2011 European Conference Report

Highlights from ISAM and Global Addiction

CONGRESS HIGHLIGHTS

13th Annual Meeting of the International Society of Addiction Medicine, Oslo, Norway
6–10 September 2011

Global Addiction 2011, incorporating the 6th European Association of Addiction Therapy Congress, Lisbon, Portugal
5–7 December 2011

CONTENTS

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Introduction

The 13th annual ISAM meeting was held on 6–10 September 2011 at the Radisson Blu Scandinavia Hotel Oslo, Norway, while Global Addiction 2011, incorporating the 6th European Association of Addiction Therapy (EAAT) congress, was held on 5–7 December 2011 at the Portuguese Catholic University in Lisbon, Portugal. International experts gathered to present and discuss the latest medical research into addiction medicine, and to learn from different management approaches around the world. This report summarises some of the key presentations on opioid addiction and the available therapeutic options, with a focus on international experiences to date with medication-assisted treatment (MAT).

Noticeable differences in the standard of care for opioid-dependent patients across Europe were reported as a significant problem, especially for access to treatment, continuity of care in prison, primary care integration and dosing (pages 2–5). In addition, strict treatment rules such as daily supervision and weekly urine drug screens were posed as significant barriers to treatment access. Speakers agreed that country-specific treatment policies impact patients in a negative way, through the promotion of non-evidence-based care over well-researched interventions. Politics was shown to play a key role in the development of treatment systems, which often focuses on the wellbeing of society rather than the wellbeing of the patient.

Speakers reported that integration of primary care with addiction medicine services is an effective and necessary solution for increasing the uptake and quality of treatment services, with excellent results obtained with provision of primary healthcare in needle and syringe programmes. Significant problems with treatment access for HIV and hepatitis C services were shown as widespread, which could be addressed through integration of services providing MAT (pages 6–7).

Encouraging research was presented showing that providing MAT improves outcomes provided that therapeutic doses and misuse-prevention strategies are employed, the latter to reduce the likelihood of misuse and diversion (pages 8–10). Study findings also confirmed the feasibility of buprenorphine/naloxone (bup/nx) as first-line therapy, showing that switching from other pharmacotherapies is well-tolerated and assists patients in their road to recovery. Recovery was placed at the forefront of the treatment agenda, with a number of studies showing the beneficial effects of buprenorphine-based therapy in reaching this endpoint. Flexible treatment was shown as a feasible option with buprenorphine and buprenorphine/naloxone (bup/nx) pharmacotherapy, offering good retention rates while increasing access to treatment (pages 11–15).

Speakers agreed that long-term maintenance strategies with effective pharmacotherapy following a structured approach are key to a successful recovery, as shown by high rates of adverse outcomes with early treatment discontinuation (pages 16–18). Furthermore, personalised treatment was described as the future of addiction medicine, through the targeting of key neurobiological circuits implicated in addiction disorders, although dopamine was shown to not play as significant a role in opioid dependence as previously thought (pages 19–20).

The 2011 European conference report was made possible as part of the ongoing educational commitment of Reckitt Benckiser Pharmaceuticals (RBP) to support healthcare professionals treating opioid dependence. The views expressed in this report reflect the opinions and clinical judgement of the speakers.

Drug policy and treatment access

Reforming national policy: the key to standardising care?

Findings presented at Global Addiction showed that significant differences in the standards of care for opioid-dependent individuals exist between countries in Europe, demonstrating an urgent need for standardisation of treatment delivery systems along the lines of those for other chronic diseases. This situation is often complicated by governments' health policies, which often prioritise societal wellbeing in favour of patient health. Preliminary findings from the European Quality Audit of Opioid Treatment (EQUATOR) study presented by Dr João Goulão confirmed non-equality among European countries in many treatment aspects and patient demographics, including access to treatment, continuity of care in prison, primary care integration and dosing. Presenting findings from the 2009 IMPROVE study, Dr Heino Stöver also showed that significant barriers exist to treatment access in the general community and in prisons within Germany. Strict treatment rules such as daily supervision and urine drug testing were reported as significant barriers to treatment, with over two-thirds of patients forced to discontinue MAT upon entry into prison.

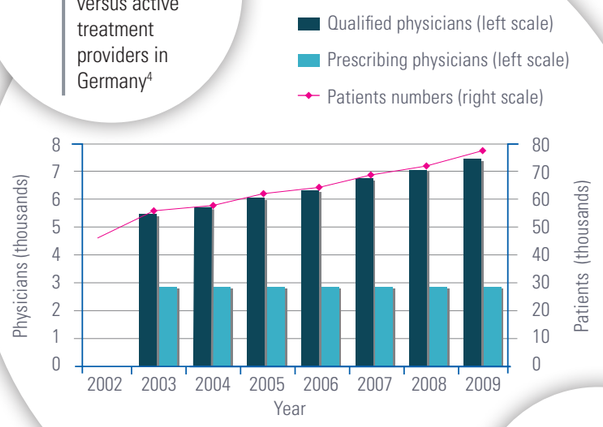
National policy impacts treatment provision through its influence on the modelling of treatment systems, with non-evidence-based care often being promoted in favour of well-researched interventions. During her presentation, Dr Chris Ford explained how the promotion of healthy drug policies is key to securing optimal patient outcomes through a model of integrated care. Country case studies were presented showing how research-based and patient-focused policies improve outcomes, while punitive treatment systems fail in the long term. Finally, Professor Mike Trace discussed how politics often influences the development of treatment systems and presented the key elements that make up an effective system.

Dr Heino Stöver
University of Applied Sciences
Frankfurt, Germany

Addressing treatment gaps through informed policy change: findings from the IMPROVE study

Significant barriers to treatment access in the general community and within prisons continue to exist, showed findings from the 2009 IMPROVE study presented by Dr Heino Stöver. Attention was drawn to the impact stigma has over prescribing practices, and how unfavourable conditions such as mandatory counselling and daily supervision can act as barriers to treatment access. Worryingly, over two-thirds of patients entering prison in Germany are required to have their medication discontinued. Stöver called for greater physician support and training, and greater integration of prison and community healthcare services to address these issues.

Figure 1. Number of opioid-dependent patients versus active treatment providers in Germany[4]



Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM). Bericht zum Substitutionsregister. Bundesopiumstelle. January 2010; 84:1. Reproduced by permission of BfArM.

Gaps in treatment provision

Despite general practitioners with 50 hours of addiction medicine training being able to provide MAT, a significant proportion of these physicians often stop prescribing after 5 years, which is most likely a result of the continuing stigma attached to MAT.[1] Dr Heino Stöver explained that the problem is compounded by the large gaps in provision of treatment, where patient numbers have increased exponentially while the number of active prescribing physicians remains the same (Figure 1). Data were presented showing that 32.4% of authorised physicians never provide MAT and 35.3% discontinue prescribing.[2] Reasons given for lack of MAT prescribing were shown to be linked to several unfavourable prescribing conditions, including increasing administration duties, juridical consequences, increasing comorbidity, low remuneration and missed psychosocial care appointments that are mandatory for patients wishing to continue receiving MAT. "In this context, psychosocial care is more a barrier to commencing or continuing MAT than a tool of retention", said Stöver.

Barriers to treatment access

In light of these findings, Stöver and colleagues launched the IMPROVE study,[3] which aimed to obtain a greater understanding of the barriers to treatment access, retention and quality. In total, 400 opioid-dependent patients out of treatment and in treatment, and 152 treating and non-treating accredited physicians were surveyed. Findings showed that MAT access and provision were inadequate, especially outside major cities. Patients reported high levels of difficulty in accessing treatment, with only 38% of physicians stating that access to MAT in their area was easy or very easy. The most significant barriers restricting patients from entering treatment included strict treatment rules (eg urine testing, daily supervision, mandatory counselling and abstinence), lack of treating physicians and related waiting lists for entering a treatment programme. Improvements in the regulatory framework and required conditions for MAT could therefore encourage more physicians to provide treatment and increase treatment access. The study also revealed that medication misuse and diversion do occur and are a significant concern for physicians. "These results highlight the need for providing sufficient guidance to support physicians in providing high-quality clinical care based on a sound understanding of the advantages and disadvantages of different pharmacological therapies and the individual needs of each patient", said Stöver.

MAT provision in prisons

The IMPROVE study also painted a problematic picture of prison treatment in Germany, showing that 70% of patients who were currently receiving treatment for opioid dependence were required to have their medication stopped. This is of great importance, given that the average number of prison terms for patients was 2.8 and 4.0 for users outside of treatment. "At the moment, in many ways, one of the key features of MAT is stability and treatment continuity is being disrupted", Stöver told delegates. Indeed, opioid pharmacotherapy is currently provided within a prison setting in only 23 countries in Europe out of 33 globally,[5] despite study findings showing that the risks for intravenous drug use and needle sharing are reduced significantly by 55–75% and 47–73%, respectively, when MAT is provided in prisons.[6] "Prisons must recognise consensus on the role and efficacy of MAT and other evidence-based interventions", said Stöver, adding that a close connection between prisons and community healthcare services is necessary for successful outcomes.

Dr João Goulão
Instituto da Droga e da Toxicodependência
Lisbon, Portugal

Between-country differences in treatment: a call for integrated health policy

Preliminary study findings from the European Quality Audit of Opioid Treatment (EQUATOR) study presented by Dr João Goulão confirmed significant differences in patient demographics, physical and mental health, comorbidities, drug use and prison treatment across Europe, suggesting an urgent need for the standardisation of treatment delivery systems. It was explained that differences exist across Europe in terms of the availability and ease of access to treatment, participation of general practitioners in treatment delivery, utilisation of a range of pharmacotherapies, and quality and continuity of patient care. In addition, significant variations are present for medication dose, requirements for supervised dosing, levels of diversion and misuse, and appropriate outreach and education for out-of-treatment drug users. "Better understanding of between-country differences in treatment delivery and outcomes would inform health policy decision making, with the goal of optimising treatment benefits", explained Goulão. The complete study findings from 900 physicians, 2,600 patients and 1,100 out-of-treatment opioid users across 11 European countries will be published in early 2013.

The EQUATOR study

To assess treatment perspectives from physicians who treat opioid-dependent patients both in and out of treatment, Goulão and other teams in the studied countries administered a survey to physicians involving telephone or face-to-face interviews, as well as questionnaires to patients in Italy, Portugal, Germany, Austria, Greece, France, Denmark, Norway, Sweden, Switzerland and the UK. The research was modelled on the 2009 IMPROVE study presented by Dr Heino Stöver, and topics addressed included treatment practices (ease of access, therapeutic goals, medications, doses, counselling, regulations and guidelines) and experiences (satisfaction, barriers to treatment entry and retention), clinical and public health outcomes (drug use, treatment retention, misuse and diversion), and demographic characteristics of users and patients. In addition to a core set of questions common to all surveys, some individual studies included additional questions specific to the local environment. The EQUATOR study is one of the largest studies in Europe to date in terms of understanding treatment quality and barriers to treatment access, thus providing a unique and powerful data set that will help address some of the gaps in treatment across countries. As with the majority of studies, Goulão noted that the employed survey methodology could be associated with potential biases in terms of achieving a representative sample and reliance on self-reported data.

Findings with reaching implications

Preliminary analysis of completed findings from six of the included countries was presented in an interactive panel discussion with Dr Heino Stöver and Prof Gabriel Fischer. Worryingly, access to opioid treatment in prison was shown to vary greatly across Europe, with treatment frequently being discontinued or changed to lower-cost options such as methadone upon entry into prison. Opioid users outside of treatment were more likely to report treatment discontinuation upon prison entry than patients, raising the question of whether stopping treatment contributes to a return to drug use upon release. Findings also showed that being in treatment was associated with a reduced likelihood of imprisonment. The results are of importance, given that approximately 0.5 million opioid-dependent individuals go through the prison system annually.[7] Fischer communicated an encouraging situation in Austria where drug policy has changed and education is provided for all individuals working in prisons, with a range of pharmacotherapeutic options routinely offered for those who require it.

Demographic considerations

Variability in patient demographics was observed among countries, with age, employment, physical and mental health, and self-reported HIV and hepatitis C rates showing the greatest variability. Speakers agreed that age and gender-specific treatment services are needed to address the variability among countries. The higher incidence of opioid dependence among individuals aged 30–39 years in Portugal was explained by Goulão to most likely be a result of an aging population and fewer young patients taking up heroin use. Conversely, Fischer said that the higher number of younger patients in Austria is most likely a result of greater treatment access through general practitioners, thus allowing for earlier detection of opioid-dependent patients. Patients in treatment were found to be significantly older, less likely to be single and to have been in prison compared with those outside of treatment. Rates of overdose were also shown as significantly different between countries, although patients in treatment had a lower risk. When specific pharmacotherapies were compared, bup/nx was associated with the lowest rate of on-top drug use for heroin, other opioids and other drugs. Indeed, concomitant consumption of drugs was higher among those outside of treatment, thus confirming the protective effect of MAT.

Q. What efforts are being made to look at the quality of MAT from the perspective of additional drug use, such as benzodiazepines and alcohol?

A. Psychiatric comorbidities are often underdiagnosed, which is directly related to increased rates of benzodiazepine and alcohol use. There is a need of putting addiction medicine into general medicine so treatment can be more accessible, although specialist psychiatric help should be available as well. The Australian model is a good example of an integrated approach to addiction medicine. Addiction is much more than a mono-dependency, and we need to look at the reasons why patients are using other drugs on top. This may be linked to the practice of underdosing in Europe, with doses of 14–16 mg/day often common practice for buprenorphine and bup/nx. These doses are far too low and also have implications for benzodiazepine medication.

Q. It is interesting to see how HIV and hepatitis C percentages across countries varied as a result of drug policy. In the UK, there is a very low HIV rate that can be attributed to the introduction of needle-exchange clinics before HIV was introduced. Portugal's figures remain suboptimal, but are encouraging, given the reduction from 65% when there was no integrated treatment to 20–30%. But I would like to know if there is any specific reason for the low rates of employment seen in the UK?

A. We do not have such information available as of yet. However, I would like to have greater attention drawn to Eastern European countries that lack standardised care and could benefit from seeing the findings of this report.

Employment

A significant difference in employment rates was seen between countries, with Italy and Portugal showing the highest employment rates. Goulão noted that the observations for Portugal were most likely a result of reductions in stigma associated with the decriminalisation of drug use and increasingly positive attitudes towards employment of drug addicts. Findings also showed that patients in treatment were nearly three-fold more likely to be employed than those outside of treatment. Despite these encouraging findings, Stöver noted that they must be analysed in the context of individual take-home country policies, as these will ultimately impact rates of employment through daily supervision acting as a barrier to employment.

Physical and mental health

Analysis of health problems experienced by patients in and out of treatment showed a very high rate of psychological problems that was comparable between groups. Hepatitis C was also a significant issue for both groups of patients, although rates were higher among those in treatment, which was attributed to greater rates of diagnosis. Rates of HIV and gastrointestinal, neurological and cardiovascular disease were found to be comparable for patients both in and out of treatment. Findings also showed that HIV incidence was generally very low among all countries apart from Portugal, which showed a rate higher than five-fold that of other countries. Goulão told delegates that these figures are indeed an accurate reflection of the situation in Portugal, although this is a marked improvement among injecting drug users based on the initial situation. Furthermore, mental and physical health was rated as good or very good by a significantly higher percentage of patients on bup/nx compared with methadone or buprenorphine alone. Rates of infectious, neurological, cardiovascular and cutaneous diseases were also significantly lower among bup/nx-treated patients. Stöver said that the findings should be interpreted with caution as bup/nx is routinely prescribed to more stable patients, which may account for these observations.

Dr Chris Ford
IDHDP
London, UK

Reforming drug policies through promotion of evidence-based care

There is a serious need to promote healthy drug policies to improve drug treatment for those who have drug problems. "We as doctors need to be involved in drug policy reform to improve care of people who use drugs", said Dr Chris Ford. Research shows that national drug policy directly affects patients, mostly in negative ways, through promotion of punitive, opinion-based treatment systems. Delegates were told that drug policy is particularly vulnerable to political influence that has little to do with evidence-based medicine, probably more so than any other area of health. "It is important to identify this and challenge where it is happening", said Ford.

Physician involvement

The International Doctors for Healthy Drug Policies (IDHDP) aims to increase the participation of medical doctors in drug policy reform and bridge the gap between evidence-based practice and drug policy in countries that need it. IDHDP now has members in 49 countries and puts a key emphasis on international lobbying to influence changes in drug policy through promotion of harm reduction and healthy drug policies. Questionnaire findings from IDHDP members (approximately 170 physicians) showed that all respondents felt that drug treatment systems are affected by their national drug policy mostly in a negative way, due to drug policies that go against evidence-based medical treatment. Despite the wide range of surveyed countries, many reported similar problems with stigma, treatment interference by law enforcement and how changes in government interrupt progress in improving policy by experience in practice. Ford also stressed that evidence showed that punitive drug policies did not reduce the amount of drug use, but rather increased it at times and always resulted in poorer health of drug users in those countries.

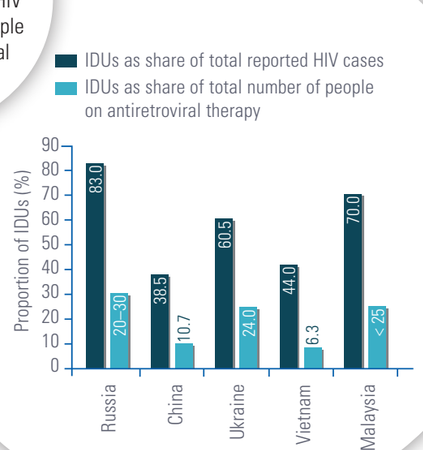
Promoting healthy drug policies

An integrated package addressing prevention, supply and development of a comprehensive and realistic treatment system providing harm reduction (MAT and needle-exchange programmes) and reintegration is key for securing a healthy drug policy. Furthermore, it is necessary to have a balanced integrated policy that is based on evidence rather than opinion. Good evidence-based treatment puts patients at the forefront, by providing harm reduction, MAT, psychological interventions, rehabilitation, reintegration and general healthcare. Unfortunately, politicians often place the drug problem as an issue of national security rather than one of public health, explained Ford.

Shining examples of success

Attention was drawn to Switzerland and Portugal, where changes in drug policy have reaped positive outcomes. Implementation of a 'four pillars' approach integrating policing, harm reduction, and prevention and treatment in Switzerland has resulted in a greater than 50% decrease in drug-related deaths between 1991 and 2004, with an eight-fold decrease in new HIV infections over a 10-year period.[8,9] Furthermore, Switzerland has experienced a 90% reduction in property crime committed by drug users, with 70% of injecting drug users now receiving treatment.[9] Decriminalisation of drug use in Portugal has resulted in significant decreases in street overdose, from 400 to 290 annually, and significantly reduced illicit drug use among 15–19-year-olds since 2003.[10] "When you decriminalise drug use, young people have open discussions about them and can make informed decisions... pushing the war on drugs is actually making things worse", said Ford. Importantly, a significant increase in the number of patients receiving treatment has occurred, from 6,000 in 1999 to over 24,000 in 2008, without an accompanying increase in drug use.[11] The number of individuals injecting heroin has also significantly decreased from 45% to 17%, with injecting drug users now accounting for 20% of Portugal's HIV cases compared with 56% before decriminalisation.[12] Ford told delegates that decriminalisation of drug use allows physicians to work to provide medical care without the stigma associated with treating individuals who the law considers to be criminals.

Figure 2. Injecting drug users (IDUs) as a proportion of HIV cases and people on antiretroviral therapy



Impact of damaging policies

In Russia, needle-exchange programmes and MAT are outlawed, resulting in 37% of the 1.8 million drug-injecting population being infected with HIV.[13] Indeed, countries with suboptimal treatment systems have shockingly high percentages of HIV infection in injecting drug users, with a concomitant low number of injecting drug users accounting for the total number of individuals receiving antiretroviral medications (Figure 2).[13] In these same countries, MAT was shown to be available in less than 2% of injecting drug users.[13] This is in stark contrast to countries with long-established harm reduction programmes such as the UK, Australia and Germany, where HIV rates remain below 5%.[13] "HIV in intravenous drug users is a preventable disease; we can prevent this disease completely by implementing the right policies", said Ford. Echoing views from Professor Mike Trace, Ford stated that putting individuals into drug detention centres and calling it treatment is "barbaric" and that doctors should campaign to close these centres. "Good evidence-based treatment for people who use drugs set in a healthy integrated drug policy works", concluded Ford, adding that "doctors need to step up as leaders to influence policy in their own country".

Professor Mike Trace
International Drug Policy Consortium
London, UK

Political agendas and treatment systems development: a cause for concern

Professor Mike Trace discussed optimal models for treatment systems and how they vary according to country, presenting the key elements of what a humane and effective treatment system would look like. To achieve such a model, delegates were told that one must examine the reasons behind providing treatment, target the correct patient populations, provide a range of different treatments to suit individual needs and be flexible with the endpoint of treatment, while focusing on the ultimate goal of recovery.

Reasons for treatment provision

Opening the presentation, Trace explained that drug-dependence treatment is geared primarily towards protecting the health of drug users, reducing social exclusion and crime, and undermining the illicit drug market through reduction of demand. "There are some real political and public-opinion challenges about the interaction between these reasons for investing in drug treatment", he said. For physicians, the main driver of treatment availability is to provide good health and social services for dependent individuals who wish to recover, while governments place greater importance on reducing the societal impact of addiction. Addressing crimes committed while on drugs and for the purpose of obtaining drugs is a key priority for many European countries. Despite the majority of European and developed Western countries being able to strike a balance between patient health and societal protection, protecting society from drug users remains the number one reason for directing funding.

Targeting patient populations

It is important to define the objectives of treatment (eg reducing crime or blood-borne viruses) in order to identify the target population and structure the treatment system accordingly. "Very few governments or health systems do this in a very explicit way, as choosing who treatment should be made available to often happens accidentally", said Trace. A major issue that many governments around the world are struggling with is the '10% dilemma', where systems make no distinction in the targeting of treatment between drug users and drug-dependent individuals with significant psychopathology that make up about 10% of this group. This is a significant problem in Asia, where this distinction does not exist and treatment is often compulsory for anyone who is a drug user. "In this case treatment resources are not being directed very wisely because resources are going to a vast majority of people who don't need dependence interventions at all", said Trace, adding that the USA has a similar problem, as many minor drug offenders are being diverted to treatment through mandatory drug court rulings. In the past 10–15 years a great amount of work has been conducted on how to determine what treatment is best suited to individual patients. Countries that have a long track record of investing in treatment services provide a number of different services for individuals, according to the stage of treatment each patient is on.

A menu of treatment services

Trace told delegates that despite research establishing that pharmacotherapy is necessary for individuals with opioid dependence, and that certain treatment paths may be more appropriate for some than others, further research is necessary. "We know very little about the clear evidence base on how to shape a treatment system. Clearly the correct approach to take is to talk about a 'menu of services' and try to integrate these as best as possible", he said. Research suggests that the setting in which treatment is provided is important, especially in the context of intensity. Individuals who are in prison often require high-intensity treatments due to much more complex life situations, and provision of anything less is ineffective. Recent UK and US research suggests that the quality of the therapeutic relationship between the treatment provider and the patient is key to successful outcomes. "This seems to be the most important indicator of the quality of the services, namely the quality of the staff and how much a patient's needs are being met, and how much a patient will feel and receive this", said Trace. Recovery is also a useful target to focus on in treatment, delegates were told, as long as one is not too prescriptive about what this means, should it be abstinence or an individual target.

When to terminate treatment

The decision to discontinue therapy is one that should not be made lightly, and extremes still exist when determining the ultimate endpoint of treatment. Trace told delegates that systems like the one in Russia work on the premise that everyone is expected to overcome their addiction, and do not offer the possibility of ongoing treatment beyond a certain period. Not encouraging or believing that patients can fully recover can result in a group of patients who never intend or attempt to progress towards abstinence. Defining the endpoints of treatment has many political implications, as they impact society on many different levels (eg discontinuing pharmacotherapy, not committing crime, getting back to work and off benefits). "When we are so focused as practitioners on getting our model right, getting our service provision right, it is important to take a step back and not only think about what project or model we want to fund, but think of the treatment service as a system", concluded Trace.

Q. From a policy perspective, are you looking at approaching the problem of addiction much more broadly rather than focusing on just drugs?

A. The United Nations has the official position on addiction as a biopsychosocial disorder. There are clearly neurological and biological elements to addiction, which are linked to the disease model. But there are also emotional and psychiatric mental health issues surrounding this...taking a purely mechanistic brain science approach one will miss these important issues. I would also like to emphasise the social aspect of addiction...you have to recognise that the trauma and the pain that some individuals suffer they do not want to confront, and this is when individuals turn to addiction. People will react to their social context, so if you ignore that then we are thinking too narrowly and missing the point. The only thing I worry about is when there is research or policy that comes out from a particular country that focuses on only one aspect of addiction, such as the brain science or the sociology.

Integrating treatment for optimal outcomes

An effective partnership between primary care and addiction medicine

Research presented at ISAM suggests that patients with opioid dependence often experience a number of comorbid conditions that require treatment outside the realm of addiction medicine, supporting the need for integrated care. Dr Gavin Bart highlighted the benefits and effectiveness of integrating primary care into addiction treatment, and presented new resources available for training primary care physicians on opioid dependence treatment. Dr Paul Haber also presented study findings showing that provision of primary healthcare to injecting drug users attending needle and syringe programmes through a nurse-led low-threshold primary health clinic significantly increased the uptake of addiction treatment services with minimal cost. In a separate talk, Dr Ivan Montoya drew attention to the challenges to new treatment availability through use of strict outcome measures such as abstinence, suggesting that multidisciplinary dynamic interventions with multiple non-abstinence goals better reflect the chronic, relapsing nature of opioid dependence.

Dr Ivan Montoya
National Institute of Drug Abuse
Maryland, USA

Defining meaningful treatment endpoints for dependent patients

During his talk on the differences between clinical and scientific realities for treatment efficacy, Dr Ivan Montoya reminded delegates of the complexity of drug addiction, which has implications for defining what constitutes a meaningful treatment goal. "Although stopping the use of illicit drugs is of paramount importance, it should not be the only outcome measure of treatment efficacy," he said. The new definition of addiction developed by the American Society for Addiction Medicine was viewed as an important milestone, helping to further define suitable outcome measures of treatment. The definition of drug abuse as a chronic, relapsing, compulsive disorder associated with multiple clinical manifestations, complications and brain changes builds the case for long-term multidisciplinary dynamic interventions that have multiple treatment goals.

Different treatment realities

Montoya explained that although evidence-based treatments are in principle supported by scientific research, the realities of clinical and research frameworks can differ significantly. Clinicians measure treatment efficacy according to individual patient needs within the context of services offered in the treatment setting. In contrast, researchers place emphasis on a set of outcome measures that are pre-determined by research protocol. Using measures such as treatment abstinence is unreliable, as other treatment measures such as the rate of comorbidities, complications and eventual rehabilitation are important. "We know as clinicians that there are many other outcomes that are extremely relevant for drug abuse that go beyond abstinence, and we know how important is the symptomatic treatment of drug abuse such as treatment of cravings, withdrawal and intoxication", said Montoya. He also explained that defining the length of treatment within studies is suboptimal, as it is difficult to determine how long it will take until a patient shows meaningful signs of recovery. Non-abstinence endpoints such as drug use, cravings, quality of life (QoL) and psychosocial functioning would therefore be suitable alternatives to better reflect patient outcomes. Both clinicians and researchers can now access a central core of outcome measures and a ring of specialty measures that are suitable alternatives to abstinence-oriented measures. Indeed, preliminary study findings by Montoya found that 50% reductions in positive urine tests were significantly associated with meaningful reductions in cravings.

Dr Paul Haber
University of Sydney
Australia

Integrating primary healthcare within needle and syringe programmes – an effective approach

Study findings presented by Dr Paul Haber showed that uptake of addiction treatment services can be increased without increasing cost by providing primary healthcare to injecting drug users (IDUs) attending needle and syringe programmes (NSPs) through a nurse-led low-threshold primary health clinic. NSPs provide the opportunity of acting as a point of contact between the healthcare system and IDUs, and may therefore provide opportunistic primary healthcare for this group of marginalised patients who often report difficulty accessing treatment.

Focusing on patient needs

Haber noted study findings from a review citing international experience with IDU-targeted primary health clinics, which showed the importance of easy accessibility, flexible arrangements, opening hours based on patient needs, confidentiality and cost-free services. In addition, clinics must be willing to operate on a principle of harm reduction and be able to accept that patients are often reluctant to receive conventional healthcare. Significant problems reported with such services are mainly financial issues with NSPs and a lack of integration with the general system of care, which could result in questionable service quality.

A nurse-led approach

To investigate the feasibility of a nurse-led low-threshold primary care facility, Haber and team aimed to define the patterns of service utilisation, drug use, risk behaviours and uptake of referrals made to other health and social services over a 4-year period. In this nurse-led clinic, both users requesting needles and those referred from other rehabilitation centres were provided access to primary healthcare within the clinic. A visiting doctor was available on a part-time basis to assist the nurse and review difficult cases and abnormal screening results. Clinical protocols were available for treating hepatitis C and a number of services were available including referral, assessment, screening, management of wounds, veins, abscesses, informal counselling and welfare.

Positive outcomes

Study findings revealed a steady case load of both new patients and those coming back for treatment, with the majority (57%) requiring blood-borne virus testing and vaccination followed by drug health and psychosocial services (23%) and sexually transmitted disease check-ups (18%). Patients attended the clinic on average 3.5 times, with 83% attending more than once. Furthermore, 62% of patients reported GP access outside the clinic. Importantly, unpublished local data presented by Haber identified that the main reason IDUs visited a GP was to 'doctor shop' for drugs. "One of the advantages of this clinic is that it is nurse-led so no prescriptions can be made," said Haber. Further analysis showed that patients who reported buprenorphine and benzodiazepine use in the preceding 12 months were 3.8- and 2.3-fold more likely than other patients to report GP access, respectively.

Of the 249 patients offered hepatitis B vaccination, 50% completed the schedule, which according to Haber was not necessarily a negative finding given the study population. Analysis of 337 patient referrals for health and welfare services showed an average 55% uptake that was also considered as an encouraging finding, and included referrals to a liver clinic (29%), GP (27%), sexual health services (13%) and drug treatment services (13%). Concluding the talk, Haber pointed out that in addition to reported patient benefits, the clinic is extremely cheap to run and provides the opportunity for continuation of care to this vulnerable patient population.

Dr Gavin Bart
Hennepin County Medical Center
Minneapolis, USA

Integrated care of opioid-dependent patients with comorbidities

Opioid-dependent patients experience a high number of infectious comorbid diseases that require different treatment approaches, which are often not integrated. The majority of opioid-dependent patients seek treatment either for their addiction or comorbid conditions within primary care, which is poorly equipped to diagnose and treat opioid dependence. In a two-part talk, Dr Gavin Bart discussed the complex psychosocial factors and organisational barriers for achieving quality patient care, and presented educational resources within a Physician Clinical Support System (PCSS) framework for assisting primary care physicians in the treatment of opioid-dependent patients.

Barriers to integration

Opening the presentation, Bart drew attention to the over-representation of common ailments among patients with substance use disorders (SUDs) in primary care compared with non-addicted patients seeking treatment (Figure 3). Integrating primary care into addiction treatment could help reduce health utilisation costs and bridge the gap between treatment services in addiction medicine, which was shown to be significantly larger at 80% than conditions such as hypertension (40%) and depression (56%).[14] However, a potential disadvantage of using this approach could be the episodic nature of treatment that would only target those in treatment, whereby treatment and monitoring for long-term comorbid conditions would cease after resolution of the SUD. Indeed, presented study findings showed that HIV+ patients who had their treatment continuously monitored had the best improvement in viral load and CD4 cell counts.[15]

An effective approach

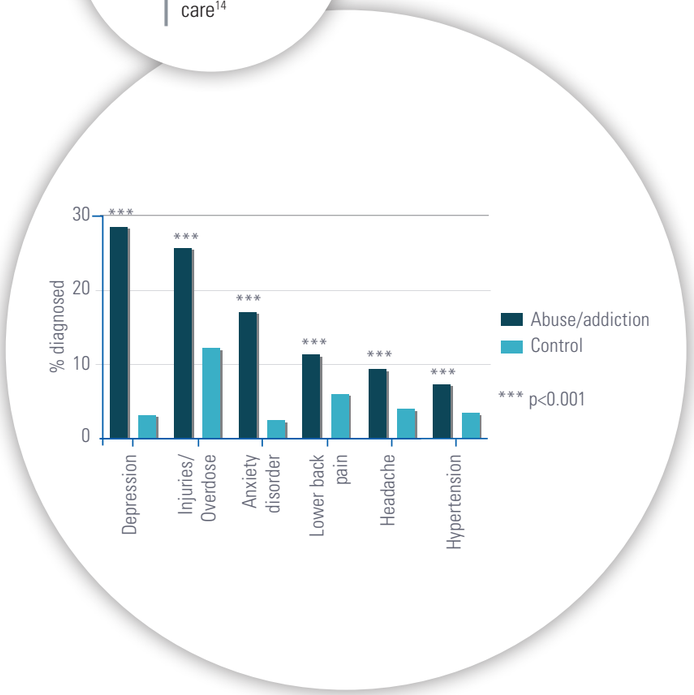
Findings from various studies integrating primary care into addiction treatment were presented, which showed improvements in 12-month addiction severity outcomes that did not differ according to whether treatment was provided onsite or offsite.[16] Furthermore, addiction treatment significantly reduced the percentage of patients using outpatient services (62% to 41%), emergency room visits (47% to 23%) and hospital visits (42% to 13%).[17] Study findings also showed that integrated treatment results in incremental cost savings of USD$1,581 per abstinent patient despite being initially more expensive.[18]

Addiction treatment in primary care

It was estimated that about 25% of primary care patients have problems with drug use or a diagnosed SUD, and this figure is often higher in HIV primary care settings.[19] "To reduce morbidity and mortality related to these problems, detection and treatment within a primary care setting becomes essential", said Bart. Despite numerous studies demonstrating the effectiveness of addiction treatment, screening and brief intervention in primary care settings, lack of knowledge in the diagnosis of addiction, unfamiliarity with treatment options, and fear of non-adherence or drug–drug interactions are cited as common barriers to integration.

To overcome these barriers, several interactive web-based tools have been developed, as well as provision of PCSSs incorporating email and telephone support, online resources, direct line advice and cooperation with local medical societies. Specific training on buprenorphine and methadone treatment is also provided for primary care physicians, with courses and practice webinars available online at www.pcssb.org and www.pcssprimarycare.org, respectively. Another useful tool available to physicians is NidaMed (www.drugabuse.gov/nidamed), an online resource providing a simple screening test with advice on clinical decision-making and other resources for addiction. "If you create a one-door system where patients can access integrated care for their addiction and comorbid conditions, addiction and healthcare outcomes will improve with the added benefit of reducing treatment costs," said Bart.

Figure 3. Over-representation of common conditions among SUDs in primary care[14]



Role of MAT in harm reduction

Addressing HIV and hepatitis C with buprenorphine treatment

Opioid-dependent patients infected with HIV and hepatitis C do not receive appropriate levels of care and often have difficulty accessing treatment, suggested study findings presented at ISAM by Prof Frederick Altice and Dr Paul Haber. Integration of HIV treatment with MAT was shown as important, given that buprenorphine was reported to increase the likelihood of initiating and staying within antiretroviral therapy, achieving viral suppression and improving QoL and indicators of quality HIV care. Indeed, suppression of viral loads to non-detectable levels was shown to significantly reduce HIV transmission. A similar problematic picture was described by Dr Paul Haber, who drew attention to the high number of injecting drug users infected with hepatitis C and the problems in accessing treatment. Development of a partnership between clinics was able to increase hepatitis C treatment access as was treatment with buprenorphine, thus playing an important role in prevention of a future liver disease epidemic. Dr Robert Haemmig then presented study findings suggesting that integrating MAT within a safe injecting facility effectively increases treatment uptake.

Professor Frederick Altice
Yale University School of Medicine
Connecticut, USA

HIV treatment and MAT – the key to harm reduction

Study findings presented by Prof Frederick Altice showed the importance of integrating buprenorphine pharmacotherapy and HIV treatment services for reducing harm and improving treatment outcomes in opioid-dependent patients.[20] Buprenorphine treatment was reported to increase the likelihood of initiating antiretroviral therapy, achieving viral suppression,[21] improving patient QoL[22] and indicators of quality HIV care.[23] In another study, encouraging findings among HIV+ opioid-dependent ex-prisoners showed high levels of retention, satisfaction and reduced craving with buprenorphine treatment. In addition, findings were reported from a separate study showing that suppression of viral loads to non-detectable levels were able to markedly reduce HIV transmission to negligible levels, irrespective of engagement in high-risk sexual behaviours, suggesting the need to develop effective strategies to initiative antiretroviral therapy and maintain adherence and retention in care.

Reducing HIV transmission

Altice told delegates it is estimated that 1.1 million individuals in the USA are infected with HIV, of which 21% are unaware of their HIV status.[24] This 21% was said to contribute to 54% of new HIV infections. Looking at the proportion of HIV+ patients engaged in various stages of care, a 20–30% decrease in each stage was presented, leaving only 19% of patients virally suppressed (Figure 4). "We really need to increase the proportion of HIV-infected individuals in care to at least 60% in order to reverse the trend of 56,000 annual new HIV infections…ineffective treatment of substance use disorders is going to significantly impact these figures", said Altice. Indeed, areas such as Eastern Europe and Central/Southeast Asia that have high levels of drug use and do not have strategies in place for integration of antiretroviral therapy were said to have a 25% increase in HIV transmission. Of particular relevance were findings from a recent study of serodiscordant couples receiving antiretroviral therapy, which showed that antiretroviral medication reduced HIV transmission by 96%, with transmission occurring only among one couple not complying with treatment.[25]

Improving HIV outcomes with MAT

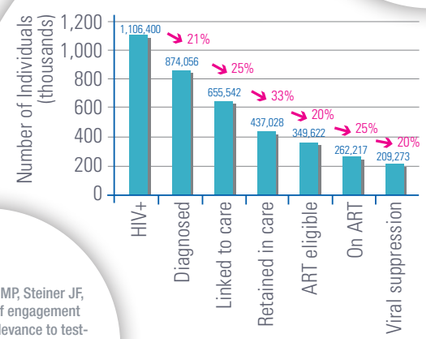
A number of studies were mentioned, all showing that MAT increases the likelihood of receiving and adhering to antiretroviral medication, thereby achieving viral suppression among opioid-dependent HIV+ patients.[21] Recent preliminary study findings confirmed that discontinuation of MAT actually reversed this benefit. Altice explained that treatment integration is key to achieving positive outcomes, noting that the capability of primary care physicians in treating addiction should not be underestimated. BHIVES study findings showed that buprenorphine increased the likelihood of initiating antiretroviral therapy (from 59.7% in treatment at baseline to 68.4% at 1 year) and improving CD4 cell counts (from 354.9 cells/ml at baseline to 404.5 cells/ml at 1 year).[21]

Furthermore, being on buprenorphine was associated with a 10.3-fold increased likelihood of achieving viral suppression, and a longer time spent on bup/nx (<3 quarters vs 3 or 4 quarters) was associated with a 1.5-fold increased likelihood of receiving antiretroviral therapy.[21]

HIV and prison

HIV outcomes following release from prison were shown as poor (Figure 5),[26] but significantly improved following buprenorphine treatment in a 12-week follow-up study of 23 released HIV+ opioid-dependent patients.[40] Opioid cravings decreased significantly within 3 days, with retention rates of 74%. Furthermore, viral load and CD4 cell counts remained constant, which "suggested for the first time that treating the SUD actually engages patients in care for a longer period of time", said Altice. He added that preliminary findings from an upcoming study show that retention on buprenorphine for 20 or 24 weeks was associated with a 5.6-fold increased likelihood of having a viral load below 50 at 6 months.

Figure 4. Proportion of HIV patients engaged in various stages of care[24]



Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clin Infect Dis. 2011; 52:793–800. Reproduced by permission of Oxford University Press.

Dr Paul Haber
University of Sydney
Australia

Problematic access to hepatitis C treatment – a hidden epidemic

Approximately 50–60% of IDUs are infected with hepatitis C, with liver disease quickly becoming the leading cause of death among opioid-dependent patients (Figure 6). Addressing the hepatitis C epidemic is of great importance as infected patients suffer from liver complications, significant morbidity and experience discrimination and social insecurities. In addition, hepatitis C poses a significant economic burden to society, estimated to cost AUD$46,300 (€34,600) per case.[27] These consequences are of great significance, given that 75% of patients receiving opioid pharmacotherapy are hepatitis C positive.[28]

Treatment barriers

Despite patients showing a high willingness to get treatment, patients currently receiving MAT are 78% less likely to receive hepatitis treatment than those out of treatment.[28] "There are barriers to having this treatment at multiple levels. We know that in our routine clinics, fewer than 5% of patients are accessing treatment for hepatitis C", said Dr Paul Haber. A number of barriers to treatment were presented, which were seen among patients, clinicians and systems of care (Figure 7, page 10).

The ETHOS programme

To address these barriers, Greg Dore, Haber and colleagues adopted a hepatitis C treatment partnership model among a network of nine clinics in New South Wales, Australia. Within this treatment partnership, the Enhancing the Treatment for Hepatitis C in Opioid Substitution Settings (ETHOS) programme was developed. In total, 237 patients with a history of injecting drug use and chronic hepatitis C infection have been recruited to date.

Factors linked to treatment

Preliminary analyses of this patient cohort showed that 49% of patients had never sought treatment for hepatitis C. Reasons cited for not taking up treatment were a lack of knowledge about hepatitis C infection (30%), concerns about treatment side effects (12%) and asymptomatic disease (11%). However, the majority (80%) of patients were willing to receive hepatitis C treatment. Of the 66% of patients referred to a hepatitis C specialist, 44% attended their appointment. Of these, 19% initiated treatment. "We think this is an excellent result compared to usual care", said Haber. Factors positively associated with hepatitis C treatment uptake included having a 2/3 genotype versus a 1 genotype (adjusted odds ratio [aOR]=4.20), current buprenorphine treatment versus none (aOR=4.20) and a high school/tertiary education (aOR=2.29). Conversely, patients who reported benzodiazepine use in the past 6 months or suicidal ideation were significantly less likely to receive treatment (aOR=0.28 and 0.09, respectively). "Access to hepatitis C treatment assessment and delivery within the clinic network should ensure that a greater number of IDUs are assessed and treated for hepatitis C", concluded Haber.

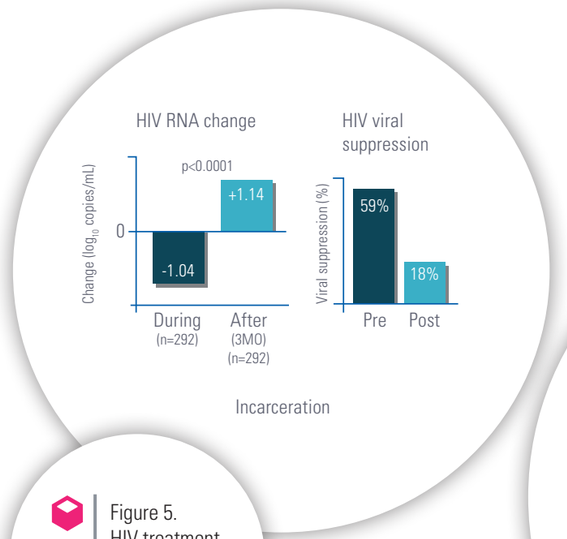
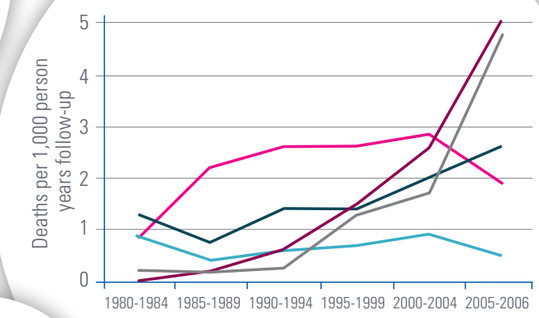


Figure 5. HIV treatment outcomes during and after incarceration[26]

Figure 6. Causes of death among opioid-dependent patients[29]



Gibson A, Randall D, Degenhardt L. The increasing mortality burden of liver disease among opioid-dependent people: cohort study. Addiction. 2011; 106:2186–2192. Reproduced by permission of John Wiley and Sons.

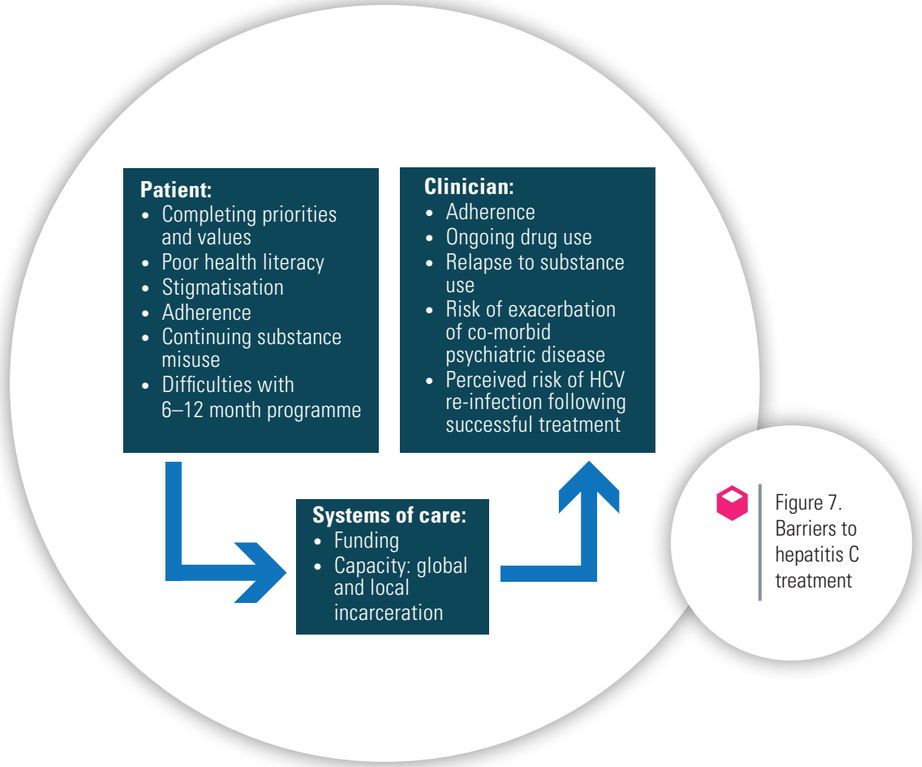


Figure 7. Barriers to hepatitis C treatment

Provision of MAT within a safe injecting facility increases treatment uptake

Supporting the concept of harm reduction in opioid-dependent users, Dr Robert Haemmig (University Psychiatric Services, Bern, Switzerland) presented preliminary study findings showing that integrating MAT within a safe injecting facility (SIF) is effective for increasing treatment uptake. The programme, which started earlier this year, has so far resulted in 6 out of 11 patients referred to a specialised treatment centre from the SIF. The findings are of importance, given that preliminary findings from a 2010 survey of opioid-dependent users showed that 31% of 231 studied users were not receiving treatment. Approximately 50% of these opioid-dependent individuals said they would be prepared to start MAT within the SIF. This approach could therefore serve to establish an initial point of contact between users and the healthcare system.

Q. Do physicians in Australia show any objections to treating patients on methadone maintenance and do you have any experience with the new protease inhibitors in patients on MAT?

A. We do not have any experience with protease inhibitors among patients on MAT as this group of patients has been excluded from the initial trials of these agents. One of the challenges of getting hepatologists to do this work is that they are not always willing to work with drug users. However, more and more hepatologists are realising that there are serious liver problems among individuals with addiction and they are looking for strategies to link the patients into treatment. This has partly been driven by the high number of patients developing cirrhosis. It is much easier to treat patients at the early stages of the disease rather than waiting until advanced liver disease emerges.

Q. Do patients show increased drug use when receiving hepatitis C treatment?

A. Findings from another Australian study show that this is not the case, despite 30% of patients experiencing depression that was successfully treated.

Benefits and experiences of buprenorphine maintenance

Improving outcomes and facilitating recovery with buprenorphine

Therapies incorporating buprenorphine or bup/nx play a key role in improving treatment outcomes, promoting recovery and increasing access to treatment, showed a number of study findings presented at ISAM. Dr Neil McKeganey showcased data suggesting that bup/nx plays an important role in recovery as it is associated with greater reductions in illicit drug use and improved QoL compared with methadone. Findings from the Buprenorphine and HIV Evaluation & Support Collaborative (BHIVES) study presented by Prof Patrick O'Connor also showed that bup/nx is an effective therapeutic modality for HIV+ opioid dependents, which results in improved treatment retention, reduced drug use, fewer drug–drug interactions and an increased likelihood of entering treatment compared with methadone. Dr Ziv Carmel and Dr James Finch also presented their experience with take-home buprenorphine and bup/nx treatment, reporting successful outcomes and reduced drug use, even with minimal psychosocial intervention. Indeed, take-home buprenorphine was posed as a solution for limited accessibility to treatment while offering good retention rates.

Dr Neil McKeganey
Centre for Drug Misuse Research
Glasgow, Scotland

The role of buprenorphine/naloxone in recovery

Opening his talk, Dr Neil McKeganey cited recovery as the priority at the forefront of treatment strategies within the UK, rather than an approach focused primarily on harm reduction. "The worry is that patients have then become dependent on the treatment services themselves", he commented. Findings presented from a study of 109 opioid-dependent patients receiving bup/nx or methadone for at least 6 months showed that bup/nx-treated patients had significant progress in multiple clinical outcomes and showed better signs of recovery than those maintained on methadone.

Reducing illicit drug use

Structured interviews among drug users, prescribers and pharmacists in Scotland performed at baseline, 1 month and 8 months showed that 80% of patients treated with methadone reported injection drug use compared with 60% of bup/nx-treated patients. Bup/nx-treated patients also reported higher scores on a readiness to treat measure than those maintained on methadone. Compared with bup/nx, methadone was associated with higher baseline and 8-month follow-up rates of illicit drug use (70.3% vs 34.2% at baseline; 43.2% vs 31.6% at 8 months), benzodiazepines (70.3% vs 36.8% at baseline; 51.4% vs 39.5% at 8 months) and stimulants use (43.2% vs 18.4% at baseline; 35.1% vs 7.9% at 8 months). When patients' self-assessment of problem drug use was analysed, nearly double the number of patients in the bup/nx group reported having no "problem" drug use compared with those on methadone, at 60.5% versus 31.4%, respectively.

Improving employment and QoL

Similar findings were seen for employment, with patients maintained on bup/nx showing significantly higher rates of employment and financial self-support within the past 6 months compared with methadone at baseline (11.2% vs 5.4% and 13.2% vs 8.1%, respectively). The rate of housing problems was also significantly lower among those treated with bup/nx, while several measures of self-assessed health were significantly better among bup/nx-treated patients. Both treatments improved regularity of bedtime, although it was noted that methadone-maintained patients had more difficulty keeping a regular wake time compared with buprenorphine-maintained patients at 8 months (40.5% vs 23.7%). Alcohol use was reported to a similar extent in both groups, with comparable numbers of patients reporting no problem to moderate alcohol problems. However, extreme drinking was observed only among methadone-maintained patients, at 8.1%. Sleep quality was similar between both groups, although significantly more patients maintained on methadone reported very poor sleep quality at baseline (32.4% vs 7.9%) and 8 months (27.0% vs 18.9%).

Patient and prescriber viewpoints

Analysis of the qualitative interview data showed that prescribers judged bup/nx as easier and quicker to reach stabilisation with a less sedative effect, fewer drug–drug interactions, better cognitive functioning, reduced risk for concurrent opioid use, and as being suitable for individuals with high motivation. Cost, diversion and need to switch to methadone in some cases were seen as negative aspects of treatment. Opioid-dependent patients reported bup/nx as being more discrete due to its tablet form and as the pharmacotherapeutic option with a more 'clean' and 'clear-headed' feeling. Patients also reported it reduced their temptation to use other opioids on top of treatment. However, patients reported a higher risk for withdrawal symptoms and difficulty with switching treatment, although it was suggested that this may be due to poor patient education and anxiety surrounding the transfer. "The indications here are that there may be real merit in considering which drug users currently on methadone might benefit from switching to bup/nx," said McKeganey, adding that the readiness to treat measure may help identify those who would benefit from such a switch.

An issue of cost

McKeganey explained that bup/nx is not as widely available as one might think, and that a reason for this may be its high cost. "It's very easy to do a simple contrasting cost and say that one drug is more expensive than another, but when you start to look at the positive changes associated with its use coupled with how widely it is prescribed, there are clearly issues of the relative cost here that need more detailed consideration", he said.

Dr James Finch
North Carolina Governor's Institute on Substance Abuse
Durham, USA

Improving patient outcomes with take-home buprenorphine/naloxone

During his review of the US clinical experience with bup/nx, Dr James Finch reported positive findings during his experience as a physician treating 71 patients with bup/nx over a 2-year period. Bup/nx treatment with take-home dosing was described as successful, although knowledge and skills of the treating physician were considered important for success: "Clinicians have to be using reasonable treatment standards of dosing, monitoring and intervening to minimise the likelihood of misuse". Finch also explained that a successful induction is the cornerstone of successful treatment: "I believe the induction process is very important in terms of building a relationship and trust between the clinician and the patient and allows one to observe the clinical response and address any anxiety when switching from a drug that patients are familiar with to one they don't necessarily know".

A positive experience

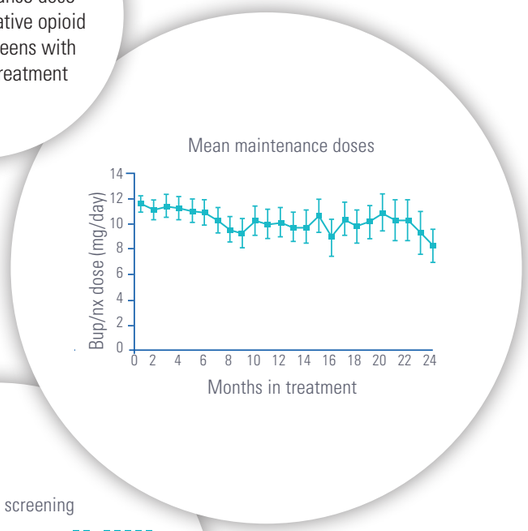
Describing the induction protocol, Finch explained that the initial dose was administered at the outpatient office followed by subsequent doses taken at home, although patients were not kept under direct observation as with earlier protocols. The lengths of prescriptions were then increased progressively to once per month depending on patient reliability and urine screening results. Finch noted that with bup/nx mean maintenance doses tended to decrease over time with increasing stability (Figure 8). This pattern was described as different from what he had seen with methadone, where doses often tended to steadily increase. In total, 43% of patients continued in ongoing treatment with bup/nx, 7% of patients transferred to methadone treatment and 21% successfully withdrew from their medication voluntarily. Only 24% failed induction or dropped out of treatment. Finch drew attention to the low number of positive drug screens seen with bup/nx, most of which occurred during initial treatment stages (Figure 8). "Often, the last drug screen positive for opioids was the one done at admission. Clinically it is just amazing to see a medication that within days can turn around drug-using behaviour," he said.

Dr Ziv Carmel
Harbetim Clinic
Tel Aviv, Israel

Improving treatment access with take-home buprenorphine

Study findings presented by Dr Ziv Carmel suggest that take-home buprenorphine maintenance with minimal psychosocial intervention is an effective treatment option, which increases access to MAT while providing comparable retention rates to those observed in intensive treatment settings. Although minimal psychosocial intervention is not an ideal setting for long-term treatment, increasing clinic resources through reduction of such services could serve as a short-term solution for the lack of treatment accessibility in many countries. However, it was cautioned that adequate patient selection would be crucial for such an intervention to be effective.

Figure 8.
Mean opioid maintenance dose and negative opioid urine screens with bup/nx treatment



Limited accessibility – a widespread problem

Opening his presentation, Carmel explained that in Israel there is limited accessibility to buprenorphine maintenance treatment in government-funded centres, in addition to a small number of private clinics offering opioid-dependence treatment. Comprehensive psychosocial interventions form an integral part of treatment in these clinics; however, this leads to long waiting lists due to the strain on treatment resources. To address this issue, the team developed the Office-based Buprenorphine Maintenance Treatment with Minimal Psychosocial Intervention (OBMMPI) model, where admission to the clinic was performed by a physician and followed by take-home buprenorphine induction and weekly attendance to the clinic during the first month and monthly thereafter. Psychosocial intake was performed within 1 month of admission and focused interventions were tailored according to patient findings, with psychotherapy offered on admission. Patients received physician follow-up once every 3 months, and psychiatric interventions were carried out when necessary.

Retaining patients with take-home

Results from the retrospective analysis of 226 patients admitted to the clinic in 2008 showed that 10.6% did not attend the clinic for a second visit. Drop out was found to be significantly higher among females compared with males, at 24.0% versus 9%. Carmel noted that patients who were self-medicating with buprenorphine before admission were less likely to drop out than those who did not self-medicate, at 0.0% versus 36.0%, respectively. Overall, 52.5% of patients who completed induction with buprenorphine were still in treatment after 12 months. The findings are encouraging, given that 87.0% of patients reported multiple substance abuse before or on admission. Furthermore, 24.8% and 49.1% of patients reported psychiatric and physical comorbidities at admission, respectively.

Factors associated with adherence

It was shown that patients who were single, previously self-medicated with buprenorphine, abused benzodiazepines and lived in close proximity to the clinic were significantly more likely to adhere to treatment than those who did not have these characteristics. Patients with a history of criminal activity were significantly more likely to also have a history of buprenorphine self medication, and thus had better rates of adherence to treatment following attendance to the clinic.

Q. What was the average buprenorphine dose used in the study and how did you monitor for misuse and diversion?

A. Patients received an average 16 mg of buprenorphine per day and regular urine screening was performed. However, it is possible that tampering of samples occurred.

ISAM/GLADD 2011– Benefits and experiences of buprenorphine maintenance

Professor Patrick O'Connor
Yale University School of Medicine
Connecticut, USA

Integrating HIV care through bup/nx treatment

Discussing the positive impact bup/nx has had on treatment uptake in the USA, Prof Patrick O'Connor provided various study findings describing the benefits of bup/nx for the treatment of HIV-infected opioid-dependent patients, and highlighted potential challenges in the integration of HIV and opioid-dependence treatment in primary care that need to be addressed. "The BHIVES study has shown in a very important way that bup/nx can be effectively integrated into HIV treatment and patients can do quite well in terms of important substance abuse outcomes," said O'Connor. The findings help shed light on problematic issues encountered when treating this group of opioid-dependent patients with specific HIV comorbidity, and confirm a lack of physician screening for HIV infection in the broader general population of patients receiving office-based treatment of opioid dependence.

Bup/nx in primary care

Delegates were told that in the USA bup/nx is widely prescribed, with prescriptions increasing exponentially since its introduction in 2002. Despite this increase, the overall proportion of prescribing physicians in primary care remains low, standing at about 12,000 out of the approximately 350,000 practicing primary care health professionals in the country.[30] Nearly half (46%) of all bup/nx prescriptions originate from primary care, with about 21% of prescriptions administered by psychiatrists.[31] Attention was drawn to preliminary study findings showing that only 46% of bup/nx providers screen for HIV in general healthcare settings, despite recommendations by the Centers for Disease Control and Prevention that support universal screening.

Integrating HIV treatment: BHIVES study

Results from the 1-year BHIVES study of 303 HIV-infected opioid-dependent patients treated with bup/nx showed several positive outcomes in treatment retention, drug use and drug–drug interactions. Bup/nx treatment of patients with averages of 17.2 and 12.2-years opioid dependence and HIV diagnosis history, respectively, showed treatment retention rates comparable to non-HIV-infected patients treated with buprenorphine, ranging from 100% at baseline to 48.2% by the end of follow-up.[32] In addition to a decrease in self-reported opioid use from baseline, investigators noted that stimulant and sedative use were also significantly decreased from baseline, from 58.3% to 38.7% and 17.9% to 11.5%, respectively.[32] Further findings from another BHIVES study showed cocaine use persisted during treatment (65%), although it did not significantly impact retention.[33]

A major concern with treatment of HIV-infected opioid-dependent patients is the possibility of adverse drug–drug interactions. BHIVES study findings showed that buprenorphine doses remained consistent among both patients who received bup/nx with HAART regimens containing atazanavir and those treated with HAART regimens without atazanavir, at 19.7 versus 18.9 mg/day, respectively.[34] Furthermore, bup/nx treatment was shown to have no significant impact on liver enzymes.[34]

The probability of receiving opioid agonist treatment over a 12-month period of time was significantly higher among patients treated with buprenorphine within the HIV clinic compared with those referred offsite for methadone treatment,[35] which "supports the concept that offering buprenorphine onsite not only improves the likelihood of entering treatment but increases the chance of receiving and remaining in treatment over 12 months", said O'Connor. The same study also showed that patients who received onsite buprenorphine had significantly less drug use than those referred to offsite methadone programmes.[35]

Benefiting from buprenorphine treatment: retaining positive outcomes, addressing key issues

Treating patients with buprenorphine-based pharmacotherapies benefits both patients and physicians, provided that key issues such as appropriate patient selection, dosing to a therapeutic standard and taking steps to minimise the likelihood of diversion and misuse are appropriately managed, according to findings presented at Global Addiction. Dr Paolo Mezzelani showed that both patients and physicians reported positive experiences with buprenorphine, with the majority of physicians dosing to recommended therapeutic doses between 12–24 mg/day. Professor Icro Maremmani revealed that buprenorphine treatment is especially beneficial for severely dependent patients with low QoL, as it results in greater QoL compared with methadone. However, physicians reportedly expressed concerns over diversion and misuse, which were shown to be dependent on a number of patient-related factors. Encouraging findings from a CME initiative presented by Professor Sharon Walsh showed that educating physicians on misuse-prevention strategies was effective for reducing negative clinical practices conducive to misuse and diversion, such as subtherapeutic dosing and incomplete assessment of withdrawal at intake. Finally, Dr Gary Tanner and Mr Duncan Hill reported positive experiences in using bup/nx as first-line therapy, showing that patients tolerate switching to this pharmacotherapeutic modality very well and that it has assisted many on the road to recovery.

Dr Paolo Mezzelani
University of Verona
Italy

Positive physician, patient experiences with buprenorphine

Survey findings on Italian physicians' experiences with buprenorphine, presented by Prof Paolo Mezzelani, revealed positive feedback on various aspects of treatment, including safety profile, ease of induction, long-term maintenance, take-home therapy and use with first-time and relapsed patients. In addition, buprenorphine was viewed positively by both family members and health workers. However, physicians reported concerns over the diversion and misuse potential of mono-buprenorphine and the difficulties in withdrawing medication principally due to a lack of low-dose tablets. Therapeutic daily doses above 12 mg during maintenance treatment were regularly reported, despite over one-third of physicians following their own clinical experience rather than complying with national guidelines. "Because Italy is a country with a large number of patients in buprenorphine treatment, results from this survey could be useful to other geographic areas", said Mezzelani.

An Italian perspective

Describing the current situation in Italy, Mezzelani told delegates that approximately 180,000 drug users attend one of the available 544 publicly funded specialist centres, of which 106,000 receive agonist-maintenance treatment. The majority of patients receive methadone treatment, with 25% and 13% treated with bup/nx and buprenorphine, respectively. Take-home treatment is commonly provided in 40–50% of cases. To assess buprenorphine-prescriber attitudes, Mezzelani and team administered a written questionnaire assessing safety, acceptability and efficacy of maintenance treatment to 305 randomly selected Italian physicians who had at least 6 months experience with buprenorphine prescribing in 2006.

Encouraging prescribing practices

Buprenorphine prescribing was highly rated by the majority of physicians, who reported feeling most comfortable prescribing buprenorphine to heroin users receiving treatment for the first time (69%) and to patients who relapsed to heroin use (58%) than those in other scenarios. Induction to buprenorphine from heroin or methadone was not rated as significantly problematic by 83% and 78% of physicians, respectively, with an additional 74% reporting little to no difficulty during

administration of take-home therapy. Indeed, physicians rated the ease of use in unsupervised treatment to be a winning feature for buprenorphine (30%), followed by the smaller risk of overdose (22%) and less associated stigma (17%), compared with methadone. Despite the reported ease of take-home therapy, the greatest disadvantage of buprenorphine treatment was its diversion potential (31%), followed by difficulty in medication withdrawal mainly as a result of a lack of low-dose tablets (28%).

In total, 90% of physicians agreed that buprenorphine was well-indicated for treatment periods lasting longer than 6 months and at doses above 12 mg/day (62%). Indeed, the majority of physicians routinely prescribed buprenorphine doses of 12–24 mg/day in practice. Despite this encouraging finding, only 27% of physicians used guidelines to inform their dosing practice, with 38% preferring clinical experience.

Patient treatment benefits

Mezzelani and team found that 44% of physicians reported increased compliance rates with buprenorphine relative to methadone, with 58% of patients regularly requesting buprenorphine. Furthermore, 70% of patients specifically attended centres to receive buprenorphine treatment. Benefits were also observed by families who judged buprenorphine as a better treatment compared with methadone (62%), and by health workers who valued the option of providing buprenorphine (74%). These encouraging findings confirm the feasibility of buprenorphine treatment for both physicians and patients.

Professor Sharon Walsh
University of Kentucky
Lexington, USA

Buprenorphine misuse: a multi-faceted issue

A review of available research on misuse and diversion of buprenorphine pharmacotherapy by Prof Sharon Walsh showed that bup/nx carries the least risk of misuse, which can be influenced by a number of individual factors such as route of administration (intranasal or intravenous), other opioids in the system and dependence state. Indeed, buprenorphine and bup/nx were said to have comparable effects when taken intranasally in non-dependent patients, while ongoing studies will soon clarify differential effects in opioid-dependent individuals. Delegates were told that data suggest some cases of injection of buprenorphine are driven by subtherapeutic dosing. Educating physicians on misuse-prevention strategies, such as careful evaluation of withdrawal symptoms during induction, therapeutic dosing, continued monitoring and patient education, were shown as effective in increasing knowledge and providing sustained positive changes in clinical practice behaviours.

An emerging problem

A number of studies have shown that bup/nx – a formulation originally developed to deter parenteral misuse and diversion – produces negative or blunted effects in people who attempt to inject it under certain conditions.[36,37] "[These findings] suggest that the intent behind the design of this drug – using naloxone as a deterrent against injection – actually works in real practice", said Walsh. However, numerous reports of intranasal misuse have emerged in the past few years, with up to 30% of patients in France prescribed take-home buprenorphine misusing their medication through this route.[38] Presented findings showed that buprenorphine bioavailability for the single and combination products are similar for both the intranasal and sublingual routes, while naloxone was shown to be well absorbed with the 8/2 mg bup/nx dose during intranasal misuse, providing a bioavailability of 27%.[39] "We believe that if we were to give the same dose in opioid-dependent patients it would likely precipitate withdrawal, but this study hasn't been done yet", said Walsh. It was explained that both buprenorphine and bup/nx have moderate abuse potential in non-dependent patients for all routes, while those dependent on opioids are less likely to derive benefit. Ongoing studies will soon clarify the potential differential effects of buprenorphine and bup/nx when taken intranasally.

Predictors for misuse

Findings from a study of 307 opioid-dependent patients showed that younger patients aged 15–20 years are more likely to misuse their medication than those aged 21–25 and 26–30 years, respectively (67% vs 41% and 18%).[40] When patients gave their reasons for misuse, 30% attributed this to management of residual withdrawal symptoms.[40] A separate survey of 111 patients also revealed suboptimal dosing (odds ratio [OR]=2.9) as a significant risk factor for intravenous use, while a previous history of intranasal drug use was predictive for intranasal medication misuse (OR=5.6).[38,41] Walsh also noted that buprenorphine was reported infrequently as the drug of choice for misuse among individuals dependent on prescription opioids (<3%), with 3-year survey findings from over 1,000 patients showing that the majority of these individuals preferred full agonist formulations such as oxycodone and hydrocodone, with only 20% reporting using buprenorphine products to get high.

Outcomes of physician education

Findings from a teaching CME course that taught clinical practice behaviours, pharmacology and legal knowledge about buprenorphine to 67 treating physicians showed that practice behaviours were improved and changes were sustained at 3-month follow-ups.[42] For the study, emphasis was placed on comprehensive patient evaluations to ensure correct diagnosis on opioid dependence, including urine testing, consistent patient history, corroborating medical examination and use of the Clinical Opioid Withdrawal Scale at all times. In addition, Walsh noted that it is important that physicians understand the rationale for why patients must be in withdrawal, and why nonadherence to intake and screening protocols may result in enrolling pseudopatients. Indeed, findings from the study showed that education on pharmacology resulted in a significant 30% increase in the number of physicians initiating MAT only when evident signs of withdrawal were present in 81–100% of their patients.[42] Delegates were told that an additional useful practice for reducing the likelihood of misuse is discussing the harms and consequences associated with this practice, such as stroke, necrosis and granuloma formation.

Dr Gary Tanner and Mr Duncan Hill
NHS Lanarkshire
Motherwell, Scotland

First-line bup/nx treatment reduces mortality, improves outcomes

Findings from two studies presented by Dr Gary Tanner and Mr Duncan Hill showed that patients report positive experiences with bup/nx, and demonstrated the successful use of bup/nx as first-line therapy and how this choice of pharmacotherapy has assisted many in the road to recovery. Preliminary study findings also showed that patients tolerate switching from buprenorphine to bup/nx very well, provided that adequate support is provided. The team also showed that implementation of new guidelines incorporating revised sections on benzodiazepine prescribing, overdose prevention and therapeutic doses resulted in a greater than 50% reduction in mortality.

MAT in Scotland

Opening the presentation, Tanner explained that opioid and benzodiazepine use in Scotland is on the rise, showing a 7.7% increase since 2006.[43] Prevalence rates for the older population (35–64 year olds) have shown a significant rise over this time period, increasing from 0.89% to 1.18%, while prevalence rates for younger age groups have declined. Following a successful trial with buprenorphine in Lanarkshire county during 2003–2006, the decision was made to switch all opioid-dependent patients receiving buprenorphine to bup/nx in 2007. Despite this change, and the reported benefits associated with buprenorphine, Tanner noted that 80% of patients still receive methadone.

Patient buprenorphine/naloxone experiences

To investigate patients' experiences with methadone and bup/nx, structured interviews were performed in nine methadone and bup/nx-treated patients, and free narrative accounts were obtained from an additional twelve patients who were successfully switched from methadone to bup/nx and were still in treatment. A number of consistent themes were identified among patients, with improved confidence, reduced stigma and opportunity for better engagement with treatment services reported as significant benefits of bup/nx. Indeed, 50% of patients reported having greater confidence and said that switching to bup/nx had helped them gain employment. However, the greater clarity of mind associated with bup/nx was reported as problematic for a number of patients as a result of their increased awareness, which was suggested as a risk for relapse if insufficient psychosocial support is provided. "Switching clients from methadone to bup/nx can be part of a recovery journey, which is based on moving patients forward towards abstinence… and can be part of the social re-integration process involving training, employment, education, family responsibility and general lifestyle change", said Tanner. He stressed the importance of comprehensive psychosocial support during the switch, in order to minimise the likelihood of relapse and improve outcomes.

A straightforward switch

Reporting preliminary findings from approximately 200 opioid-dependent patients transferred to bup/nx from buprenorphine, Hill told delegates that the decision to transfer patients was based on bup/nx's superior harm-reduction profile, lack of street value, comparable pricing and cost benefits in relation to supervised dosing compared with buprenorphine. Patients were transferred on the date of their new prescription, maintaining previous supervision protocols. All patients received nurse counselling before the switch and were successfully transferred without complaints or issues. The only negative feedback was related to the loss of supplementary income through diversion of buprenorphine tablets. Hill reported that a number of new patients have come to the clinic asking specifically for bup/nx, with a large number of existing patients on methadone requesting transfer to bup/nx.

New guidelines

Following the study findings, new guidelines for Lanarkshire county were developed to standardise prescribing practice and clarify recommendations. Hill noted that recommendations were included in the guidelines on how to manage prescribing for patients taking benzodiazepines and on MAT, with daily dispensing required in these instances. In addition, a section has been included on benzodiazepine prescribing, which states that 2 mg diazepam tablets should be used due to the increased risk of diversion with higher dose formulations. Implementation of these new guidelines have resulted in a greater than 50% decrease in mortality and a 12.3% reduction in diazepam prescribing over a 6-month period. Delegates were told that the observed first-time decrease in mortality was most likely related to the increased use of therapeutic doses and correct choice of treatment, higher treatment uptake, reduced benzodiazepine prescriptions and greater use of overdose-prevention strategies.

Looking to the future

Delegates were told that the cost of medication is not everything, as one must consider the total costs of delivering treatment including the ability to reduce supervision costs associated through take-home. In addition, the presence of a ceiling effect on respiratory depression makes bup/nx a safer option for both the patient and victims of accidental ingestion. Alternate day supervision was posed as an option to be explored, as patients would be able to come to the pharmacy on a less regular basis and thus have greater freedom. Hill called for availability of the film preparation of bup/nx in the UK, concluding that it is paramount to "have the correct selection criteria for patients starting bup/nx therapy".

Considerations for optimal buprenorphine management – an interactive discussion

Following presentations on aspects of buprenorphine pharmacotherapies for the treatment of opioid dependence, Prof Neil McKeganey, Prof Icro Maremmani and Prof Sharon Walsh answered delegates' queries and provided a fruitful discussion on important issues and aspects of buprenorphine treatment.

Q. Is there any data on the impact that providing physician CME training has on street practice?

A. Unfortunately, we have not been able to collect such data, but I would like to note that in the USA the majority of patients who misuse buprenorphine – in contrast to other opioid pharmacotherapies – are getting it from their physicians. Physicians are the number one providers of buprenorphine in the context of misuse. In contrast, drugs like oxycodone, hydrocodone and morphine products are being obtained on the street. Trying to intervene with physicians is really key to reducing misuse, although this may be very specific to our setting.

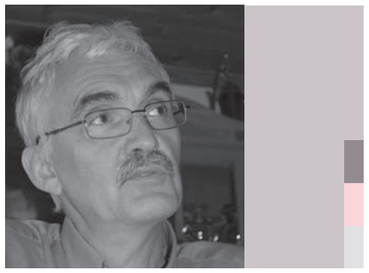
A. We must also stress the role of underdosing in the practice of buprenorphine misuse. When a medication dose is too low, patients who supplement their treatment with injecting often do better than those who do not. It is therefore very important that physicians prescribe a therapeutic stabilisation dose; in this way we will be able to reduce the practice of misuse. If we don't control cravings through an adequate dose, there will be pseudo-misuse as patients will try to increase the potency of their prescribed dose.

A. I would also like to draw attention to the shorter induction process with buprenorphine, which allows for the opportunity to stabilise patients much more quickly than with other opioid medications. Doses should be neither too high nor too low, but must be tailored to each individual patient so that they feel good and well.
It is difficult to quantify the dose at which a patient 'feels well' as it cannot be measured objectively. In almost all of the available treatment guidelines, an adequate dose is one that objectively reduces or eliminates drug use. However, cravings often remain. This is a major problem for physicians as we need to understand what the endpoint of treatment is and what this means for patient QoL. An anti-withdrawal dose is not the correct dose for stabilisation. Suppression of withdrawal and stopping drug use are pharmacological phenomena, while craving and high QoL are not solely related to pharmacology. MAT is there to support and stabilise patients, but other work needs to be done.

Best practice in opioid dependence

Completion of long-term maintenance: the key to recovery

Patients have a better chance of recovering from opioid dependence if they receive long-term maintenance with MAT, suggested study findings presented by a number of speakers at ISAM showing poor outcomes with early discontinuation. Dr Ivar Skeie and Prof Thomas Clausen presented data showing that patients who are both not in treatment and discontinue MAT have higher rates of mortality, drug-related somatic disease, crime and poorer QoL than those in treatment. Durations lasting less than 40 weeks were explained as negating the benefits of entering treatment due to the high-risk period 1 month after entering and subsequently leaving treatment. Discussing the implications of these findings, Prof Helge Waal stressed the importance of long-term therapy, stating the importance of flexible treatment schedules with take-home MAT and easy re-integration into the treatment system should de-stabilisation following discontinuation occur. Dr Lorenzo Somaini and Prof Icro Maremmani highlighted the importance of completing all phases of treatment, with successful withdrawal from MAT only possible once induction, stabilisation and an adequate length of maintenance are achieved. Attention was also drawn to the confusion surrounding therapeutic dosing, with many treatment providers unaware of the importance of higher doses at the beginning of treatment.



Dr Ivar Skeie
Oslo University Hospital
Norway

Long-term treatment with MAT improves patient outcomes

Dr Ivar Skeie presented study findings showing that being in treatment with MAT is associated with a reduction in drug-related acute somatic disease incidents. Preliminary findings based on the same cohort of 200 patients also showed that improvements seen during MAT treatment were associated with improvements in various quality-of-life measures, which deteriorated when patients discontinued or interrupted their treatment.

Reducing drug-related disease incidents

For the study, Skeie and his team performed a retrospective analysis of all hospital contact due to acute/subacute somatic disease incidents 5 years before, during and after MAT treatment among 200 opioid-dependent patients. Significant reductions in drug-related incidents were observed during treatment compared with before treatment for non-fatal overdose (64%), injection-related incidents (83%) and other drug-related incidents (81%) (Figure 9). However, once patients discontinued treatment, these reductions were no longer seen. Indeed, non-fatal overdoses were five times as frequent after treatment compared with during treatment and twice as likely as before treatment.[44] A similar pattern was observed for injection-related incidents, which were 14 times as frequent after and more than twice as likely before treatment.[44] Other drug-related incidents increased 15-fold after versus during treatment and were 3-fold more likely after compared with before treatment. Non-drug-related morbidity increased during treatment, but this was explained as being most likely due to closer contact with health services.

Factors associated with QoL

In response to the study findings, a follow-up study investigating self-perceived QoL in relation to treatment stage was performed. Preliminary findings showed that patients reported significant improvements in physical and mental health and overall QoL during maintenance treatment compared with before entering treatment. These were mainly associated with improvements in social functioning. However, some patients reported reduced QoL during treatment, which was associated with a number of treatment-related factors. Importantly, patients who had discontinued treatment reported worse QoL than when they were receiving treatment, which builds the case for long-term maintenance therapy with MAT. "When we first take patients into treatment, we should try to keep them there," said Skeie.

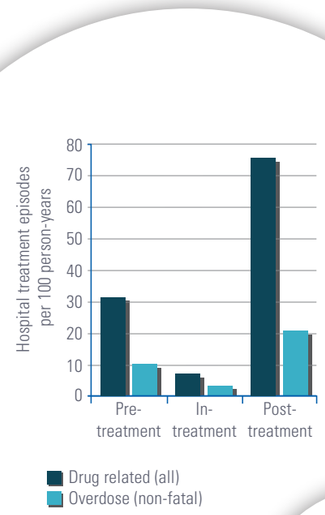


Figure 9. Drug-related incidents and overdose within treatment[44]

Note: *Buprenorphine and bup/nx are not licensed for the treatment of cocaine or alcohol abuse, and are only indicated for treatment of opioid dependence. The views expressed on these pages reflect the opinions and clinical judgement of the speakers and this section has been included for academic interest only.*

Professor Thomas Clausen
University of Oslo
Norway

Reducing mortality through long-term MAT

Prof Thomas Clausen presented a number of studies showing high rates of mortality, drug-related incidents and crime among patients outside of MAT. He explained that the first month after initiating or discontinuing treatment are found to be high-risk periods, which may outweigh the benefits of entering treatment with durations of less than 40 weeks. Findings from these studies suggest that clinicians need to remain vigilant during transition between treatment phases, and that patients who decide to terminate treatment must be informed of this high-risk period. "If we accept that there is a high risk of mortality at the beginning of treatment then we need to balance this with prolonged treatment", said Clausen.

Improving outcomes

A study of 3,221 patients initiating treatment with buprenorphine (average dose 16 mg) or methadone (average dose 110 mg) showed that 64% had continuous treatment, 16% had two or more multiple treatment episodes and 20% terminated treatment.[45] The highest rates of mortality were seen among patients who left treatment, which was comparable to that seen before entering treatment.[45] Importantly, the study showed that being in treatment was associated with a 50% reduction in mortality compared with being out of treatment (Figure 10). Study findings were also presented showing over 50% reduction in conviction rates during treatment compared with being out of treatment (Figure 10). Clausen also referred to study findings presented by Dr Ivar Skeie showing significant reductions in somatic drug-related incidents during MAT (Figure 9).

A high-risk period

Delegates were then shown recent study findings suggesting that the first month starting and discontinuing treatment were associated with a high risk of death.[46] In addition, this study concluded that treatment lasting 40 weeks on average was associated with a 65% reduction in mortality, while longer durations approaching or exceeding 1 year reduced the likelihood of mortality by 85%.[46] Clausen added that Skeie's study also showed that both patients who had continued drug use at the end of treatment and those who terminated in a stable abstinent condition had comparable levels of relapse within the first year after leaving treatment.[44] "There should be interventions and support other than medication that patients leaving treatment could benefit from", said Clausen. Nevertheless, he concluded that it is not ideal to maintain patients indefinitely on MAT.

Professor Helge Waal
University of Oslo
Norway

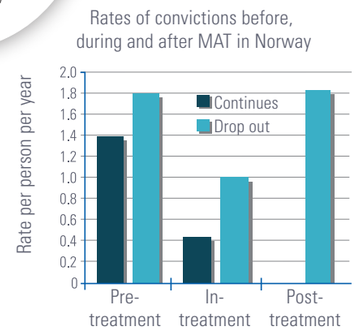
Implications of neuroadaptation for deciding treatment length

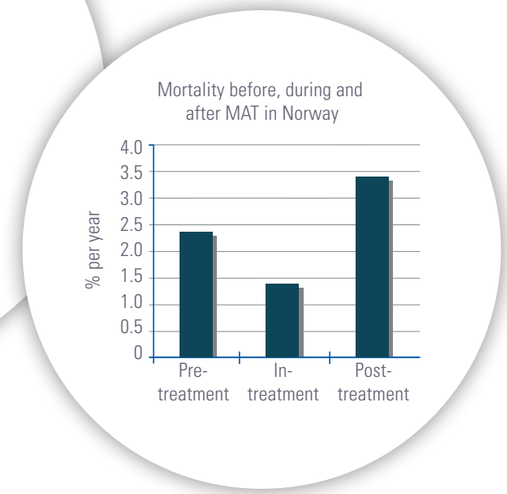
Professor Helge Waal explained that the treatment framework in Norway is built around the assumption that maintenance therapy for opioid dependence may be life-long, and that treatment programmes should therefore be structured accordingly to include this possibility. However, patients who do wish to pursue abstinence should be supported but re-intake into treatment programmes must be easy in case of relapse or destabilisation. These findings reflect Prof Thomas Clausen's presentation showing that the main benefits of treatment occur when in maintenance. "Post-treatment, the typical development is recurrence of drug use and social and health problems", said Waal.

The role of neuroadaptation

Neuroadaptive changes were said to play an important role in supporting addictive behaviour, which could progress to alterations in normal cell functioning. "I do not propose that this explains addiction, but that we need to take this into consideration when understanding the long-term problems of opioid-dependent persons," said Waal. It remains unknown whether these neurological changes can be reversed, and thus has implications for the length of treatment with agonist pharmacotherapy as disturbances can be rectified but only while receiving medication.

Figure 10. Rates of convictions and mortality before, during and after MAT in Norway[45,47]





Methadone impairs rehabilitation

Waal explained that methadone's full agonist properties mean that it produces a competing blockade at high doses but does not block the receptors as such. "This is important because if there is no effective blockade there can be no cure of possible disturbances in the opioid system, which also means that after long-term methadone maintenance you have the same level (or worse) of neuroadaptive problems at the end of treatment", he said. Waal added that this happens to an extent with buprenorphine as it also stimulates the mu-receptor, although there is an upper limit to its effect.

Long-term treatment and flexibility

Regardless of treating patients with a continuing care or rehabilitation model, Waal stressed that patients should be informed of better outcomes with long-term therapy. Importantly, physicians should not terminate treatment against a patient's will as this has been shown to result in adverse outcomes. Patients should be allowed to decide when it is best to withdraw from treatment, and this choice should be planned in advance with support systems in place should coming back to treatment be necessary.

Take-home medication schedules could prove beneficial, as Waal recommended that treatment programmes should be compatible with ordinary life in society, including the normalisation of medication dispensing and providing a sense of empowerment to patients.

Dr Lorenzo Somaini
Health Local Unit Biella
Cossato, Italy

Abstinence-oriented short-term treatment – an ineffective approach

Long-term treatment delivers significantly better outcomes than abstinence-oriented therapies, said Dr Lorenzo Somaini in his review of the literature investigating both types of treatment. Numerous studies support the role of long-term pharmacotherapy in the treatment of opioid dependence, showing that it decreases illicit opioid use, morbidity and mortality, HIV infection risk, illegal activities and promotes overall functioning. Indeed, MAT creates a 'window of opportunity' during which patients can receive psychosocial interventions to reduce the risk for relapse.

Previous studies support maintenance therapy lasting a minimum of 3 months in order to be successful, with results supporting the concept that time in treatment and successful completion of treatment result in better outcomes.[48,49] However, choice of MAT is important as some patients are unable to achieve normative levels of psychosocial functioning with methadone. This result has led to promotion of time-limited MAT in some patients, leading to the question of whether all patients require life-long treatment.

A review of six studies investigating time-limited MAT treatment programmes showed that the majority of patients required subsequent treatment as high rates of relapse were observed with this approach.[50–55] Conversely, studies of planned detoxification following a stabilisation period showed significantly improved outcomes, with fewer patients returning for treatment.[56–58] Study findings showing high levels of abstinence-oriented therapies among treatment centres in Italy both in new (49.7%) and re-treated (45.3%) patients also confirmed their lack of effectiveness, as 50% of patients dropped out of treatment after 101 days compared with after 307 days with maintenance therapy.[59] Somaini concluded that a major challenge lies in delivering existing treatments more effectively.

Professor Icro Maremmani
University of Pisa
Italy

High-threshold maintenance treatment effective for dual-diagnosis patients

Effective withdrawal from MAT can only be achieved once induction, stabilisation and an adequate length of maintenance have been completed, said Prof Icro Maremmani during his overview of the PISA-opioid agonist treatment model for severely dependent patients with or without dual diagnosis. "Effective detoxification is not possible without having completed these four phases", he said. High MAT doses that provide effective blockade are able to give effective protection against overdose and help reduce long-term cravings even during abstinence. After 1–2 years of maintenance, patients will then be typically able to start reducing their dose. Most importantly, euphoria and withdrawal should never be present at this stage of treatment, he noted.

Why provide MAT?

Opioid dependence destroys the reward system but agonist treatment is able to reverse this damage, keeping patients in a state of normality rather than cycling between euphoria and withdrawal. Delegates were told that correct dosing is key to success, with low doses being only partially effective. Many treatment providers are often confused about adequate dosing due to the differences in effectiveness at certain stages of treatment. "The problem is that low doses are fully effective but only after a period of high MAT dosing", said Maremmani, adding that it is important to have long-term treatment, as doses will only be effective within this framework. Previous study findings from his group showed that patients completing all four steps of treatment showed the highest reduction in opioid-positive urines (98.9%) compared with those who underwent rapid detoxification, had poor treatment adherence or were treated with low doses (78.2%).[60] Separate study findings also showed that craving for and abuse of illicit substances during treatment were correlated with low MAT doses.[61]

Effective treatment in dual dependence

Delegates were then shown data suggesting that alcohol use during MAT is a significant problem, with 15 of 99 studied alcoholics showing a history of heroin addiction.[62] Furthermore, psychopathological symptoms were higher among patients consuming alcohol and cocaine. It is therefore evident that therapeutic dosing can function to reduce this risk. "The shifting from heroin to alcohol also means a transition to a highly curable disease, such as heroin addiction, to a poorly curable one, such as alcoholism", said Maremmani. Within the PISA-opioid agonist treatment framework, patients with dual diagnosis stay in treatment for longer periods of time and at higher doses demonstrated by the reduction in psychopathological symptoms achieved with high dose-MAT.[63] "I think that MAT programmes are not only useful for opioid dependence, but for treating psychopathology as well", he concluded.

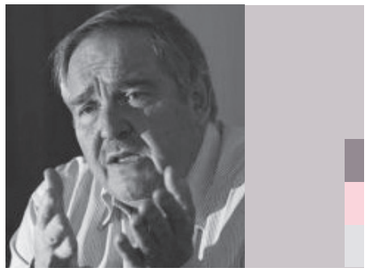
Q. A number of delegates reported their clinical experiences with treatment, with one delegate stating that in his clinic patients are given the freedom to initially decide how their treatment should progress. Over a 4-year period, patients were able to withdraw successfully from treatment after 1 year, with 25% of patients previously unable to withdraw from methadone being able to withdraw after switching to bup/nx. Another delegate explained that patients seem to initially want to stay on treatment for a short period of time, but after 2 years on maintenance many seem reluctant to withdraw from their medication. It was said that it is indeed difficult to navigate the correct balance between pushing patients to stop and letting them stay on treatment for too long.

A. Commenting on delegates' experiences, Somaini said that when considering termination of treatment, it is important to bear in mind that many patients suffer from dual-diagnosis. Patients who cannot withdraw from treatment often have comorbid mental health disorders that make discontinuing treatment problematic. If treatment is discontinued in this group of patients, they will most likely be at a high risk for relapse.

Neurobiological implications of opioid dependence

Neurotransmitters in addiction disorders: the key to individualised medicine

Describing the role of neurotransmitters in addiction disorders during his presentation at Global Addiction, Professor David Nutt drew attention to misconceptions on the role of dopamine in opioid dependence and presented key findings from research in the field of neuropsychopharmacology. His review of the literature supports the development of a personalised approach to treatment in addiction medicine through the targeting of key neurobiological circuits implicated in specific aspects of addiction disorders.



Professor David Nutt
Imperial College London, UK

Neurobiological considerations for treating addiction

During his presentation on the role of neurotransmitters and the specific brain circuits they affect in addiction disorders, Prof David Nutt clarified misconceptions about the role of dopamine in opioid dependence, stating that opioid drugs do not result in dopamine release as is commonly misconstrued. Variations in pharmacokinetics were described as key to determining the addictive potential of drugs, and the role of the endogenous opioid system and glutamate in addiction were reviewed. "The role of dopamine, opioid and GABA-A receptors in regulating these processes is leading to the development of new approaches to treatment, such as dopamine and opioid receptor partial agonists and subtype selective agonists", said Nutt.

An integrated model of addiction

Addiction is a complex disorder, with multiple neurological and psychological constructs mediating its development. Targeting these processes provides the opportunity for developing new treatments and enables the possibility of selectively treating different aspects of addiction. A number of neurotransmitters are involved in the development of addiction disorders, which individually affect processes implicated in their progression (Figure 11). Nutt told delegates that an important propagator of addiction is withdrawal, which is directly related to the duration of action and the dose of the administered drug. In addition, one of the major variables in terms of the genetic predisposition of drug use is the rate of drug clearance by the CYP450 system. "Accelerated clearance leads to greater dependence because after withdrawal more aversion occurs, leading to greater drug use", said Nutt. This can be reflected by the cyclical pattern of heroin use, which is directly related to its short half-life. Pharmacotherapy, such as buprenorphine or methadone, which has slower kinetics than heroin due to differences in formulation and route of administration, reduces the chaotic effects of opioids and blocks on-top use by restoring regularity to altered pharmacokinetics.

Dopamine in opioid dependence

There is a large focus on dopamine and its involvement in addiction, as stimulants have been shown to release dopamine in the brain. Thus increases in brain dopamine are regularly associated with the rewarding effects of psychostimulants in humans. "This notion has been transmuted into general theory that all drugs release dopamine, and that the pleasure derived from all drugs is dopaminergic, which is not true", said Nutt. Delegates were presented with findings showing that individuals who received 50 mg intravenous heroin experienced pleasurable effects, but with no associated dopamine release.[64] "We, and others, have never been able to show that heroin releases dopamine, so the high of heroin is not dopaminergic. This explains why people continue to inject opioids even when they are taking dopamine-blocking drugs", he said. In addition, the decreased levels of dopamine receptors observed in patients with stimulant and alcohol addiction has not been seen among those dependent on opioids.[64]

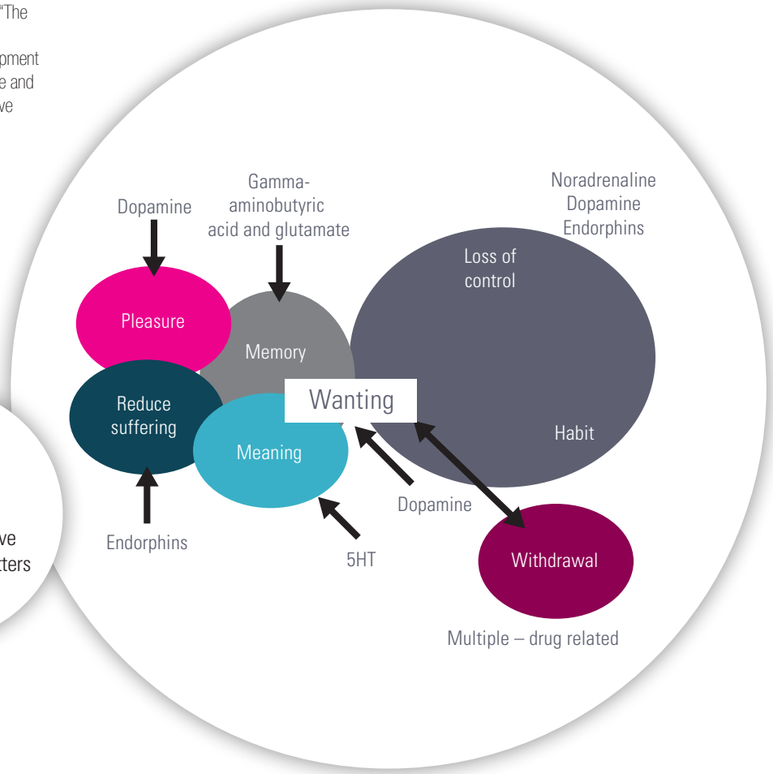


Figure 11. Elements of addiction and their respective neurotransmitters

Another role for dopamine?

It has been established that dopamine-rich areas such as the nucleus accumbens are involved in the response to drug cues and reward, and that dopamine-releasing medications such as L-DOPA can lead to the development of addictive behaviours. Researchers have suggested that the effects of dopamine may be involved in habit formation, as the majority of dopaminergic circuits run through the basal ganglia, and that motor programming for drug taking is laid down in the caudate – an area involved in drug-seeking behaviour.[65] Nutt also said that it is possible that different dopamine phenotypes exist, with individuals who have low levels of dopamine receptors more likely to engage in addictive behaviours as a result of the increased pleasure derived from stimulant use.[66] Delegates were presented with research findings showing that drug use in compulsive stimulant users was differentially affected by a dopamine blocker or agonist, depending on the behavioural pattern of drug use.[67] This suggests that the therapeutic benefits of different drugs depend on the individual. Current studies are underway to investigate the potential use of dopamine D3 receptor blockers to reduce drug-seeking behaviour, and dopamine beta-hydroxylase blockers to prevent low levels of dopamine commonly associated with the withdrawal syndrome.

Endorphins and addiction

Endogenous opioids play an important role in the process of addiction, with imaging studies showing increases in opioid receptors in the brain standing at 15% among opioid-dependent patients in withdrawal.[68] "Whether this reflects more receptors or a deficiency of endorphins competing for the receptor is not yet understood…this is an intriguing endophenotype that may help explain the nature of relapsed vulnerability through craving", Nutt told delegates. Study findings were then presented showing that amphetamines release endorphins in the putamen, suggesting that opioid pharmacotherapy could be used to regulate dysfunction in stimulant users.[69] "If we are going to improve treatment we are going to have to be more subtle and understand that these different processes apply differentially to patients. We are going to have to target these particular processes selectively to develop different treatments. If we do this we may end up with a personalised medical approach to treatment, which is likely the best way forward in the long term", concluded Nutt.

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