SUBMISSION FROM THE NATIONAL DRUG RESEARCH INSTITUTE, CURTIN UNIVERSITY

PRESCRIPTION STRONG (SCHEDULE 8) OPIOID USE AND MISUSE IN AUSTRALIA – OPTIONS FOR A REGULATORY RESPONSE:

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PRELIMINARY COMMENTS

The National Drug Research Institute welcomes circulation of the *Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response* Consultation Paper[1]. It is timely that the TGA is looking to experiences with the opioid crises elsewhere, especially in North America; is noting increasing opioid use and overdose in the Australian data; and is asking what regulatory tools it has within its remit and how they could be exercised as part of the policy response to prevent further escalations in opioid use and adverse events in this country.

We note the TGA has particular defined powers under the *Therapeutic Goods Act 1989* and Regulations, as outlined on page 9 of the Consultation Paper, and that the Consultation Paper and the options canvassed are largely limited to those actions available to it. We also recognise that the Consultation Paper is limited largely to higher risk Schedule 8 opioids although some S4 opioids are also within scope. However we also appreciate the reference to other actions which could be taken within the wider medicines control mechanisms in the Australian system, such as the various State and Territory Poisons Schedules and the annexures to those. We urge the Australian Government Department of Health, along with the TGA, to explore with its State and Territory partners what sensible and balanced steps can be taken across the regulatory landscape to mitigate the expansion of opioid misuse and associated harm.

The Consultation Paper acknowledges that the Australian Government has made funds available to implement a national real-time prescription monitoring system, the Electronic Recording and Reporting of Controlled Drugs (ERRCD). This system aims to assist physicians and pharmacists to identify people at risk of harm or potential 'doctor shoppers' accessing S8 (and selected S4) medicines. **Overall we see the ERRCD as a welcome development that will hopefully reduce opioid-related harm, although the effect it will have is yet to emerge.**

As well as some likely benefits, the change may also have some unintended adverse consequences. This could include a shift from prescription drug use to illicit opioid use, or an increase in illicit opioid use, particularly for heroin injectors who may be using S8 medications to manage their opioid withdrawals between heroin injections. Although the extent to which this is an issue will only unfold once the scheme is implemented and settles in, it is something worth monitoring.

We note that **Australia does not have a dedicated national opioid strategy.** We have a National Ice Action Strategy [2], a National Tobacco Strategy [3], and a (currently draft) National Alcohol Strategy [4]. To our knowledge the most recent national strategy specifically addressing opioid use in Australia was the 2001 *National Heroin Overdose Strategy* [5]. We believe that developing a national opioid strategy that encompasses both licit and illicit opioid use and related harms and benefits, and addresses the full range of regulatory, law enforcement, educational, treatment, peer based and other strategies to prevent and manage opioid use and related harms including opioid overdose, would be timely.

The TGA rightly notes that the factors contributing to an opioid crisis go beyond regulated drug availability. They include both licit and illicit drug domestic production, importation and, nowadays,

must include online availability of both pharmaceutical opioids and illicit opioids in both the 'clear' and 'dark' web, and secondary supply from such importations. This broader context would need to be the focus of a national opioid strategy. **Support from the TGA for the development of a national opioid strategy would be welcomed.**

DECLARATION OF INTERESTS

Prof. Simon Lenton, one of the authors of this document, was appointed to the Mundipharma Australia Nyxoid (intra-nasal naloxone) Advisory Board. Prof. Lenton does not accept any honorarium for his involvement although his travel and accommodation costs to attend the meetings of the Board are covered by Mundipharma.

ABOUT NDRI

The National Drug Research Institute's (NDRI) mission is to conduct and disseminate high quality research that supports evidence informed policy, strategies and practice to prevent and minimise alcohol and other drug-related health, social and economic harms among individuals, families and communities in Australia. Since its inception in 1986, the Institute has grown to employ about 30 research staff, making it one of the largest centres of drug research and public health expertise in Australia. It is a World Health Organization Collaborating Centre for Alcohol and Drug Abuse. Researchers have completed about 500 research projects, resulting in a range of positive outcomes for policy, practice and the community. For example, NDRI research has significantly informed and contributed to policy and evidence-based practice such as the National Amphetamine-Type Stimulants (ATS) Strategy, the National Drug Strategy and the National Alcohol Strategy; contributed to Australia's involvement in international strategies, such as WHO Global and Regional Strategy to Reduce Harmful Use of Alcohol; directly contributed to Australian and State government alcohol and illicit drug policy, including cannabis policy and naloxone availability; significantly contributed to international evidence-based school interventions; influenced NHMRC guidelines to reduce alcohol health risks; and been cited in development of policy documents for Aboriginal Australians.
The Institute's work was described as *"research considered truly internationally competitive and making a major contribution to the advancement of knowledge"* in the Research Quality Framework.

CONSIDERATION OF REGULATORY OPTIONS

In this submission, NDRI limits its discussion to the options outlined in the Consultation Paper most relevant to its research. We note however that several of the eight regulatory options canvassed, on face value, appear to be sensible, including Option 5, a review of label warnings and revision to the Consumer Medicines Information. We do not have any other specific comments on Option 5, nor do we offer comment on Option 7 or Option 8.

Option 1: Consider the pack sizes for Schedule 8 opioids

On face value, having smaller pack sizes available for patients requiring short term analgesia of 1-3 days, such as post minor surgery, appears a sensible intervention. Accepting the evidence that the standard pack sizes (30 or more) and default settings for clinical prescribing software in Australia are far greater than would be needed for the treatment of most acute non-cancer pain, suggests such an intervention would potentially limit the number of S8 medications 'lying around' in people's medicine cupboards, which would reduce the likelihood of subsequent use, misuse and overdose.

While patient education and warning labels about risks (see Option 5) and the Return of Unwanted Medicines (RUM) (see Option 5) are worth pursuing, preventing or reducing the availability of unused medications in the first place is likely to be an important preventive intervention.
We support the view **the TGA consider reduced pack sizes for some settings in which S8 opioids are used, notably for patients requiring short term analgesia of 1-3 days such as post minor surgery.**

Option 2: Consider a review of the indications for strong opioids

Given the reported inconsistencies between products and classes and patient groups in the Australian Register of Therapeutic Goods (ARTG) for Approved Indications and Patient Information, we support the notion that **the TGA review Approved Indications and Patient Information for S8 medications in light of current best practice clinical guidelines and the most up-to-date scientific literature**. We note it is imperative that such revisions ensure people in severe pain and in need of prompt pain management are not disadvantaged as a result of any tightening of such indications and any accompanying regulatory changes.

Option 3: Consider whether the highest dose products should remain on the market, or be restricted to specialist / authority prescribing

These are questions worthy of regular consideration and review, although NDRI does not have any evidence to suggest particular products should be removed from sale or access further restricted. We note that in this Section there is a discussion of the wider availability of naloxone in the context of the concerns about fentanyl-related overdoses in Canada. NDRI has been intimately involved in research and research-based advocacy in support of the wider availability of naloxone in Australia [6-16]. **There is no question that increasing the availability of naloxone is an important component of a multi-faceted overdose prevention and management response** [12, 17]. We will address naloxone availability more generally under Option 6, but notably for this option, while take-home naloxone (THN) programs have proved helpful in responding to overdoses where street heroin samples are adulterated with fentanyl [18, 19], several factors mitigate the effect of naloxone on fentanyl overdoses. These are: (i) the dose of naloxone required is likely to be very high (but is yet to be determined); (ii) fentanyl overdoses are characterised by rapid onset (seconds or minutes) rather than the 20-30 minutes for many heroin overdoses [20], allowing far less time for intervention, and (iii) the effective half-life of some fentanyl-based synthetic opioids [18] is far longer than heroin. To date it appears that the majority of fentanyl-based overdoses we are seeing in this country appear to be associated with diversion of pharmaceutical fentanyl products, almost exclusively transdermal patches, which account for 99% of the market [21, 22]. This contrasts with the situation in North America, which has witnessed the adulteration of street heroin with illicitly manufactured fentanyl or counterfeit analgesic pills (e.g. 'oxycodone') containing fentanyl available through illegitimate online pharmacies on the dark and clear web [18]. Further, Roxburgh and colleagues have demonstrated that while morphine and oxycodone are the major contributors to opioid deaths in Australia, the rate of fentanyl deaths per Oral Morphine Equivalent (OME) dispensed increased on average 31% p.a. between 2002 and 2012 [23]. Given this, there is an opportunity for the TGA to significantly contribute to a reduction in fentanyl-related overdose fatalities. **To that end, the TGA should explore supply-side strategies to limit the availability and diversion of the existing oral and, particularly, transdermal fentanyl patch products on the market.**

Option 4: Strengthening risk management plans for opioid products

The proposal for the TGA to work with product sponsors to update their risk management plans seems a logical initiative. We endorse the adoption, following the US FDA initiative, of requiring all sponsors of opioid products to provide RMPs, including continuing professional development (CPD) training meeting the requirements of the relevant clinical colleges. Although, like any regulatory measures, this will only have a significant impact if compliance is monitored and there are penalties for non-compliance.

Naloxone

An issue not addressed in the consultation paper is the **co-prescribing of naloxone** for patients prescribed strong opioids. In the US, the American Medical Association [24] and the Centre for Disease Control [25] have recommended patients prescribed large doses of opioids (>50mg OME or with other risk factors such as concurrent substance abuse disorder or concurrent benzodiazepine use) be co-prescribed naloxone. Resources are also provided to assist the doctor to raise the issue of naloxone prescription [26] in the context of broader opioid prescribing clinical guidelines and resources [27]. Recent research with pain patients in San Francisco co-prescribed naloxone in primary care found that 57% had positive responses to being offered it, 22% were neutral, 37% reported positive behaviour changes having been prescribed naloxone and 5% reported that the naloxone had been used to revive them in an overdose situation [28]. It is important to note that co-prescribing naloxone should not, however, be a substitute for more controlled prescribing of the opioids themselves, as canvassed elsewhere in the Consultation Paper.

Nonetheless we recommend **the TGA consider requiring naloxone co-prescribing in Australia, and undertake consultation with key stakeholders to explore relevant conditions under which it should occur, and to develop practice guidelines appropriate for the Australian context.**

Stigma

The Consultation Paper offers eight options for amending the regulation of opioids in Australia, primarily Schedule 8 (S8) drugs with some implications for Schedule 4 (S4) drugs. The document rightly discusses the importance of ensuring that regulatory changes made to opioids including S8 drugs do not stigmatise patients by endorsing the goals of the National Pharmaceutical Drug Misuse Framework for Action (2012-2015), which included the goal to "enhance the quality use of pharmaceutical drugs without stigmatisation or limiting their accessibility for therapeutic use" (p.7). However, aside from this early mention in the document, the issue is not referred to again.

Stigma is a very important issue that needs to be considered when developing regulatory approaches to opioid use in Australia. It is well known that people who consume opioids are stigmatised in the popular media [55], when accessing health services [56] and within workplaces [57]. Indeed the stigmatisation of certain alcohol and other drug consumption practices is a fundamental part of how such practices are understood [58] and has significant negative effects on health and well-being [60]. Importantly, stigma is negatively associated with the attainment of individual health goals including the cessation of drug consumption [56].

The issue of stigma is most relevant for Option 4 (p15). One aspect of this option is to develop topics for education programs for health professionals on issues relevant to opioids in Australia. The consultation document makes some suggestions for important topics that could be included, but does not mention stigma (p16). NDRI suggests the TGA recommend that the stigma faced by people who consume opioids in Australia be a central part of education programs about opioid consumption targeting health professionals. Stigma should be explored through the following specific issues:

- The influence of stigma on people's willingness and desire to disclose opioid consumption to health professionals
- The influence of stigma on help-seeking practices of people who consume opioids
- The influence of stigma on general health and well-being
- The challenges faced by those trying to reduce the stigmatisation of people who consume opioids within a prohibitionist legislative context.

Stigma affects both those with experience of criminalised consumption such as heroin and those who consume opioids to manage health issues such as chronic pain. **Stigma is an essential topic for any education programs for health professionals focussed on opioids and S8 drugs in Australia.**

Option 6: Consider incentives for expedited TGA review of improved products for pain relief and opioid antidotes

Under this option, in addition to exploring non-opioid alternatives for pain control, the Consultation Paper raises the issues of abuse-deterrent formulations for opioids and presentation of antidotes. Regarding abuse-deterrent formulations, the paper states (p18):

> *There should not be the need to develop TGA-specific guidance for abuse-deterrent opioids, as there are no local manufacturers for these products, and the Australian market would be small on a global scale, and secondly because there remains some uncertainty on which technologies may be the most effective for deterring abuse while avoiding transfer of the abuse to an alternative and more dangerous opioids.*

However, overseas experiences of the approval of abuse-deterrent opioid pharmaceutical formulations have indicated they are easily subverted and can have unintended adverse consequences. The most infamous of these examples was Purdue Pharma's 1995 release and promotion of the 'abuse-deterrent' form of 'long acting' Oxycodone OxyContin® [29]. This formulation contained a hard coating and was marketed as safe for use in non-pain specialist settings [30]. However, drug users quickly discovered they could crush the tablet and release the '12hr dose' in a single injection [29], contributing to what became known as the 'epidemic' of 'hill-billy heroin' use. This was the beginning of the escalation of the pharmaceutical opioid problems we now see in the U.S. [31].

Mindful that Consultation Paper authors are well aware of this history, we are not arguing against expedited review for 'tamper-proof' formulations but rather for the need for caution about the challenges in determining whether such new products are indeed as resistant to tampering as is claimed.

To this end, **should the TGA have a role in reviewing the abuse potential of opioids, we suggest that consideration be given to seeking advice from persons familiar with illicit drug use practices as part of the review process.** A possible resource here is the Australian Injecting and Illicit Drug Users League (AIVL), the national peak body representing state and territory peer-based drug user organisations. AIVL has a 25 year history of working with government, researchers and other organisations, bringing the voice of people who use drugs to produce community informed policy treatment and other responses. We believe AIVL is well placed to work with the TGA to provide expert community input regarding new opioid medications and their abuse potential, tamper-proof properties and any potential unintended consequences of these.

We are very supportive of the proposition that: 'New formulations of antidotes that allow carers to administer antidotes more simply could also be reviewed in an expedited manner.' (p.18)
The World Health Organization has noted that timely naloxone administration is crucial in preventing morbidity and mortality associated with opioid overdose and that expanding access to this medicine is a positive step towards reducing the morbidity and mortality of opioid overdose [47]. Accumulating international evidence shows that the provision of take-home naloxone, with appropriate training, to people who are likely to witness an opioid overdose (including opioid users themselves, friends, family and service providers) can lead to successful opioid overdose reversals and that it is a remarkably safe and cost-effective intervention with few, if any, adverse effects [e.g. 32, 33-44]. Opioid users experiencing reduced tolerance due to total or partial abstinence on a voluntary (treatment) or enforced (prison) basis, are at greatly increased risk of overdose should they use opioids again when discharged or released [45]. Indeed, one study found risk of overdose for prisoners in the first two weeks after custody is 34 times greater than at other times [46].

In Australia, the first take-home naloxone (THN) program commenced in 2012 in Canberra [48], but programs quickly followed in Sydney [10], Perth [8] and Melbourne [11]. As at November 2017, across the evaluations of these THN programs in Australia, we have some 358 participants trained and formally followed up with 142 (40%) overdose reversals using THN reported. Outside of these evaluations, there have been more than 2500 additional trainings and provision to PWID with 359 anecdotal reports of reversals [49].

However, THN programs are unlikely to have an impact on overdose rates unless they can be scaled up to ensure that many potential overdose witnesses have access to the medicine and the basic knowledge needed to manage an overdose, including administering naloxone [11]. There are a number of barriers to getting naloxone into the hands of illicit opioid users, who are most likely to witness an overdose, and price is an important one of these [9, 50]. Many illicit opioid users are financially disadvantaged. While they may be able to cover the cost of their day-to-day living expenses, the cost of a medicine which is not immediately needed (although having the potential to save their life or the life of someone else at some time in the future) may be lower on the budget hierarchy, and for some it is not affordable. The cost of naloxone is currently listed as $74.50 (exclusive of dispensing fee) OTC for Phebra's Prenoxad® (comprising 2mg; five 400 microgram doses in a single-use syringe with a needle and patient instructions). Under the Pharmaceutical Benefits Scheme, it is available for $39.50, or $6.10 on concession.

Naloxone is also available as ampoules (5 x ampoules of 400 micrograms each) for $79.00 on private prescription, $38.50 under PBS and $5.40 on concession (but this is without needles or syringe to administer and without patient instruction for lay administration). Recent research explored the issue of affordability and willingness to pay. In 2016, 827 regular injecting drug users interviewed as part of the Illicit Drug Reporting System were asked how much they would be willing to pay OTC at a pharmacy for naloxone in a prefilled syringe with accompanying needle and instruction materials. Some 41% said it should be free and 15% said they were willing to pay either $5 or $15 [51]. This clearly falls well short of the price of the currently available product.

We are also aware that Mundipharma has its intranasal (IN) product (Nyxoid®) before the TGA for consideration. Intranasal (IN) naloxone, has advantages over intramuscular (IM) injection, especially for people not familiar with injection practices, thereby potentially making naloxone training simpler while at the same time eliminating the risk of blood borne virus transfer [36, 52-54]. **Having an IN naloxone product available in Australia is well overdue and we would very much welcome its prompt approval. Nevertheless it is important that any naloxone product is provided at a price point that makes it accessible to potential overdose witnesses.**

There is a range of community settings and contexts where naloxone could be made available to those at risk of opioid overdose and those likely to witness it. These include, but are not limited to:

- drug user organisations who service active drug users (where many of the current Australian THN programs take place)
- custodial services just before prison release
- drug addiction treatment upon discharge
- emergency departments on leaving subsequent to a non-fatal overdose
- accommodation shelters
- pain management services

While a great deal of work has been, and is being, done on developing appropriate training and participant information materials, the cost of naloxone remains a substantial barrier to access. This is an issue where consumers are required to pay, e.g. in community pharmacies, or where government or community agencies need to find budget to pay for the medicine if they are providing it at no charge to their clients. It appears there are at least three potential factors here:

- the price of the product as delivered by the supplier;
- any subsidy by the Federal Government under the PBS and or other schemes such as s85 or s100, and;
- the capacity of state and territory government agencies or non-government agencies to offset the cost of the medicine to supply at zero or low cost in community settings.

We encourage the TGA and other related agencies, such as the PBAC, to explore mechanisms to facilitate naloxone being made available at the lowest possible cost to potential overdose victims and witnesses.

REFERENCES

[1] Therapeutic Goods Administration Department of Health (Australia). Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response: Consultation paper. Canberra. Available at: https://www.tga.gov.au/consultation-invitation/consultation-prescription-strong-schedule-8-opioid-use-and-misuse-australia-options-regulatory-response (Accessed 19 Janurary 2018): Department of Health (Australia), 2018.

[2] Commonwealth of Australia Department of the Prime Minister and Cabinet. National Ice Action Strategy Canberra. Available at: https://www.coag.gov.au/sites/default/files/communique/2015%20National%20Ice%20Action%20Strategy.pdf (Accessed 13 Feb 2018): Commonwealth of Australia, 2015.

[3] Intergovernmental Committee on Drugs. National Tobacco Strategy 2012–2018. Canberra. Available at: http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/publishing.nsf/Content/D4E3727950BDBAE4CA257AE70003730C/$File/National%20Tobacco%20Strategy%202012-2018.pdf (Accessed 13.02.18), 2012.

[4] Commonwealth of Australia. Consultation Draft National Alcohol Strategy 2018–2026. Canberra. Available at: http://www.health.gov.au/internet/main/publishing.nsf/Content/55E4796388E9EDE5CA25808F00035035/$File/Consultation%20Draft%20National%20Alcohol%20Strategy%202018-2026.pdf (Accessed 14 December 2017): Department of Health (Australia), 2018.

[5] Commonwealth Department of Health and Aged Care. National Heroin Overdose Strategy - Summary. Canberra: Commonwealth of Australia, 2001.

[6] Nielsen S, Lenton S. Weekly Dose: Naloxone, how to save a life from opioid overdose. The Conversation. 2016. Available from: https://theconversation.com/weekly-dose-naloxone-how-to-save-a-life-from-opioid-overdose-63459

[7] Farrugia A, Fraser S, Dwyer R. Assembling the Social and Political Dimensions of Take-Home Naloxone. Contemporary Drug Problems. 2017;44:163-75.

[8] Nelson M, Lenton S, Dietze P, Olsen A, Agramunt S. Evaluation of the WA Peer Naloxone Project – Final Report. Perth: National Drug Research Institute, Curtin University, 2016.

[9] Lenton S, Dietze P, Jauncey M. Perspective: Australia reschedules naloxone for overdose. Medical Journal of Australia. 2016;4:146-7.

[10] Chronister KJ, Lintzeris N, Jackson A, Ivan M, Dietze P, Lenton S, et al. Findings and lessons learnt from implementing Australia's first health service based take-home naloxone program. Drug and Alcohol Review. [Article in Press]. 2016.

[11] Lenton S, Dietze P, Olsen A, Wiggins N, McDonald D, Fowlie C. Working together: Expanding the availability of naloxone for peer administration to prevent opioid overdose deaths in the Australian Capital Territory and beyond. Drug and Alcohol Review. 2015;34:404-11.

[12] Lenton S, Dietze P. Explainer: what is naloxone and how can it help save drug users who overdose? The Conversation [serial on the Internet]. 2015: Available from: https://theconversation.com/explainer-what-is-naloxone-and-how-can-it-help-save-drug-users-who-overdose-48812.

[13] Dietze P, Cogger S, Malandkar D, Olsen A, Lenton S. Knowledge of naloxone and take-home naloxone programs among a sample of people who inject drugs in Australia. Sydney: NDARC. Available nat: https://ndarc.med.unsw.edu.au/resource/knowledge-naloxone-and-take-home-naloxone-programs-among-sample-people-who-inject-drugs. (Accessed 21/8/2015), 2015.

[14] Lenton SR, Dietze PM, Degenhardt L, Darke S, Butler TG. Now is the time to take steps to allow peer access to naloxone for heroin overdose in Australia. Drug and Alcohol Review. 2009;28:583-5.

[15] Lenton SR, Dietze PM, Degenhardt L, Darke S, Butler T. Naloxone for administration by peers in cases of heroin overdose. Medical Journal of Australia. 2009;189:469.

[16] Dietze PM, Stare M, Cogger S, Nambiar D, Olsen A, Burns L, et al. Knowledge of naloxone and take-home naloxone programs among a sample of people who inject drugs in Australia: Variations across capital cities. Drug and Alcohol Review.n/a-n/a.

[17] Olsen A, McDonald D, Lenton S, Dietze PM. Assessing causality in drug policy analyses: How useful are the Bradford Hill criteria in analysing take-home naloxone programs? Drug and Alcohol Review. 2017:n/a-n/a.

[18] Fairbairn N, Coffin PO, Walley AY. Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. International Journal of Drug Policy. 2017 8//;46:172-9.

[19] Somerville NJ, O'Donnell J, R. Matthew Gladden, Zibbell JE, Green TC, Younkin M, et al. Characteristics of Fentanyl Overdose — Massachusetts, 2014–2016. US Department of Health and Human Services/Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report. 2017;66:382-6.

[20] Darke S, Duflou J. The toxicology of heroin-related death: Estimating survival times. Addiction. [Article in Press]. 2016.

[21] Karanges EA, Blanch B, Buckley NA, Pearson S-A. Twenty-five years of prescription opioid use in Australia: a whole-of-population analysis using pharmaceutical claims. British Journal of Clinical Pharmacology. 2016;82:255-67.

[22] Gisev N, Larance B, Cama E, Nielsen S, Roxburgh A, Bruno R, et al. A nationwide study of the extent and factors associated with fentanyl use in Australia. Research in Social and Administrative Pharmacy. [Article in Press]. 2017.

[23] Roxburgh A, Hall WD, Dobbins T, Gisev N, Burns L, Pearson S, et al. Trends in heroin and pharmaceutical opioid overdose deaths in Australia. Drug and Alcohol Dependence. 2017 2017/10/01/;179:291-8.

[24] American Medical Association. Task force to reduce prescription opioid abuse. Prescription Drug Misuse, Overdose & Death. Available at: https://www.ama-assn.org/delivering-care/prescription-drug-misuse-overdose-death (Accessed 16/02/18): AMA, 2016.

[25] Dowell D, Haegerich TM, Roger Chou. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. Morbidity and Mortality Weekly Report (MMWR). 2016;65:1-49.

[26] Prescribe to prevent.org. Prescribe to prevent. Prescribe Naloxone, Save a life. Available at: http://prescribetoprevent.org/. Accessed 16/02/18)2016.

[27] Centre for Disease Control. Opioid overdose - Guideline resources: Clinical Tools. Available at: https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html (accessed 15/02/18): CDC, 2017.
[28] Behar E, Rowe C, Santos GM, Murphy S, Coffin PO. Primary care patient experience with naloxone prescription. Annals of Family Medicine. [Article]. 2016;14:431-6.
[29] Cicero T, Inciardi J, Munoz A. Trends in abuse of OxyContin® and other opioid analgesics in the United States: 2002–2004. The Journal of Pain. 2005;662-672.
[30] United States General Accounting Office. Prescription Drugs: OxyContin abuse and diversion and efforts to address the problem. Washington. Available at: https://www.gao.gov/new.items/d04110.pdf (Accessed 21 February 2018), 2003.
[31] Whelan E, Asbridge M. The OxyContin crisis: Problematisation and responsibilisation strategies in addiction, pain, and general medicine journals. International Journal of Drug Policy. 2013;24:402-4011.
[32] Green TC, Heimer R, Grau LE. Distinguishing signs of opioid overdose and indication for naloxone: an evaluation of six overdose training and naloxone distribution programs in the United States. Addiction. 2008;103:979-89.
[33] Coffin PO, Sullivan SD. Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal. Annals of Internal Medicine. 2013;158:1-9.
[34] Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal in Russian cities. Journal of Medical Economics. 2013;16:1051-60.
[35] Bennett T, Holloway K. The impact of take-home naloxone distribution and training on opiate overdose knowledge and response: An evaluation of the THN Project in Wales. Drugs: education, prevention and policy. 2012;19:320-8.
[36] Doe-Simkins M, Walley AY, Epstein A, Moyer P. Saved by the Nose: Bystander-Administered Intranasal Naloxone Hydrochloride for Opioid Overdose. American Journal of Public Health. 2009;99:778-91.
[37] Enteen L, Bauer J, McLean R, Wheeler E, Huriaux E, Kral A, et al. Overdose Prevention and Naloxone Prescription for Opioid Users in San Francisco. Journal of Urban Health. 2010:1-11.
[38] Maxwell S, Bigg D, Stanczykiewicz K, Carlberg-Racich S. Prescribing Naloxone to Actively Injecting Heroin Users: A Program to Reduce Heroin Overdose Deaths. Journal of Addictive Diseases. 2006;25:89-96.
[39] McAuley A, Lindsay G, Woods M, Louttit D. Responsible management and use of a personal take-home naloxone supply: A pilot project. Drugs: education, prevention and policy. 2009.
[40] McAuley A, Best D, Taylor A, Hunter C, Robertson R. From evidence to policy: The Scottish national naloxone programme. Drugs: Education, Prevention, and Policy. 2012;19:309-19.
[41] Markham Piper T, Stancliff S, Rudenstine S, Sherman S, Nandi V, Clear A, et al. Evaluation of a Naloxone Distribution and Administration Program in New York City. Substance Use and Misuse. 2008;43:858-70.
[42] Tobin KE, Sherman SG, Beilenson P, Welsh C, Latkin CA. Evaluation of the Staying Alive programme: Training injection drug users to properly administer naloxone and save lives. International Journal of Drug Policy. 2009;20:131-6.

[43] Piper T, Rudenstine S, Stancliff S, Sherman S, Nandi V, Clear A, et al. Overdose prevention for injection drug users: Lessons learned from naloxone training and distribution programs in New York City. Harm Reduction Journal. 2007;4:3.

[44] Kim D, Irwin KS, Khoshnood K. Expanded Access to Naloxone: Options for Critical Response to the Epidemic of Opioid Overdose Mortality. American Journal of Public Health. 2009 March 1, 2009;99:402-7.

[45] Darke S, Hall W. Heroin overdose: research and evidence-based intervention. Journal of Urban Health. 2003;80:189-200.

[46] SR S, RP B, SM G. Mortality from overdose among injecting drug users recently released from prison: database linkage study. BMJ. 1998;316:426-8.

[47] World Health Organization. Community management of opioid overdose. Geneva, 2014.

[48] Olsen A, McDonald D, Lenton S, Dietze P. Independent evaluation of the 'Implementing Expanded Naloxone Availability in the ACT (I-ENAACT)' Program, 2011-2014, final report. Canberra. : ACT Health. Available at: http://www.atoda.org.au/wp-content/uploads/Naloxone-Evaluation-Report-FINAL_August-2015_BI.pdf (Accessed 7/10/15), 2015.

[49] Lenton S. Take-Home Naloxone in Australia: past, present, future. Invited presentation at NDARC 30th Anniversary Symposium: Changing the Game; 3rd-4th October 2017; UNSW.

[50] Dwyer R, Fraser S, Dietze P. Benefits and barriers to expanding the availability of take-home naloxone in Australia: A qualitative interview study with service providers. Drugs: Education, Prevention and Policy. [Article]. 2016;23:388-96.

[51] Stafford J, Breen C. Australian drug trends 2016: Findings from the Illicit Drug Reporting System (IDRS) Sydney Available at: https://dlnstorage.blob.core.windows.net/drt101/1877/national-idrs_2016_finalwith-customs.pdf (Accessed 15/02/18): NDARC, 2017.

[52] Madah-Amiri D, Clausen T, Lobmaier P. Rapid widespread distribution of intranasal naloxone for overdose prevention. Drug and Alcohol Dependence. [Article]. 2017;173:17-23.

[53] Beletsky L, Rich JD, Walley AY. Prevention of fatal opioid overdose. JAMA: The Journal of the American Medical Association. 2012;308:1863-4.

[54] Kerr D, Kelly A-M, Dietze P, Jolley D, Barger B. Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. Addiction. 2009;104:2067-74.

[55] Taylor, S. (2008). Outside the outsiders: Media representations of drug use. *Probation Journal: The Journal of Community and Criminal Justice,* 55(4), 369-387.

[56] Lloyd, C. (2013). The stigmatization of problem drug users: A narrative literature review. *Drugs: Education, Prevention and Policy*, 20, 85–95.

[57] Hathaway, A. Comeau, N. & Erickson, P. (2011). Cannabis normalization and stigma: Contemporary practices of moral regulation. *Criminology & Criminal Justice,* 11 (5), 451-469.

[58] Fraser, S., Pienaar, K., Dilkes-Frayne, E., Moore, D., Kokanovic, R., Treloar, C. & Dunlop, A. (2017). Addiction stigma and the biopolitics of liberal modernity: A qualitative analysis. *International Journal of Drug Policy*, 44, 192–201.

[59] Room, R. (2005). Stigma, social inequality and alcohol and drug use. *Drug and Alcohol Review,* 24 (2), 143-155.