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Considering consent to research for patients in chronic pain and with mental illnesses

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Steel et al. deny that people dependent on opioids should be presumed incompetent to consent to research involving supervised injectable opioid assisted treatment (siOAT). They argue that the greater concern in assessing consent is exploitation, a significant risk when siOAT is not available as a medical treatment. We broadly agree with their position and suggest that the argument may be strengthened by considering how consent to research is addressed for two related populations: people in chronic pain and people with mental illnesses. Severe chronic pain can dramatically affect how patients consider risks and benefits, particularly if approved treatments have not worked for them, yet they are widely permitted to choose experimental treatments on their own. Severe mental illness can also seriously affect patients' decision making, but institutional safeguards exist to preserve their agency as much as possible. For both these patient populations, as for people dependent on opioids, an emphasis on external factors that promote direct or proxy consent will enhance the prospects for participation in beneficial research and show greater respect for members of these stigmatized groups.

Consent to research for people in chronic pain

The idea that the research consent process for people in chronic pain deserves extra scrutiny is not new. For instance, Tait (2009) notes that having chronic pain may complicate how prospective participants weigh the risks and benefits of research: "One [reason] is directly related to the aversive nature of severe pain: absent a viable alternative, prospective research subjects are likely to have a general bias toward options perceived as holding promise for pain relief and/or reduction" (p. 4).

Tait raises much the same concern about people with chronic pain as Charland (2002) raises about people dependent on opioids: The urgency of alleviating their distress may make them less attentive to research risks. But where Charland – and many others – focuses on the psychological deficiencies of people dependent on opioids, Tait focuses on ways to mitigate threats to the decision-making capacities of people with chronic pain. These threats arise not from psychological deficits, but from external circumstances that needlessly burden choice.

Echoing Steel et al.'s concern about exploitation, Tait argues that inclusion criteria requiring poorly controlled pain "capitalize on the current state of pain management where the undertreatment of pain is widespread secondary to a range of barriers: societal attitudes, political and legal concerns ... fear of opioids, and fear of prosecution for providing such treatment" (14). Like Steel et al., Tait argues that this undertreatment is not necessary for research purposes. While it is understandable from a scientific perspective to limit enrollment to subjects whose pain would be severe if untreated, "it is not clear that current pain must be poorly controlled" (14). Such a requirement plays on desperation and undermines the capacity to consent. Tait suggests that "consideration should be given to an alternative inclusion criterion, such that patients would be eligible for study participation if their clinical record reflected previously high levels of pain severity that are reasonably controlled by standard care" (14).

In both chronic pain and opioid dependence research, trade-offs may arise between more inclusive enrollment criteria and more efficient research. There may be cases in which offering siOAT as clinical treatment slows enrollment in siOAT studies; there may be cases in which modifying the inclusion criteria for chronic pain research to require only a history of severe pain, not a current presentation of it, will reduce the power of the study. But in making these trade-offs, it is critical to bear in mind the reason why clinical trials exist for people with chronic pain and/or opioid dependence in the first place: Treatments currently available in clinical care do not work well enough for everyone. This lack of adequate treatment is compounded by the fact that new treatments are typically tested in clinical trials before being offered in clinics and covered by insurance. Mistaking vulnerability to exploitation for inability to consent could therefore prevent people with chronic pain and/or opioid dependence from accessing potentially effective treatment, initially in research and then in clinical care.

Furthermore, even when it is reasonable to restrict enrollment to individuals without access to adequate pain management or opioid replacement therapy, it is important not to underestimate their decision-making capacities. Because of the lack of universally effective treatment, patients with chronic pain and/or opioid dependence are used to making trade-offs when choosing among imperfect options. Deciding whether to participate in research that has the prospect of direct benefit but carries some risks is not sufficiently different from other treatment avenues, particularly those options without much empirical evidence. In fact, in some cases, institutional review board (IRB)- approved research may lay out the risks and benefits of participation more clearly than experimental interventions not subject to the same level of regulatory oversight because they are considered "clinical care."

Consent to research for people with mental illnesses

It is also common practice for IRBs to build in safeguards for people who may not be able to consent. For instance, the Office of Human Subjects Research Protections requires the National Institutes of Health IRBs to use its Standard Operating Procedure 14E, "Research involving adults who are or may be unable to consent" (2016). This document establishes several layers of protection that aim to preserve the agency of vulnerable individuals, such as the requirement to assess capacity "through the use of a standardized measure or by

consultation with a qualified professional” if questions arise about the individual’s capacity (p. 14). Such provisions are frequently applied to individuals with mental illnesses such as depression. So too should they be applied to people with opioid dependence, particularly since depression is often co-morbid with opioid dependence (and for that matter, chronic pain).

For further evidence against preemptively labeling people as unable to consent, we turn to a systematic review of depression and decision-making capacity for treatment or research. Hindmarch, Hotopf, and Owen (2013) reported that “[t]he empirical studies reporting decision-making ability scores also highlighted impairment of appreciation but without evidence of strong impact” (p. 1).

That is, while individuals with depression may not be able to apply information to their own situation and consider the consequences of treatment as well as individuals without depression, the degree of impairment may not always be severe enough to affect overall decision-making ability.

Similarly, a recent study by Morán-Sánchez et al. (2016) found “evidence that a large proportion of individuals with [substance use disorder] had decisional capacity for consent to research,” leading the authors to conclude, “It is therefore inappropriate to draw conclusions about capacity to make research decisions on the basis of a [substance use disorder] diagnosis” (p. 1). These papers reinforce the idea that a diagnosis alone is not evidence that individuals cannot consent.

Conclusion

Regardless of whether individuals are coping with chronic pain, mental illnesses, or opioid dependence, they should be presumed competent to consent to research unless proven otherwise. Moreover, in cases where individuals are not able to consent, we should seek to enhance capacity where possible rather than immediately delegating their decision-making authority. This respect is particularly important for these members of stigmatized groups, whose capabilities – decision making among them – are frequently challenged. The clinical and research literature offer examples of how these principles work for people with chronic pain and mental illnesses, and these examples are easily adaptable for people with opioid dependence.

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