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BRIEF REPORT

Potential risk for fatal drug overdose perceived by people using opioid drugs

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Abstract

Introduction and Aims. *Combinations of drugs can increase the risk of overdose. Our aim was to examine perceptions of people dependent on opioid drugs on the potential risk of overdose from taking a prescribed dose of methadone in combination with various other recreational substances.* ***Design and Methods.*** *A peer-interviewer survey was conducted in three New Zealand regions. Recruitment was via snowballing initiated at needle exchange and opioid substitution treatment (OST) services.* ***Results.*** *Participants were 56% male, with a mean age of 37.5 years, 75% were New Zealand European, 24% Māori and 51% were receiving OST. Methadone and alcohol or benzodiazepine combinations were perceived as being of higher potential risk than methadone and stimulant or cannabis combinations. However, methadone taken in combination with alcohol or benzodiazepines was perceived as low risk by over half (55%) the participants. Factors associated with higher risk potential were area of residence, use of methadone in the previous month and a non-opioid drug injecting preference.* ***Discussion and Conclusions.*** *People who use opioid drugs continue to perceive taking opioids in combination with alcohol and benzodiazepines as low risk. Prevention efforts could be informed by greater exploration of barriers to understanding potential overdose risk and changing high-risk behaviours, and accessible and relevant opioid-related fatality data. OST must be able to attract and retain people who are dependent on opioid drugs.* [Deering DEA, Adamson SJ, Sellman JD, Henderson C, Sheridan J, Pooley S, Robertson RM, Noller G, Frampton CMA. Potential risk for fatal drug overdose perceived by people using opioid drugs. *Drug Alcohol Rev* 2017;:••]

Key words: methadone, opioids, overdose risk, polysubstance use, prevention.

Introduction

Opioid-related overdose has a devastating effect on families and communities. Factors shown to influence opioid-related overdose include tolerance, variations in rate of metabolism, systemic disease and concurrent use of other central nervous system depressants, particularly alcohol and benzodiazepines [1–3]. As methadone has been the primary medication used in opioid substitution treatment (OST) a specific focus has been on methadone-related overdose [4–7] which is of particular concern due to its potential delayed toxicity [3].

In 2009, it was estimated that the number of people in New Zealand who were daily/almost daily intravenous opioid users was about 10 000 with around half receiving OST [8], primarily methadone. Since this estimate the number of people receiving OST has remained relatively stable and not exceeded 5400

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(Ministry of Health, 2016, unpublished data). There is limited availability of heroin in New Zealand, and users of opioid drugs have typically injected a variety of pharmaceutical opioids and 'homebake' morphine/heroin illegally manufactured from codeine based products [9]. Surveys of people who are drug users have found use of opioids, including methadone which is considered to be easily accessible, tends to occur in a polydrug use context that includes use of nicotine, benzodiazepines, stimulants, cannabis and alcohol [10]. Injection of prescribed methadone and non-prescribed opioids as well as concurrent use of oral and injected benzodiazepines, stimulants, alcohol and cannabis have consistently been reported in surveys of OST clients [11,12]. Our aim was to examine perceptions of people who are opioid dependent on the potential overdose risk of taking a prescribed dose of methadone in combination with various other recreational substances.

Methods

Setting

Three New Zealand cities were selected for the survey, comprising the largest cities in both the North (Auckland) and South (Christchurch) Islands and a somewhat smaller North Island metropolitan area (Tauranga/Mt. Maunganui).

Participants

Recruitment occurred by snowballing, initiated from two sources: (i) OST services (four participants per city); and (ii) needle exchange outlets (eight participants per city). Eligibility criteria included: people currently receiving OST or who injected opioids daily/almost daily and were not receiving OST. Sample representativeness was enhanced by ensuring that two of the initially recruited participants from each of the two sources were aged under 30 years and two over 30 years, two male/two female and that at least one of the initial participants from each source identified as Māori, the indigenous people of New Zealand. Ethical approval for the study was granted by the Ministry of Health Multi-region Ethics Committee (MEC/07/04/061). Written informed consent was gained from each participant prior to the research interview. A $20 voucher was provided at the end of the interview for travel/time-related costs.

Survey questionnaire

A structured questionnaire was administered by trained peer interviewers in face-to-face interviews. The questionnaire was developed for this study and underwent initial testing of face validity and feasibility with peer interviewers. Participants were asked to rate the perceived dangerousness (potential to cause death by overdose) of each of five substances used recreationally when taken in combination with a stable daily dose of 80 mg oral methadone. This was a typical dose prescribed to OST clients within the effective dose range specified in national guidelines [13]. The five 'combination' substances and doses were decided on in consultation with peer advisors and OST clinical staff and were substances commonly used in combination with opioids in New Zealand [10]. They were defined as: (i) 12 standard drinks (120 g ethanol); (ii) 60 mg diazepam taken orally; (iii) 0.1 mg methamphetamine taken intravenously; (iv) 40 mg methylphenidate taken intravenously; and (v) three joints of cannabis (0.5 g marijuana per joint, smoked).

Response options for perceived dangerousness of each of the five methadone and other substance combinations were 'not at all', 'a little', 'moderately', 'a lot' or 'extremely'. Participants were also asked a number of demographic, substance use and treatment-related questions.

Data analysis

A potential 'higher risk' group was classified as those participants who rated use of either alcohol or diazepam in combination with methadone, as low risk ('not at all' or 'a little' dangerous). Predictors of 'higher risk' status were examined first using χ^2, with continuous variables dichotomised. Variables significant at $P < 0.10$ were entered into a multivariate logistic regression. Forward and backward models were run to test the robustness of the model. For potential predictors of high-risk status present in less than 20% of the sample there was >80% power to detect differences greater than approximately 35% as statistically significant (two-tailed alpha = 0.05). For those present in between 20% and 80% of the sample there was >80% power to detect differences greater than 30%.

Results

Ninety-seven participants were recruited and interviewed from Auckland (n = 21), Mt. Maunganui/Tauranga (n = 33) and Christchurch (n = 43). They were 56% male, with a mean age of 37.5 years (SD 9.1, range 16–58). Ethnically, 75% identified as Pakeha/European, 24% Māori and 1% Pacifika. Mean age of first drug injection was 19.4 years (SD 4.8,

range 13–40). At time of interview 51% were receiving OST, 14% had received OST in the past and 35% had never received OST.

Participants' ratings of potential risk of overdose for each of the five substances taken in combination with oral methadone are presented in Table 1. The two combinations rated as having higher perceived risk were alcohol and diazepam with 58% and 57%, respectively rating the risk as moderate or higher, while cannabis was rated as having the lowest perceived risk, with only 3% rating the risk as moderate or higher. For the stimulants, each of the substance combinations methamphetamine and methylphenidate were rated as moderate or higher risk by 25% and 22%, respectively.

Fifty-one (55%) participants rated use of either alcohol or benzodiazepines (or both) as low risk ('not at all', 'a little' dangerous) when taken in combination with a stable daily methadone oral dose of 80 mg. We defined these participants as the potentially 'higher risk' group for further analysis. Variables explored in relation to this risk category are shown in Table 2.

Four variables identified as possible candidates for a multivariate model were first examined for risk of collinearity. These were injecting drug of choice (opioids), frequency of past month injecting, any methadone use (prescribed or not) in the past month and being currently on a methadone programme. Injecting drug of choice (opioids) was not associated with the other variables (χ^2 0.02 to 0.91, all $P > 0.30$), while the remaining three were all highly associated (χ^2 9.20 to 30.50, all $P < 0.002$). Methadone use in the past month was most strongly correlated with the other two measures. Hence, neither frequency of opioid use nor being currently on a methadone maintenance programme were entered into the model.

Both forward and backward logistic regression produced the same solution, with high-risk individuals identified as those who did not live in Auckland (Wald = 7.845, df = 2, $P = 0.003$), identified non-opioids as their injecting drug of choice (Wald =5.268, df = 1, $P = 0.022$) and had used methadone in the past month (Wald = 5.781, df = 1, $P = 0.016$).

Discussion

Over half the participants in this study perceived the combination of methadone with either alcohol or benzodiazepines to be low risk for overdose. This finding is consistent with findings from other studies identifying limited understanding of overdose risk factors and prevention strategies amongst people who use opioid drugs [14] and variable appreciation of risks associated with concurrent use of opioids, benzodiazepines and alcohol [15]. Three factors were identified that predicted being in this potential 'higher risk' group. Firstly, area of residence (Christchurch and Tauranga/Mt. Maunganui). This could well be a sampling issue with a higher proportion of individuals who were more 'marginal users' surveyed in these two sites. However, regional differences have been found in injecting practices and hepatitis C virus exposure rates [16] indicating more in-depth exploration of regional differences in risk perceptions and injecting practices is warranted. Secondly, using methadone in the past month (prescribed or not) suggesting greater familiarity with the effects of methadone may lead to complacency. Thirdly, all but one of the participants who reported a non-opioid injecting preference were in the 'higher risk' group. Thereby indicating that this group within the opioid injecting population warrants further attention.

Almost half the participants were not currently engaged in OST. Of importance is that a restrictive and abstinence focussed treatment context is more likely to lead to clients leaving treatment prematurely thereby increasing potential for overdose [17,18]. Within such a context it is also unlikely that clients will willingly acknowledge the use of other substances reducing opportunities for such use to be therapeutically addressed [19].

Limitations in the present study include sample size, a small number of research sites and use of a questionnaire designed for the study. Perceptions of risk potential cannot be equated with actual high-risk practices. The New Zealand context is unusual in that there is

Table 1. *Participants' ratings of perceived dangerousness (potential to cause fatal overdose) of substances used in combination with a stable dose of 80 mg oral methadone*

Substance	*n*	Not at all (%)	A little (%)	Moderately (%)	A lot (%)	Extremely (%)
Alcohol (12 standard drinks)	93	24.7	17.2	26.9	20.4	10.8
Diazepam (60 mg orally)	92	23.9	19.6	27.2	22.8	6.5
Methamphetamine (0.1 mg IV)	89	53.9	21.3	14.6	7.9	2.2
Methylphenidate (40 mg IV)	90	54.4	23.3	15.6	5.6	1.1
Cannabis (three joints)	94	85.1	11.7	2.1	1.1	0.0

IV, intravenous.

Table 2. *Predictors of 'higher risk' status (potential to cause fatal overdose of use of alcohol or benzodiazepines in combination with a stable dose of 80 mg oral methadone perceived as 'not at all' or 'a little' dangerous)*, n = *93*

	N	High risk (*n*)	χ^2	*P*
Age			0.329	0.566
Under 30	20	60.0% (12)		
30+	72	52.8% (38)		
Birth place			0.165	0.685
New Zealand born	80	56.3% (45)		
Born overseas	12	50.0% (6)		
Ethnicity			0.066	0.797
Māori	21	52.4% (11)		
Non-Māori	72	55.6% (40)		
Gender			0.846	0.358
Male	52	59.6% (31)		
Female	40	50.0% (20)		
Location			18.533	**0.000**
Auckland	18	11.1% (2)		
Tauranga	33	72.7% (24)		
Christchurch	42	59.5% (25)		
Age first injected			0.047	0.829
Under 18	41	56.1% (23)		
18 and over+	52	53.8% (28)		
Injecting drug of choice			5.593	**0.018**
Opioids	83	50.6% (42)		
Not opioids	10	90% (9)		
Injected past month			6.139	**0.013**
Fewer than 30 times	48	66.7% (32)		
30 or more times	44	40.9% (18)		
Past month alcohol use	50	60.0% (30)	1.145	0.284
Yes				
No	41	48.8% (20)		
Past month methadone use			4.900	**0.027**
Yes	68	61.8% (42)		
No	25	36.0% (9)		
Past month benzodiazepine use			2.969	**0.085**
Yes	49	63.3% (31)		
No	44	45.5% (20)		
Currently on methadone maintenance			3.102	**0.078**
Yes	47	63.8% (30)		
No	46	45.7% (21)		

little heroin available. However, both locally produced 'homebake' morphine/heroin and a range of pharmaceutical opioids are readily available [10].

Further research and development include exploring barriers to understanding overdose-related information and changing high-risk practices, and the place of peer-educators [20]. A review of the quality of information collected on opioid-related deaths is timely, particularly in light of the availability of buprenorphine/naloxone in New Zealand and providing easily accessible take-home naloxone used to reverse opioid overdose in the community [21]. In conclusion, the prevention of opioid-related overdoses is a continuing challenge, which requires a co-ordinated strategy and further service development.

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Conflict of interest

Funding from the New Zealand Ministry of Health supported this research. SJA worked for the Christchurch Opioid Substitution Treatment site at the time of data collection. CH was manager of the New Zealand Needle Exchange Programme (trading as Needle Exchange Services Trust) at the time of data collection. The remaining authors have no conflict of interest to declare.

References

[1] White JM, Irvine RJ. Mechanisms of fatal opioid overdose. Addiction 1999;94:961–72.
[2] Corkery JM, Schifano F, Ghodse AH, Oyefeso A. The effects of methadone and its role in fatalities. Hum Psychopharmacol 2004;19:565–76.
[3] Wolff K. Characterization of methadone overdose: clinical considerations and the scientific evidence. Ther Drug Monit 2002;24:457–70.
[4] Albion C, Shkrum M, Cairns J. Contributing factors to methadone-related deaths in Ontario. Am J Forensic Med Pathol 2010;31:313–9.
[5] Pilgrim JL, McDonough M, Drummer OH. A review of methadone deaths between 2001 and 2005 in Victoria, Australia. Forensic Sci Int 2013;226:216–22.
[6] Iwersen-Bergmann S, Jungen H, Andresen-Streichert H *et al*. Intravenous methadone application as a serious risk factor for an overdose death: methadone related fatalities in Hamburg from 2007 to 2012. Int J Legal Med 2014;128:751–64.
[7] Wikner BN, Ohman I, Selden T, Druid H, Brandt L, Kieler H. Opioid-related mortality and filled prescriptions for buprenorphine and methadone. Drug Alcohol Rev 2014;33:491–8.
[8] Adamson SJ, Deering DE, Sellman JD *et al*. An estimation of the prevalence of opioid dependence in New Zealand. Int J Drug Policy 2012;23:87–9.
[9] Bedford KR, Nolan SL, Onrust R, Siegers JD. The illicit preparation of morphine and heroin from pharmaceutical products containing codeine: homebake laboratories in New Zealand. Forensic Sci Int 1987;34:197–204.
[10] Wilkins, C, Prasad, J, Wong K, Rychert M. Recent trends in illegal drug use in New Zealand 2006-2014: findings from the 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013 and 2014 illegal drug monitoring system (IDMS). Auckland: SHORE & Whariki Research Centre, Massey University Available at: http://www.massey.ac.nz/massey/fms/Colleges/College%20of%20Humanities%20and%20Social%20Sciences/Shore/reports/IDMS%202014%20Final%20Report.pdf?38B9C25FBFC4F517CCB03BCA4C7CF64A (accessed May 2016).
[11] Deering DE, Frampton CMA, Horn J, Sellman D, Adamson SJ, Potiki T. Health status of clients receiving methadone maintenance treatment using the SF-36 health survey questionnaire. Drug Alcohol Rev 2004;23:273–80.

[12] Judson G, Bird R, O'Connor P *et al*. Drug injecting in patients in New Zealand methadone maintenance treatment programs: an anonymous survey. Drug Alcohol Rev 2010;29:41–6.
[13] Ministry of Health. Practice guidelines for opioid substitution treatment in New Zealand. Wellington: Ministry of Health, 2014 Available at: http://www.health.govt.nz/publication/new-zealand-practice-guidelines-opioid-substitution-treatment-2014 (accessed April 2016).
[14] Sarasa-Renedo A, Espelt A, Folch C *et al*. Overdose prevention in injecting opioid users: the role of substance abuse treatment and training programs. Gac Sanit 2014;28:146–54.
[15] Rowe C, Santos GM, Behar E, Coffin PO. Correlates of overdose risk perception among illicit opioid users. Drug Alcohol Depend 2016;159:234–9.
[16] Noller G, Henderson C. Report of the national needle exchange bloodborne virus Ssroprevalence survey: technical report BBVNEX 2013. Wellington: Ministry of Health, 2014.
[17] Gronbladh L, Gunne LM. Mortality in heroin addiction: impact of methadone. Acta Psychiatr Scand 1990;82:223–7.
[18] Deering DE, Sheridan J, Sellman JD *et al*. Consumer and treatment provider perspectives on reducing barriers to opioid substitution treatment and improving treatment attractiveness. Addict Behav 2011;36:636–42.
[19] Lintzeris N, Neilsen S. Benzodiazepines, methadone and buprenorphine: interations and clinical management. Am J Addict 2010;19:59–72.
[20] Raki M, National Addiction Workforce Development. Consumer and peer roles in the addiction sector. Wellington: Matua Raki, 2010. Available at: http://www.matuaraki.org.nz/uploads/files/resource-assets/consumer-and-peer-roles-in-the-addiction-sector.pdf (accessed December 2016).
[21] Rowe C, Santos GM, Vittinghoff E, Wheeler E, Davidson P, Coffin PO. Predictors of participant engagement and naloxone utilisation in a community-based naloxone distribution program. Addiction 2015;1:1301–10.