prevalence of opioid use, and may do so to a substantial degree. While a variety of indirect methods have been devised for estimating opioid use, not one is without limitations. In the absence of a 'gold standard' convergence of estimates obtained from a variety of analytical methods and data sources is likely to give the most accurate results.

The majority of the research typically estimates the prevalence of opioid use but less is known about the prevalence of opioid abuse or dependence. Current research suggests that the worldwide use of opioids increased over the 1990s and has remained stable since 2000, and that New Zealand appears to have a high rate of opioid use in general relative to many other countries.

Opioid substitution is a harm reduction strategy which has a strong evidence-base for the treatment of opioid dependence. However, the number of opioid dependent individuals on waitlists for comprehensive opioid substitution treatment and the time on waitlists is a significant problem. Increased utilisation of G.Ps is currently the primary strategy for reducing wait-list for comprehensive opioid substitution treatment including interim prescribing and private treatment. An additional concern facing the presentation and treatment of opioid dependence is the "methamphetamine epidemic". It appears that many opioid users also use amphetamines; and for some, amphetamines may be a gateway into opioid use. The use of amphetamines in addition to opioids increases the risk of physical harm and complex psychopathology, and is related to worse treatment outcomes. Additional or alternative treatment strategies may need to be adopted for individuals who present with problematic use of both opioids and amphetamines.

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