

Review and Meta-Analysis

The long winding road of opioid substitution therapy implementation in South-East Asia: challenges to scale up

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Significance for public health

Several countries in the World Health Organization South-East Asia Region can be commended for introducing opioid substitution therapy (OST) to address the ongoing HIV epidemic among people who inject drugs (PWID). Local evidence shows OST is an effective drug treatment approach in the Asian context given sufficient technical and institutional support. However, despite much progress, the number of OST dispensing sites and recipients remains totally inadequate in terms of impact upon the current HIV epidemic among PWID. Ongoing advocacy is needed if countries are to achieve the WHO's target of 40% of PWID being dosed with OST. Greater political commitment a strengthened policy environment, capacity building for OST clinics, lessening the criminalisation of drug use and promoting a public health response will give many more PWID access to OST and slow the advance of the HIV epidemic.

Abstract

The South-East Asia Region contains an estimated 400,000-500,000 people who inject drugs (PWID). HIV prevalence among PWID is commonly 20% or higher in Indonesia, Thailand, Myanmar and some regions of India. Opioid substitution therapy (OST) is an important HIV prevention intervention in this part of the world. However, key challenges and barriers to scale up of OST exist, including: pervasive stigma and discrimination towards PWID; criminalisation of drug use overshadowing a public health response; lack of political will and national commitment; low financial investment; focus towards traditional treatment models of detoxification and rehabilitation; inadequate dosing of OST; and poor monitoring and evaluation of programmes. Our review of local evidence highlights that OST can be successful within the Asian context. Such evidence should be utilised more widely to advocate for policy change and increased political commitment to ensure OST reaches substantially more drug users.

Background

Global estimates indicate that there are 15.9 million (range 11.0-21.2 million) people who inject drugs (PWID) across 151 countries.^{1,2} Of these, approximately three million (range 0.8-6 million) PWID are HIV infected.¹ Furthermore, it is estimated that 10 per cent of all new HIV infections can be attributed to injecting drugs, rising to 30 per cent when sub-Saharan Africa is excluded.³ Within what the World Health Organization (WHO) define as their *South-East Asia Region* (SEAR) there are an estimated 400,000-500,000 PWID,⁴ primarily located in countries that experience a high or medium burden of illicit

drug injecting (WHO Office for SEAR covers 11 countries: Bangladesh, Bhutan, DPR Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste).

Data from several sources show that high risk behaviours among PWID are common and provision of comprehensive HIV prevention services varies (Table 1). HIV prevalence among PWID in South-East Asia was commonly identified at 20-25% and has remained consistently high in Indonesia, Nepal, Thailand, Myanmar and some regions of India.⁵ Whilst a decline was recorded in HIV prevalence among Nepalese PWID, from 68% in 2002 to 21% in 2009 and 6% in 2011,⁶⁻⁸ HIV prevalence rose in Bangladeshi PWID, from 4% in 2003-2004 to 7% in 2007,⁹ and in Punjab (India) from 13% in 2006 to 21% in 2011.¹⁰ High-risk behaviours among PWID, such as the sharing of contaminated needles and syringes, remain a major determining factor in the course of the HIV epidemic throughout Asia.¹¹⁻¹³

The ongoing HIV epidemic among PWID in South-East Asia has prompted many countries to develop HIV policies linked to national HIV strategic plans in which harm reduction interventions are increasingly viewed with understanding and acceptance.⁴ UNAIDS UNDOC and WHO outline nine interventions as part of a comprehensive package that has the greatest impact on HIV prevention, treatment and care for PWID.¹⁴ Meta-analysis and systematic reviews show conclusively that providing opioid substitution therapy (OST) together with needle and syringe programmes and antiretroviral treatment targeted towards PWID have the greatest effect in preventing HIV infection.¹⁵

In this article the focus is upon one essential harm reduction intervention, OST, and its use in countries that fall under the administrative purview of WHO's SEAR, with specific focus on Bangladesh, India, Indonesia, Maldives, Myanmar, Nepal and Thailand. We excluded Timor-Leste, Bhutan and the Democratic People's Republic of Korea due to limited data.

Methadone has been prescribed for the treatment of opioid dependency for over four decades and buprenorphine has been available since the early 2000s. Both were added to the WHO list of essential medicines in 2005, and are usually consumed orally or sublingually as maintenance treatment to relieve opioid withdrawal and to reduce cravings. Research has shown them to be effective in the reduction of HIV risk behaviours and other comorbidities.^{16,17} Due to the chronic nature of opioid dependency, treatment outcomes are better in long-term therapy incorporating adequate dosing (at least 60 mg of methadone and 8-6 mg buprenorphine per day).¹⁶

Despite the strong evidence for various benefits resulting from the use of OST – improved retention in treatment for HIV, HCV and opioid use,¹⁶ reduced illicit opioid use,¹⁷ reduced risk of HIV,¹⁸ reduced criminality, better psychosocial outcomes and decreased risk to pregnant drug-dependent women¹⁹ (during the intra-uterine, partum and post-partum period²⁰) fewer than three per cent of PWID in the South-East Asia Region have access to OST.¹² In this article we explore the histor-

ical adoption of OST, the current situation, some of the major challenges, and suggest ways to scale up OST in the SEAR.

Methods

We reviewed published and grey literature located using Medline and PubMed, WHO program documents for the countries of the SEAR, the Joint United Nations Programme on HIV/AIDS (UNAIDS), the United Nations Office on Drugs and Crime (UNODC) documents, and generic internet search engines between October 2011 and June 2013. Direct email requests were made to WHO HIV country focal points and official government counterparts for additional data and comments about OST in the SEAR between September 2010 and March 2013.

Results

Implementation of opioid substitution therapy

The amount and quality of the data available on the commencement of OST programmes, responsible agencies, the number of PWID receiving OST, and the linkages with other health and non-health systems vary considerably among the countries in South-East Asia (Table 2).

Nepal started a government-approved methadone-based OST programme in 1994.²¹ Despite satisfactory outcomes, the programme was suspended in 1998, and then restarted as an emergency response for HIV prevention in September 2007.⁴ In India, sublingual buprenorphine treatment commenced in 1993 as a pilot project and has been licensed for treatment of opioid dependence in drug treatment centres since 1999.^{22,23} Methadone maintenance therapy (MMT) commenced in India in 2011.²⁴

In Thailand, limited methadone treatment became available in 1979, primarily as a detoxification program in approved clinics. In 1989 a national clinical trial of MMT was initiated. MMT started in Bangkok as an HIV prevention measure in 1990, and gradually extended to a few clinics outside the capital.^{25,26} Buprenorphine was approved for opioid treatment in 2007, and a trial of buprenorphine-naloxone was initiated in Chiang Mai during the same year, but it is not routinely used in opioid treatment programs.²⁶

Buprenorphine was introduced in Indonesia in 2001, and the manufacturers of the drug encouraged private practitioners to prescribe the medication to drug-dependent clients.^{27,28} In 2003 the Indonesian Ministry of Health established MMT (with technical and financial assistance from WHO) in two pilot projects, one in Jakarta and one in a joint pilot within a Bali prison and a hospital. These two pilots continued until the end of 2005, serving a population of approximately 300 drug users.²⁹

Preparation for the introduction of methadone began in Myanmar in 2004, with the Ministry of Health commencing the delivery of MMT over February and March 2006 in four drug treatment centres. Around 2900 clients were receiving MMT by 2013.³⁰

In November 2008, MMT was introduced into the Maldives as part of a pilot study;³¹ buprenorphine remained unavailable due to its classification as an illegal substance.⁴

Opioid substitution therapy availability in 2009–2012

In Nepal, as of June 2011, 380 clients were receiving methadone from three sites in the cities of Kathmandu, Patan and Pokhara (Kramarz P., 2011; personal communication). The demand for methadone was reported to be high, with a long waiting list to join the

programme. In Pokhara, 88 PWID were enrolled to receive methadone and 62 were active recipients.³² In 2009, 30 Nepalese PWID received buprenorphine administered as part of a three-month tapering reduction dose rather than long-term maintenance therapy.¹² At the end of 2010, NGOs were dispensing buprenorphine from six sites to 175 clients. The three-month duration of treatment of 2–4 mg per day remained unchanged. Take-home/home delivery of buprenorphine was only granted under exceptional circumstances (Pandey B., 2010; personal communication). The provision of buprenorphine is not currently an official part of the government OST programme.

Initial Indian targets were for 40,000 PWID to receive OST by 2012, with delivery through 320 sites, primarily NGOs or government-run treatment centres.⁴ By May 2011, buprenorphine was available from 52 sites and 4810 clients were in treatment; data from December 2012 show that 120 buprenorphine sites were delivering treatment to 7500 regular patients (in India regular patients are defined as those accessing OST 24 days or more per month; those that received less frequent treatment are not included).³⁰

Apart from small pilot studies Methadone has not been available for clinical use in India following its removal from the Indian pharmacopoeia in 1982.³³ However, in early 2010 the government approved the use of methadone in a pilot study intended to involve six sites in late 2010. By 2012 four methadone dispensing sites were servicing 350 patients (Kumar R. 2013; personal communication). A buprenorphine project commenced inside Tihar prison, New Delhi in late 2008, but client numbers remain small.

In 2009 the Bangkok Metropolitan Administration funded 20 methadone clinics at two hospitals and 18 health centres,³⁴ and across Thailand an estimated 4000–5000 patients were receiving methadone.¹² In 2010, 2200 patients received methadone treatment, but probable duplication of some client records makes this number uncertain, and whether they were receiving long-term treatment is undetermined (Thanpresertsuk S., 2011; personal communication). The reasons for the apparent fall in client numbers between 2009 and 2010 are unknown (the 2009 figures are estimates only), although the general shift from opioid use to stimulant use in Thailand is likely to have contributed. In 2012, 147 sites were dispensing methadone to 2777 patients.³⁰ Methadone is the National Health Security Office's approved OST medication and was placed on the Thai Essential Drug List in 2008; it is available as part of the Universal Health Coverage package for all Thai citizens. In 2009, an estimated 150 clients were reported to be receiving buprenorphine as part of an HIV prevention trial at Chiang Mai University, which has since been completed.^{4,12}

In Indonesia, methadone expansion began in 2006 with seven clinics serving 1000 clients by the end of that year.²⁹ By April 2010 methadone was available in ten provinces from 51 clinics (five specialist hospitals; 10 general hospitals; 30 primary health centres; and six prison and detention centres) (Sarasvita R., 2010; personal communication). In June 2011, Indonesia had 68 government-funded clinics with 2540 active patients. In addition, more than 50 medical prescribers in private practices were dispensing buprenorphine to an estimated 3000 patients.³⁵

In Myanmar in January 2010, 821 patients were receiving methadone from eight sites in four states,³ and by June 2011 patient numbers had increased to 1087.³⁶ In late 2012, 13 methadone sites were dispensing to 2909 patients.^{30,37} Methadone was dispensed from drug treatment centres as part of Global Fund Round.⁹

In the Maldives, 47 patients had been enrolled to receive methadone in late 2009,⁴ but by April 2010 only 17 patients remained, decreasing to 11 by August 2010 (Mohamed A.J., 2010; personal communication); by July 2011 patient numbers had rebounded to 57 (Aminath Z., 2011; personal communication). Barriers to methadone programme enrolment in the Maldives include the need to obtain clearance from five dif-

Table 1. HIV prevalence among people who inject drugs in selected South-East Asia Region countries: interventions, behaviours and reach of HIV prevention programmes 2009-2012.

Country	Estimated number of PWID	Estimated HIV prevalence (%)	Harm reduction interventions adopted as policy for PWID (n.)	PWID report using sterile injecting equipment last time of injecting (%)	PWID reporting use of condoms last having sexual intercourse (%)	PWID reached with HIV prevention programmes (%)
Bangladesh	21,800-23,800	7 Dhaka	9	33.6 (male) 73.8 (female)	30.2	2.1
India	177,000-180,000	7	9	29-88	44-100	10-83
Indonesia	105,784 (73,663-201,131)	36	9	88.3	35.7	43.38
Maldives	793 (690-896)	0	6	69-77	6	Not available
Myanmar	75,000	22	9	81 (last month)	78	8274
Nepal	17,000-24,000	6 Kathmandu	8	50.8	99	56.9
Thailand	40,300	22	9	<50	<40	Not available

Source: WHO, UNAIDS, UNODC, UNGASS reports and Harm Reduction International (Global State of Harm Reduction Towards An Integrated Response 2012). PWID, people who inject drugs.

Table 2. Opioid substitution therapy in selected South-East Asia Region countries: start date, numbers, linkages, compulsory/court mandated, modality.

Country	Year first trialled, started OST	Key responsible agencies for OST	No. OST sites (2010-2012)	No. receiving OST (2009-2012)	OST service links with other health services	OST service has links with non-health services	Compulsory or court mandated treatment exists	Modality of OST delivery
Bangladesh	2010 - M	ICDDR,B with funding support from UNODC	2 - M	188	Based in govt detox clinic, where several psychiatrists provide support as and when needed. The OST clinic is also linked to ICDDR, B voluntary counseling testing unit	No - but plans underway	No	Government
India	1993 - B 2011 - M	MoH, Ministry of Social Justice, Empowerment, & National AIDS Control Office	120 - B 4 - M	7500 - B 350 - M	Weak to good links	Weak to good links	No	Government & NGO
Indonesia	2001 - B 2003 - M	MoH for methadone. Private practitioners dispense buprenorphine following training Largely unsupervised by Moh	68 - M ? - B (50 doctors trained in buprenorphine dispensing)	2540 - M 3000 B	Weak links	Weak Links	No	Government & Private
Maldives	2008 - M	Moh	1 - M	57 - M	No	No	No	Government
Myanmar	2004 - M	Department of Health - medical care	13 - M	1637 - M	Weak to good links	Weak to good links	Yes	Government
Nepal	1994 - M	Ministry of Home Affairs, UNODC, Hospitals, NGOs (not part of official government programs)	3 - M	386 - M 175 - B	Overall weak links but some sites have good links but with constraints	Overall weak links but some sites have good links	No	Government & NGO
Thailand	1979 - M 2007 - B	Thanyarak Institute of the Department of Medical Services, under the Ministry of Public Health	147 - M ? - B	1183 - M ? - B	Fully integrated (most OST services attached within health care settings)	Weak links	Yes	Regional drug treatment centers (of the Department of Medical Services) & Govt Hospitals

OST, opioid substitution therapy; B, Buprenorphine; M, Methadone; ICDDR,B, International Centre for Diarrhoeal Disease Research, Bangladesh; MoH, Ministry of Health.

ferent government departments to ensure no criminal cases are pending. It is reported that the methadone programme functions well, but scope for improvement remains.³⁸

In July 2010, after several years of advocacy to initiate OST, Bangladesh commence methadone provision, starting with one site in Dhaka. By early 2013 an additional site had opened and 188 clients were receiving methadone (Azim T., 2013; personal communication).

Challenges and barriers to scale up of opioid substitution therapy

Various common challenges and barriers exist to the implementation and expansion of OST services. Throughout the region drug users continue to experience high levels of stigma and discrimination due to their substance use. This impacts upon the delivery of general health services, including access to OST.³⁹⁻⁴¹ In the UK it has been noted that key government policies to assist PWID reintegration and recovery through the use of OST were highly unlikely to succeed while stigmatising attitudes towards PWID remain pervasive.⁴² Stigma and discrimination remain major barriers across South-east Asia.

Acknowledging drug use and responding to HIV risk-taking behaviour was largely delayed across Asia in comparison to many Western countries,^{43,44} and the criminalisation of drug use still commonly overshadows a public health response to address this problem.⁴⁵ Various countries in the SEAR force drug users into compulsory drug detention centres. Official reports state that 235,000 people were detained in over 1000 compulsory drug detention centres in East and South East Asia alone in 2012. Since 2012, many United Nation agencies have called for their closure for reasons including human rights abuses and a lack of evidence of their effectiveness.⁴⁶ As found in other regions of the world, the attitude that the abstinence model of drug treatment is of paramount importance persists and rejection of the concept of OST maintenance is widespread, despite opioid dependence being acknowledged as a chronic medical condition.⁴⁷ As a result, it could be argued that this has been the major reason for reduced political will, financial under-investment and lack of commitment toward the scaling up of essential harm reduction interventions, including OST.

Advocacy for and funding of OST scale-up in the countries under review remains largely driven by UN agencies and the international donor community. Initial funding of and sustainable investment in harm reduction services, including OST, remains a perennial problem. Recent global studies have revealed over 90% of HIV-related harm reduction funds in low and middle income countries stem from international donors, and total funding remains inadequate.⁴⁴ The cost of OST for individual recipients is prohibitive in many cases, and this greatly reduces the numbers of PWID in treatment. In Indonesia, while methadone could cost a client 1-2 UD Dollars (\$) per dose through a government service, an 8-12 mg dose of buprenorphine commonly costs 11-17 \$ through a private medical practitioner. As a result, many PWID can only afford to purchase an inadequate dose that proves ineffective and contributes towards ongoing injecting of illicit drugs.

Despite these problems, it is important to highlight progressive steps from Asian countries such as Malaysia and China, where governments strongly endorse OST and are expanding the OST programme nationwide. By 2009, China had 680 methadone clinics in 27 provinces with 242,000 patients (ever) enrolled, while Malaysia had 59 government facilities and nine private clinics dispensing methadone to 7065 registered clients, with an additional 10,000 clients receiving methadone through private practitioners.^{39,48} In 2011 Malaysia further expanded its methadone programme, with substantially more distribution sites: 168 public health clinics, 48 public hospitals, 24 general practitioners (GPs), 32 National Anti-Drug Agency sites, 18 prisons and two others. A cumulative 20,955 PWID have been registered in public facilities since 2006 and another 23,573 PWIDs are receiving MMT from

GPs. Due to the separate registration systems of private and public services, it is not possible to identify whether patients receiving methadone from private GPs were also registered with public facilities (Naning H., 2012; personal communication).

In all countries under review, the focus remains largely on the traditional treatment model of detoxification and rehabilitation despite strong evidence of recidivism, with rates often ranging from 60-100%.^{13,48} Despite the international evidence highlighting the broad-ranging health, social and economic benefits of OST,⁴⁹ a lack of in-depth knowledge, awareness and education about OST among policy-makers, community members, drug users and the health sector constrains the scaling up of OST.^{31,50,51} As found worldwide, one of the greatest obstacles to OST acceptance in the SEAR is limited acceptance and practice of evidence-based medicine associated with OST in the medical workforce.⁴⁷

Research has shown that it is commonly perceived that providing OST is simply *replacing one drug with another*, despite evidence that methadone is superior to non-pharmacological methods in terms of client retention in treatment, reduced self-reported heroin use and both urine and hair analysis.^{52,53} In some parts of the world, including in some Asian countries, providing OST can be viewed as a failure to deal with the criminal behaviour of drug users. Consequently, the implementation of an abstinence-based model of treatment is still strongly advocated as the primary approach to address drug dependency. In addition, tensions continue between supply/demand reduction and harm reduction approaches, and impacts upon expansion of OST services.⁵⁴

Highlighting an effective OST treatment model that builds upon local evidence can contribute towards expansion of drug treatment services for PWID. One aspect of effectiveness is to achieve an optimal dose of OST (usually greater than 60 mg of methadone) that can lead to a decrease in the use of illicit drugs and ensure a higher retention rate and decrease in HIV risk behaviours.⁵⁵ However, it is not uncommon practice for a lower dose to be prescribed for clients receiving OST in South-East Asia. For example, in Indonesia an integrated biological survey among PWID noted that most of those who received methadone in the past year were still injecting illicit opioids in the past week, and it was speculated that one reason for this was inadequate dosage.⁵⁶

Doses of methadone of more than 60 mg daily are recommended, with most clients requiring 60-120 mg daily.⁵⁷ In some countries under review, low-dose buprenorphine was common practice (<4 mg daily). Recent buprenorphine guidelines in India (2009) recommend 4-8 mg as the optimal buprenorphine dose,³² despite international evidence recommending that people be stabilised on 8-16 mg daily.⁵⁷ Overall poor monitoring and evaluation of OST programmes exists in the countries under review and this does not allow local experiences to be translated into coherently managed knowledge about a program. As a consequence this impacts upon seeking ways to improve and expand coverage of the OST service.

Discussion

Moving forward with scale-up of opioid substitution therapy

In 2005, WHO added methadone and buprenorphine to the WHO Model List of Essential Medicines, and this endorsement provided high-level official support to advocate with the appropriate government ministries for the introduction and wider use of OST in treatment programmes. However, despite the official use of OST in all countries under review, specific policies for OST either do not exist or are too underdeveloped to have the desired impact. Many countries in the region need greater official acknowledgement of PWID and the role

they play in the HIV epidemic and respond according to the epidemiological and national context.^{58,59}

A national policy would assist in establishing a set of standards for OST provision and address the needs of politicians, health administrators, program managers, clinicians and OST recipients. Such policies should reflect a national agreement about the important strategic role of OST in reducing the adverse health, social and economic consequences of drug use, and outline key objectives and procedures. Evidence of the benefits of OST in all countries under review warrants increased high-level support for and expansion of OST, as has occurred in China.³⁹

Criminalisation of drug use continues to restrict the wider utilisation of OST. As a result it is critically important to increase the law enforcement sector's understanding of OST, and to advocate for it to endorse the expansion of OST. National Working Groups or Task Forces on harm reduction, with a high priority on OST, are similarly important, requiring participation of senior officials from health, police, academia and representatives of civil society for maximum benefit.

Despite an incremental growth in knowledge of OST since its introduction in various countries of South-East Asia, building staff and institutional capacity remains critically important. The skills and knowledge of staff working on drug dependency and OST is often lacking, and consequently regular training programmes are necessary. Poly-drug use is widespread, with opioids often being mixed with benzodiazepines and other pharmaceuticals; many clinical staff are uncertain as to how to address these issues. Training programmes facilitate sustainable expansion and improved quality of OST services, and encourage long-term commitment towards OST treatment patients and PWID in general. Of equal importance is the need to conduct regular monitoring and evaluation of OST programmes at national and local level. Data identifying both effective approaches and difficulties inform policymakers and other stakeholders about how to improve quality and continue expansion of OST services.

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