



# DRUG SUBSTITUTION THERAPY: SUCCESS AND LIMITATIONS OF THE METHADONE AND BUPHRENORPHINE MAINTENANCE PROGRAMMES<sup>1</sup>

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## ABSTRACT

*Due to the severity of its drug problem, the Malaysian Government has allocated significant resources to rehabilitate drug addicts, which includes institutional drug rehabilitation and community care, all of which are mandated by the law for drug abusers charged under Section 6 (1) APD. In 2005, the government approved opiate maintenance therapies. However it was observed that in the early stages of the DST practice, there were various reports of substitute abuses in several parts of the country. Incidences of injecting subutex cocktail and oral consumption of subutex with benzodiazepines such as dormicum have been highlighted in the local press; including the exposé by the participants of the programme on the availability of these substitute drugs on the streets, have tainted the practice of DST in the country. The aim of this research to study the current DST practice in Malaysia, and the compliance to the DST protocol by the medical doctors involved in the DST; determine if there are positive outcomes of the DST among those following the programme; and to determine if there are any incidences of abuses among those involved in the programme. The study utilizes a cross-sectional survey designed to gather data from the practicing medical officers and drug dependents who have participated in the DST programme. Data was collected through several approaches; firstly via a structured interview*

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conducted on a sample of participating general practitioners in Kedah, Perlis, Penang, Kuala Lumpur and Johor who practiced DST. The interviews, among others will ascertain (i) if GPs adhered to the prescribed maintenance protocols set forth by MOH (ii) the number of clients/patients under the DST (iii) psychosocial intervention and (iv) record keeping. Data was also collected through structured interviews with drug dependents who accessed the GPs for buprenorphine or methadone maintenance therapy in hospitals. This is to ascertain (i) reasons for using DST (ii) past drug and treatment history (iii) dosage and length of time under DST (iv) familial and social support (v) dependency and possible abuse or misuse of the substitute drugs. Participants of the DST answer a Drug Profile Questionnaire, the Severity of Dependency Scale, ICD-10 Symptoms Checklist for Mental Disorders (Psychoactive substance use syndrome) and The Addiction Severity Index-Lite. More than 50% of the respondents reported benefits of the therapy; however incidences of non-adherence among the GPs were also identified. More importantly, almost half of the respondents reported abusing the substitute therapy by injecting and mixing them with other substances.

### ABSTRAK

Oleh kerana masalah dadah yang begitu serius, Kerajaan Malaysia telah menyediakan sejumlah peruntukan yang besar untuk memulihkan para penagih dadah termasuklah pusat pemulihan serta jagaan masyarakat. Kesemuanya itu dilakukan melalui peruntukan undang-undang yang diluluskan di bawah Seksyen 6 (1) APD yang diambil terhadap para penagih dadah. Beberapa pendekatan lain turut dikaji dan mulai 2005, kerajaan telah memperkenalkan program terapi gantian atau DST, yang turut diperkenalkan di banyak negara sebelum ini dan terbukti berkesan terutamanya jika ia dijalankan mengikut kaedah perubatan dan protokol yang betul. Melalui pemerhatian yang dibuat, adalah beberapa aduan diterima berhubung penyalahgunaan gantian pada peringkat awal pelaksanaan program DST di beberapa tempat di seluruh negara. Beberapa kejadian pengambilan koktail subutex melalui suntikan dan campuran subutex dengan benzodiazepins seperti dormicum yang diminum telah dilaporkan oleh media. Beberapa orang peserta program juga turut mendedahkan tentang bagaimana dadah gantian tersebut boleh didapati dengan mudah di jalanan dan hal ini sedikit sebanyak menjejaskan kelancaran program DST di negara ini. Oleh itu, kaji selidik ini mempunyai matlamat untuk melihat perjalanan program DST di negara dan sejauh manakah para doktor perubatan yang terlibat di dalam program ini mematuhi protokol yang ditetapkan; sejauh manakah terdapatnya kesan positif terhadap mereka yang mengikuti program ini dan seterusnya menentukan sama ada berlakunya penyalahgunaan di kalangan mereka yang



menerima rawatan melalui program ini. Pengumpulan data dibuat melalui kaedah tinjauan keratan rentas terhadap doktor-doktor perubatan dan para penagih dadah yang terlibat di bawah program ini. Data dikumpulkan melalui beberapa kaedah; pertamanya melalui beberapa temu ramah berstruktur yang melibatkan beberapa orang pengamal perubatan di beberapa kawasan di Kedah, Perlis, Penang, Kuala Lumpur dan Johor yang terlibat dengan DST. Temu ramah merangkumi beberapa aspek seperti (i) sama ada para pengamal perubatan tersebut mematuhi garis panduan yang ditetapkan oleh Kementerian Kesihatan Malaysia (ii) bilangan pesakit yang terlibat di bawah program DST (iii) aspek pencegahan psikososial dan (iv) penyimpanan rekod. Kaedah kedua melibatkan temu ramah berstruktur terhadap para penagih yang menggunakan saluran pengamal-pengamal perubatan untuk mendapatkan buprenorphine atau methadone bagi terapi pemulihan di hospital-hospital. Hal ini penting bagi memastikan (i) sebab-sebab mengambil DST (ii) sejarah penagihan lalu dan rawatan yang diterima (iii) sukatan ubat yang diambil serta tempoh menjalani DST dan (iv) latar belakang keluarga dan sosial mereka yang menjalani DST. Mereka yang mengikuti DST diminta menjawab beberapa soalan yang merangkumi 'Drug Profile Questionnaire', 'Severity of Dependency Scale', 'ICD-10 Symptoms Checklist for Mental Disorders' dan 'The Addiction Severity Index-Lite'. Lebih daripada 50 peratus responden mengakui akan kebaikan terapi yang diterima mereka. Walau bagaimanapun, beberapa pengamal perubatan dikesan melakukan pelanggaran terhadap garis panduan yang telah ditetapkan. Apa yang lebih penting, separuh daripada responden dikesan menyalahgunakan dadah terapi gantian dengan menyuntiknya atau mencampurkannya dengan bahan-bahan lain. Turut dibincangkan dalam kertas kerja ini implikasi dan masa depan program DST di Malaysia.

## INTRODUCTION

There are various estimates on the number of illicit drug users in Malaysia ranging from 300,000 to 500,000. In 2000, the total number of drug users identified was 30,593; new cases numbered at 14,850 with an average of 1,238 cases per month whereas the number of relapse cases was 15,743 with an average of 1,312 cases per month (National Drugs Agency, 2001). For 2005, this number increased to 32,808 with an identified 15,389 new drug addicts and 17,419 relapsed users. However, a reduction of 30.5% was observed for 2006 as compared to the previous year. From 1990 to December 2000, 14,122 drug users were identified (National Drugs Agency, 2001) and by 2006, a cumulative number of more than three hundred thousand was recorded, which accounts for more than 1% of the total population in the country (AADK, 2007).



The National Drugs Agency reported that there were 32,141 male and 667 female drug addicts in 2005. Among the first time identified drug addicts, heroin was the drug of choice (4,580 cases), followed by morphine (3,172), marijuana (3,120) and methamphetamine or syabu (2,983). Heroin is still the drug of choice for all drug addicts, i.e. for first-timers as well as relapsed cases (13,914) (National Anti-Drugs Agency, 2006).

Many of these drug addicts are legally mandated to government drug treatment programmes. In 1996, there were 48,216 drug users who were receiving rehabilitation. A total of 14,264 were placed in government rehabilitation centres; 9,107 inside correctional facilities and 24,845 in community programmes run privately by NGOs or by religious organizations (Ismail, 1998). In 2006, 5,148 drug addicts who received treatment were in government rehabilitation centres, 37,283 were in community-based programmes, 17,782 in the prison system and 6,662 in private centres.

The effectiveness of these programmes have not been systematically reported by National Anti-Drugs Agency (NADA). At present the only indicator of the programme's effectiveness is the ratio of relapsed drug users to new drug users who are mandated by the legal system for drug treatment and rehabilitation. In 2006, the ratio was 45.5% of new cases to 54.5% of relapsed cases.

### **Defining Drug Substitution Therapy**

Drug Substitution Therapy (DST) which is also known as "agonist pharmacotherapy" or "agonist assisted therapy" or "agonist replacement therapy", is defined as the administration under medical supervision of a prescribed psychoactive substance, which is pharmacologically related to the one producing dependence to people with substance dependence for achieving defined treatment (Dole, 1988; Kramber, 2001; Lesner, 1991; Marsden, 1988; NIDA, 2001). Substitution therapies have been used in the management of nicotine and opioid dependence. Substitution for opioid dependence is the focus of this study, which consists of agonist producing and opiate type effect or antagonists, a narcotic blocking agent that prevents the drug of dependence having a similar effect on the user.

The Burnet Institute fact sheet (<http://www.burnet.org>) states that drug substitution involves replacing the illicit drug that a drug user is taking with another similar acting and medically prescribed drug. Drug substitution also literally means taking the same drug but in a different way, for example, taking it sublingually instead of injecting the drug.



The pharmacologic effect of substitutes is different from the effects of opiates (Fiellin, 2002). With the substitutes, there is no euphoric effect and the regular, fixed doses wear off more slowly than opiates. Substitution treatments can stabilize a drug user's life by addressing and reducing their physical dependency and diminish various health, social and economic harms (Harden, 2002; Leavitt, 2003).

Thus, the aim of the drug substitution therapy is to reduce the risk of contracting or transmitting HIV/AIDS and other blood transmitted viruses (Payte, Zweben & Martin, 2003); to minimize the risk of overdose and other medical complications (Obadia et al., 2001); to switch from an injected to a non injected substance (Sung-Yeon, 1993); to reduce the sharing of injecting equipment (Maxwell et al., 1999); to reduce the motivation and need for drug users to commit crime to support their drug habits and to keep them out of prisons (Leavitt et al., 2000); to maintain contact with drug users; to attract drug users into counselling, referrals and treatment services (Payte et al., 2003; Resnick et al., 1992); and to help drug users stabilize their lives and reintegrate with the wider community (Payte, 2000).

The most commonly used opioid drug substitutions include methadone, buprenorphine, levo-alpha-acetylmethadol (LAAM), tincture of opium and naltrexone. In some countries, pharmaceutical heroin (diamorphine) is prescribed but this is uncommon (Stimson & Metrabian, 2003). No broadly effective pharmacological therapy has yet been identified to deal with psycho-stimulants such as cocaine and other categories of psychoactive substances. The prescribing of dexamphetamine, for amphetamine users, is being trailed in different parts of the world but its effectiveness is still under review (Reynolds, 1999).

Methadone maintenance, initiated by Dole and Nyswander in the 1950's, is the most widely researched treatment for opioid dependency (Dole, Nyswander & Kreek, 1966). Goals of the therapy include preventing the withdrawal syndrome, reducing narcotic craving and blocking the euphoric effect of illicit opioid use (Dole, 1988; Tenore, 2003). Methadone maintenance is a DST that requires the selection of a patient's suitability for a steady state of dosing, until the patient requires long-term therapy. Patients are guided towards a better quality of life by means of employment, positive familial and social relationships (Tenore, 2003; Wolff, 2002).



Methadone is the most widely researched and commonly used agonist pharmacotherapy. It is long acting (from 24-36 hours) and is taken orally once a day. When the dosage is correct (ranging from 60 – 100 mg per day) and stable, it effectively wards off withdrawal symptoms and suppresses the drug craving experienced by people dependent on opiates. Scientific evidence shows long term methadone maintenance treatment (MMT) is effective in the prevention of HIV by reducing HIV risk behaviours which is specifically related to injecting (Appel et al., 2003; Auerbach et al., 1994). It can also substantially decrease or eliminate drug use. Research shows methadone improves overall health and well-being, reduces criminal activity, increases mortality and reduces transmission of blood transmitted diseases and improves the psycho-social functioning and is also a relatively inexpensive form of treatment.

A minimum of 12 treatments with methadone is recommended so as to lead to better outcomes rather than short-term treatments. While there are many benefits to methadone, the side effects experienced by people include nausea, constipation, lethargy and a loss of libido. These symptoms usually settle down over time. Since methadone does not work for everyone, alternative drug substitutions are also needed (Leavitt, 1997; 1999, 2003b; Newman & Peyser, 1991; Payte & Khuri, 1993).

LAAM (levo-alpha-acetymethadol) is a synthetic opioid analgesic, which acts in a similar way to methadone. While it was extensively experimented in the 1970s, it was not until the 1990s that its availability and usage was increased. The major advantage of LAAM over methadone is that it has a longer half-life of 96 hours compared to 24-36 hours for methadone. This means the drug remains in the body for a longer period and therefore drug users do not have to be given a dose every day. Patients can take LAAM orally every 48 hours and in some cases every three days. This gives the patient greater flexibility and its longer effect also reduces the need to use illicit substances. The treatment's outcomes and the client retention are similar to methadone programmes. Research suggests that LAAM may cause cardiac problems and, while no longer marketed in Europe; other western countries continue to use it (Reynold, 1999; White & Irvine, 1999).

Buprenorphine, a synthetic opioid, is originally used as a painkiller. However, since the 1990s, it has been used to treat opiate



dependency. Buprenorphine is an alternative to methadone, possesses agonist/antagonist properties, providing a long duration of action, and can be administered on alternate days (NIDA, 2001). Unlike methadone, buprenorphine is poorly absorbed orally and thus needs to be taken sublingually (under the tongue). It has a relatively milder withdrawal symptom compared to methadone, and a high safety record (an overdose of buprenorphine alone is very difficult). Buprenorphine blocks the euphoria of exogenous opioid, prevents opioid withdrawal and has decreased the potential for abuse or overdose compared to methadone (Luty, 2003; McCrance-Kraz, 2004; Payte, 2002).

Subutex, which contains buprenorphine HCL, was approved by USFDA in October 1992. It is intended for use at the beginning of treatment for drug abuse (NIDA, 2001). Buprenorphine which has demonstrated efficacy in maintenance therapy, is available alone or in combination with naloxone (Suboxone). The addition of naloxone to Suboxone is actually intended to prevent an abuse of buprenorphine during the addiction treatment (NIDA, 2001).

Both substitutes are available as 2-mg and 8-mg tablets and its dosage is thrice a week. Although buprenorphine has the potential to be abused, it is considered to have less abuse potential compared to methadone. Moreover, unlike methadone, buprenorphine has shown minor cardiovascular effects across a wide range of doses, and buprenorphine antagonist effects are at higher doses thus making it difficult for an overdose. (McCrance-Kraz, 2004).

Naltrexone is classified as an opioid antagonist, which blocks the euphoric effects of opioid. It can help people stay off heroin after they have successfully withdrawn from the drug. It is a long acting drug (up to 72 hours depending on the dose) and is usually taken orally or grafted under the skin for slow release over a long period of time. The effectiveness of naltrexone often depends on the individuals' motivation to stay off heroin and the level of support provided to the individual. The side effects are minimal but research shows a poor acceptance of the drug and consequently a relapse to heroin is very common (Payte et al., 2003; O'Brien, 1996). Naltrexone is expensive, hence deemed inappropriate for poor countries. It was piloted in Malaysia in the late 1990's but was not widely accepted due to the negative side effects, which were reported as being quite adverse by the participants (Lasimon, 2006).



## DST in the Primary Care Setting

For a drug substitution programme to be successful, it needs to be effective for drug users. Programmes work better when they are tailored accordingly to the individual's characteristics and needs. Research has demonstrated that drug substitution provides many benefits for drug users and the wider community has become a key component in the drug treatment (Marsden, 1998). Drug substitution can help drug users regain control of their lives. But it needs to be coupled with the appropriate psychosocial care and practical assistance from medical practitioners and various specialized services in order to achieve long term positive outcomes (Watson, 1991; Strang, 1999).

As such, more treatment opportunities for opioid users are now available in primary care clinics. In the case of heroin dependence, the primary-care setting may decrease some of the potentially "negative" aspects of opioid maintenance programmes, including opportunities for interaction with patients who continue to use illicit drugs. For some opioid-dependents, the primary-care clinics may be preferred because it is less stigmatizing and offers easier access (McCance-Kraz, 2004). Furthermore, integrating substance abuse treatment and primary care may enhance the access of this group to the much-needed medical services such as preventive health care and the management of medical problems associated with drug use such as HIV infection.

However, one issue affecting the potential effectiveness of primary-care-based opioid maintenance treatment involves the level of psychosocial services available in this setting. In general, primary-care clinics provide only limited psychosocial services, as a more intensive or specialized drug counselling may not be feasible in this setting. Primary care-based maintenance programmes will only be able to provide brief medically focused counselling to patients. (Chowdhury et al., 1990; Moatti et al., 1998).

There are criterias that must be fulfilled by opioid dependents entering DST as stated in the Diagnostic and Statistical Manual 4<sup>th</sup> Edition (DSM – IV) the criteria includes the opioid dependence, opioid-positive urine toxicology, and should be at least 18 years old with a one year history of opioid addiction as well as evidence of physiologic dependence for methadone maintenance. Drug dependents were excluded if they were currently using and are dependent on alcohol, cocaine, benzodiazepines, or sedatives, or with a suicide or homicide risk, or had acute medical or psychiatric conditions.



Buprenorphine are provided in tablet forms of 2 or 8 mg, which are administered sublingually. The Yale Buprenorphine Clinic prescribes the following protocols: Following a one week induction, treatment is to be administered at 24 mg on Monday and Wednesday and 36 mg on Friday. The dosage protocol allows for two dose upgrades to 28, 28, and 40 mg for the first upgrade and 32, 32, and 48 mg for the second upgrade. The buprenorphine dosage was increased for the continued positive urine toxicology or the patient's discomfort due to withdrawal. During detoxification, treatment was administered at 16mg on Monday and Wednesday and 24 mg on Friday during the first week and 8 mg on Monday and 4 mg on Wednesday and Friday during the second week.

At the same time, patients should receive psychosocial support in various forms either from clinics or peripheral support services. The Yale Clinic provides Medical Management (MM), which is a manual-guided treatment provided in thrice weekly sessions with a nurse that lasts approximately 20 minutes. Additionally, patients will meet monthly for approximately 20 minutes with a general internist physician or counsellor. All sessions used a brief counselling format. The sessions covered: (1) a review of recent drug use or efforts to maintain abstinence, (2) a review of attendance at self-help groups, (3) support for efforts to reduce drug use or remain abstinent, (4) brief advice on how to achieve or maintain abstinence, and (5) thrice weekly urine sample collection and review. Half of the patients received MM as well as manual-guided drug counselling which was provided on-site during the weekly 45-minute sessions.

## **PROBLEM STATEMENT**

### **Misuse and Abuse of Substitution Drugs**

The availability of methadone and buprenorphine for the treatment and maintenance programme for opiate drug users has been a welcoming development for treatment specialists all over the world. Theoretically, the use of drug substitution is safe with consistent monitoring by attending medical officers and counsellors or social workers to manage their treatment over time. However, both methadone and buprenorphine has the potential of being abused by individuals in a maintenance programme or by those not in the programme (Belluck, 2003; Gendreau-Webb, 2004).

Incidences of misuse and abuse of methadone and buprenorphine is evident, though not well documented in the literature. Most of the



abuse cases are related to overdose of the substitutes usually in a cocktail mixture with other illicit drugs or medications (Chowdhury & Chowdhury, 1990; Grichard et al., 2003) and by injecting the cocktail intravenously (Grichard et al., 2003; Jenkinson et al., 2005; Faizal, 2006; Loo et al, 2005).

The issue of non-compliance with therapy and undesirable dropout rates is a common problem during the addiction treatment and this includes DST and MMT (Luty 2003). While adequate methadone doses can be effective in reducing or eliminating illicit-opioid abuse (Leavitt 2003b), some studies have found illicit-drug use of any sort persisting in 1 of every 5 MMT patients during any given month (Wechsberg et al. 2001), with about half of them also continuing to misuse opioid (Marion 1993).

Lejeure (1989) commented on the British drug legalization programme whereby under the Misuse of Drug Act, 1969, British doctors can treat known drug users and addict, but are obliged to register their names which is primarily for statistical purposes with the advent of methadone. In his observation, some doctors prescribed methadone in large quantities instead of progressively reducing the addict's dosage. One reason for such an act is because the demand is so great and there were many clinics that offer maintenance treatment. In his article, Lejeure also attributed the failure of the methadone programme to the many addicts who were on a methadone regime and added illegal drugs to their methadone ration or sold methadone to acquire heroin. He also identified that some doctors supplied methadone that could be injected and this was more popular with addicts because it acts faster.

In Germany, Newman (1995) stated that with the initiation of the methadone pilot programme, there was a dramatic drop in heroin usage among the programme participants. Several methadone programmes all over Germany have indicated the success of the endeavour and all published reports were positive. He however cautioned that there were failures in the methadone programmes, which have not been reported in the country.

In the US, where there was an increase in methadone-related deaths, the methadone that was abused appeared to be in the form of tablets prescribed for pain. These are sold or sometimes given to addicts by people who have stolen them from patients or, in some cases, given by the patients themselves (Baden, 1970). Addicts either swallow the tablets or grind them into powder that can be inhaled or turned into liquid and injected. Methadone has been produced in the liquid form;



however it must only be used in drug clinics. Many clinics across the U.S abide by federal guidelines designed to make methadone treatment more accessible. But many have stopped requiring patients to take all their daily doses at the clinic, and instead are allowing them to take home doses of methadone once a week or more. This opened the possibilities for more abuse.

Belluck (2003) reviewed methadone-related deaths in several states in the U.S and attributed it to methadone overdose because it is more readily available with a prescription. In states where methadone-related deaths are high, the usual abuse cases are usually with methadone tablets where it is easily passed on from one person to the next illegally. Also recorded were death-related cases attributable to injecting methadone.

There are also records of methadone abuse in forms other than those stated in the research reports. In a testimony of Michael Chitwood (2003), Chief Police of Portland, Maine, he stated his experience in observing the Methadone abuse that had grown to epidemic proportions. In 2002, Methadone was identified as the cause of 30 deaths in Maine, mainly due to accidental overdose. In his testimony, Chitwood stated that Methadone dispensed in some clinics were for increasing profit because they increased the dosage and gave high take home supplies whilst little monitoring was done on these clinics by the state office of substance abuse. ([http://www.senate.gov/ngov.aff\\_files/080603chitwood.htm](http://www.senate.gov/ngov.aff_files/080603chitwood.htm)).

Similar natures of abuse were also noted in Florida where the Florida Office of Drug Control (ODC) issued a safety alert in 2002 after 254 deaths were confirmed to be related to the abuse of the prescription drug Methadone between January to Jun 2002 as well as an increase of 31% in the prescriptions as compared to the previous 6 months (<http://www.fdle.state.fl.us/alerts/2002/methadone-alert.html>).

CSAT (2004) reported that deaths cause by methadone had tripled from 24 to 76 between 1998 and 2002 with a total of 225 deaths in just a span of 5 years. Methadone related emergencies increased by 230% between 1994 till 2004. In Baltimore alone, there were 8.2 emergency methadone cases for every 100,000 of its population. Among the contributing factors was an increased sale of methadone in the state, where there was a rise of 167% in sales between 1998 and 2002 of which included the usage of methadone as a pain reliever (Dolphine) and the abuse by opioid drug users in MMT.



The same situation has been observed for buprenorphine. The National Drug Intelligence Centre (NDIC) in its September 2004 Bulletin warned that buprenorphine is a synthetic opiate that can produce euphoric effects and are sought by opiate abusers and therefore it is susceptible to abuse. It can be crushed, turned into liquid and injected, either by itself or mixed with other substances.

Five European member States in 2003 reported a post-mortem on the findings of buprenorphine in the blood. Eight reported cases in France and 44 in Finland were linked to Subutex. The difference between the two countries is striking given that in France, approximately 72,000 to 85,000 people were receiving buprenorphine substitution treatment, whereas in Finland, 460 patients were treated in 2004 with buprenorphine. In Finland, buprenorphine is frequently used as substances for abuse, and in 2003, 90% of the users undergoing the treatments were injecting it. But in France, about one-third of those using buprenorphine outside the protocol injected the substance. Finally, two deaths associated with buprenorphine were reported in Luxembourg and two in Sweden.

When the data on the number of deaths related to methadone misuse and the number of deaths related to buprenorphine misuse were compared, buprenorphine appeared to be associated with a lower risk as compared to methadone (Buster, 1996). For instance in France in 2003, eight deaths that were related to buprenorphine were reported out of 72,000 to 85,000 people who were receiving buprenorphine substitution treatment; as compared to eight deaths related to methadone, out of a total of 11,000 to 17,000 treatment clients (French National Report).

Buprenorphine has opioid agonist effect and therefore individuals who were not physically dependent on opioid can abuse it. However, if buprenorphine is mixed with other substances such as benzodiazepines, it has a strong potential to be abused (Maremmani & Shinderman, 1999). Deaths due to buprenorphine misuse are very rare, and it is thought that the risk of overdose is lower with buprenorphine than with other opioid because of its agonist-antagonist pharmacological characteristics (i.e. beyond a certain dose, a further increase does not result in any further increase in effect) and because it's usual administration is sublingual.

Pirnay et.al (2004) investigated buprenorphine and methadone associated deaths and concluded that it is difficult to determine the role of substitution drugs in the death process as many other factors may be involved including the circumstances surrounding the death, past history



and drug usage patterns (especially benzodiazepines and neuroleptics). The potential for a synergistic effect in particular and opioid, benzodiazepines and alcohol together with buprenorphine and methadone must be reconsidered.

The Institute of Mental Health, Singapore stated that there were 4,000 patients who were prescribed buprenorphine in 2004. Even though the dispensation and the usage of subutex is theoretically safe, there is evidence of abuse (Loo, et al, 2005). Faizal (2006) observed that several deaths among buprenorphine users in Singapore were associated with the blockage of blood vessels. This incident is frequently observed among those who combined buprenorphine and benzodiazepines such as dormicum and by injecting the cocktail intravenously. Loo et al. (2005) reported severe upper limb complications caused by the abuse of subutex in Singapore, and these were due to injecting subutex. Singapore banned subutex which is now categorised as Class A Drug, since August 2006 (NCB, 2007).

Jenkinson et al. (2005) observed that a third of 156 IDU sampled for their study in Melbourne, Australia injected buprenorphine in their lifetime and 33.0% had injected the drug in the last 6 months. About 47% of those who reported a recent injection obtained the drugs illicitly. The study concluded that buprenorphine injecting is serious and required monitoring and intervention.

Chowdhury and Chowdhury (1990) found that over two and half years experience of opiate addiction cases at a de-addiction clinic revealed its increasing rate of abuse, especially as a substitute for heroin. Reynand et al. (1998) found that the cause of death is linked to a concomitant use of buprenorphine and benzodiazepines. Their study concluded that the dispensing of both drugs must be observed, as it is open for abuse.

Grichard et al. (2003) did a cross-sectional study on 197 methadone and 142 buprenorphine that was used at drug dependence clinics and several general practitioners in France. They found that 35.4% of the methadone group and 36.6% of the buprenorphine group used at least one illicit drug as a substitute; 25.7% reported injected drugs and 15.3% injected the substitution drugs. Injecting was more common in buprenorphine maintained individuals (40.1%) as opposed to methadone-maintained individuals (15.2%).

Obadia et al. (2001) sampled 343 IDUs who were attending community pharmacies; needle exchange programmes and syringe vending machines to ascertain the injecting misuse of buprenorphine in



France. They found that 33.8% were poly drug users who occasionally injected buprenorphine whereas 23.9% had injected the substitute in the last 6 months. The study concluded that there is a substantial risk of injecting misuse and it was associated with large-scale diffusion of buprenorphine DMT and called for a more stringent regulation for medical distribution of buprenorphine.

There were also studies that investigated the perception and attitude of the medical community towards DST. Moatti et al. (1998) assessed the attitudes of general practitioners towards buprenorphine maintenance drug abuse treatment right after it was introduced in the French ambulatory care in 1996. They found that a minority number of GPs (24% took care of IDU patients and 30.8% of this group) were ready to prescribe to buprenorphine (i.e., only 7.5% of the sample).

Although the general attitude is positive, however, not all GPs accepted IDUs into their treatment. While the benefits of methadone and buprenorphine have been very encouraging, however, from the literature review, there were also distinctive misuse and the occurrences of the drug substitute abuse in the treatment and maintenance of opioid dependence. This is attributed to the non-adherence to the treatment protocols such as oversupplying the drugs to patients and not having any provision of psychosocial intervention with the maintenance programme.

### **DST in Malaysia**

Malaysia has identified its drug problems since its pre-independence days. In the early 70's, it can be seen that several government initiatives had been undertaken to reduce and eradicate the problem. Its approach has always been on the supply and demand reduction up to the year 2005.

Methadone was introduced in the late 50's and is widely used in many parts of the world. However, there have been no records on the application of methadone in any drug rehabilitation programme in Malaysia. An interview with the National Anti-Drugs Agency indicated that there have been some efforts to bring methadone in the country during its early stage of development and trials, but it was banned in Malaysia in 1972.

It was not until 2005 that the Malaysian government reconsidered the use of drug substitution as a mode of treatment and rehabilitation in



the country. It was reconsidered due to the following reasons: most drug users are opiate abusers, especially heroin; 75% of all HIV cases recorded in Malaysia are among the IDUs and the demand reduction approach has not been very successful in rehabilitating drug users.

The methadone programme was launched as a pilot project that involved 1,200 drug users in 10 government hospitals and 2 private clinics. The second stage included about 5,000 drug users who were given free methadone as an effort to reduce their heroine addiction (MOH, 12-06-06, <http://www.moh.gov.my>).

Many of the strategies to combat drug addiction in Malaysia recommend the demand reduction approach. In the past, there have also been several efforts to introduce harm reduction strategies in Malaysia. Advocates of these strategies outlined three main strategies to reduce the negative effect of addiction on the individual, his family and the community at large. These strategies are:

- Information, education and communication (IEC), that is providing information on HIV prevention and educating the drug users using peer based education and outreach programmes;
- Needle or syringe exchange programme (NEP), that is to ensure IDUs have access to clean syringes and needles as this is claimed to be the cheapest way of preventing HIV transmission among injecting drug users; and,
- Drug substitution programme or therapy (DST) which is aimed to reduce infectious diseases such as HIV and Hepatitis among DUs and IDUs, to improve the general health of drug users, reduce drug-related crimes and to complement the traditional addiction care by diversifying the treatment options.

From the existing literatures, DST is presented as a logical alternative to the present drug treatment and rehabilitation system for opioid dependency. The Malaysian government has allocated significant resources to treat and rehabilitate drug addicts. The estimated cost of rehabilitation at the Serenti Drug Treatment centre is RM19.77 per person per day (AADK, 2006) and this excludes the cost of continuing community care which is mandated by the law for drug abusers charged under Section 16 (1)(6) APD and for those who have completed the institutional programme for another two years. Thus, it is necessary to allocate some cost of treatment onto the person such as maintenance therapies. As pointed



out in the literature, the efficacy of DST has been proven in many countries especially when it is conducted in line with proper treatment guidelines and protocols. Furthermore, the purpose of DST and harm reduction in general is not to achieve total abstinence, but to provide an alternative path to recovery as defined, by having employment and education opportunities, reducing criminal activities, build positive family relationships and maintaining higher social responsibilities among drug using community (Resnick et al. 1992; Tenore, 2003; McCance-Kraz, 2004).

However, in the early stages of the DST practice, there were various reports of subutex abuses in several parts of the country. Incidences of injecting subutex cocktail and oral consumption of subutex with benzodiazepines such as dormicum was highlighted in the local press; including the exposé by the participants of the programme on the availability of these substitute drugs on the streets, had tainted the practice of DST in the country.

Therefore, to ensure the success of DST in Malaysia, the following questions need to be addressed. Who are the clients of DST, what is the state of current practice of DST in Malaysia in terms of conformity or adherence to the DST protocol or guidelines by the participating medical doctors? Are there any positive (or at least short term) outcomes of DST, and finally, are the drug users in Malaysia abusing these substitutes?

## OBJECTIVES

In general, the objective is to ascertain the success and limitations of the methadone and buprenorphine maintenance programmes. Specifically, this study will:

- i. Identify the users of DST, its current practice in Malaysia, and the compliance to the DST protocol by the medical doctors involved in the DST;
- ii. Determine if there are positive outcomes of DST among those following the programme; and
- iii. Determine if there are any incidences of abuses among those participating in the programme

## METHODS

This study is a cross-sectional survey. Data are collected from practicing medical officers and drug dependents who have participated in the DST programme between June to August 2006.



There are two categories of respondents in this study; thus, two groups were identified. First are the medical officers or general practitioners who have obtained license to dispense methadone or buprenorphine for the maintenance therapy of opiate drug users. The list is as provided by the National Anti-Drug Agency (NADA) and the Ministry of Health. The second group in this study are the participants of methadone or buprenorphine programmes, either for the purpose of the maintenance therapy or those who use, misuse or abuse the medication. An estimate by Dr Mahmud Mazlan from the Substance Abuse Centre (SAC), Muar, stated that there are approximately 25,000 subutex users based on the 15 kilograms of buprenorphine imported in 2006, while MOH has about 1,500 participants of the methadone programme at government hospitals.

Data was collected through the following approaches. Firstly, a structured interview was conducted on a sample of participating general practitioners in Kedah, Perlis, Penang, Kuala Lumpur and Johor area who practice DST. The interviews, among others will ascertain (i) if the GPs adhere to the prescribed maintenance protocols set forth by MOH (ii) the number of clients/patients under the DST programme (iii) psychosocial intervention and (iv) record keeping.

Secondly, another structured interview was conducted for the drug dependents who consulted the GPs for buprenorphine or methadone maintenance therapy. This is to ascertain (i) reasons for using DST (ii) past drug and treatment history (iii) dosage and length of time under DST (iv) familial and social support (v) dependency and possible abuse or misuse of the substitute drugs. Participants of the DST will answer a Drug Profile Questionnaire, Severity of Dependency Scale (Gossop et al. 1995), ICD-10 Symptoms Checklist for Mental Disorders (Psychoactive substance use syndrome) (Janca et al. 1994) and The Addiction Severity Index-Lite (McLellan et al. 1980).

## FINDINGS

The respondents totalled to 225 drug substitutes users of which 204 (90.7%) were male and 21 (9.3%) were female. A large number (n=189; 84.8%) were from the Malay ethnic background, while 21 (9.4%) were Chinese and 12 (5.4%) were Indians. Most of them were single (n=118; 53.2%); 55 (24.8%) were married and 49 (22.1%) were either separated or divorced. More than 95% have received their education up to the Form 5 level and mostly (25.8%) work in the construction sector.



Almost all respondents are lifetime polydrug users. Table 1 presents the type of substance frequency used by the respondents. All of them used heroin, morphine, candu or other forms of opiates and its substitutes. However, many respondents also used ganja (30.6%), psychoactive pills (24.8%) and ATS, specifically syabu (20.8%). This indicates that while all respondents fit the criteria of opiate users for the DST, they also used other illicit substances such as marijuana, psychoactive pills and ATS, and as such, this may pose to be a limitation to the efficacy of the DST.

**Table 1: History of Drug Usage**

Substance	Frequency	Percentage %
Alcohol	7	3.1
Heroin/morphine and opiate	225	100
Ganja	69	30.6
Psychoactive pills	56	24.8
ATS/Syabu	47	20.8
Methadone or Subutex	7	3.1

The respondents have been using drugs between the range of 1 to 50 years with a mode of 10 years and a mean of 13.21 years. Some took drugs as early as 10 years old and as late as 34 years old with a mode of 20 years old, and a mean of 18.92 years old. A significant number (40.5%) used drugs due to peer pressure and curiosity (28.8%). A total of 183 respondents have undergone prior treatment programmes, mainly at Serenti.

Their family backgrounds and profiles were as follows: A total of 57% have fathers who are still alive, and 75% reported that their mothers were still alive; 63.1% reported that their parents were still living together. Most of the respondents (63.1%) were living with their families, whereas those who did not lived either with their siblings (18.3%), by themselves (25%), with friends (18.3%), other family members (15.0%) and with their spouses (10%). A majority of them reported that their family has knowledge of their drug problems. Their fathers were mostly retirees (20.7%), operated their own businesses (17.1%) or worked as farmers (17.1%), while their mothers were mostly housewives (64.8%).

As for their living environment, a total of 119 (53.4%) resided in towns or cities while 104 (46.6%) lived in villages and rural areas; 118



(54.1%) lived in a “kampung” house, 32.6% (n=71) in suburban residential parks or ‘taman’, around 7.8% (n=17) in flats, 3.7% (n=8) in bungalows and 4 respondents (1.8%) lived in squatter houses in slum areas. There were approximately 1 to 12 people living in their dwellings with a mode of 4 persons and a mean of 4.92 persons. When respondents were asked on the number of drug users and addicts near their homes, 49.3% (n=108) admitted there were some but not many; 34.4% (82) said that there were many drug users around while 13.2% said there weren’t many. However, most of the respondents who informed that there were many drug users around their homes was among those living in the squatter areas, flats and bungalows but those living in residential parks (taman) and villages only reported the presence of a few drug users though not many.

Most of the respondents (n=199; 88.9%) said that their friends were also using drugs, in fact, a total of 135 persons (61.1%) said that their friends were tested and found to be HIV positive. One main reason for this is that 180 respondents (81.1%) said that their friends injected the drugs.

On their current drug usage, most of the respondents interviewed in this study used Subutex (n=160, 84.2%) while 6(3.2%) used Methadone and 2 (1.1%) used naltrexone. About 20(10.5%) switched alternately between Subutex and Methadone.

It is interesting to note that when respondents were asked on drug substitutes used before their current usage, quite a number had tried other substances in an effort to control their addiction (Table 2).

**Table 2: Substitute Drugs Used Before Current Substitute Therapy**

Substitutes Used in the Past	N	%
Candu, heroin, morphine	4	1.7
Alcohol	2	1.7
Ketum/kratom	9	0.09
Erimin pills	39	17.4
Subutex	74	32.9
Methadone	21	9.4
Naltrexone	7	3.2



Cough medicine/codeine	1	0.45
Syabu	3	1.35
Ganja	2	0.09

It is also important to note that 74 respondents used Subutex and 21 used Methadone, indicating that some may have switched to the other drug for their current usage. It is also possible that some are using both substitutes now (Tables 3).

This study also looks at the severity of addiction with the types of substitutes they are using now. It was found that there is no difference between the type of drug substitutes used with the severity of their addiction or their level of dependency as noted by the Severity of Dependency Scale (Gossop et al. 1995) and the ICD-10 Symptoms Checklist for Mental Disorders (Psychoactive substance use syndrome) (Janca et al. 1994) (Table 15)

**Table 3: Three Types of Substitutes Currently Used**

	Frequency	Percent (%)
Subutex	160	84.2
Methadone	6	3.2
Naltrexone	2	1.1
Others	2	1.1
Subutex & Methadone	20	10.5
Total	190	100.0

**Table 4: Severity of Addiction with The Type of Substitutes**

		Sum of Squares	Df	Mean Square	F	p
Severity	Between Group	5.395	4	1.349	.433	.789
	Within Group	539.352	173	3.118		
	Total	544.747	177			
ICD 10	Between Group	23.453	4	5.863	.824	.511
	Within Group	1209.404	170	7.114		
	Total	1232.657	174			



Current users of substitutes got the information about DST from various sources. A significant number (75.2%) stated their friends as the source of information; 8% obtained it from medical doctors and 4% each, obtained information on DST from friends and family members. This is as reflected in Table 5. As with the initiation of the drug used, 169 (75.2%) reported that they knew about DST from friends, followed by medical doctors (n=18; 8%), NADA and family members (each 4.0%). They have used substitutes for an average of 33.2 months.

**Table 5: Source of Information for DST**

Who Inform Respondents About DST	Frequency	Percent
National Anti-Drug Agency	9	4.0
Friends	169	75.2
Medical Doctors	18	8.0
Family Members	9	4.0
Employer	1	0.45
Info from Media	9	4.0
NGOs	1	0.45

A small number (n=34; 13.4%) said they also used substitution with other substances, which they considered as a part of the medication regime, mostly with ketum leaves (n=14) and psychoactive pills (n=12) (Table 6).

**Table 6: Other Substances Currently Taken with Substitutes**

	Frequency	Percent
Candu	1	0.45
Daun ketum	14	6.2
Eramin 5	1	0.45
Heroin	1	0.45
Psychoactive pill	12	5.3
Syabu	2	0.9
Xanax	1	0.45
Sleeping pills	2	0.9



Most users of substitutes (161) said that DST was suggested by their friends followed by doctors 6=30, 13.4% and family members (n=14; 6.3%) (Table 7).

A total of 121 (53.8%) said they abided by the instructions of the medical doctors pertaining to the usage of substitutes; 104 (46.2%) said they did not follow the instructions, 84 said they injected it, while the others mixed the substitutes with other substances (cocktail) and swallowed it (Table 8).

**Table 7: Who Suggested to the Respondents to Use Substitutes**

Suggested by	Frequency	Percent
AADK	2	0.9
Doctors	30	13.4
Friends	161	71.6
Family	14	6.3
Employer	2	0.9
NGO	2	0.9
Self	11	4.3

**Table 8: How Do You Use Subutex/Methadone?**

	Frequency	Percent
As instructed by doctors	121	53.8
Not as instructed	104	46.2
a. Injected	84	37.4
b. Cocktail	20	8.9
Total	225	100

When asked about the effects of the substitutes drugs on them, a total of 164 (44.5%) responded that it could stop the withdrawal symptoms; 20.7% felt relaxed and 17.7% experienced some degree of “being high” (Table 9).



**Table 9: Effects of The Substitutes**

	Frequency	Percent
Can work	10	6.1
“High”	29	17.7
Stop withdrawal	73	44.5
Hot	6	3.7
Thirsty	5	3.0
Manage Pain	2	1.2
Relaxing	34	20.7
No Effects	3	1.8
Feel Weak	2	1.2
Total	164	100.0

Only 92 (45.3%) of the substitute’s users obtained their medication from the same doctors while the remaining 111 (54.7%) did not. About 37.5% went to two doctors and 30.7% went to three doctors (Table 10). On the average, the respondents met between one doctor to 3.4 doctors (sd 1.64). A total of 164 (85.4%) said that the doctors told them the right way of taking the substitutes. Similarly, 106 (74.6%) respondents also said the doctors provided some counselling prior to the start of the programme, while 36 (25.4%) admitted that no counselling was provided to them.

**Table 10: The Number of Doctors Visited for DST**

Number of Doctors Visited for DST	Frequency	Percent
2	33	37.5
3	27	30.7
4	7	8.0
5	7	8.0
6	7	8.0
7	7	8.0
Total	88	100.0



In addition, 62 (32.5%) informed that they always purchased substitutes from the clinic counter or dispensary, 57 (29.8%) said they sometimes purchased the substitutes from the dispensary while 72 (37.7%) only purchased them directly from the doctors. However, 81.5% did not go to the same doctor and the doctor did not tell them how to use the medication as opposed to 47.6% who visited different doctors but the doctors did inform them on how to properly use the medication (Table 11). Furthermore, 74.1% reported that they did not use the medication properly and that the doctors did not inform them on how to properly use the medication as opposed to 33.7% who used the medication properly even when the doctors did not inform them on how to properly use the medication (Table 12).

In addition, Table 13 indicates that clients of DST stated a higher severity as measured by the ICD-10 Symptoms Checklist for Mental Disorders (Psychoactive substance use syndrome) (Janca et al. 1994) for those who tend to obtain medication from many doctors ( $t=-2.59, p<.05$ ). This shows that the respondents who obtained DST from several GPs had a higher level of substance dependence then those who obtained the medication from one GP only. No differences were noted with the dependence as measured by the Severity of Dependency Scale (Gossop et al. 1995).

**Table 11: Did You Obtain the DST from the Same GP?**

		Obtain from Same GP	Not from the Same GP	Total
Do doctors inform you on the right way to use DST	Yes	86	78	164
		52.4%	47.6%	100%
		94.5%	78.0%	85.9%
		45.0%	40.8%	85.9%
	No	5	22	27
		18.5%	81.5%	100%
		5.5%	22.0%	14.1%
		2.6%	11.5%	14.1%
	Total	91	100	191
		47.6%	52.4%	100%
		100%	100%	100%
		47.6%	52.4%	100%



**Table 12: Did You Follow the GP's Instructions?**

		Follow GP's Instruction	Did Not Follow GPs Instruction	Total
Do doctors inform you on the right way to use DST?	Yes	108	55	163
		66.3%	33.7%	100%
		93.9%	73.3%	85.8%
		56.8%	28.9%	85.8%
	No	7	20	27
		25.9%	74.1%	100%
		6.1%	26.7%	14.2%
		3.7%	10.5%	14.2%
	Total	115	75	190
		60.5%	39.5%	100%
		100%	100%	100%
		60.5%	39.5%	100%

**Table 13: Severity of Independence and ICD-10 for Respondents Who Obtained the DST from the Same GP**

Get DST from Same GP	N	Mean	sd	t	p
Severity	85	7.69	1.58	1.06	.28
ICD-10	84	7.17	3.02	-2.59	.01

Respondents were also asked on how to evaluate the effect of the substitute therapy. This is reflected in Table 14. Almost 50% of the respondents said that they can work, or go to school, and that they did not feel that they needed the drugs, about 31.3% said they did not crave for the drugs and 22.7% said that they have good familial relationships. However, 18.7% said they did not feel any difference at all.

**Table 14: Evaluation of Respondents on the Effects of DST**

Evaluation on the Effect of DST	n	%
Can work /school	112	49.7
Have good family relationship	51	22.7
Do not crave drugs	68	30.3
Do not feel that they need drugs	112	30.3
Not much difference	42	18.7

### Adherence to the DST Guidelines

The first objective is to identify the current practice and the degree of conformity or adherence to the DST protocol by the medical doctors involved in the DST.

A total of 26 private clinics that dispensed subutex responded to the study. Most of them (17 or 68%) have obtained proper rights to practice DST from the Ministry of Health, while others operated as private medical clinics. Only 50% (12) submitted their reports to the Agensi Antidadah Kebangsaan (AADK).

At the beginning of the DST treatment session, most clinics confirmed that they conducted initial interviews to determine the severity and suitability of the case (96.2%) and the majority performed medical tests on their patients (92.4%). Nevertheless, only a total of 84.6% checked on every patient who came in for the treatments and almost all kept records of patients undergoing DST with them (Table 15).

**Table 15: DST Practices at Clinics**

GP RESPONSES TO DST	YES (%)	NO (%)
Have licence / agreement from MOH to practice DST	17 (68%)	8 (32%)
Conduct initial interview to determine severity of cases	25 (96.2%)	1 (3.8%)
Perform medical check-up before beginning treatment	24 (92.4%)	2 (7.6%)



Check on every patient who comes in for DST	22 (84.6%)	4 (15.4%)
Record treatment dosage given to patients	23 (88.5%)	3 (11.5%)
Patient must see doctors before treatment	19 (76%)	6 (24%)
Who dispenses the medication		
i. Doctors	15 (57.7%)	
ii. Doctors and dispensary	11 (42.3%)	

The DST treatment guidelines or protocol outlined by the Ministry of Health specifies that a medical officer must dispense the DST. However, only 57.7% of clinics agreed that mostly doctors dispensed the medication while 11(42.3%) respondents said that at times, it was dispensed by the doctors and sometimes by the dispensary (nurse, clinic personnel). A total of 88.5% recorded all treatments that were given while another 3 (11.5%) only recorded it sometimes. Only 19 (76.0%) said that they required the patients to see the doctors before taking the medication (Table 15).

DST guidelines also required medical doctors to investigate and identify signs of misuse and abuse. Only 20 (83.3%) clinics asked if other drugs were used during the treatment, 20 (80.0%) asked if any other medications were used during the treatment; 18 (69.2%) looked for signs of abuse such as needle puncture marks; 18 (69.2%) asked about social and familial support that the patients received and 21 (84%) enquired about the patients' school or occupational status (Table 16).

**Table 16: DST Adherences at Clinics**

ADHERENCES	NO (%)	SOMETIMES (%)	YES (%)
1. Clinic asks clients the types of drugs currently used	1 (4.2%)	3 (12.5%)	20 (83.3%)
2. Clinic asks on types of medication used by clients during DST	1 (4%)	4 (16%)	20 (80%)
3. Clinic looks for signs of abuse (eg needle marks)	1 (3.8%)	7 (26.9%)	18 (69.2%)



4. Clinic asks about social/ familial support	1 (3.8%)	7 (26.9%)	18 (69.2%)
5. Clinic asks about school/occupation of clients	-	4 (16%)	21 (84%)
6. Clinic investigates if medication are taken as prescribed	-	3 (12%)	22 (88%)
7. Clinic investigates on the general health of clients	-	6 (24%)	19 (76%)
8. Clinic investigates on signs of overdose	3 (12.5%)	5 (20.8%)	16 (66.7%)
9. Clinic investigates sign of relapse	1 (4%)	5 (20%)	19 (76%)
10. Know actual health status of clients	1 (4%)	1 (4%)	23 (92%)
11. Observe psychiatric condition of clients	1 (17.4%)	-	19 (82.6%)
12. Clinic permits doses to be taken at home	3 (12%)	-	22 (88%)

However, most of the clinics (n=22 or 88%) did investigate if the dosage taken was as prescribed but not as many looked into the general health of the patients (19 or 76%); some clinics investigated for signs of overdose (n=16 or 66.7%); while some investigated for signs of relapse (n=19 or 76%) (Table 16).

However, if patients were found to be abusing the treatment, most of the clinics (n=14 or 58.3%) gave advice, 6 clinics (25%) responded that they would drop the patients from the programme, 2 clinics (8.3%) responded that they would provide counselling and 1 each (4.2%) would give warning or take no action at all (Table 16). Most clinics (64%) answered that they would adjust the dosage of the medication based on the requirements of their patients (Table 17).



**Table 17: How Does The Clinic Manage and Adjust The Dosage of The Medication**

	Frequency	Percent
Observation	3	12.0
Depends on patient	16	64.0
Doctors' discretion	1	4.0
Reduce dosage	2	8.0
Increase dosage	3	12.0
Total	25	100.0

In general, most clinics (92%) knew the health status of their patients because they came in quite regularly to obtain their medication, and most of them (n=19 or 82.6%) observed their patients for any psychiatric conditions. Most of the clinics (n=22 or 88%) permitted dosages to be taken at home but this depended on the requirements of the patients (Table 16).

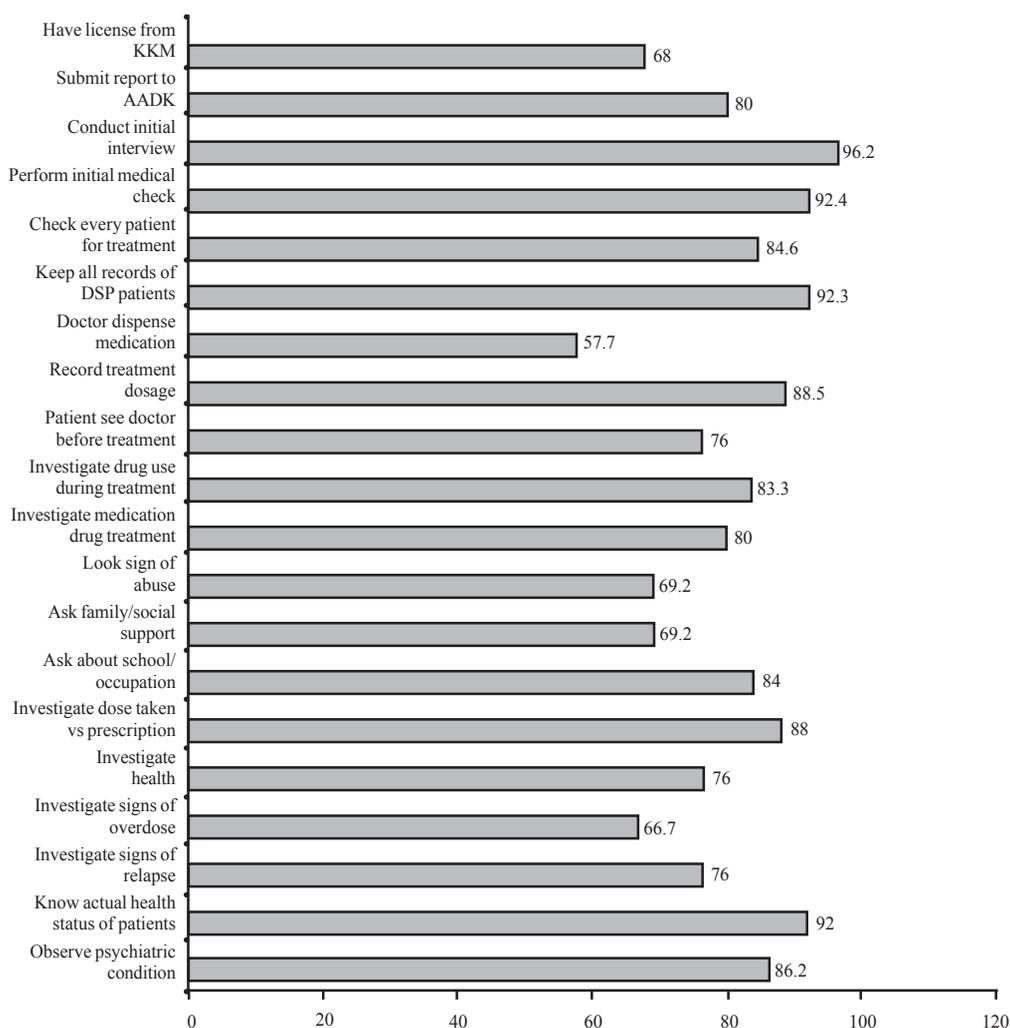
Figure 1 provides a summary of the adherence of GPs towards the practice of DST. In general, the study concluded that the adherence was satisfactory and this can be averaged out to 70-80%.

**Table 18: How DST Is Misused**

	Frequency	Percent (%)
Mix with other substances	4	4.4
Smoke	1	1.1
Inject	84	93.3
Swallow	1	1.1
Total	90	100.0

The adherence towards DST was also observed for the drug users who came in for treatment at private clinics. This is important so as to identify signs of misuse and abuse. The study found that only 56% used the medication as instructed by the doctors, whereas 44% did not use it as instructed. Misuse included injecting the mixture (93.3%), mixing it with other substances (4.4%), smoking it (1.1%) and swallowing it (1.1%) (Table 18).

**Figure 1: Adherence of GPs Towards The Practice of DST**



Finally, the objective of the study was to determine if there were any positive outcomes of the DST among the drug users who were in the programme.

### **The Outcome of DST**

There were both positive and negative outcomes of the DST. While negative aspects of the programme can be labelled as the misuses and abuses of the DST, the outcomes must be viewed as the positive aspects that will give benefit to the participants of the programme.



First, substitutes was observed in that 160 respondents reported using Subutex and Methadone (Table 16) and 20 respondents said that they used both simultaneously. A large number (75.2%) obtained information about DST from their friends (Table 16) and on the average, the respondents have been on DST for 33.2 months. More than half (53.8%) abided by the instructions and guidelines prescribed by their doctors on the usage and doses of Subutex and Methadone and 45.3% obtained their substitutes from the same doctor, while 37.5% went to two different doctors for their supplies.

The majority reported positive outcomes of the DST; 44.5% reported that they did not experience any withdrawal effects; 6.1% reported that they could maintain their employment or work; 20.7% said that it was relaxing and 1.2% reported that it could manage their pain (Table 20). Many also reported positive effects of DST such as being able to work or attend schools or programmes (49.7%); did not feel that they needed drugs (30.3%); did not crave for the drugs (30.3%); and had good family relationships (22.7%).

Thus in general, it was observed that at least half of the participants who were involved with DST reported favourable outcomes of the programme.

### **The Misuse and Abuse of DST**

While there are obvious positive outcomes of DST, it is also the aim of this study to identify incidences of misuse and abuse of the substitute therapy. Misuse and abuse of DST can be contributed by the participating medical doctors or the participants of the programme.

There were some incidences of non-adherence to the DST guidelines among the participating medical doctors. The study identified only one respondent (doctor) who did not conduct the initial interview or medical check up, or even check on all his clients who came in for treatment. However, some clinics did not properly dispense the medication, for example 42.3% stated that sometimes the doctors dispensed the medication, and sometimes it was just dispensed at the counter. Moreover, 11.5% did not properly record their treatment dosage to clients and 8% did not see the clients at all before giving medication, while 16% only saw the clients once in a while.



The DST guidelines also require medical doctors to investigate the use of other medication, look for signs of abuse and ascertain if the medication was properly taken. Only 4 clinics (16.7%) did not ask the clients or only asked them sometimes on any other drugs currently used by the participants; 5 clinics (20%) did not or only sometimes asked on the current medication used; 8 clinics (30.7%) did not or only sometimes looked for signs of abuse like needle punctures on the arms; 8 clinics (33.3%) did not or only sometimes investigate signs of overdose; 6 clinics (24%) did not or only sometimes looked for signs of relapse; and 3 clinics (12%) never or only sometimes asked their clients if they took the medication as prescribed. Many clinics though, (88%) permitted their clients to take the medications at home.

Among the participants of DST, all were opiate users but they also used other substances such as alcohol (30.6%), marijuana (30.6%), psychoactive pills (24.8%) and ATS or syabu (20.8%). In addition, 10.5% used both Subutex and Methadone as part of their DST regime.

There were also other substances that were mixed with the current substitute drugs. Many also used ketum leaves (n=14; 6.2%) and psychoactive pills (n=12; 5.3%).

A total of 104 respondents (46.2%) reported some degree of misuse and abuse. From this number, 84 (37.4%) injected the substitutes and 20 (8.9%) took them as cocktails, usually with benzodiazepines (dormicum).

When asked on the effects of the substitutes, 29 (17.7%) reported feeling "high" and some reported feeling "hot" (3.7%); thirsty (3.0%), weak (1.2%) and not having any effect at all (1.8%). Though most of the respondents reported positive outcomes of DST, 42 (18.7%) of them reported that they felt "no difference" to the substitution therapy.

## DISCUSSION

The efficacy of DST has been proven in many countries. With the advent of methadone in the late 50's, drug rehabilitation has been introduced with a different approach in order to attain successful intervention. Total abstinence is no longer the target but a set of new indicators of success was introduced. Thus the purpose of DST is generally harm reduction which is to provide an alternative path to recovery as defined by having employment and education opportunities, reducing criminal activities, positive family relationships and maintaining higher social



responsibilities among the drug using community (Resnick et al. 1992; Tenore, 2003; McCance-Kraz, 2004).

In Malaysia, DST, especially methadone was introduced in 2005, and with that, subutex (buprenorphine) was also prescribed by many GPs around the country. In the early stages of the DST practice, there were various reports on drug substitute abuses in several parts of the country, but not in methadone programmes because it was highly controlled and regulated in government hospitals with collaborative efforts between MOH, AADK and the Anti-Narcotic division of the Royal Malaysian Police Force. The less regulated and monitored subutex substitution by the GPs was highly criticized by the media, ex-drug users and even some concerned DST therapists. Incidences of injecting subutex cocktail and oral consumption of subutex with benzodiazepines such as dormicum has been highlighted in the local press; including the exposé by the participants of the programme on the availability of these substitute drugs on the streets have tainted the practice of DST in the country.

The objectives of this study were to ascertain the success and limitations of the methadone and buprenorphine maintenance programmes. Specifically, this study was set to identify the users of DST, its current practice in Malaysia, and the compliance to the DST protocol by the medical doctors involved in the DST; to determine if there are positive outcomes of the DST among those following the programme; and to determine if there were any incidences of abuses among those undergoing the programme.

The current practice of DST in Malaysia is relatively new, and not much regulation has been set forth to monitor and regulate the practice. Some GPs view their clients as drug users and not as patients, thus providing substitutes are seen as a “better” alternative rather than taking the hard drugs itself.

With more than 50% of the participants of the programme expressing the benefits of the DST, it is an alternative programme for drug users who are termed as hard-core of whom did not benefit much from any demand reduction programme in the past and also for drug users who can maintain a high level of social, familial and occupational functionality.

The compliance to the DST protocol by the medical doctors involved in the DST has been good for the methadone programme, but



only fair by the GPs involved in the buprenorphine maintenance programme. A total of 26 private clinics that dispensed subutex responded to the study. Most of them (17 or 68%) have obtained proper rights to practice DST from the Ministry of Health, while others operated as private medical clinics. At the beginning of the DST treatment sessions, most clinics (96.2%) confirmed that they conducted initial interviews to determine the severity and suitability of the case, and the majority (92.4%) also performed medical tests on their patients. In general, most clinics (92%) knew the health status of the patients because they came in quite regularly to obtain their medication and most of them (82.6%) observed if there were any psychiatric conditions. However, only a total of 84.6% checked on every patient who came in for the treatment and almost all kept records of the patients who were undergoing the DST with them.

The DST treatment guidelines or protocol outlined by the Ministry of Health specifies that a medical officer must dispense the DST. However, only 57.7% clinics agreed that mostly doctors dispensed the medication while 11 (42.3%) respondents said that it was sometimes dispensed by the doctors and sometimes by the dispensary (nurses and other clinic personnel). A total of 88.5% recorded all treatments that were given, while 36 (11.5%) only recorded it sometimes. Only 19 (76.0%) said that they required the patients to see the doctors before taking the medication. These are some of the examples of non-compliance by the participating clinics involved in the buprenorphine maintenance programme.

The DST guidelines also required medical doctors to investigate and identify signs of misuse and abuse, but only 20 (83.3%) clinics asked if other drugs were used during the treatment, 20 (80.0%) clinics asked if other medications were used during the treatment; 18 (69.2%) clinics looked for signs of abuse such as needle puncture marks; 18 (69.2%) clinics asked about the patients' social and familial support received from their families or other significant individuals and 21 (84%) clinics enquired about their patients' school or occupational status. This indicates that about 20% of the participating clinics failed to comply with the guidelines that were set.

However, most clinics (88%) did investigate if the dosage taken was as prescribed but not as many looked into the general health of the patients (76%); or investigate for signs of overdose (66.7%); or investigate for signs of relapse (76%). Still, between 12 - 25% did not comply with the guidelines.



This study is unable to specify the percentage of the participating clinics in the buprenorphine maintenance programme that complied with the guidelines provided by the MOH. However, approximately 80% are estimated to comply with the protocol. Other countries also experienced this, for example Great Britain, whereby the British drug legalization programme, under the Misuse of Drug Act, 1969, with the advent of methadone, British doctors can treat known drug users and addicts. Lejeune (1989) however, observed that some doctors prescribed methadone in large quantities instead of progressively reducing the addict's dosage because the demand was so great and there were many clinics that offered the maintenance treatment. Lejeune also attributed the failure of the methadone programme to the fact that there were too many addicts on the methadone regime who simply added illegal drugs to their methadone ration or sold methadone to attain heroin.

There are obvious positive outcomes of the DST among those who participated in the programme. Firstly, there is a positive compliance towards the programme by more than 50% of the participants. A total of 53.8% abided by the instructions and guidelines prescribed by their doctors on the usage and doses of Subutex and Methadone, 45.3% obtained their substitutes from the same doctor, while 37.5% went to different two doctors for their supplies.

Moreover, 49.7% said they could work or attend schools or programmes; 44.5% reported that they experienced no withdrawal effect (which is the main aim of DST); 30.3% did not feel that they needed drugs or did not have the craving for drugs; 22.7% reported enjoying good familial relationships, and 6.1% reported that they could maintain their present employment; and 1.2% reported that it helped them manage their pain. This is in line with the aim of the drug substitution therapy which is to reduce the motivation and need for drug users to commit crime to support their drug habits and to keep them out of prisons (Leavitt et al., 2000); to maintain contact with drug users; to attract drug users into counselling, referral and treatment services (Payte et al., 2003; Resnick et al., 1992); and to help drug users stabilize their lives and reintegrate with the wider community (Payte, 2000)

These findings are also in line with several evidences that show methadone does improve the overall health and well being, reduce criminal activities, increase mortality, reduce the transmission of blood related diseases and improve psycho-social functioning and is also a



relatively inexpensive form of treatment. Research has also demonstrated that drug substitution provides many benefits for drug users and the wider community and consequently has become a key component of drug treatments (Marsden, 1998). Drug substitution can help drug users regain control of their lives. But it needs to be coupled with psychosocial care and practical help from medical practitioners and various specialized services in order to achieve long-term positive outcomes (Watson, 1991; Strang, 1999).

Methadone and buprenorphine has the potential of being abused by individuals in a maintenance programme as well as by those who aren't (Belluck, 2003; Gendreau-Webb, 2004). This was observed in many countries where most of the abuse cases are related to an overdose of the substitutes usually in cocktail mixtures with other illicit drugs or medications (Chowdhury & Chowdhury, 1990; Grichard et al., 2003) and injecting the cocktail intravenously (Grichard et al., 2003; Jenkinson et al., 2005; Faizal, 2006; Loo et al, 2005).

In this study, even though all participants were opiate users, but they also have a history of using other substances such as alcohol (30.6%), marijuana (30.6%), psychoactive pills (24.8%) and ATS or syabu (20.8%). The guidelines clearly states that DST is only for opiate users and addicts and that this criteria must be fulfilled as described in the Diagnostic and Statistical Manual 4<sup>th</sup> Edition (DSM – IV) criteria for opioid dependence. Drug dependents must be excluded if they were currently using and are dependent on alcohol, cocaine, benzodiazepines, or sedatives, or with a suicide or homicide risk, or had acute medical or psychiatric conditions. However, this was not particularly observed by the GPs and most of them in the Subutex programme are polydrug users.

Also, it was noted that a total of 104 respondents reported some forms of misuse and abuse. Out of this total, 84 (37.4%) injected the substitutes and 20 (8.9%) took them as cocktails, usually with benzodiazepines (dormicum). Buprenorphine has a stronger potential to be abused when mixed with other substances such as benzodiazepines (Maremmani & Shinderman, 1999) and this has been demonstrated in this study.

One of the principal strategies of harm reduction is to prevent the sharing of needles in order reduce the transmission of HIV/AIDS and other blood borne viruses (Payte, Zweben & Martin, 2003); to minimize the risk of an overdose and other medical complications (Obadia et al., 2001); to switch from an injected to a non injected substance (Sung-Yeon,



1993); and to reduce the sharing of injecting equipment (Maxwell et al., 1999). However, the abuse of the DST by injecting a cocktail of substitutes clearly contradicts with the purpose of DST and the principles of harm reduction. Injecting substitute drugs also demonstrates that the participants are still dependent on opioid and are using the substitutes as a means of complementing their drug supply. This was supported by their answers when asked on the effects of the substitutes, where 17.7% reported feeling “high” and some reported feeling “hot” (3.7%); thirsty (3.0%), weak (1.2%) and as not having any effect at all (1.8%). Furthermore, 42 respondents (18.7%) reported a “no difference” reaction to the substitution therapy.

There were also cases of misuse where some did continue using opioid or other drugs. This is similar with the findings of some studies where they found illicit-drug use of any sort, persisting in 1 of every 5 MMT patients during any given month (Wechsberg et al. 2001), with about half of those persons also continuing to misuse opioid (Marion 1993).

### **Limitations of Current DST Practice**

After 12 months of implementation, naturally, several limitations and problems could be identified from this programme. This provides opportunities for future improvements. Responses stated here are from the interviews with respondents on their reaction to the practice of DST in Malaysia.

Private GPs involved with the buprenorphine programme pointed out several limitations to DST, which engulfs the capacity of patients to support the cost of the substance, screening and testing as well as the psychosocial interventions:

- i. On the average, GPs stated that 50-60% of their patients were regular maintenance patients, 40-50% had the tendency to abuse. This is due to several factors, many of which were highlighted in the MOH guidelines.
- ii. Patients are more interested to obtain the substitute drugs and did not wish to engage in counselling or psychosocial intervention.
- iii. Patients did not have additional funds to undergo urine screening test, therefore it was an additional cost to the clinics to identify if they were actually using or abusing other drugs.



- iv. Usually, patients just have enough money to purchase the substitute drugs; at times they did not even have the funds for their daily sustenance.
- v. Patients often carry several treatment record books from several clinics
- vi. If a particular clinic refuse to sell them the drugs (signs of abuse), patients could go to other clinics to buy their supplies (many also acknowledged that their counterparts are not following the guidelines provided by MOH)
- vii. Patients will shy away from participating clinics if they knew the presence of police (anti-narcotics) at the clinic, hence they obtain their supply from other clinics.
- viii. Most of the time, AADK is unable to assist clinics in conducting random urine test or testing for suspected Subutex abuse cases.
- ix. Sometimes police raided their clinics for details of their patients to be remanded.
- x. Patients who are on subutex programme, in general did not want to enrol in the MMT programme conducted by the government because of too many "red tapes".

At the same time, participants of the programme also expressed several problems and limitations to the implementation of the programme. Among others, the participants expressed that;

- i. Many times the supply of subutex was not consistent. They had to resort to several clinics to get their daily dosage. That is the reason why some carried several cards.
- ii. The DST provides them with another choice of drug therapy, which they can manage independently.
- iii. Most clinics will do the initial interview to gather records but after which will dispense drugs from the counter. There was little interactions between the GPs and their clients or patients.
- iv. Some clinic did not ask questions as to how much they wanted to purchase, but most sales were limited to a maximum of a week's supply
- v. Supply could be purchased from a number of clinics if you register with them.
- vi. Most of them only have enough money to purchase the drugs, not for other screenings.
- vii. Some clinics dispense dormicum with buprenorphine, because they justified that it would help them sleep. Some provided unknown mixture of cocktail to assist them if they had withdrawal symptoms. All these cost more money.



## **Implication and Suggestions**

This study and many others elsewhere have pointed out the potential benefits of DST, however, there are several implications if the current trend of practice is to proceed:

- i. The incidence of abuse will increase because of the compliance issues among the GPs. Regulations and monitoring should be enhanced to increase the efficacy of the service.
- ii. While the supply of methadone is consistent, however the supply of subutex could be improved. At the time this report was prepared, subutex was replaced by suboxone. Very limited supply of subutex was available after January 2007. Drug users on maintenance therapy must get their regular dosage. Failure to do so will make them resort to other illicit drugs.
- iii. The success of DST is very dependent on the quality of psychosocial intervention provided to the participants. Most GPs are not able to provide this service, while the methadone programmes at the hospitals utilizes drug counsellors from AADK. Proper intervention services must be outlined with the assistance of AADK and relevant NGOs.
- iv. Most drug users who are in the programme do not have adequate finances to purchase the substitute drugs (at the time of data collection, 2mg of subutex cost between RM10-12, and an 8mg pill cost between RM30-34), thus there is a possibility that some will resort to cheaper alternatives when they do not have the money for the substitute (for example ketum leaves). The implication for failure and abuse is high. Thus, it is necessary for the government to supply subutex as with the supply of methadone. Dispensing can be done at Pusat Khidmat AADK, which can be set up in all districts all over the country. Existing drug counsellors can be utilized to provide counselling and psychosocial support. Group meetings and support groups could be set up to provide additional services for the participants of the programme.



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