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PATIENT VIEWS OF OPIOID PHARMACOTHERAPY BIO-DELIVERY SYSTEMS: QUALITATIVE STUDY TO ASSIST TREATMENT DECISION MAKING

Joanne Neale[1, 2] **(Corresponding author)**
Qualifications: BA (Hons); MA; DPhil; CQSW
Tel: +44(207) 848 0835; Mobile: +44(7876) 641399
Email: joanne.neale@kcl.ac.uk

Charlotte N. E. Tompkins[1]
Qualifications: BA (Hons); MSc; PhD
Tel: +44(207) 848 0727
Email: charlotte.tompkins@kcl.ac.uk

Rebecca McDonald[1]
Qualifications: Dipl-Psych; PhD
Tel: +44(207) 848 0727
Email: rebecca.s.mcdonald@kcl.ac.uk

John Strang[1, 2]
Qualifications: MBBS; FRCPsych; MD; F Ac Med Sci
Tel: +44(207) 848 0727
Email: john.strang@kcl.ac.uk

[1]King's College London, National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, 4 Windsor Walk, London, SE5 8AF, United Kingdom.

[2] South London and Maudsley NHS Foundation Trust, Bethlem Royal Hospital, Monks Orchard Road, Beckenham, Kent, BR3 3BX, United Kingdom.

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ABSTRACT

The technology for delivering opioid pharmacotherapy (OPT) is expanding. It is important to know what OPT patients think of these developments, and to find ways of enabling patients and clinicians to make informed decisions about which bio-delivery system to choose. We explored the views of current and former OPT patients with a history of heroin use to identify factors influencing their preferences regarding routes of OPT administration. Data were generated via seven focus groups conducted in London, United Kingdom. Participants (n=44) considered standard bio-delivery systems (liquid/linctus, tablet, injectables), emergent systems (implants, depot injections), and a hypothetical system (nasal sprays). Groups were audio-recorded, transcribed verbatim, coded using qualitative software, and analyzed inductively via Iterative Categorization. Participants were cautious of, but willing to consider, new ways of receiving OPT and they welcomed having more choice. Their preferences and decision-making processes were influenced by nine interconnected factors: 1. personal dislike of particular bio-delivery systems; 2. desired feelings following OPT administration; 3. perceived effectiveness of OPT bio-delivery systems; 4. concerns about side effects; 5. ability to control the OPT; 6. impact on daily lives; 7. concerns about OPT-related stigma; 8. need for psychosocial support; and 9. personal treatment goals. This complexity may make it difficult for patients and clinicians to evaluate the pros and cons of the expanding array of OPT bio-delivery systems and to arrive at clear conclusions. We therefore use the findings to

construct a checklist that may facilitate discussions with patients when decisions about OPT need to be made.

KEYWORDS

Opioid pharmacotherapy (OPT); heroin users; treatment; decision making; qualitative

PUBLIC SIGNIFICANCE STATEMENT

This study indicates that people who need pharmacological treatment for opioid use disorder welcome having increased choice about how they receive their medication (including liquid/linctus, tablets, implants and depot injections), but their preferences depend on a complex range of interconnected factors. A simple checklist is provided to help clinicians and their patients jointly consider and decide on the best way of receiving medication for opioid use disorder when faced with an increasing number of options.

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Preliminary data from the study were presented at the 19th International Society of Addiction Medicine (ISAM) annual conference in Abu Dhabi (October 2017). A paper from the same data set and by the same authors: "Implants and depot injections for treating opioid dependence: qualitative study of people who use or have used heroin" has been accepted for publication in the journal *Drug and Alcohol Dependence.* A paper from a linked data set has been published in the journal *Addiction*: Neale, J., Tompkins, C., McDonald, R., & Strang, J. (2018). "Improving recruitment to pharmacological trials for illicit opioid use: findings from a qualitative focus group study". *Addiction*. Early online doi: 10.1111/add.14163.

JS conceived of the study. JN and JS designed the study. CNET and RM conducted the focus groups. CNET and JN analysed the data. JN prepared the first draft of the paper and revised it following comments from JS, CNET and RM. All authors have approved the final article.

JN receives honoraria and some expenses from *Addiction* journal in her role as Commissioning Editor and Senior Qualitative Editor. JS is a researcher and clinician who has worked with a range of types of treatment and rehabilitation service providers. He has also

worked with a range of governmental and non-governmental organizations, and with pharmaceutical companies to seek to identify new or improved treatments from whom he and his employer (King's College London) have received honoraria, travel costs and/or consultancy payments. This includes work with, during past 3 years, Martindale, Indivior, Mundipharma, Braeburn/Camurus and trial medication supply from iGen and from Camurus. His employer (King's College London) has registered intellectual property on a novel buccal naloxone formulation and he has also been named in a patent registration by a pharmaceutical company regarding a concentrated nasal naloxone spray. For a fuller account, see JS's web-page at http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx RM has undertaken an unpaid student industry placement with Mundipharma Research Ltd. RM and JS have both worked as consultants for the United Nations Office on Drugs and Crime (UNODC). Subsequent to the submission of this article, JN, JS and CNET received a research grant from Camurus AB to undertake further qualitative research exploring long-acting buprenorphine.

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PATIENT VIEWS OF OPIOID PHARMACOTHERAPY BIO-DELIVERY SYSTEMS: QUALITATIVE STUDY TO ASSIST TREATMENT DECISION MAKING

BACKGROUND

Opioid pharmacotherapy (OPT) is an effective and evidence-based approach to treating opioid dependence (Bell, 2012; NICE, 2007; SAMHSA, 2018; WHO/UNODC/UNAIDS, 2004). There is an extensive literature evaluating and comparing different types of OPT, but studies are largely confined to analyses of detoxification versus maintenance, and assessments of specific medicines, such as methadone, buprenorphine, lofexidine, levomethadyl acetate (LAAM), and naltrexone (Kleber, 2007; Mattick et al., 2014; Stotts et al., 2009). Whilst most of this literature is based on biomedical or clinical studies, social scientists have used qualitative and quantitative methods to capture both treatment provider perspectives (e.g. Berg et al., 2009; Eversman, 2010; Larance et al., 2011; Lin et al., 2010; Philbin & Zhang, 2010) and patient perspectives (e.g. Anstice et al., 2009; Conner & Rosen, 2008; Harris & McElrath, 2012; Lin et al., 2011; Nyamathi et al., 2007; Treloar et al., 2007). For example, numerous qualitative studies have used one-to-one interviews and focus groups to provide in-depth insights into patients' views and experiences of accessing and receiving methadone, the most frequently prescribed treatment for opioid use disorder globally (e.g. Jones et al., 1994; Koester et al., 1999; Murphy & Irwin, 1992; Neale, 1998, 1999a,b; Sohler et al., 2013).

Despite this wide literature, there has been a lack of research exploring patient and provider views of the bio-delivery systems by which OPT medications are administered. This likely relates to the fact that historically almost all OPT has been consumed in liquid/linctus or tablet formulations, apart from rare instances of countries or clinicians providing injectable OPT for a minority of patients who have repeatedly failed to benefit from oral delivery systems (Ferri et al., 2011; Strang et al., 2015; Zador, 2001). Furthermore, many service providers have not had access to a choice of bio-delivery systems due to restricted licensing, policies, regulations and resources (at national, regional and local service levels). Recently, however, global increases in opioid use and poor adherence to existing opioid medications have generated interest and investment in the development of new OPT medications and bio-delivery systems (Sigmon et al., 2006; Sigmon & Bigelow, 2016). This is already resulting in a diversification of treatment options for opioid use disorder, including rapid dispersal film or tablets and long-acting implant or depot injection formulations (Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group, 2017; Sigmon et al., 2006; Sigmon & Bigelow, 2016). Currently, we do not know what OPT patients think of these new bio-delivery systems, whether they prefer them over more conventional routes of administration, and the reasons for their preferences.

More generally still, relatively little is known about how OPT prescribing decisions are made when a patient and clinician meet. In the United Kingdom (UK), the introduction of national guidelines was followed by a two-fold overall increase in methadone and buprenorphine prescribing, in the direction of the guidelines' recommendations (Strang et al., 2007). Yet, international data suggest that treatment decisions are more influenced by patient preferences than by clinical guidelines (Fischer & Stöver, 2012). The EQUATOR (European Quality Audit of Opioid Treatment) study, which was conducted in ten European countries, found

that patients mostly received the OPT treatment they requested even though less than half consulted physicians or pharmacies for information and most had limited knowledge of the available OPT options (Benyamin & Stöver, 2012; Dale-Perera et al., 2012; Fischer & Stöver, 2012). A survey conducted in London, UK, similarly found that patient preference influenced providers' prescribing decisions, with patients preferring methadone over buprenorphine treatment having higher odds of receiving their preferred medication (and vice versa) (Ridge et al., 2009).

These findings are consistent with calls to increase patient participation in treatment decision making (Neale, 1998; Rance & Treloar, 2015; Trujols, 2012, 2017), but fall short of recommendations that OPT decision making should be 'shared' between patients and clinicians (Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group, 2017; Joosten et al., 2008; Kampman & Jarvis, 2015). Shared decision making has the potential to enhance patient adherence to treatment and, in turn, to improve patients' health and related outcomes (Bowling & Ebrahim, 2001). However, it requires conversations that carefully bring together the health care professional's knowledge (for example, on treatment options, risk and benefits) with the patient's own expertise (for example, on their personal preferences, circumstances, goals, values and beliefs) (Bowling & Ebrahim, 2001; The Health Foundation, 2014). Furthermore, for OPT treatment decision making to be truly shared, patients must be well-informed about the available treatment options, able to communicate openly with clinicians, and equal partners in decision-making processes (Yarborough et al., 2016).

With the substantial expansion of types of OPT medications and bio-delivery systems entering the market, it will become increasingly important to find ways of enabling patients

and clinicians to make informed joint decisions about which bio-delivery system to choose. The aim of this paper is to begin this process. To this end, we explore current and former heroin users' views of a range of OPT bio-delivery systems in order to identify factors influencing their preferences. We then use the findings to construct a checklist that clinicians may wish to use to facilitate discussions with patients when they are considering initiating or changing OPT medications.

METHODS

Our study received ethical approval from the UK NHS Research Ethics Service. During 2017, we conducted focus groups (FGs) with current or former OPT patients with a history of heroin use. Focus groups were chosen over one-to-one interviews since the former are particularly useful when participants may feel they have little to say or existing knowledge of a subject is limited. This is because the group format allows participants the opportunity to develop and refine their ideas through interaction with others (Foster-Turner, 2009; Powell & Single, 1996). In this case, we were concerned that participants might struggle to articulate views on bio-delivery systems that they had not personally experienced or previously considered, and we believed that group discussions would enable them to reflect and then form and express opinions.

Participants were recruited from drug and alcohol services, a peer support recovery service, and a homeless hostel in London, UK. These locations were chosen in order to ensure a mix of people receiving different medications, former OPT patients with no current street opioid use, and former OPT patients with current street opioid use. Recruitment occurred in several

ways: i. posters with the researchers' contact details were displayed in the services; ii. researchers approached potential participants in the waiting rooms at the services; iii. workers and volunteers at the services encouraged service users to contact the researchers; and iv. participants from the earlier focus groups introduced the study to their peers. All people expressing interest in participating (n=76) were provided with further information about the study and asked to complete a basic questionnaire covering gender, age, ethnicity, substance use, prescribed medications, and contact details.

Using data from the questionnaire, the 76 people expressing interest were first stratified based on their current OPT treatment status: oral linctus methadone, buprenorphine tablets, injectable OPT, former OPT (no current street opioids), and former OPT (current street opioid use). This was because we did not want to mix people on different treatments within FGs. Specifically, we did not want to bring people in stable treatment or currently abstinent into contact with people currently using street opioids in case this prompted (re)lapses. Equally, we did not want to bring people who were receiving oral OPT into contact with people receiving injectable OPT in case this prompted requests for injectable treatment (which is not commonly available in the UK). In addition, we stratified people by current treatment status as some homogeneity of group composition tends to make it easier for participants to engage in sharing and comparing, particularly when discussing topics that might be considered deviant behavior (Morgan, 2006).

To avoid having more than 10 participants in a single FG (Foster-Turner, 2009), both the oral linctus methadone and buprenorphine tablet groups were split into two. Next, the lists of people for each group were reviewed to ensure that there was, in so far as possible, a balanced mix of men and women, age groups, ethnic backgrounds, and duration of current

treatment. During this process 27 people were omitted (mostly people in current receipt of methadone or buprenorphine), leaving 49 current or former OPT patients who were all contacted and invited to attend one of the following seven groups: oral liquid/linctus methadone (FGs 1 and 2); buprenorphine tablets (FGs 3 and 4); injectable diamorphine or injectable methadone (FG5); previously in receipt of OPT but now not using any opioids at all (FG6); and previously (but no longer) in receipt of OPT and now all using street opioids (FG7). Of the 49 people invited to attend a group, 44 (28 men and 16 women, aged 33-66 years) arrived and participated on the day (3 sent apologies and 2 did not show). Additional details about the participants in each group (including their current street opioid use and current and previous OPT treatment) are shown in Table 1.

Table 1

All participants provided written informed consent before the start of their group and received £10 as a gesture of thanks at the end. Each group was facilitated by two researchers (CNET and RM) who used a topic guide comprising questions relating to common OPT bio-delivery systems (liquid, tablet, injectable routes), emergent OPT bio-delivery systems (implants, depot injections), and a hypothetical OPT bio-delivery system (nasal sprays). Participants were asked to discuss any personal experiences of taking OPT via different routes, including what they liked and disliked about each, as well as their views on, and willingness to try, other ways of taking OPT. Throughout the emphasis was on the bio-delivery system, rather than the actual drug (pharmaceutical agent) or dosage. When participants began to conflate these issues, the researchers gently steered the discussions back to the bio-delivery system.

Groups lasted between 41 and 63 minutes and were audio-recorded. The audio recordings were transcribed verbatim by a professional transcriber and coded and analysed according to the principles of Iterative Categorization (Neale, 2016). To this end, each participant was first given a unique identifier that denoted their focus group, gender and participant number within their group (for example: FG2, female, participant 3). Next all data were coded using the qualitative software programme MAXQDA (version 11). The coding frame comprised deductive codes derived directly from the topic guide and inductive codes emerging from the data. One researcher (CNET) undertook all coding to ensure consistency and transparency (Barbour, 2001). All coded data (with participant identifiers) were then exported from MAXQDA into Microsoft Word documents and analysed inductively by two of the researchers (CNET and JN).

In the first stage of the analyses, all Word documents were reviewed line-by-line to produce descriptive accounts of whether and why participants liked, disliked and would be willing to try different OPT bio-delivery systems. Participant identifiers were retained so that it was possible to link all comments directly back to the individuals making them. In the second stage of the analyses, the descriptive findings were reviewed more analytically to extract factors influencing participants' preferences across all the bio-delivery systems. Again, participant identifiers were retained, so that it was also possible to explore the extent to which the factors identified varied by FG (and therefore current treatment status) or other variables. Once these analyses were complete, RM reviewed the findings to check that they corresponded with her subjective memory of the groups. No discrepancies were identified.

FINDINGS

Across all groups, participants generally reported that they were willing to consider receiving OPT in a range of ways. Indeed, they welcomed the prospect of having some choice. They argued that it was important to have options since opioid users have different needs and preferences, know their own bodies better than professionals, and have a right to decide what medication they take. Moreover, choice would enable them to try out different bio-delivery systems to discover what worked best for them personally. As one participant explained:

> "Not one thing suits everybody. So… even to try a couple of things and find what's best for you. So, yeah, to have a choice of two, three, whatever things would be amazing." (FG2, female, participant 3)

Analyses indicated that participants' preferences for OPT bio-delivery systems were underpinned by nine factors. These are each described below and illustrated by anonymized verbatim quotations. For the most part, participants considered the bio-delivery systems with reference to their own personal drug use and treatment histories. However, they also sometimes reflected on what they thought others might want or need. Although participants within groups often expressed different opinions about particular bio-delivery systems, the same discussions tended to replicate across all seven groups. Where differences between sub-groups of participants were evident in the analyses, we document them below.

1. Personal dislike of particular OPT bio-delivery systems

Participants in all FGs frequently voiced strong reasons why they did not want to receive their medication by a particular bio-delivery system, and they routinely linked these explanations back to their own personal experiences of both OPT and illicit drug use. Sometimes participants referred to physical aversions: for example, liquid OPT made them feel, or actually be, nauseous; they found drinking large dosages of liquid OPT physically uncomfortable; they had difficulty swallowing tablets; the aftertaste from tablets was too chalky or unpleasant; their venous access was too poor to inject medications; or sinus problems would make it difficult for them to use medication via a nasal spray. On other occasions, their dislike of a particular bio-delivery system was more psychological: for example, they were afraid of needles; needles reminded them of an injecting history that they were trying to forget; they were worried about using nasal sprays because of their associations with snorting drugs or because they might prompt them to snort drugs; or they did not like the idea of having a foreign body '*implanted*' inside them.

- "It's just the actual liquid going down… just makes me feel sick." (FG1, female, participant 2)
- "I don't like the idea of it [implant] actually being in your skin or under the skin. It's the actual thought about it being there, under my skin, and I'd feel it." (FG3, male, participant 5)
- "The nasal spray, it reminds me of like snorting cocaine… So that would be like memories." (FG4, female, participant 2)

2. Desired feelings following OPT administration

A further key factor influencing participants' medication preferences was how they wanted any OPT to make them feel. Thus, some expressed a desire for slow-release medication delivered by an implant or depot injection, since this would keep them feeling '*on a level*', '*the same*', or '*normal*' throughout the day for many days at a time. In contrast, others (mostly – but not exclusively - participants currently receiving oral linctus methadone and injectable formulations) emphasized that they did not want to feel constantly '*on a plateau*', as this would be '*boring*'. Instead, they preferred OPT with a shorter duration of action that would require more frequent consumption but also allow them to feel the ebb and flow of the medication's effects. Expanding upon this, several participants explained how liquid OPT in particular permitted them to experience mild withdrawal symptoms as the medication was eliminated from their system, followed by warmth and slight intoxication on further dosing. Meanwhile, participants who were currently prescribed injectable OPT emphasized that this was '*superior'* to all other bio-delivery systems since they really '*liked the feelings'* that the injected medication produced.

- "I don't like the sound of that [depot injection]… Because it means that you're on a level for the whole month." (FG6, male, participant 1)
- "I don't want to feel flat… I want to feel human and alive." (FG5, male, participant 1)
- "I like to be able to feel a bit of something, and then I like to be a bit straight too… I like to be a little bit stoned… very stoned… to have variations on a theme." (FG5, female, participant 1)

3. Perceived effectiveness of OPT bio-delivery systems

Participants' views of OPT bio-delivery systems were also influenced by how effective they believed the medication administered would be. For example, participants in all FGs generally emphasized that they wanted medication to take effect or '*kick in*' immediately. In this regard, short-acting injectable OPT and nasal administration were considered better than other bio-delivery systems. However, participants also routinely said that they wanted their OPT to '*hold them*' or '*last*' for at least 24 hours. On this latter criterion, tablets were considered more effective than liquids, and implants and depot injections were considered most effective of all. In addition, participants routinely expressed concerns about withdrawal symptoms if OPT proved ineffective. For example, they worried that liquids and tablets might not be absorbed if somebody vomited shortly after ingestion and that OPT delivered by nasal sprays might '*get blown away in the wind*' or be poorly absorbed if a patient had nasal damage, hay fever, breathing difficulties, sinus problems, or even a cold. Several participants were also concerned about the abuse potential of nasal sprays, commenting that ease of administration might tempt people to use too much or people might remove the liquid from the spray container and inject it. Lastly, some expressed uncertainty about the effectiveness of implants and depot injections, particularly how the dose would disperse once administered and what would happen to the dose towards the end of the implant or depot injection.

- "[The] good thing about injecting is that… it's immediate. There's no period of waiting for the medication to take effect." (FG5, male, participant 1)
- "That [nasal spray] sounds very tempting to me… [to just have] a quick one [additional dose from nasal spray]." (FG6, male, participant 2)

- "If you have to have it [implant] put in every month, do you end up with all these empty capsules inside, or do they totally dissolve?" (FG2, female, participant 2)

4. **Concerns about OPT side effects**

Participants from all FGs discussed the potential for negative side effects from each of the OPT bio-delivery systems. For example, they worried about vomiting after swallowing liquids; respiratory problems or harm to the nose and its membranes from nasal sprays; pain and vein or skin damage from injected medications; infections, haematomas or skin damage from implants; and increased risk of overdosing if they used street drugs '*on top of*' an implant or depot injection. Additionally, there was a general concern about increased dependence when transitioning to any new OPT bio-delivery system, including fear of finding it difficult to reduce and come off OPT and becoming addicted to two substances rather than one. Many participants were also worried that OPT delivered by implants and depot injections might interact with other street drugs or medicines they were taking or make it difficult for them to receive pain relief if they were involved in an accident.

- "Because once it [implant] is in, once it's there, it might be difficult to remove. Suppose you use on top, the potential for overdose might be high." (FG7, female, participant 2)
- "Anything you keep snorting up your nose is going to… rot up your fucking inside… It burns… no one wants to be snorting". (FG7, female, participant 1)
- "[A depot injection is] a mad idea of a medication… Lots of medications interact with each other. So what happens if you get unwell and you're in a hospital and it's already

> in you, and you might need some medication that interacts with it. It just seems really toxic and scary for me." (FG6, female, participant 1)

5. Ability to control the OPT

Participants, again in all FGs, routinely reported that they liked to feel in control of their own OPT. This included being in control of the dose they received each day, but also the time they took the dose. In this respect, conventional bio-delivery systems (liquids and tablets) were universally preferred over long-acting systems (implants and depot injections), especially when liquids and tablets were prescribed as a take-home dosage. Participants were particularly worried about having a slow-release medication, which they could not change or control once injected or implanted inside them. This, they said, would make them feel powerless and remove any sense of autonomy or responsibility they felt for their own treatment. Despite this, views also differed. Thus, some reported that it was easier to manage a liquid than tablets as they could drink as little or as much as they needed. Others stated that it was difficult to measure out liquid medication precisely; consequently, they preferred tablets as they were easier to dose. Those receiving injectable medications often complained that they were being prescribed an insufficient amount for their needs and this undermined their ability to manage or control their medication. However, others liked the fact that they could take their injectable OPT home to use when it suited them. In relation to nasal sprays, views were mixed with some participants reporting that it would be hard to get the dosage right (so difficult to control) and others reporting that it would be easy to take as and when needed (so easy to control).

- "It's easier to control yourself when it's in tablet form… I've found that I'm able, when it's tablet form, to leave a tablet out. And suddenly you get to the end of the week and you think 'Wow - I've left all these tablets out'." (FG2, female, participant 2)
- "It [implant] is out of question… I want to be in control, not some substance under my skin." (FG4, male, participant 4)
- "[I] take it [injectable OPT] home… do it in my own time, and without any hassle… I wouldn't want to be monitored by anybody." (FG5, male, participant 3)

6. Impact of OPT on everyday life

Participants from all FGs groups frequently reported that they wanted OPT medication to facilitate rather than impede their daily lives. Thus, many stated that they did not want a bio-delivery system that required them to attend a pharmacy every day as this would limit their opportunities to do '*normal'* things, such as work, go to college, travel or look after their children. According to these participants, extended-release medication delivered via an implant or depot injection was more attractive than liquid, tablet or injectable formulations that required daily dosing. Once the implanted or depot medication was administered, they welcomed the prospect of not having to use street drugs or to attend treatment services. Others in receipt of take-home medication reported that they did not want a bio-delivery system that would hamper their ability to do everyday things because it was inconvenient or precarious to carry around. Accordingly, they disliked liquids which they described as '*heavy'*, '*sticky'*, '*bulky'* and prone to spillage or leakage especially when travelling. In

response to this, some expressed interest in nasal spray delivery systems as they felt that these would be very portable and easy to use whilst '*out and about*'.

- "For me, it [my preference] would be the implant… I'll be free, practically free. Go on holidays when I want… All of that shit." (FG1, female, participant 1).
- "Workwise, it [implant] is going to help, because you don't have to worry about getting to the chemist." (FG3, male, participant 3)
- "Because you know it [depot injection] is there. It's good, it's brilliant. Because you can get on with your life and stuff. It frees you up." (FG2, male, participant 1)

7. Concerns about OPT-related stigma

When reflecting on the various bio-delivery systems, many participants (again all FGs) spontaneously discussed the stigma associated with being a heroin user and with receiving OPT. To help counter this, they wanted their medication delivery system to be discreet. Having to collect liquid or tablet OPT from a pharmacy was often described as embarrassing and shameful, particularly if it had to be consumed in front of other customers in the pharmacy shop. Many participants reported that liquid methadone was especially stigmatizing since it was highly visible and made them look and feel '*different*' from other pharmacy customers. Tablets were generally deemed more discreet than liquids, but still '*humiliating'*, especially if the pharmacist required them to open their mouth to demonstrate that pills had been swallowed. Overall, participants thought that nasal administration of OPT would be less conspicuous and stigmatizing than liquid and tablet OPT. Meanwhile, implants

and depot injections were considered least stigmatizing of all given that they would be invisible to others once they had been fitted or administered.

- "When I've taken my medication [tablets], they keep wanting me to open my mouth… I feel violated." (FG3, male, participant 2)
- "[Tablets] they're less stigmatizing… In a liquid form…, everybody in the chemist knows… If you're getting some tablets across the counter..., you're much more like the rest of the people that are using the pharmacy." (FG6, male, participant 4)
- "I like it [implant] because… there's less stigma attached to something that nobody can see. You don't drink it, you don't take it, you're just another person, and nobody has to know that you've got that under your skin." (FG2, female, participant 2)

8. Perceived need for adjunctive psychosocial support

As above, participants routinely reported that they liked implants and depot injections because they freed them from constantly having to attend pharmacies and drug services. Nonetheless, others - mostly those who had more recently started treatment and those who also reported mental health problems – said that they were happy with short-acting delivery systems (liquid, tablet or injectable formulations) that required regular service attendance because they valued the support and reassurance provided by professionals. Indeed, several participants explained that they would find it difficult to manage their own medication every day, so they wanted to be monitored. Others liked having to attend services regularly as this offered them social contact, alongside the routine and structure of having to go to the pharmacy or drug service. Indeed, a minority said that having to collect their medication daily

was important because it '*got them out of the hous*e' and/ or provided them with the only social interaction they had each day. Accordingly, they did not want a slow-release medication that would require minimal or no professional contact once fitted or administered. Likewise, they did not like the idea of a nasal spray formulation that might be given to them in large take-home quantities without close subsequent monitoring to ensure that they were taking it correctly.

- "I'm pissed off that I have to go [to the pharmacy]. But also at the same time it's a safety net… There are some pharmacists that are really good and give you that care while you're going through it, the support." (FG4, female, participant 3)
- "Going to the chemist on a daily basis actually gets me outside the house. Because I don't go outside. I really don't do anything. I'm clinically depressed… Can you believe it, I look forward to actually getting up and going to the chemist in the mornings?" (FG2, male, participant 5)
- "I think there's also a negative side of it [nasal spray]… The lack of engagement with services… You could give someone a month's worth of supply… How do you know they're actually taking that?... They could have relapsed, they could have gone over [overdosed]." (FG4, female, participant 1)

9. Personal treatment goals

Lastly, participants' preferences for particular bio-delivery systems were influenced by their commitment to entering and remaining in OPT and their desire to avoid street drugs or to become totally abstinent. For example, some participants reported that they wanted to collect

and take their medication (liquid, tablet or injectable) daily to provide a ritual to replace their use of street drugs. In contrast, others perceived the daily routine of collecting and taking OPT as a negative extension of drug-taking behaviours. They therefore expressed a preference for long-acting OPT bio-delivery systems (implants and depot injections) that would help them to break rituals associated with drug use. Participants who wanted to stop using street opioids but could not imagine being abstinent in the near future were particularly interested in implants and depot injections as they liked the idea of receiving guaranteed stable treatment for several weeks or months. Others were conversely anxious about long-acting formulations, stating that medication delivered in this way was not easily reversed once administered and could create problems if they wanted to alter the dose, use street drugs, or be completely drug-free.

- "I have really severe PTSD [post-traumatic stress disorder], so sometimes I use [street drugs]… And I'm having a hit [injection of street drugs] or two, done. But I pass the peak… For me the peak is very bad. So that's why something which is irreversible, and will keep you away for a month or two, it's too much for me." (FG6, male, participant 4)
- "You don't know if you're going to get on with it [depot injection]… You could hate it. And then… you can't take it out. With the implant you can [take it out], but with that [depot injection] you can't…. Once you're signed up, 'Shit, I'm screwed for the next two months'." (FG5, female, participant 2)
- "If I wasn't ready to get clean [be abstinent], yeah, then I would do it [have an implant]. But it's releasing 8 ml in me every day, you know… My goal is to get clean [be abstinent]." (FG3, male, participant 1)

DISCUSSION

Until recently, the technology for delivering OPT has been relatively limited with options largely restricted to liquid and tablet formulations. As new bio-delivery systems enter the market, it is important to know what potential patients think of these developments, and what factors will influence their decisions to accept and/or adhere to new ways of taking OPT medication. Our findings indicate that current and former heroin users are cautious of, but willing to consider, new OPT bio-delivery systems and welcome the idea of having more choice. However, their preferences and decision-making processes are influenced by multiple interconnected factors. These include whether they have a pre-existing dislike of particular bio-delivery systems; how they want OPT to make them feel; how effective they believe the OPT bio-delivery system will be; whether they think that the bio-delivery system will have side effects; how much control they will have over the medication; how the OPT received will likely impact on their daily lives; whether they are concerned about the stigma of receiving OPT; how much psychosocial support they feel they need; and what they want to achieve from OPT.

Our findings show notable overlap with the Treatment Satisfaction with Medicines Questionnaire (SATMED-Q) (Ruiz et al., 2008). SATMED-Q is a generic instrument, with good psychometric properties, designed for use with patients undergoing pharmacological treatment for any chronic disease. The first four domains of the SATMED-Q are: undesirable side effects of the medicine; efficacy of the medicine; convenience and ease of use of the medicine; and impact of the medicine on everyday life (the remaining two domains are medical review of the medical condition and overall opinion of the medicine and health).

This likeness to the SATMED-Q suggests that heroin users have similar priorities and concerns to other patient populations experiencing chronic health problems when it comes to receiving medication. Meanwhile, other issues identified by our participants may also be relevant to non-heroin using patient groups, particularly those prescribed opioid pain medications. For example, participants generally liked medication that had a rapid effect, addressed their symptoms for at least 24 hours without further dosing, was portable, and was discrete. In contrast, they worried about withdrawal symptoms, becoming dependent on medication, interactions with other drugs, and their ability to receive effective pain relief in the event of an accident (c.f. Frank et al., 2016; Penney et al., 2016).

Overall, we found few differences between participants' responses based on their current treatment status (*sic* focus group attended). This likely related to the fact that participants generally drew upon their diverse treatment and drug use histories when responding, but also because they considered what others might want or need. Reflecting this, preferences regarding OPT bio-delivery systems varied within FGs more than across FGs, and there were many issues on which participants disagreed. For example, most did not want to have to attend a pharmacy daily; whereas some valued daily attendance since it provided routine, structure, reassurance and support. Most wanted to feel in control of their own OPT, but expressed different views on which bio-delivery systems were easiest to control. Others, conversely, did not want or feel able to be in control.

In short, participants did not express clear preferences for one particular bio-delivery system over another. Instead, they tended to like and dislike aspects of each. For example, they might value the discretion of implants, but worry about their side effects or irreversibility once administered. Equally, they might appreciate the structure and routine of collecting liquid or

tablet OPT from the pharmacy, but dislike the stigma of having to consume it in front of others. Preferences also varied depending on commitment to treatment and recovery. Decisions about which bio-delivery system will be most appropriate for any given individual will therefore reflect a wide range of contradictory and dynamic pharmaceutical, physical, psychological, social, and lifestyle factors.

Such complexity, combined with the recent diversification of new bio-delivery systems even for the same pharmacological agent, is likely to make it difficult for patients and clinicians to evaluate the pros and cons of different routes of OPT administration and to arrive at clear conclusions. However, difficulty does not diminish the importance of discussing treatment options and sharing decision making with people receiving healthcare. Responding to each individual patient's needs and circumstances at any particular point in time, and sharing decision making with them, is at the heart of both patient-centred medicine and person-centred care. Patient-centred medicine seeks to focus medical attention on the individual patient's needs and concerns, rather than the doctor's (Bardes, 2012). Person-centred care is a broader concept that involves supporting people with healthcare needs to live independent and fulfilling lives by focusing on their emotional, social and practical circumstances, and not just their medical symptoms and clinical outcomes. People using services should be treated as equal partners in planning, developing and monitoring care, and care must be provided 'with' them rather than done 'to' or 'for' them (The Health Foundation, 2014).

The challenges of involving people experiencing addiction as partners in treatment decision making have previously been documented (Fischer et al. 2007, Fischer & Neale, 2008). Patients may not want to be involved, they may have unrealistic expectations about treatment options, they may not understand the different treatment options, or they may prefer medical

professionals to make treatment decisions for them. Furthermore, individual clinicians' willingness to involve patients will likely differ and be constrained by structural factors such as regulations, financial resources (including the patient's insurance), time, competing priorities, and the available treatment options (Fischer & Neale, 2008). Prescribing OPT is already a complex process subject to bureaucracy, appointments, waiting times and monitoring (Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group, 2017; Neale, 2013). We have no desire to compound this by creating further work or unnecessary hurdles. However, patients with opioid use disorders have a right to be involved in medical treatment decisions in the same way as patients with other health conditions (Friedrichs et al., 2016). Thus, it is incumbent on clinicians to try to facilitate this.

Our findings highlight a number of issues that patients and clinicians might beneficially consider together when decisions about OPT bio-delivery systems need to be made, and we have collated these into a checklist (see Table 2). We caution, however, that the data on which the checklist is based derive from a single qualitative study involving just 44 current and former heroin users in London, UK. The study did not explicitly ask about all potential bio-delivery systems (for example, rapid dispersal tablets, lozenges, gum, patches or suppositories). Additionally, the list has been constructed without input from pharmacists, physicians or other treatment providers (although one of the authors is an addiction psychiatrist) and without reference to other contextual factors that may need to be taken into account, such as the broader health care system within which decisions are being made or individual patient factors such as co-morbidities. Given these limitations, we welcome any feedback (from patients, clinicians or researchers) to help develop or refine the items included.

Table 2

To conclude, we call for further research, involving patients and other relevant stakeholders, to co-produce a more developed decision tool or algorithm that will enable shared decision making in respect of OPT more broadly. This might include whether or not to prescribe OPT at all, what medications/ pharmaceutical agents to prescribe, what dosing regimens to choose, over what time period to prescribe, as well as which bio-delivery systems to select. We note the excellent online decision tool already developed by the U.S. Department of Health and Human Services for people wanting information on medications in treating opioid use disorder (SAMSHA, 2016) and also the various national guidelines offering health professionals practice recommendations on evidence-based treatment approaches for opioid use disorder (Bruneau et al., 2018; Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group, 2017; Gowling et al., 2014). Nonetheless, we suggest that there is an additional need for a tool that directly assists clinicians in their conversations with patients. Such a tool is likely to become increasingly important as the options for OPT bio-delivery systems and pharmaceutical agents expand and the number of treatment decisions needing to be made multiplies.

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Table 1: Participant details

Demographic characteristics	FG[a]1 Oral methadone (n=4)	FG2 Oral methadone (n=8)	FG3 Buprenorphine tablets (n=8)	FG4 Buprenorphine tablets (n=8)	FG5 Injectable OPT[b] (n=6)	FG6 Former OPT: no current street opioids (n=6)	FG7 Former OPT: current street opioid use (n=4)	All (n=44)
Gender								
Male	2 (50%)	5 (63%)	6 (75%)	5 (63%)	4 (67%)	4 (67%)	2 (50%)	28 (64%)
Female	2 (50%)	3 (38%)	2 (25%)	3 (38%)	2 (33%)	2 (33%)	2 (50%)	16 (36%)
Ethnicity								
White /White British[c]	2	4	6	6	5	4	2	29 (66%)
Asian /Asian British	0	0	0	0	0	0	0	0 (0%)
Black /Black British	2	2	1	0	0	2	1	8 (18%)
Mixed or Multiple	0	1	1	1	0	0	0	3 (8%)
Other	0	1	0	1	1	0	1	4 (8%)
Age								
Mean age (range)	49 (42-59)	51 (43-58)	46 (33-55)	40 (34-47)	56 (47-66)	47 (39-58)	45 (35-53)	48 (33-66)
Street opioid use								
Currently using street opioids	4 (100%)	6 (75%)	4 (50%)	2 (25%)	2 (33%)	n/a	4 (100%)	22 (53%)
Mean years of street opioid use (range)	26 (22-30)	33 (25-39)	22 (2-37)	17 (0-33)	39 (27-50)	n/a	22 (9-31)	26 (0-50)
Mean age of first street opioid use (range)	23 (16-33)	18 (14-22)	24 (14-31)	23 (14-35)	18 (15-27)	22 (15-32)	23 (18-26)	22 (14-35)
Current treatment[d]								
None	0	0	0	0	0	6	4	10 (23%)
Buprenorphine (tablets)	0	0	8	8	0	0	0	16 (36%)
Methadone (oral)	4	8	0	0	2	0	0	14 (32%)
Methadone (injection)	0	0	0	0	2	0	0	2 (5%)
Diamorphine (injection)	0	0	0	0	4	0	0	4 (9%)
Mean years on current treatment (range)	10 (2-20)	10 (0-26)	4 (0-12)	1 (0-6)	31 (3-46)	n/a	n/a	11 (0-46)
Previous treatment								
Buprenorphine	1	3	2	0	0	4	3	13 (30%)
Methadone	2	1	7	7	3	6	4	30 (68%)
Naltrexone	0	0	0	0	0	1	0	1 (2%)
Diamorphine (injection)	1	0	0	0	0	0	1	2 (5%)

[a] Focus group; [b] Opioid Pharmacotherapy; [c] 21 participants identified as 'British', 4 as 'Italian', 3 as 'Irish', and 1 as 'European'; [d] 2 participants were prescribed a combination of opioid medications (injectable + oral). The denominator used for the calculation of percentages across all subjects was n=44. Because two subjects from FG5 were included in the percentages for 'Current treatment' twice, the total percentage across all 44 subjects adds up to 105%.

Table 2: Checklist to facilitate shared decision making on OPT bio-delivery systems

1. **Does the patient have a pre-existing dislike of particular OPT bio-delivery systems?**
   Probe: How willing is the patient to try out new ways of taking OPT? Does the patient have a dislike of, or concern about, any particular OPT bio-delivery system?

2. **How does the patient want OPT to make them feel?**
   Probe: Does the patient want OPT to make them feel 'on a level' all of the time or does the patient prefer to feel changes in the medication's effects?

3. **What does the patient know or understand about the effectiveness of the available OPT bio-delivery systems?**
   Probe: How important is it to the patient that OPT has an instant/ immediate effect? How important is it to the patient that OPT lasts at least 24 hours? How worried is the patient about withdrawal symptoms? How worried is the patient about their absorption of OPT?

4. **What does the patient know or understand about side effects from the available OPT bio-delivery systems?**
   Probe: Is the patient worried about side effects? How worried is the patient about becoming addicted to OPT? How worried is the patient that OPT might interact with other street drugs or medications they are taking, including pain relief in the event of an accident?

5. **How does the patient feel about being in control of their own OPT?**
   Probe: Does the patient want to control the dose of OPT they receive each day? Does the patient want to control the time they take OPT each day?

6. **How does the patient think OPT will impact on their daily lives?**
   Probe: Is the patient happy to go to the pharmacy daily? Does the patient have commitments (e.g. work or family) that might make it difficult to attend a pharmacy daily? Does the patient need OPT that is portable/ easy to carry around?

7. **How concerned is the patient about the stigma of receiving OPT?**
   Probe: Is the patient worried about other people knowing they are taking OPT? Does the patient have concerns about taking OPT in a pharmacy?

8. **How much psychosocial support does the patient feel they need?**
   Probe: Does the patient think that it will be helpful to have regular contact with professionals (e.g. pharmacy staff, prescriber, drug worker)? What kind of psycho-social support and/ or monitoring does the patient desire? Is the patient worried they might misuse/ abuse OPT?

9. **What are the patient's treatment goals?**
   Probe: Does the patient think they might want to stop taking OPT over the coming days or weeks? Does the patient think they might want to alter their dose of OPT? Does the patient think they might want to use street drugs? Does the patient hope to be drug free/ abstinent soon?