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Factors associated with non-adherence and misuse of opioid maintenance treatment medications and intoxicating drugs among Finnish maintenance treatment patients

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ABSTRACT

Background: The intravenous (IV) use of opioid maintenance treatment (OMT) medications and other intoxicating drugs among OMT patients is a challenge for many OMT units and affects treatment outcomes. The aim of this study is to examine factors associated with IV use of OMT medications and other intoxicating drugs among Finnish OMT patients.
Methods: A cross-sectional study was conducted among all Finnish OMT patients of whom 60% (n = 1508) participated. The data were collected by anonymous questionnaire. Binominal regression analysis with unadjusted and adjusted ORs was conducted to evaluate predictors for IV use.
Findings: Factors associated with the injection of a patient's own OMT medication were: being treated with buprenorphine-naloxone (BNX) (OR 2.60, p = 0.005) with a low dose (<9.0 mg/day; OR 5.70, p < 0.001) and being treated in a health-care centre (OR 2.03, p = 0.029). Factors associated with the injection of illicit OMT medications were: being treated with BNX (OR 5.25, p < 0.001) with a low dose (<9.0 mg/day; OR 2.89, p = 0.017), lack of psychosocial support (OR 2.62, p < 0.001) and concurrent use of psychotropic medications from illicit sources (OR 4.28, p < 0.001). Associated factors for the injection of other intoxicating drugs were: concurrent use of illicit drugs (OR 1.72, p = 0.015), psychotropic medications from illicit sources (OR 4.78, p < 0.001) and from a doctor (OR 1.93, p = 0.004).
Conclusions: More effort should be made to reduce concurrent injecting use during OMT. This may be done by addressing concurrent substance use orders more effectively, by ensuring that patients receive an optimal BNX dose and by providing more psychosocial support.

1. Introduction

Opioid maintenance treatment (OMT) has been proven effective in the treatment of opioid dependency, as it retains people in treatment (Mattick et al., 2009,2014), suppresses illicit opioid use (Marsch, 1998; Mattick et al., 2003, 2009, 2014), decreases criminal activity (Marsch, 1998; Mattick et al., 2009; Vorma et al., 2013) and the occurrence of high-risk injecting practices (Gowing et al., 2011, 2006; Marsch, 1998; Mattick et al., 2009). In Finland, 2439 of the estimated 13,000 to 15,000 problem opioid users in the country received OMT at the end of 2011 (Ollgren et al., 2014; Partanen et al., 2014). OMT in Finland includes oral liquid methadone (MET), buprenorphine-naloxone (BNX) tablets and soluble films (Suboxone®, Reckit-Benckiser). In 2008 buprenorphine (BUP) was withdrawn and placed under special licence (pregnancy only). According to Finnish clinical guidelines, take-home allowances of OMT medications are only granted to stable and motivated patients. MET and BUP are mostly dispensed by addiction treatment services and take-home doses of MET are often diluted with water to discourage injecting. Finnish OMT programmes are divided into rehabilitation and harm reduction approaches (MSAH,

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2008). In rehabilitation programmes, where detoxification is one of the goals, urine screening and assessment of injection sites are part of the treatment protocol. In harm reduction programmes less supervision is involved. The level of psychosocial support during OMT also varies depending on the programme and treatment service.

However, in Finland and elsewhere, misuse and non-adherence of OMT medications amongst patients attending OMT remains a major concern. Adverse outcomes such as non-fatal and fatal overdoses (Bretteville-Jensen et al., 2014; Iwersen-Bergmann et al., 2014), and injection related injuries and diseases (Degenhardt et al., 2008; Jenkinson et al., 2005) are well documented.

1.1. Definitions

Misuse refers to use of a substance for a purpose not consistent with legal or medical guidelines, as in the non-medical use of prescription medications (WHO,1994). In this paper, the term misuse is used to describe intravenous (IV) use of intoxicating drugs or illicit OMT medications, which were obtained from outside an OMT service. Internationally, injecting rates of illicit OMT medications vary widely. In France, injection rates of BUP range from 15.3% to 46.5% among samples of patients receiving OMT (Guichard et al., 2003; Roux et al., 2008a,b; Vidal-Trecan et al., 2003) while in Australia injection rates of BUP range from 9% to 26.5% and of MET from 17% to 33% (Winstock and Lea, 2010; Winstock et al., 2008).

Non-adherence refers to any use of a medication by the person to whom it was prescribed where the medication is not taken according to prescription directions. During OMT, this may include escalation or reduction in dose, removal of supervised doses, stockpiling medication, missing doses and the injection of medication (Larance et al., 2011b). In this paper, the injection of a patient's own OMT medication is referred to as non-adherence. Most studies on the occurrence of non-adherence, where patients inject their own OMT medications, have been conducted in Australia. In these studies, injection rates of own medication have been found to vary from 13% to 24% for MET patients and from 13% to 19% for BNX patients (Degenhardt et al., 2009; Larance et al., 2011a, 2014). These studies indicate that IV use of both own and illicit OMT medications during treatment is still an ongoing challenge.

Psychotropic medications are defined as any pharmaceutical medications that mainly affect the central nervous system. When ingested, they affect mental processes, e.g., cognition (WHO, 2009). In Finland, they are legally available only with a prescription. In this paper, *any intoxicating drugs* refer to any substances that cause a state of intoxication. This may include own and illicit OMT medications, other psychotropic medications or illicit drugs.

'*Psychosocial support*' refers to interventions such as cognitive and behavioural approaches and contingency management techniques (WHO, 2009).

1.2. Factors associated with non-adherence and misuse

Existing research has identified a number of factors associated with non-adherence and misuse. This includes an inadequate BUP dose (Comer et al., 2010; Roux et al., 2008a; Vidal-Trecan et al., 2003), high doses of BUP (Guichard et al., 2003) and previous IV use of other intoxicating drugs such as BUP and other prescription opioids (Carrieri et al., 2003; Horyniak et al., 2011; Vidal-Trecan et al., 2003). In addition, social factors such as living on social benefits, not living in a stable relationship or having a prison background, together with health related issues such as depression and previous suicide attempts have been associated with non-adherence and misuse (Carrieri et al., 2003; Horyniak et al., 2011; Roux et al., 2008a, 2008b; Vidal-Trecan et al., 2003). Patients themselves have reported injecting in order to reduce cravings and to prevent withdrawal ('self-treatment'). Only rarely has the search for pleasure been reported (Moratti et al., 2010; Schuman-Olivier et al., 2010).

However, generalisation of the results from previous studies has been difficult, as they have been conducted among a subset of patients, for example within a single treatment service (Moratti et al., 2010). In addition, some results have been contradictory to each other, for example the results regarding BUP dose (e.g., Guichard et al., 2003; Vidal-Trecan et al., 2003). A better understanding of the factors related to non-adherence with OMT is essential to developing and improving treatment regimes. The aim of this study is to identify the factors associated with non-adherence, misuse of illicit OMT medications and intoxicating drugs among Finnish OMT patients.

2. Methods

2.1. Study sample and data collection

The study was conducted by the University of Helsinki and the National Institute for Health and Welfare (THL) between May and July, 2013. A questionnaire consisting of 18 multiple-choice and 4 free-text questions (see Supplementary material 1) was distributed to all treatment services providing OMT in Finland, excluding prisons. The questionnaire included questions concerning patients' background information, concurrent substance use, IV use of own and illicit OMT medications, IV use of other intoxicating drugs and diversion of OMT medications. Results regarding diversion have been published elsewhere (Launonen et al., 2015).

A total of 2512 questionnaires were sent to treatment services, whose staff distributed them to OMT patients to be completed anonymously. A cover letter to staff and OMT patients, explaining the study objectives and directions on distribution and collection was attached. To avoid duplicated surveys, each patient was provided with one questionnaire only.

Patients were asked to complete questionnaires anonymously and return them to staff in sealed envelopes. Patients were advised to seal their envelopes with a sticker to ensure they remained unopened until the point of analysis. Responses were voluntary and participants were reassured that return/non-return would not have any impact on treatment. The questionnaire informed OMT patients of the purpose of the study and confidentiality of responses. The importance of answering honestly was emphasised. Staff returned the sealed envelopes in prepaid postal pouches to THL.

All the completed questionnaires were registered and numbered. In addition, municipality numbers were registered so that regional coverage and comparison could be assessed. However, no personal or treatment centre identifying information was registered.

2.2. Data analysis

The data were described using percentages, means, standard deviations and medians. Binominal logistic regression models were used to analyse factors associated with non-adherence and misuse of OMT medications and intoxicating drugs. The dependent variable in each model was dichotomous (IV use of own or illicit OMT medications or intoxicating drugs yes or no). The explanatory variables were gender, age, duration of OMT, OMT medication and its dose, dispensation of OMT medication, treatment service, psychosocial support during treatment and concurrent substance use during the past six months. These were selected on the basis of factors that had been identified in previous literature as being associated with non-adherence and misuse (for example, Comer et al., 2010; Guichard et al., 2003; Roux et al., 2008a, 2008b; Vidal-Trecan et al., 2003; Carrieri et al., 2003; Horyniak et al., 2011), as well as new areas of

interest, which included OMT medication collection method and perceived psychosocial support. Statistically significant variables (p-value < 0.05) in univariate analysis were included in the multivariate analysis. In multivariate models, group with the lowest prevalence with relation to the endpoint was consistently used as a reference group. The results were presented as odds ratios (ORs) and 95% confidence intervals (95% CI). Data were analysed using SPSS version 21.

2.3. Ethical conduct of study

The study was conducted according to EU and Finnish regulations (KL 313/2004 and 295/2004) regarding clinical research. A notification to the THL Ethics Committee for study approval was filed and approved (reference number # THL/354/6.02.01/2013). The study was conducted in accordance with the Personal Data Protection rule of THL, the ICH guidelines for Good Clinical Practice and the Helsinki Declaration of 1964.

3. Results

Completed surveys were received from 1508 patients, a response rate of 60% calculated on the basis of sent forms (2512). Of all treatment services included in the survey (206), 83% (170) participated in the study and a satisfactory regional coverage was reached. Compared to the total number of OMT patients in Finland (Partanen et al., 2014), respondents represent about 62% of all OMT patients.

3.1. Characteristics of OMT patients

Two thirds of respondents were male (n = 1 015, 68%) and one third female (n = 477, 32%). Respondents' mean age was 34 years (S.D. 7.5 years; median 33 years; range 19–60 years) and the mean duration of OMT was 46 months (S.D. 41.3 months; median 32 months; range 0.5–216 months). Average daily dose was 14.8 mg/day (range 1.0–30.0 mg/day, S.D. 5.0 mg) for BNX, 92.0 mg/day (range 2.0–270.0 mg/day, S.D. 42.5 mg) for MET and 11.8 mg/day (range 2.0–24.0 mg/day, S.D. 5.3 mg) for BUP. Basic characteristics are shown in Table 1.

Table 1
Characteristics and treatment details of OMT patients (n = 1508).

	n	%
Gender (n = 1492)		
Male	1 015	68
Female	477	32
Total	1 492	100
Age (years, n = 1494)		
19–29	415	28
30–34	462	31
35–39	305	20
≥40	312	21
Total	1 494	100
Duration of OMT (months, n = 1424)		
<6	127	9
6–11	145	10
12–23 (1–2 years)	228	16
24–35 (2–3 years)	229	16
36–59 (3–5 years)	258	18
60–83 (5–7 years)	160	11
≥ 84 (≥7 years)	277	20
Total	1 424	100
OMT medication (n = 1409)		
Buprenorphine-naloxone (BNX)	908	61
Methadone (MET)	538	36
Buprenorphine (BUP)	29	2
Other/Unclear	23	2
Total	1 498	100
OMT service (n = 1506)		
Primary health care centre[a]	327	22
Specialist drug treatment services (outpatient)	964	64
Specialized medical care (inpatient)	188	13
Other	27	2
Total	1 506	100
Location (n = 1505)		
Helsinki metropolitan area	530	35
Other areas	975	65
Total	1 505	100
Dispensation of OMT medications and other psychotropic medications (n = 1453)		
OMT medication collected from treatment service	554	38
BNX collected from pharmacy	52	4
Other psychotropic medications collected according to a pharmacy agreement[b]	718	49
BNX collected from pharmacy[c] and other psychotropic medications collected according to a pharmacy agreement	81	6
Answer not clear	48	3
Total	1 453	100

[a] Primary health care services operated by general practitioners, equivalent to general practice in the UK.
[b] An agreement that compels a patient to collect their medication from one pharmacy only, usually signed to monitor and restrict the use of psychotropic medications among patients with a risk of misuse.
[c] Pharmacy distribution of BNX in Finland is restricted to stable patients who agree to sign a contract compelling them to collect their BNX from one pharmacy only.

3.2. Concurrent substance use and IV use of intoxicating drugs in general

OMT patients were asked about their concurrent substance use during the past six months. The distribution of answers is shown in Table 2.

Respondents were asked whether they had injected any intoxicating drugs during the past six months. Of all respondents, 36% (n = 487) reported IV use, compared to 64% (n = 882) who reported no IV use.

IV use during the past six months was analysed in relation to gender, age, duration of OMT, OMT medication and dose, collection method, treatment service, perceived psychosocial support and concurrent substance use (for prevalence, see Table 3). After adjusting the only factors that remained independently associated with IV use of intoxicating drugs were concurrent use of illicit drugs (OR 26.29, 95% CI 16.09–42.97), psychotropic medications from illicit sources (OR 5.49, 95% CI 3.72–8.10), cannabis (OR 2.19, 95% CI 1.46–3.28) and alcohol (OR 1.49, 95% CI 1.01–2.20) and lack of psychosocial support during treatment (OR 2.11, 95% CI 1.38–3.24). In addition, increasing length of OMT was associated with a lower risk of IV use (OR 0.987, 95% CI 0.982–0.993) (Table 4).

3.3. Non-adherence and misuse of illicit OMT medications

In terms of non-adherence, 84% (n = 439) of injecting patients reported no IV use of their own OMT medication during the past six months, while 16% (n = 85) reported IV use. Five percent (n = 24) reported injecting on a regular basis, while the remaining 12% (n = 61) reported injecting less frequently than on a monthly basis. Table 6 shows the reasons reported for injecting own medication.

The injection of own OMT medication during the six months prior to the survey was analysed in relation to gender, age, duration

Table 2
Concurrent substance use during the past six months (n = 1464).

Used substance/s	Frequency	Distribution (%) between answers	Share (%) of respondents
Alcohol	846	28	58
Cannabis	552	18	38
Other illicit drugs[a]	366	12	25
Psychotropic medications[b] from a doctor	633	21	43
Psychotropic medications from illicit sources	494	16	34
Own OMT medication only	179	6	12
Total	3 070	100	210[c]
Only alcohol	213		15
Only psychotropic medications from a doctor	120		8
Only alcohol and psychotropic medications from a doctor	129		9

[a] Illicit drugs are referred to as any psychotropic substances, of which the production, sale, or use is prohibited. The use of cannabis, however, was asked separately, although it is regarded as an illicit drug in Finland.
[b] Psychotropic medications are referred to as any pharmaceutical medications that mainly affect the central nervous system. In Finland, they can only be legally obtained with a prescription.
[c] Total sum exceeds 100% as multiple responses were allowed.

Table 3
IV use of own and illicit OMT medications and other intoxicating drugs during the past six months in relation to patients' demographic background and treatment related factors.

Background variable	IV use in general[a] during the past 6 months			IV use of own OMT medication			IV use of illicit OMT medications			IV use of other intoxicating drugs[b]		
	Yes, n (%)	No, n (%)	Total	Yes, n (%)	No, n (%)	Total	Yes, n (%)	No, n (%)	Total	Yes, n (%)	No, n (%)	Total
Gender												
−male	349 (38.2)	565 (61.8)	914	56 (14.9)	321 (85.1)	377	112 (33.4)	223 (66.6)	335	250 (70.8)	103 (29.2)	353
−female	130 (29.3)	314 (70.7)	444	29 (20.6)	112 (79.4)	141	43 (34.7)	81 (65.3)	124	90 (66.2)	46 (33.8)	136
Total	479	879	1358	85	433	518	155	304	459	340	149	489
OMT medication												
−BNX	288 (34.5)	547 (65.5)	835	67 (21.7)	242 (78.3)	309	122 (42.8)	163 (57.2)	285	205 (70.4)	86 (29.6)	291
−MET	183 (38.0)	299 (62.0)	482	14 (7.1)	183 (92.9)	197	28 (17.2)	135 (82.8)	163	124 (66.3)	63 (33.7)	187
Total	471	846	1317	81	425	506	150	298	448	329	149	478
BNX dose (mg/day)												
<9.0	37 (30.6)	84 (69.4)	121	16 (42.1)	22 (57.9)	38	21 (58.3)	15 (41.7)	36	26 (66.7)	13 (33.3)	39
9.0–15.9	85 (36.8)	146 (63.2)	231	22 (25.0)	66 (75.0)	88	49 (58.3)	35 (41.7)	84	61 (70.1)	26 (29.9)	87
>15.9	164 (34.2)	316 (65.8)	480	27 (14.9)	154 (85.1)	181	51 (31.1)	113 (68.9)	164	116 (71.2)	47 (28.8)	163
Total	286	546	832	65	242	307	121	163	284	203	86	289
Treatment unit												
−Primary Health care centre	66 (22.0)	243 (78.0)	300	20 (28.6)	50 (71.4)	70	22 (33.8)	43 (66.2)	65	42 (64.6)	23 (35.4)	65
−A-clinic[c]	320 (36.9)	548 (63.1)	868	49 (14.0)	302 (86.0)	351	90 (29.4)	216 (70.6)	306	231 (69.4)	102 (30.6)	333
Total	386	782	1168	69	352	421	112	259	371	273	125	398
BNX collected from pharmacy												
−yes	46 (37.4)	77 (62.6)	123	12 (24.5)	37 (75.5)	49	23 (52.3)	21 (47.7)	44	38 (82.6)	8 (17.4)	46
−no	413 (35.4)	754 (64.6)	1 167	71 (16.0)	372 (84.0)	443	122 (30.9)	273 (69.1)	395	285 (67.7)	136 (32.3)	421
Total	459	831	1290	83	409	492	145	294	439	323	144	467
Psychosocial support												
−yes	296 (30.1)	688 (69.9)	984	52 (16.5)	264 (83.5)	316	79 (27.9)	204 (72.1)	283	198 (66.0)	102 (34.0)	300
−no	164 (50.6)	160 (49.4)	324	30 (16.8)	149 (83.2)	179	70 (43.8)	90 (56.3)	160	123 (71.9)	48 (28.1)	171
Total	460	848	1308	82	413	495	149	294	443	321	150	471
Concurrent substance use[d]												
−alcohol	308 (39.9)	463 (60.1)	771	61 (18.5)	268 (81.5)	329	113 (38.4)	181 (61.5)	294	223 (70.3)	94 (29.7)	317
−cannabis	285 (56.1)	223 (43.9)	508	41 (13.8)	256 (86.2)	297	88 (33.5)	175 (66.5)	263	212 (74.4)	73 (25.6)	285
−other illicit drugs	305 (88.4)	40 (11.6)	345	45 (14.6)	263 (85.4)	308	95 (34.5)	180 (65.5)	275	222 (75.8)	71 (24.2)	293
−PM[e] from a doctor	223 (38.9)	351 (61.1)	574	49 (20.2)	193 (79.8)	242	76 (34.7)	143 (65.3)	219	178 (76.4)	55 (23.6)	233
−PM[e] from illicit sources	316 (69.1)	141 (30.9)	457	52 (15.8)	277 (84.2)	329	132 (44.3)	166 (55.7)	298	259 (80.9)	61 (19.1)	320
Own OMT medication only	10 (5.8)	161 (94.2)	171	5 (45.5)	6 (54.5)	11	2 (25.0)	6 (75.9)	8	3 (30.0)	7 (70.0)	10

[a] IV use in general may include the IV use of illicit drugs, OMT medications or other psychotropic medications.
[b] IV use of other intoxicating drugs may include, for example, IV use of psychotropic medications, excluding OMT medications.
[c] Specialist treatment unit for substance abusers.
[d] During the past 6 months.
[e] Psychotropic medications, referred to as any pharmaceutical medications that mainly affect the central nervous system. In Finland, they can only be legally obtained with a prescription.

of OMT, OMT medication and dose, collection method, treatment service, perceived psychosocial support and concurrent substance use (for prevalence, see Table 3). After adjusting (Table 5), factors that remained independently associated with injection of own medication were BNX as OMT medication (OR 2.60, 95% CI 1.34–5.06) and BNX medication dose (OR 0.88, per one mg increase, 95% CI 0.82–0.95). As presented in Table 5, model 1.3, we also conducted an additional analysis of BNX dose according to a low, medium or high dose classification. The purpose of this was to support practical application of the results. This model shows that those with a daily dose of less than 9.0 mg/day and 9.0–15.9 mg/day were at a higher risk of injecting their own medication as compared with patients with a daily dose of higher than 15.9 mg/day (OR 5.70, 95% CI 2.41–13.46 and OR 2.52, 95% CI 1.20–5.28, respectively). In addition, injecting was more likely among patients treated in primary health care centres (OR 2.03, 95% CI 1.08–3.84) as compared with patients treated in specialist treatment services for substance abusers.

Table 4
Multivariate analysis of factors associated with IV use in general during the past six months.

Background variable	IV use in general during the past 6 months[a]			
	Unadjusted OR (95% CI)[d]	p[e]	Adjusted OR (95% CI)	p
Gender				
–female	1	<0.001	1	0.736
–male	1.49 (1.17–1.90)		0.93 (0.61–1.42)[f]	
Age (years, continuous)[b]	0.959 (0.944–0.975)	<0.001	0.978 (0.950–1.006)[f]	0.122
Duration of OMT[b] (months, continuous)	0.991 (0.988–0.994)	<0.001	0.987 (0.982–0.993)[f]	<0.001
OMT-medication				
–BNX[c] medication	1	0.205		
–MET medication	1.16 (0.92–1.47)			
BNX[c] daily dose[b] (mg, continuous)	0.999 (0.971–1.028)	0.948		
MET daily dose[b] (mg, continuous)	0.995 (0.991–1.000)	0.044	0.998 (0.989–1.007)[g]	0.664
Treatment unit	1 2.07 (1.53–2.81)	<0.001	1 1.07 (0.66–1.75)[f]	0.781
–Primary health care centre				
–Specialist treatment unit for substance abusers (e.g. A-clinic)				
BNX[c] collected from pharmacy OMT med. collected from treatment unit	1 1.09 (0.74–1.60)	0.658		
Psychosocial support				
– yes	1	<0.001	1	0.001
– no	2.38 (1.84–3.08)		2.11 (1.38–3.24)[f]	
Concurrent substance use during the past 6 months: no concurrent substance use	1		1	
– Alcohol	1.52 (1.21–1.91)	<0.001	1.49 (1.01–2.20)[f]	0.043
– Cannabis	4.12 (3.25–5.22)	<0.001	2.19 (1.46–3.28)[f]	<0.001
–Other illicit drugs	35.10 (24.32–50.67)	<0.001	26.29 (16.09–42.97)[f]	<0.001
–Psychotropic medications from a doctor	1.25 (1.00–1.56)	0.052		
–Psychotropic medications from illicit sources	9.65 (7.44–12.51)	<0.001	5.49 (3.72–8.10)[f]	<0.001

[a] IV use in general may include the IV use of illicit drugs, OMT medications or other psychotropic medications.
[b] Per one unit increase.
[c] Buprenorphine-naloxone.
[d] Separate unadjusted logistic regression models for each variable (dependent variable IV use of any intoxicating drugs during the past 6 months, yes vs. no).
[e] Variables with p-value < 0.05 were included in the multivariate analysis.
[f] Adjusted for gender, age, duration of OMT, treatment service, psychosocial support, use of alcohol, cannabis, other illicit drugs and psychotropic medications from illicit sources. Nagelkerke R square = 0.594. 1 041 cases included in the analysis.
[g] Adjusted for MET dose, gender, age, duration of OMT, treatment service, psychosocial support, use of alcohol, cannabis, other illicit drugs and psychotropic medications from illicit sources. Nagelkerke R square = 0.611. 371 cases included in the analysis.

In terms of misuse of illicit OMT medications, 67% (n = 308) of injecting patients reported no IV use of illicit OMT medications, whereas the remaining 33% (n = 155) reported IV use. The injection of illicit OMT medications was analysed in relation to the same factors as the injection of own OMT medication. After adjusting (Table 5), factors that remained independently associated with injection of illicit OMT medications were BNX as OMT medication (OR 5.25, 95% CI 2.88–9.55) and BNX medication dose (OR 0.88, 95% CI 0.83–0.95). As above, we also analysed BNX dose according to a low, medium or high dose classification (Table 5, model 2.3). This showed that among those with a daily dose of less than 9.0 mg/day and 9.0–15.9 mg/day the odds of injecting illicit OMT medication increased more than two fold compared with patients with a daily dose of higher than 15.9 mg/day (OR 2.89, 95% CI 1.21–6.91 and OR 2.59, 95% 1.38–4.86, respectively). In addition, the odds of injecting illicit OMT medications were higher among those who reported not receiving enough psychosocial support (OR 2.62, 95% CI 1.59–4.32). Those who reported concurrent use of psychotropic medications from illicit sources were more likely to inject illicit OMT medications (OR 4.28, 95% CI 3.44–7.49).

3.4. Concurrent misuse of other intoxicating drugs

In regards to misuse of other intoxicating drugs (including any intoxicating drugs other than OMT medications such as psychotropic medications), 67% (n = 306) of injecting patients reported IV use of intoxicating drugs, while 33% (n = 152) reported no IV use. Of all respondents, 42% (n = 194) reported injecting less frequently than on a monthly basis, whereas 24% (n = 112) reported injecting on a regular basis. Table 6 shows the reasons reported for injecting intoxicating drugs. The injection of other intoxicating drugs was analysed in relation to the same factors as the injection of own and illicit OMT medications. After adjusting (Table 5), factors that remained independently associated with injection of other intoxicating drugs were concurrent use of psychotropic medications from illicit sources (OR 4.78, 95% CI 3.08–7.39) and from a doctor (OR 1.93, 95% CI 1.24–3.01) as well as concurrent use of illicit drugs (OR 1.72, 95% CI 1.11–2.67).

3.5. Injecting behaviour as a problem

Respondents were asked about problem injecting. Over half of the respondents stated that their injecting was a problem 'to some extent' (52%, n = 260), while for 29% it was 'occasionally' a problem, and for 3% 'constantly' a problem. However, nearly half of respondent reported that their injecting was not problematic (47%, n = 237). Only 18% (n = 89) of respondents stated that they would like to stop injecting, with 22% (n = 113) reporting that they needed help to do so. 74% (n = 373) of respondents stated that they did not need help to stop injecting, while 4% (n = 20) did not know.

4. Discussion

This is the first large-scale study, conducted with a target group of all OMT patients within one country, to report on factors associated with non-adherence and misuse of illicit OMT medications and other intoxicating drugs. The factors associated with injecting use during ongoing treatment is a topic which to date has been relatively under-explored. However, understanding these factors is essential to enhancing adherence to treatment, as well as to improving patients' overall well-being and their treatment outcomes.

Table 5
Multivariate analysis of factors associated with IV use of own OMT medication, illicit OMT medications and other intoxicating drugs during the past six months.

Background variable	IV use of own OMT medication				IV use of illicit OMT medications				IV use of other intoxicating drugs[l]			
	Unadjusted OR[c]	p[d]	Adjusted OR	p	Unadjusted OR[c]	p[d]	Adjusted OR	p	Unadjusted OR[c]	p[d]	Adjusted OR	p
Gender												
−female	1.48 (0.90–2.44)	0.120			1.06 (0.69–1.63)	0.802			1.24 (0.81–1.89)	0.318		
−male	1				1				1			
Age (years, continuous)[a]	0.98 (0.94–1.02)	0.259			0.95 (0.92–0.98)	0.003	0.97 (0.93–1.01)[h]	0.096	0.97 (0.95–1.00)	0.052		
Duration of OMT[a] (months, continuous)	1.001 (0.994–1.008)	0.754			0.998 (0.992–1.004)	0.505			1.000 (0.994–1.005)	0.888		
OMT-medication												
−BNX[b] medication	3.62 (1.97–6.64)	<0.001	2.60 (1.34–5.06)[e]	0.005	3.61 (2.26−5.77)	<0.001	5.25 (2.88–9.55)[h]	<0.001	1.21 (0.82–1.80)	0.341		
−MET medication	1		1		1		1		1			
BNX[b] daily dose[a] (mg, continuous)	0.91 (0.86–0.97)	0.004	0.88 (0.82–0.95)[f]	<0.001	0.88 (0.83−0.93)	<0.001	0.88 (0.83–0.95)[i]	<0.001	1.03 (0.97–1.08)	0.375		
BNX[b] dose **(mg/day)												
<9.0	4.15 (1.93–8.90)	<0.001	5.70 (2.41–13.46)[g]	<0.001	3.10 (1.48−6.51)	0.003	2.89 (1.21–6.91)[j]	0.017	1.17 (0.52–2.63)	0.699		
9.0–15.9	1.90 (1.01–3.58)	0.046	2.52 (1.20–5.28)[g]	0.014	3.10 (1.80−5.35)	<0.001	2.59 (1.38–4.86)[j]	0.003	1.23 (0.59–2.61)	0.581		
>15.9	1		1		1		1		1			
MET daily dose[a] (mg, continuous)	0.99 (0.97–1.00)	0.163			0.99 (0.98−1.01)	0.297			0.99 (0.99–1.00)	0.138		
Treatment unit												
−Primary health care centre	2.47 (1.35–4.49)	0.003	2.03 (1.08–3.84)[e]	0.029	1.23 (0.70−2.17)	0.480			1	0.451		
−Specialist treatment unit for substance abusers (e.g. A-clinic)	1		1		1				1.24 (0.71–2.17)			
BNX[b] collected from pharmacy	1.70 (0.85–3.42)	0.137			2.45 (1.31−4.60) 1	0.005	1.44 (0.70–2.94)[h]	0.324	2.27 (1.03–4.99) 1	0.042	2.04 (0.87–4.82)[k]	0.095
OMT med. collected from treatment unit	1				1				1			
Psychosocial support												
− yes	1				1		1		1			
− no	1.02 (0.63–1.67)	0.930			2.01 (1.34−3.02)	0.001	2.62 (1.59−4.32)[h]	<0.001	1.32 (0.88–1.99)	0.185		
Concurrent substance use during the past 6 months: no substance use	1				1				1			
−Alcohol	1.55 (0.93–2.58)	0.095			1.79(1.17–2.72)	0.007	1.66(0.98–2.81)[h]	0.059	1.10 (0.74–1.64)	0.652		
−Cannabis	0.64 (0.40–1.02)	0.058			0.95 (0.65–1.41)	0.813			1.70 (1.15–2.50)	0.008	1.51 (0.98–2.34)[k]	0.065
−Other illicit drugs	0.72 (0.45–1.15)	0.166			1.07 (0.72–1.59)	0.727			2.03 (1.38–3.00)	<0.001	1.72 (1.11–2.67)[k]	0.015
−PM[m] from a doctor	1.68 (1.05–2.69)	0.031	1.63 (0.94–2.83)[e]	0.085	1.07 (0.73–1.57)	0.733			1.86 (1.25–2.75)	0.002	1.93 (1.24–3.01)[k]	0.004
−PM[m] from illicit sources	0.88 (0.54–1.41)	0.588			4.57 (2.80–7.46)	<0.001	4.28 (2.44–7.49)[h]	<0.001	4.50 (2.99–6.78)	<0.001	4.78 (3.08–7.39)[k]	<0.001

[a] Per one unit increase.

[b] Buprenorphine-naloxone.

[c] Separate unadjusted logistic regression models for each variable.

[d] Variables with *p*-value <0.05 were included in the multivariate analysis. Due to highly correlated variables separate models were conducted in order to avoid multicollinearity.

[e] Model 1.1: adjusted for OMT-medication, treatment unit and concurrent use of psychotropic medications from doctor. Nagelkerke R square = 0.088. 398 cases included in the analysis.

[f] Model 1.2: adjusted for BNX daily dose (continuous), treatment unit and concurrent use of psychotropic medications from doctor. Nagelkerke R square = 0.120. 243 cases included in the analysis.

[g] Model 1.3: assessed BNX dose according to a low, medium or high dose classification, to support practical application of the results in addition to model 1.2. Adjusted for BNX daily dose (classified), treatment unit and concurrent use of psychotropic medications from doctor. Nagelkerke R square = 0.144. 243 cases included in the analysis.

[h] Model 2.1: adjusted for age, OMT-medication, psychosocial support, OMT medication collection method and concurrent use of alcohol and psychotropic medications from illicit sources. Nagelkerke R square = 0.303. 399 cases included in the analysis.

[i] Model 2.2: adjusted for BNX daily dose (continuous), age, psychosocial support, OMT medication collection method and concurrent use of alcohol and psychotropic medications from illicit sources. Nagelkerke R square = 0.311. 261 cases included in the analysis.

[j] Model 2.3: assessed BNX dose according to a low, medium or high dose classification, to support practical application of the results in addition to model 2.2. Adjusted for BNX daily dose (classified), age, psychosocial support, OMT medication collection method and concurrent use of alcohol and psychotropic medications from illicit sources. Nagelkerke R square = 0.302. 261 cases included in the analysis.

[k] Model 3.1: adjusted for OMT collection method, concurrent use of cannabis, other illicit drugs, psychotropic medications from doctor and from illicit sources. Nagelkerke R square = 0.224. 463 cases included in the analysis.

[l] IV use of other intoxicating drugs may include, for example, IV use of psychotropic medications, excluding OMT medications.

[m] Psychotropic medications, referred to as any pharmaceutical medications that mainly affect the central nervous system. In Finland, they can only be legally obtained with a prescription.

Table 6
Reasons for injecting own OMT medication and other intoxicating drugs.

Reasons for injecting own OMT medication, n = 87	n	Distribution between answers (%)	Share of respondents (%)
Some other reason	35	33%	40%
Injecting out of habit	34	32%	39%
OMT medication dose too low	27	26%	31%
Desire to become intoxicated	10	9%	12%
Total	106	100%	122%
Reasons for injecting any intoxicating drugs, n = 316			
Desire to become intoxicated	126	31%	40%
Some other reason	97	24%	31%
OMT medication dose too low	94	23%	30%
Injecting out of habit	86	21%	27%
Total	403	100%	128%

This study has demonstrated that over one third of respondents (36%) reported injecting intoxicating drugs in the six months prior to the study. Although this finding is in line with previous studies (Guichard et al., 2003; Roux et al., 2008a; Vidal-Trecan et al., 2003), it is nonetheless striking. Factors associated with IV use in general were concurrent use of illicit drugs, psychotropic medications from illicit sources and alcohol. In addition, perceived lack of psychosocial support was associated with more than twice as high odds for injecting. IV use was also found to decrease by the length of OMT (OR 0.997 per one month increase). This finding is consistent with previous studies (Gowing et al., 2011, 2006; Marsch, 1998; Mattick et al., 2009) suggesting that OMT may provide a degree of stability for those on the programme over a longer period of time.

Misuse of illicit OMT medications was found to be significantly more common than the injection of own OMT medication, with rates of 44% versus 16%, respectively. The prevalence of the injection of a patient's own medication is in concordance with previous studies (Degenhardt et al., 2009; Larance et al., 2011a, 2014; Winstock et al., 2008), as were the self-reported reasons behind this behaviour. According to the present study, the most common reasons stated for non-adherence were injecting 'out of habit' and 'OMT medication dose too low'. This finding supports previous studies that suggest that the search for pleasure is not the main reason for non-adherence (Moratti et al., 2010; Schuman-Olivier et al., 2010). Instead, factors such as the avoidance of withdrawal and self-treatment are more often cited.

Nevertheless, some of the factors associated with both non-adherence and misuse of illicit OMT medications were found to be similar. These were BNX as OMT medication and low daily doses of BNX. Among those receiving doses of less than 9.0 mg/day of the odds of injecting their own and illicit OMT medications were between two to five times higher as opposed to those patients receiving >15.9 mg/day doses. The more frequent IV use of BNX as compared to MET can be explained both by availability and ease of injecting, as BNX is often considered less difficult to inject than oral liquid MET (Guichard et al., 2003). BNX is more commonly prescribed in OMT in Finland and it is also possible to collect it unsupervised from a pharmacy. However, according to our study, receiving BNX unsupervised from a pharmacy was not associated with increased injection use. The association between sub-optimal dosing of BNX and its IV use has been described in previous studies (Comer et al., 2010; Mattick et al., 2014; Roux et al., 2008a; Vidal-Trecan et al., 2003) and the present study supports these findings. According to the EQUATOR project assessing the state of OMT across Europe there is a need for less pressure to reduce treatment doses among OMT patients (Dale-Perera et al., 2012). The EQUATOR study recommends the provision of adequate therapeutic doses for effective stabilization, and the current study seems to support these findings.

Interestingly, among those experiencing a lack of psychosocial support during treatment the odds for injecting illicit OMT medications was higher. In addition, concurrent use of psychotropic medications from illicit sources was associated with injecting of illicit OMT medications. Perceived lack of psychosocial support as a risk factor for injection has not been clearly described in earlier studies, although dissatisfaction with the treatment as a whole has been found to increase the risk of IV use (Roux et al., 2008b).There is also evidence to show that combining OMT with psychosocial support may improve treatment outcomes and reduce injecting (Chen et al., 2013; Schottenfeld et al., 2005; Wang et al., 2014). However, further studies are needed to explore the potential role of psychiatric comorbidities in non-adherence and IV use among OMT patients.

Concurrent misuse of other intoxicating drugs was declared by 67% of injecting OMT patients, which indicates that misuse of intoxicating drugs is a more notable problem than the injecting of OMT medications. However, this finding should not be generalized without caution, as in other countries the form of misuse in OMT may vary due to different kind of treatment settings. Self-reported reasons for misuse of intoxicating drugs differed from those for non-adherence as 'desire to become intoxicated' was the most common reason for misuse. In addition, factors associated with the injection of intoxicating drugs differed from those related to injection of OMT medications. For IV use of intoxicating drugs, associated factors were concurrent use of cannabis, illicit drugs and psychotropic medications from illicit sources and from doctor, which are all quite self-explanatory as risk factors as they are often used intravenously.

The present study revealed concurrent substance use to be relatively common among OMT patients. Only 12% of respondents reported using only their OMT medication during the past six months, while concurrent use of alcohol (58%), cannabis (38%), illicit drugs (25%) and psychotropic medications from a doctor (43%) and from illicit sources (34%) were more common. Assessing the results it should be noted that restrictions and guidelines regarding concurrent substance use during treatment vary between countries. However, these results indicate that more efforts should be made in order to decrease the use of illicit substances during OMT, given the correlation with injecting use which inevitably has several health-related risks.

Finally, a majority (52%) of respondents declared IV use to be problematic for them, although only one fifth reported needing help to stop injecting. This suggests that current support for addressing injection use during treatment is inadequate.

5. Conclusions

Summarizing the results of this study, we suggest that more attention is given to addressing concurrent injection use among OMT patients given the health related risks to the patient, the negative effects on treatment outcomes, and the costs of related complications. It is also important for public acceptance of OMT.

Although IV use might slowly decrease by the length of OMT more effort is needed to reduce this, especially in the early phases of treatment. Given that injecting is a highly conditioned behaviour, it is understandable that it is likely to continue for some time after treatment initiation. Tools to address the issue may include, for example, different kind of psychosocial and behavioural treatments such as contingency management or group therapy. However, more research is needed to determine the effectiveness of these kinds of interventions in terms of abstinence from injecting. According to the present study intoxicating drugs other than OMT medications account for the majority of substances used IV during OMT. Thus, we suggest other psychiatric comorbidities to be treated more effectively as part of OMT. IV use of OMT medications may be reduced by providing patients with an optimal, individually defined BNX dose. For patients who do not receive an adequate dose of BNX, IV use can be perceived as the only way to avoid withdrawal. Another measure that may reduce the injection of OMT medications is providing patients with more psychosocial support during treatment. In the light of the results, we suggest that IV use, to some extent, could be decreased by adjusting treatment-related factors such as optimal dosing and psychosocial support.

5.1. Strengths and limitations

This study has its limitations. Self-selection may have led to recruitment bias, which in this case would mean only highly motivated patients participating. However, the demographic profiles of respondents were found to be comparable with those of Finnish OMT patients in terms of treatment service types, regional distribution and OMT medication (Partanen et al., 2014). Another limitation is that the results are based on patients ' self-response, so it is possible that patients have under-reported some sensitive information regarding concurrent substance use and misuse in fear of punitive responses. However, all the participants were reassured that all the responses are used for research purposes only. The lack of information about psychiatric comorbidities can also be regarded as a weakness of this study.

The strength of this study is its satisfactory return rate (60%) and the comparability of the participants with the whole target group. Judging from the return rate, Finnish OMT patients seemed willing to report on their situation and participate in the improvement of treatment practices.

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Contributors

The original idea and the first draft of the study design and the questionnaire came from author Kaarlo Simojoki. The study protocol, design and questionnaire were finalized in cooperation with authors Kaarlo Simojoki, Hannu Alho and Elina Kotovirta. Author Elina Kotovirta updated the registry of the treatment units and sent out the questionnaires to the clinics and operated as a contact person. Author Essiina Launonen received and registered the completed questionnaires, managed the literature searches and wrote the first draft of the paper. Isla Wallace significantly contributed to the interpretation of data through writing and critical revision of the manuscript for important intellectual content. Statistical analyses were conducted by Essiina Launonen. All authors contributed in writing the manuscript and approved the final version.

Conflict of interest

Hannu Alho has received travel support from Reckit-Benckiser Pharmaceuticals and given expert lectures paid by Reckit-Benckiser pharmaceuticals.

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Essiina Launonen, Isla Wallace and Elina Kotovirta declare they have no conflict of interest.

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Appendix A. Supplementary data

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