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## Original Article

# Methadone-maintained patients in primary care have higher rates of chronic disease and multimorbidity, and use health services more intensively than matched controls

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### KEY MESSAGES:

- Methadone-maintained patients (MMPs) have more chronic disease and use health services more intensively than controls, independent of drug-related care.
- Methadone maintenance programme design should be cognisant of the broad range of services MMPs receive from their GP.
- Resource allocation and health policy must support GPs in providing such services.

### ABSTRACT

**Background:** Methadone maintenance treatment in primary care is cost-effective and improves outcomes for opiate-dependent patients. A more developed understanding of the evolving needs of this important cohort will facilitate further improvements in their integrated care within the community.

**Objectives:** The aim of this study was to compare the burden of chronic disease, multi-morbidity and intensity of health-service use between methadone-maintained patients (MMPs) and matched controls in primary care.

**Methods:** This is a retrospective matched case-control design. Data on chronic disease and health service use was collected in 13 computerized GP surgeries on 414 patients (207 MMPs and 207 controls). Twelve months of records were examined. MMPs were compared with controls matched by gender, age, socio-economic status (SES) and GP surgery.

**Results:** MMPs suffered more chronic disease (OR = 9.1, 95% CI: 5.4–15.1,  $P < 0.001$ ) and multi-morbidity (OR = 6.6, 95% CI: 4.3–10.2,  $P < 0.001$ ). They had higher rates of respiratory, psychiatric and infectious disease. MMPs of lower SES had more chronic disease than their peers (OR = 7.2, 95% CI: 2.4–22.0,  $P < 0.001$ ). MMPs attended the doctor more often with medical problems (OR = 15.4, 95% CI: 8.2–28.7,  $P < 0.001$ ), with a frequent requirement to have medical issues addressed during methadone-management visits. Their care generated more telephone calls (OR = 4.4, 95% CI: 2.8–6.8,  $P < 0.001$ ), investigations (OR = 1.8, 95% CI: 1.2–2.7,  $P = 0.003$ ), referrals (2.6, 95% CI: 1.7–4.0,  $P < 0.001$ ), emergency department visits (2.1, 95% CI: 1.3–3.6,  $P = 0.004$ ), outpatient attendances (2.3, 95% CI: 1.51–1.43,  $P < 0.001$ ) and hospital admissions (3.6, 95% CI: 1.6–8.1,  $P = 0.001$ ).

**Conclusion:** Correcting for routine methadone care and drug-related illnesses, MMPs had a higher burden of chronic disease and used both primary and secondary health services more intensively than matched controls.

**Keywords:** Methadone, primary health care, chronic disease, health care costs, health policy

### INTRODUCTION

The European Monitoring Centre for Drugs and Drug Addiction estimates the current prevalence of problem opioid use in Europe at 0.41% of the adult population (1). This equates to 1.4 million problem opioid users, of

whom 197 000 are in specialized treatment for opiate use. Ireland has the highest rate of problem opiate use in Europe at 7 cases per 1000 of the population, however, of these only 60% are currently in treatment (2). In view of this discrepancy, a recent review of the Irish Opioid Treatment Protocol advocates expansion of

community methadone services, backed by initiatives to foster greater GP participation in this area (3).

Methadone maintenance treatment (MMT) is effective in opioid dependence (4,5). Benefits include retention in treatment, reductions in heroin use and risk behaviours, improvements in health, social and criminal justice outcomes, and savings to society (6–11). Stable patients requiring MMT can be managed effectively in primary care settings (12–16).

A paucity of objective data exists concerning health service use among methadone-maintained patients (MMPs). Large quantitative studies, which explicitly examine chronic disease and multimorbidity in MMPs are also lacking in the international literature. Patients with a history of opiate dependence subjectively report poorer physical health than controls in self-rated health studies, and higher rates of mental illness and addiction (17–19). Prescribing patterns indicate that older MMPs (> 50 years) are more likely to have COPD and depression (20). A high prevalence of mood disorders and substance use has been identified among opioid addicts maintained on buprenorphine (21).

The aim of the current study is to compare the burden of chronic disease and multi-morbidity, and the rate of health-service utilization, between MMPs and matched controls in primary care. An Irish pilot study of modest sample size examined this area and found a trend towards higher levels of chronic disease and multi-morbidity, and higher levels of health service use among MMPs (22). The current study builds upon this preliminary work by obtaining a larger sample size and providing a greater breadth and depth of information about health service utilization by MMPs.

## METHODS

### *Design*

A matched case-control design of MMPs attending 13 primary care medical teaching practices in Dublin, Ireland was conducted. Ethical approval was received from the ethics committee of the Trinity College Dublin & Health Service Executive (TCD/HSE) Specialist Training Programme in General Practice.

### *Sample size*

A power calculation was conducted during the study design phase. Based on between-subjects differences using a standard *t*-test, it was estimated that a sample of 180 MMPs would be required for an 80% power to detect differences in rates of chronic disease and health service utilization versus controls. The final sample size exceeded this target.

### *Selection of practices, patients and matched controls*

The research network of the TCD/HSE GP Training Scheme consists of GP practices, which have undertaken a commitment to training GP registrars and facilitating research, widely distributed throughout the greater Dublin area. Within this network, 13 practices equipped with electronic patient records are involved in the provision of MMT. All 13 practices agreed to participate in this study, amounting to a pool of 230 MMPs. Patients were included if they attended the practice for both MMT and primary health care for at least one year prior to data collection. Sixteen MMPs did not meet these inclusion criteria. In total 414 patients were included in the final analyses; 207 MMPs, and 207 matched controls.

In Ireland MMT visits are free for all patients; otherwise a two-tiered system of payment exists for general medical care. Thirty-eight per cent of the population are entitled to free medical care under the General Medical Services scheme (GMS) based on means testing (23). The remainder pays directly for their medical care and are referred to as private patients. GMS eligibility was thus included in the matching process as a surrogate marker for socio-economic status. Patients were matched according to practice to mitigate possible effects of geographic variability in consulting habits and deprivation levels. MMPs and controls were also matched according to sex and age.

### *Data collection*

Data was collected from electronic patient medical records in participating practices by three researchers. Demographic details relating to age, sex and GMS eligibility were collected. Chronic disease data included number and type of chronic diseases, number of repeat medications and information regarding smoking, alcohol, non-opiate substance use and obesity. Health service utilization data included number and nature of GP and nurse consultations, telephone calls to and from the practice, referrals to and attendances at outpatient services, emergency department attendances, acute admissions, and out-of-hours GP service use. Multi-morbidity was defined as two or more chronic diseases (24).

The data collection template used by the research team was piloted to ensure consistency and clarity. Inter-rater reliability was tested with a random sample of 10 methadone patients and 10 matched controls resulting in a Cohen's Kappa co-efficient of 0.97, indicating excellent congruence amongst data extractors.

### *Data analysis*

Data was analysed using SPSS version 20. Basic descriptive statistics were used to analyse demographics. Chronic disease and health service utilization patterns

were investigated using independent samples *t*-tests, Pearson chi-squared tests, risk estimation, and binary logistic regression (25). Results were expressed as chi-squares with *P*-values, means with *t*- and *P*-values and odds ratios with 95% confidence intervals.

## RESULTS

### Demographics

There were no differences between MMPs and controls with respect to age (mean age = 39.2 years,  $t = -0.009$ ,  $P = 0.992$ ), gender or GMS Status ( $\chi^2 = 0.000$ ,  $P = 1.0$ , in both cases). Forty-three per cent of the sample was female, 57% were male; 16% were private patients, and 84% were GMS eligible. Mean dose of methadone among MMPs was 72.6 mgs (SD = 25.7 mgs), and mean duration of MMT was 8.2 years (SD = 4.0 years).

### Chronic disease and multi-morbidity

MMPs were more likely to have chronic diseases and multimorbidity than controls (Table 1). They had 2.0 chronic diseases on average, compared to 0.9 for controls, and 2.6 repeat medicines versus 1.4 for controls. MMPs were more likely to smoke, consume alcohol excessively and use potentially addictive substances such as benzodiazepines, Z-hypnotics, or non-opiate street drugs.

MMPs were more likely to have psychiatric illness, respiratory disease, and infectious disease (Table 2). MMPs were more likely to be obese. They had a lower mean number of cardiovascular diseases 0.06 (SD = 0.25) than controls 0.14 (SD = 0.5)  $t = -2.0$   $P = 0.04$ . No differences were found with respect to endocrine or 'other' chronic diseases.

### Health service utilization

MMPs had a mean of 32.4 primary care visits annually (of which 30.3 involved methadone assessments),

Table 2. Comparison of methadone maintained patients (MMPs,  $n = 207$ ) and controls ( $n = 207$ ) by chronic disease subtype.

	Odds ratio MMP/control (95%CI)	$\chi^2$	<i>P</i> -value
Psychiatric disease	6.1 (3.9–9.3)	72.4	< 0.001
Respiratory disease	3.3 (1.9–5.9)	18.5	< 0.001
Infectious disease	118.5 (28.8–489.9)	144.6	< 0.001
Obesity	1.7 (1.03–2.9)	4.3	0.038
Cardiovascular disease	0.5 (0.2–1.1)	2.8	0.1
Endocrine disease	1.5 (0.9–2.2)	2.5	0.1
Other chronic disease	0.8 (0.4–1.4)	0.8	0.4

compared to 3.4 visits for controls. To help delineate use of primary care services, we defined three categories of patient assessment, which were not mutually exclusive, i.e. 'medical,' 'nursing,' and 'methadone' assessments (Table 3). Overall, MMPs were more likely than controls to require medical assessments and nursing assessments, 87% of medical and 20% nursing assessments happened during a scheduled methadone consultation. Nursing involvement in MMT provision was low overall, averaging 2.4 nurse methadone visits per MMP annually.

MMPs were more likely to generate practice telephone calls, to have investigations organized by the practice and to require referral to OPD services by their GP. MMPs were more likely to attend hospital outpatient services, to attend the emergency department, and to be admitted to hospital. No difference was found in out-of-hours service use.

Hierarchical binary logistic regression was performed to assess the risk of chronic disease conferred by being an MMP, controlling for the effects of gender, age, GMS status, smoking status and drug-related infections. The model was statistically significant ( $\chi^2 53.1$ ,  $P < 0.001$ ). It explained between 30.0% and 41.1% of the variance in chronic disease, and correctly classified 74.8% of cases. Being an MMP carried an odds ratio of 7.3 (95% CI: 4.1–13.1) for chronic disease.

Table 1. Comparison of methadone maintained patients (MMPs,  $n = 207$ ) and controls ( $n = 207$ ) by presence of chronic diseases and related factors.

	Odds ratio MMP/control (95%CI)	$\chi^2$	<i>P</i> -value
Chronic disease	9.1 (5.4–15.1)	83.9	< 0.001
Chronic disease (excluding HIV/hepatitis B/hepatitis C)	4.2 (2.7–6.4)	44.8	< 0.001
Multimorbidity	6.6 (4.3–10.2)	79.1	< 0.001
Repeat meds	5.8 (3.7–8.9)	66.1	< 0.001
Smoking	4.8 (3.2–7.2)	57.3	< 0.001
Alcohol excess	2.9 (1.6–5.2)	14.1	< 0.001
Substance use	141.2 (63.3–315.3)	276.1	< 0.001

Table 3. Comparison of methadone maintained patients (MMPs,  $n = 207$ ) and controls ( $n = 207$ ) by health service use patterns.

	Odds ratio MMP/control (95%CI)	$\chi^2$	<i>P</i> -value
Medical assessment	15.4 (8.2–28.7)	100.3	< 0.001
Nursing assessment	5.9 (3.7–9.3)	62.9	< 0.001
Phone call	4.4 (2.8–6.8)	46.6	< 0.001
Investigation	1.8 (1.2–2.7)	8.8	0.003
Referral	2.6 (1.7–4.0)	21.3	< 0.001
Attended OPD	2.3 (1.51–1.43)	15.8	< 0.001
Attended emergency department	2.1 (1.3–3.6)	8.1	0.004
Acute hospital admission	3.6 (1.6–8.1)	10.4	0.001
Used out-of-hours service	1.09 (0.6–2.0)	0.09	0.767

Binary logistic regression was also performed within the MMP group alone. The model contained five independent variables (age, sex, GMS status, current dose of methadone, and smoking status). The full model containing all predictors was statistically significant ( $\chi^2 = 30.4$ ,  $P < 0.001$ ), explained between 14% and 27% of the variance in chronic disease, and correctly classified 89.4% of cases. Two of the independent variables made a unique statistically significant contribution to the model (GMS status and current dose of methadone). The strongest predictor of chronic disease was being a GMS patient, recording an odds ratio of 7.2 (95%CI: 2.4–22.0). A positive correlation between methadone dose and risk of chronic disease was found, represented by an odds ratio of 1.02. To express this differently, a 10 mg dose increase would incur a 1.2-fold increased risk of having one or more chronic diseases.

## DISCUSSION

### *Main Findings*

MMPs had a substantially higher burden of chronic disease and multi-morbidity than controls. This remained the case after removing drug-related infections from the analysis (Hepatitis B/C and HIV were disproportionately represented in the MMP group). Irrespective of the effect of gender, age, GMS status, smoking status and drug-related infections, being an MMP carried a 7-fold increased risk of having one or more chronic diseases compared to controls.

Respiratory, psychiatric and infectious disease (chiefly hepatitis C) accounted for most of the surplus disease burden among MMPs. MMPs who smoked had higher rates of respiratory disease than controls who smoked, suggesting increased cigarette consumption by MMPs, or an increased vulnerability to their damaging health effects.

The rate of GP attendance was similar for GMS and private MMPs, but the former were seven times more likely to exhibit chronic disease. GMS MMPs raised more medical problems per visit, saw the nurse more often, and had more investigations organized by the practice. This suggests that GMS MMPs are a sicker cohort of patients than private MMPs. This may be related to deprivation, as GMS eligibility is a surrogate marker for socio-economic status. Alternatively, private MMPs may represent a subgroup deriving greater than average functional benefit from MMT, reflected by relative increases in both wealth (hence GMS ineligibility) and health (hence less chronic disease).

MMPs had higher levels of health service utilization at a practice and secondary care level. They generated a higher workload for GPs' and increased administrative tasks for primary care services. They spent more time in emergency departments, inpatient beds and outpatient clinics. These findings imply that MMPs generate

increased costs for the health service above and beyond the known costs of MMT.

### *Strengths and limitations*

This study involved a diverse sample of 13 methadone-prescribing GP practices across urban and suburban Dublin. Methadone patients and controls were well matched. A high level of inter-rater reliability was achieved between data collectors. Given the depth of data collected, and the timescale examined, the sample size of 414 patients is considered a major strength of this study.

As this study involved chart review, the quality of the final data is dependent on the completeness of patient data-recording in participating practices. Data was extracted from electronic patient records maintained in well-established, fully computerized teaching practices. Each consultation and all correspondence were read and analysed individually. This approach is thought to provide more accurate prevalence data than other strategies, such as questionnaires or analysis of administrative data at a population level (26,27).

It is possible that certain underestimations occurred, although these predominantly affected the methadone group. Specialist medicines prescribed through outpatient clinics were not found to be systematically documented in the GP chart; thus only regular medications prescribed in the GP practices were analysed. Examples of medications, which were not included, were antiviral regimes for patients suffering from HIV or hepatitis C, anti-epileptic medications, and certain specialist psychiatric medications. Outpatient attendance rates were calculated from outpatient correspondence scanned into the patient record. Delays in such correspondence are common in the Irish health care system, and on certain occasions, correspondence does not occur. Thus, outpatient attendances for both groups of patients may be underestimated.

The opioid treatment protocol requires MMPs to attend their GP regularly for methadone visits, which could theoretically increase the likelihood of disease documentation in their electronic records. However, the opposite effect was empirically observed during data collection. Medical problems among MMPs tended to arise as unanticipated 'door-handle symptoms' during time-pressured, protocol-driven methadone appointments, rather than during a dedicated medical appointment as in the case of controls. Accordingly, non-methadone-related documentation in MMT visits tended to suffer in terms of detail.

### *Comparison with existing literature*

Observed rates of hepatitis C (51%), smoking (69%) and alcohol dependence (23%) among MMPs were

comparable to international studies, suggesting the MMP cohort in this study is a representative sample (1,28,29). Our findings of increased rates of respiratory disease and mental illness among MMPs are mirrored in the international literature (20,21,30). Little international data appears to exist in relation to health service use among MMPs.

### Recommendations

The results of this study suggest that provision of health care to MMPs should be approached in a holistic fashion, aiming to integrate addiction-related care with management of overall health needs. Care must also be systematic and structured to assist the manifest need for intensive risk factor reduction and high quality chronic disease management in this group. The roll-out of a national methadone electronic care plan is to be recommended, where such a framework is absent. Brief targeted interventions for smoking and alcohol have been shown to be effective, and are to be particularly recommended in the routine care of MMPs (28). Systematic coding of chronic disease is to be encouraged, to allow for effective risk factor assessment and management. These recommendations reflect the findings of the recent Irish review of the opioid treatment protocol (3).

This study identified the practice nurse as an under-used resource in the management of MMPs in Ireland. We recommend an increased role for the practice nurse in provision of methadone related care, coupled with greater involvement of the multidisciplinary primary care team in general.

Appropriate incentives for GPs to become formally trained in the provision of methadone treatment are necessary to ensure the continued viability of community-based care for MMPs. Any formal review of remuneration for GP methadone prescribers must take into account the special nature of the 'methadone consultation,' which frequently involves both protocol-driven care of drug dependence, and simultaneous management of complex chronic disease and multi-morbidity. This is accompanied by a disproportionate increase in both consultation workload and complexity for the primary care physician and increased organizational pressures for the practice, which will accelerate, as MMPs age further.

### Conclusion

After correcting for routine methadone care and drug-related illnesses, MMPs attend the GP more frequently and have a higher burden of complex medical disease than matched controls. This must be reflected in health care policy, which may otherwise focus on drug-related issues alone.

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### REFERENCES

1. European Monitoring Centre for Drugs and Drug Addiction. European Drug Report 2013: Trends and developments. Lisbon: EMCDDA, Publications office of the European Union; 2013. pp. 38–42.
2. European Monitoring Centre for Drugs and Drug Addiction. The state of the drugs problem in Europe. Annual Report 2012. Luxembourg: EMCDDA, Publications Office of the European Union; 2012. pp. 72–6.
3. Farrell M, Barry J. The introduction of the opioid treatment protocol. Dublin: Department of Health, Health Service Executive; 2010. pp. 33–6.
4. World Health Organization. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. Geneva: World Health Organization, Department of Mental Health and Substance Abuse; 2009. pp. 31.
5. World Health Organization. Proposal for the inclusion of methadone in the WHO model list of essential medicines. Geneva: World Health Organization, Department of Mental Health and Substance Use; 2004. pp. 22.
6. Connock M, Juarez-Garcia A, Jowett S, Frew E, Liu Z, Taylor RJ, et al. Methadone and buprenorphine for the management of opioid dependence: A systematic review and economic evaluation. *Health Technol Assess.* 2007;11:1–171.
7. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst Rev.* 2011;CD004145.
8. Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De Angelis D, et al. Survival and cessation in injecting drug users: Prospective observational study of outcomes and effect of opiate substitution treatment. *Br Med J.* 2010;341:c3172.
9. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev.* 2009;CD002209.
10. National Treatment Agency for Substance Misuse. Why invest? How drug treatment and recovery services work for individuals, communities and society. London: NHS, National Treatment Agency for Substance Misuse; 2011. pp. 7.
11. Salamina G, Diecidue R, Vigna-Taglianti F, Jarre P, Schifano P, Bargagli AM, et al. Effectiveness of therapies for heroin addiction in retaining patients in treatment: Results from the VEdette study. *Subst Use Misuse* 2010;45:2076–92.
12. Martin E, Canavan A, Butler R. A decade of caring for drug users entirely within general practice. *Br J Gen Pract.* 1998;48: 1679–82.
13. Keen J, Rowse G, Mathers N, Campbell M, Seivewright N. Can methadone maintenance for heroin-dependent patients retained

- in general practice reduce criminal conviction rates and time spent in prison? *Br J Gen Pract.* 2000;50:48–9.
14. Keen J, Oliver P, Mathers N. Methadone maintenance treatment can be provided in a primary care setting without increasing methadone-related mortality: The Sheffield experience 1997–2000. *Br J Gen Pract.* 2002;52:387–9.
  15. Keenan E, Barry J. Managing drug misuse in general practice. Republic of Ireland has set up scheme to regulate methadone prescribing by GPs. *Br Med J.* 1999;319:1497.
  16. Gossop M, Marsden J, Stewart D, Lehmann P, Strang J. Methadone treatment practices and outcome for opiate addicts treated in drug clinics and in general practice: Results from the national treatment outcome research study. *Br J Gen Pract.* 1999; 49:31–4.
  17. Gossop M, Marsden J, Stewart D, Lehmann P, Edwards C, Wilson A, et al. Substance use, health and social problems of service users at 54 drug treatment agencies. Intake data from the national treatment outcome research study. *Br J Psychiatry* 1998; 173:166–71.
  18. Rosen D, Smith ML, Reynolds CF 3rd. The prevalence of mental and physical health disorders among older methadone patients. *Am J Geriatr Psychiatry* 2008;16:488–97.
  19. Ryan CF, White JM. Health status at entry to methadone maintenance treatment using the SF-36 health survey questionnaire. *Addiction* 1996;91:39–45.
  20. Maruyama A, Macdonald S, Borycki E, Zhao J. Hypertension, chronic obstructive pulmonary disease, diabetes and depression among older methadone maintenance patients in British Columbia. *Drug Alcohol Rev.* 2013;32:412–8.
  21. Savant JD, Barry DT, Cutter CJ, Joy MT, Dinh A, Schottenfeld RS, et al. Prevalence of mood and substance use disorders among patients seeking primary care office-based buprenorphine/naloxone treatment. *Drug Alcohol Depend.* 2013;127:243–7.
  22. Cullen W, O'Brien S, O'Carroll A, O'Kelly FD, Bury G. Chronic illness and multimorbidity among problem drug users: A comparative cross sectional pilot study in primary care. *BMC Fam Pract.* 2009;10:25.
  23. Primary Care Reimbursement Service. Statistical analysis of claims and payments 2010. Dublin: Department of Health, Health Service Executive; 2011. pp. 42.
  24. van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: Prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol.* 1998;51:367–75.
  25. Tabachnick BG, Fidell LS. Logistic regression. In: *Using multivariate statistics*. 5th ed. Boston: Allyn & Bacon; 2007. pp. 437–504.
  26. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. *Ann Fam Med.* 2005;3:223–8.
  27. Fortin M, Hudon C, Haggerty J, Akker M, Almirall J. Prevalence estimates of multimorbidity: A comparative study of two sources. *BMC Health Serv Res.* 2010;10:111.
  28. Darker CD, Sweeney BP, El Hassan HO, Smyth BP, Ivers JH, Barry JM. Brief interventions are effective in reducing alcohol consumption in opiate-dependent methadone-maintained patients: Results from an implementation study. *Drug Alcohol Rev.* 2012;31:348–56.
  29. Nahvi S, Richter K, Li X, Modali L, Arnsten J. Cigarette smoking and interest in quitting in methadone maintenance patients. *Addict Behav.* 2006;31:2127–34.
  30. Palmer F, Jaffray M, Moffat MA, Matheson C, McLernon DJ, Coutts A, et al. Prevalence of common chronic respiratory diseases in drug misusers: A cohort study. *Prim Care Respir J.* 2012;21:377–83.