Opiate Addiction and Overdose: Experiences, Attitudes and Appetite for Community Naloxone Provision.

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ABSTRACT

Background: Over 200 overdose deaths occur annually in Ireland. Overdose prevention and management, including naloxone provision, should be a priority for healthcare services. Naloxone is an effective overdose treatment and is now being considered for wider lay use.

Aim: To establish General Practitioners’ (GP) views and experiences of opioid addiction, overdose care and naloxone provision.

Design: An anonymous postal survey.

Setting: GPs affiliated with Academic General Practice, University College Dublin, Ireland.

Method: We invited 714 GPs to complete an anonymous postal survey. Results were compared with a parallel GP trainee survey.

Results: A total of 448/714 (62.7%) responded. Approximate thirds were urban, rural and mixed-area GPs. Over 75% of GPs had patients who used illicit opiates, and 25% prescribed methadone. Two thirds of GPs were in favour of a project to increase naloxone availability in the community; almost one third would take part in such a scheme. Intranasal naloxone was much preferred to single (p<0.001) or multiple dose (p<0.001) intramuscular naloxone. Few GPs objected to wider naloxone availability.

Conclusion: GPs report extensive contact with people who have opioid use disorders but provide limited opiate agonist treatment. They support wider availability of naloxone and would participate in its expansion. Development and evaluation of an implementation strategy to support GP-based distribution is urgently needed.

How this fits in: The role of general practice in opiate overdose prevention and naloxone distribution has yet to be established. This study suggests that GPs commonly provide healthcare for patients with opiate use disorder and support naloxone distribution within the community.

Keywords: Substance-related disorders, Medical Education, Family Practice, Overdose Education and Naloxone Distribution, Methadone
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INTRODUCTION

Overdose continues to drive mortality among people with opiate use disorders worldwide (1). There are approximately 1.3 million people with opiate use disorder in Europe (2), with Ireland having one of the highest rates of all European countries (3). Irish general practitioners (GPs) play a key role in providing opiate agonist treatment (primarily methadone), and have frequent contact with people who use opiates (4, 5). Ireland experiences a high rate of fatal drug overdose, with many cases involving people who have an opiate use disorder. For instance in 2013, more people died due to opiate overdose than all those who died in road traffic accidents (249 vs 190) (6, 7). Overdose prevention and management have been recognised as key issues for GPs who care for patients with opiate use disorders (8).

Naloxone is an effective opiate antagonist that can be distributed in the community to treat opiate overdose (9); however, to date, its use in Ireland has largely been limited to doctors, nurses and paramedics. The World Health Organisation recommends that people likely to witness an opiate overdose should have access to naloxone and be instructed in its administration (10). Coordinated take-home naloxone schemes have been available in Scotland and Wales since 2011 (11); however, despite a significant problem with opiate-related deaths, Ireland has lagged behind its neighbours on this issue (12). Policy initiatives to allow lay access to naloxone are being developed (13) but the role of general practice in such initiatives has not been established, despite frequent contact with people who use opiates. Previous work by this group has explored the experience and views of trainee GPs, in relation to opiate addiction (14). The perspective of established Irish GPs is also highly relevant, but
has not previously been documented. Ultimately this group determine the policies and procedures of their own practices and influence the education and training of future GPs. The purpose of this study is to examine the views and experiences of Irish GPs toward opiate addiction and overdose, to inform policy and practice in this area.

METHODS

We contacted all GPs (N=714) affiliated with the Department of Academic General Practice, University College Dublin (UCD) by mail in October 2015 and invited them to participate in a paper-based, anonymous postal survey. A reminder letter was sent three weeks after the initial mailing. The cohort of GPs surveyed maintain links with UCD through their roles as undergraduate tutors in general practice, or by involvement in UCD general practice research projects (15). This sample of GPs represents a significant cross section of Ireland’s total resource of approximately 2900 individual GPs (16). The results of this study are compared to selected results from an earlier study involving general practice trainees that is reported elsewhere (14). The UCD Human Research Ethics Committee granted exemption from full ethical review prior to the commencement of data collection.

Our study instrument was informed by previous studies concerning the epidemiology of opiate overdose and a pilot evaluation of an educational session to support overdose prevention and naloxone distribution by GP trainees (17, 18). The study instrument was an adapted version of a tool already used to examine the views and experiences of Irish GP trainees toward opiate addiction and overdose. It included sections on demographics and practice profile, as well as questions relating to experience of and attitudes toward problem opiate use, overdose and naloxone treatment. Data was analysed using Microsoft Excel (2013) and IBM SPSS (Version 20). Means and proportions are reported as appropriate. Chi-
square tests for association were performed to evaluate relationships between categorical variables, and a Friedman test with post hoc Wilcoxon Signed Ranks tests carried out to assess differences in ranked naloxone route preferences. Not all questions were completed by all participants and denominator data is reported where relevant.

RESULTS

Our survey of GPs achieved a response rate of 62.7% (448/714) which included GPs from all four provinces of Ireland. The majority of GPs were male (64.8%, 287/443), worked full time (88.4%, 390/441) and were either a principal or partner at their practice (93.6%, 412/440). Approximate thirds worked in rural (29.1%, 127/437), urban (38.2%, 167/437) or mixed (32.7%, 143/437) settings. Respondents represented an experienced cohort of GPs with only four per cent (18/445) reporting fewer than five years’ experience and the majority (61.3%, 273/445) reporting more than 20 years’ experience. GPs reported a median of 3500 patients per individual practice with a range of 200 to 60,000. Almost half of GPs provided postgraduate training within their practice setting (47.8%, 211/441). Tables 1-3 illustrate the key data obtained from this survey, and, for the purposes of comparison, data obtained from our earlier survey of GP trainees (14).

In excess of 90% of the responding GPs indicated that they provided services to GMS patients who comprised a mean of 42.6 % of their patient mix. In Ireland, General Medical Services (GMS) patients are the cohort for whom the state finances primary care on the basis of need and financial circumstance. GMS eligible patients represent approximately 35% of the total population, with this figure set to rise (19). Three quarters of respondents provided medical care for patients known to have an opiate use disorder, while approximately one third
were aware that a patient of their practice had experienced an opiate overdose in the past. Despite these observations only one quarter of GPs reported that their practice prescribed the opiate agonist therapy methadone, although one third had completed the pre-requisite training to provide this treatment (Irish College of General Practitioners, Substance Misuse Management Course).

Just over one third of GP respondents reported that they had used naloxone to treat opiate overdose in the past, and in 44.2% of cases this was outside the hospital setting. Two thirds of GPs were in favour of a planned initiative to increase the availability of naloxone by allowing access to trained lay bystanders (13). Almost a third reported that they would consider taking part in such a project, while a significant proportion (29.8%, 132/443) remained undecided.

For the 110 GPs prescribing methadone versus the 331 GPs who do not, methadone prescribers were more likely to work in an urban area (63% vs 30% p<0.001), have patients using illicit opiates (93% vs. 70%, p<0.001) and be willing to take part in a naloxone distribution project (43% vs 28% p<0.01). Regarding whether a GP was in favour of wider naloxone distribution, there was no significant difference between those prescribing and those not prescribing methadone (74% vs 64% p>0.05). Intranasal naloxone was the preferred route for lay delivery of naloxone (mean rank = 1.34), when ranked from first (1) to fourth (4) preference, and a large majority of GPs who responded (81.7% 331/405) reported it as their first preference. This was significantly higher than formulations of naloxone with an injectable single dose (mean = 2.35, p<0.001) or an injectable multi-dose (mean = 3.22, p<0.001), with only 12.8% (47/367) and 3.3% (11/338) respectively of those who replied expressing these as their first preference.
DISCUSSION

Summary

Our study captured a cross-section of GPs in Ireland involved in undergraduate education and postgraduate training. This cohort represents an experienced, predominantly male and primarily full-time group of GPs. In contrast, the GP trainees from our earlier study were mostly younger and female. It is possible that these contrasts reflect shifting patterns in the demographics of Irish general practice. Nevertheless, both fully qualified GPs and trainee GPs reported significant experience of patients with opiate use disorders.

While both qualified and trainee GPs reported experience of naloxone use, significantly more trainees had used naloxone to treat opiate overdose; however, this was more frequently in the hospital setting. Although patients who use illicit opiates were commonly encountered in the general practice setting, only a minority of general practices provided methadone treatment and only a small minority of GP training practices provide exposure to this essential opiate agonist treatment (20). A significant proportion of GPs and GP trainees were supportive of the wider distribution of naloxone in the community. Smaller, but nonetheless significant proportions were willing to take part in that distribution; however, among GPs, a willingness to take part in distribution of naloxone was predominantly in practices already prescribing methadone. While the difference between being supportive and being willing to take part may reflect the well documented current demands already placed on busy GPs (21), other barriers to participation may exist but have not been elicited in this study.
Strengths and limitations

Although this study involved a substantial cross section of Irish general practice, the fact that it involved a targeted sample of GPs affiliated to a major academic centre may limit its representativeness of the wider GP population. The survey instrument used for this study and our earlier study of GP trainees was developed specifically for these purposes and has not been formally assessed in terms of reliability and validity, although it was piloted at one practice site and revised prior to large-scale use. While this study achieved a response rate of 63%, it is possible that non-responding GPs may have differed in their experience and attitudes toward opiate addiction and overdose, potentially skewing results. Despite the above limitations, this study is helpful in identifying a sub-population of GPs who provide care to patients with opiate addiction, who see a benefit in wider naloxone distribution and who support distribution initiatives.

This study offers an important perspective concerning overdose response and will be helpful in informing future policy initiatives. Despite this observation, the findings must be viewed as representing the clinician’s perspective, and one that will need to be balanced with a pragmatic, real-world, community understanding. In reality, when an individual suffers an overdose, it will be the reaction of the surrounding bystanders - whether peers, family members or other individuals - that will be crucial to survival. Research from Ireland has demonstrated high levels of experience of witnessed drug overdose among people with opiate use disorder (22). Previous studies have shown a clear willingness to intervene on the part of those who witness opiate overdose (23, 24). Any planned initiative for GP naloxone provision will need to integrate the clinician’s perspective with a pragmatic understanding of
the real-world challenge of lay response to witnessed opiate overdose in Ireland. In turn, however, GPs may be well placed to recruit and support family members or friends of drugs users as ‘naloxone rescuers’, given their local knowledge, continuing relationships with patients and families and potential to identify drug users at higher risk.

Comparison with existing literature

Previous research has suggested that GPs express a negative view toward working with substance users (25). This observation was not supported by our research where both GPs and GP trainees demonstrated encouraging support for this type of work via community naloxone provision. Although the relevance of this issue for general practice has traditionally received little attention, there is some evidence that GPs elsewhere support the concept (26-28). Research in Canada has demonstrated that family physicians considered naloxone provision to be a potentially effective and lifesaving intervention within their practice, and suggested that the community medicine setting may offer advantages for patients in terms of ease of access and capacity for follow-up (28). Further research from Scotland suggested that, while some GPs perceived community naloxone provision to be more appropriate for specialist drug services, GPs did express tentative willingness to be involved (27). However, this important study did highlight concerns expressed among GPs regarding training, knowledge and the level of experience necessary to enable participation. The issue of medico-legal uncertainty regarding innovative schemes has also been raised as a further barrier to community naloxone provision (28, 29). These issues, among others were not addressed in our study and will need to be explored further elsewhere.

Our research finding that only a minority of general practices and an even smaller percentage of GP training practices provide the opiate agonist treatment methadone,
compares poorly with data from other countries. In Scotland, 44% of GPs were providing methadone in 2008 (30), while in some regions of Switzerland, GPs are known to provide the majority of opiate agonist treatment (31). Research from England and Wales suggested that over time an increasing number of GPs have become involved in opiate agonist provision. However, in keeping with the findings from our study, more patients with opiate use disorder were seen for general medical care than were prescribed methadone by their GP (32). This observation may suggest a discrepancy between the exposure to people with an opiate use disorder in general practice and the discipline’s capacity or willingness to provide opiate agonist treatment. An external review of the Irish Methadone Treatment Protocol recommended that all doctors completing GP professional training should have demonstrable competence to provide methadone treatment (33). Our findings suggest that this 2010 recommendation has not been achieved.

The GPs in our study expressed a clear preference for an intranasal (IN) means of naloxone delivery in the community. Intranasal naloxone has been used internationally by pre-hospital emergency services for some time (34) and is currently an option available to statutory emergency services in Ireland (35). There is evidence of its efficacy from other jurisdictions compared with naloxone delivered intramuscularly (36, 37). Interestingly, a recent editorial has questioned the expansion of unlicensed improvised intranasal naloxone kit use in many jurisdictions (38). The authors, who acknowledge a conflict of interest due to involvement in the development of such a product, caution that despite a lack of pharmacokinetic and bioavailability data concerning naloxone delivered by this route, IN naloxone has been incorporated into standard clinical practice in numerous regions as an off-label route. Of note, the United States Food and Drug Administration (FDA) has recently approved an IN naloxone product suitable for community use (39). This development may
help allay concern and pave the way for wider naloxone availability in the community setting.

Implications for future research and clinical practice

Three important conclusions can be drawn from the findings of our study. Firstly, significant differences emerge between the quarter of GPs whose practices prescribe opiate agonist treatment and the three quarters who do not. GPs who prescribed methadone appear to be more willing to participate in an initiative to increase access to naloxone in the community, and as such would be a logical cohort to pilot a take-home naloxone programme in primary care. Previous research in Ireland has identified the high-risk geographical locations where overdose occurs most frequently (17). GPs who are working in these areas and are already prescribing methadone could be targeted in the first instance. The relatively low level of involvement of GPs in opiate agonist treatment and their concentration in urban areas in the east of the country, contrasts sharply with the well-reported increase in opiate dependence in all areas of the country (40). Efforts to engage larger numbers of GPs in poorly served parts of the country, are also essential.

Secondly, the observation that a majority of training practices do not provide exposure to opiate agonist treatment is likely to be a major limiting factor in the future development of competency in this area. Currently, GP trainees are unlikely to have acquired the necessary training and experience to enable participation in either opiate agonist treatment
or overdose prevention in general practice. This issue should be addressed as a matter of urgency.

Finally, GPs express a clear preference for intranasal naloxone. To date, there is no licenced preparation of intranasal naloxone available in Ireland, however as previously mentioned the US FDA has recently approved a bespoke intranasal product (39). Given the wide prevalence of problem opiate use and lethal potential for overdose, an appropriate take-home intranasal product and primary-care training package should be developed as a matter of urgency.
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Ethics committee

Competing interests
The authors have stated that there are none.

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Tables 1-3 Opiate overdose in Irish General Practice: demographics, experience and attitudes.

**Table 1: Comparison of GPs and GP Trainees- Demographics**

<table>
<thead>
<tr>
<th></th>
<th>GP Trainee n (%) n = 136</th>
<th>GP n (%) n = 448</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>30/128 (23.4%)</td>
<td>287/443 (64.8%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>≤40 years</td>
<td>125/128 (97.7%)</td>
<td>68/445 (15.3%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>41-50 years</td>
<td>3/128 (2.3%)</td>
<td>104/445 (23.4%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>0/128 (0%)</td>
<td>273/445 (61.3%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Proportion of trainees in general practice setting</td>
<td>88/129 (68.2%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table 2: Comparison of GPs and GP Trainees- Experience of Addiction and Overdose**

<table>
<thead>
<tr>
<th></th>
<th>GP Trainee n (%) n = 136</th>
<th>GP n (%) n = 448</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice provides care for patients who use illicit opiates</td>
<td>63/88 (71.6%)</td>
<td>324/430 (75.3%)</td>
<td>0.775</td>
</tr>
<tr>
<td>Practice prescribes methadone</td>
<td>15/88 (17.1%)</td>
<td>110/441 (24.9%)</td>
<td>0.148</td>
</tr>
<tr>
<td>Patient of practice had OD</td>
<td>8/88 (9.1%)</td>
<td>148/430 (34.4%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Used naloxone for OD</td>
<td>83/132 (62.9%)</td>
<td>155/446 (34.8%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Of which, in hospital</td>
<td>80/82 (97.6%)</td>
<td>87/152 (57.2%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Of which, in general practice</td>
<td>1/82 (1.2%)</td>
<td>21/152 (13.8%)</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

**Table 3: Comparison of GPs and GP Trainees- Attitudes toward Naloxone**

<table>
<thead>
<tr>
<th></th>
<th>GP Trainee n (%) n = 136</th>
<th>GP n (%) n = 448</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In favour of lay naloxone project</td>
<td>84/132 (63.6%)</td>
<td>292/442 (66.1%)</td>
<td>0.741</td>
</tr>
<tr>
<td>Would take part in project</td>
<td>71/123 (57.7%)</td>
<td>140/443 (31.6%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>1st preference single use injectable naloxone</td>
<td>26/123 (21.1%)</td>
<td>47/367 (12.8%)</td>
<td>0.035*</td>
</tr>
<tr>
<td>1st preference multi-dose injectable naloxone</td>
<td>23/117 (19.7%)</td>
<td>11/338 (3.3%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>1st preference intranasal naloxone</td>
<td>73/124 (58.9%)</td>
<td>331/405 (81.7%)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

All tests are 2x2 chi-square tests for association, as the variables are categorical and independent. Missing values were excluded.