Journal of Clinical Epidemiology 116 (2019) 146–149

COMMENTARY

The moral and legal status of Health Care Workers in Cluster Randomized Trials: a response to Weijer and Taljaard

Rieke van der Graaf[a,*], Ghislaine J.M.W. van Thiel[a], Esther Oomen-de Hoop[b], Karel G.M. Moons[c], Diederick E. Grobbee[c], Johannes J.M. van Delden[a]

[a]*Department of Medical Humanities, University Medical Center Utrecht, Utrecht University, Julius Center of Health Sciences and Primary Care, Utrecht, The Netherlands*

[b]*Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands*

[c]*Department of Epidemiology, University Medical Center Utrecht, Utrecht University, Julius Center of Health Sciences and Primary Care, Utrecht, The Netherlands*

Accepted 20 August 2019; Published online 23 August 2019

Abstract

In 2012, Weijer et al published "The Ottawa Statement on the ethical design and conduct of cluster randomized trials". In 2015, we reflected on this statement and argued that three recommendations in this statement need to be further refined. Weijer and Taljaard have responded to our comments in this issue of the journal. They agree with one of the proposed revisions but not with two others. In this commentary, we argue that the main reason why there is disagreement about two of our refinements is that we have different views on the moral and legal status of the health care workers as "research participants" in cluster randomized trials (CRTs). In this commentary, we clarify misunderstandings about our view expressed in 2015 and elaborate on the positions of health care workers in CRTs. We argue that there is sufficient reason to doubt whether the rights and interests of health care workers (HCWs) should be protected by means of ethics guidance documents and laws on human subjects research. Their interests are protected in the first place by professional codes of conduct which ensure that they cannot provide substandard care. Furthermore, protection of HCWs by ethics guidance on human subjects research will create an enormous burden for principle investigators and research ethics committees. Further debate is essential to determine how the interests of HCWs in CRTs can be protected best.

Keywords: Cluster randomized trial; Research ethics; Ottawa statement; Role of physician; Health care worker; Research participant

1. Introduction

In 2012, Weijer et al. [1] published "The Ottawa Statement on the ethical design and conduct of cluster randomized trials". Although this statement consists of a comprehensive and well-designed set of ethical guidelines, we have argued that certain issues in these guidelines deserve further clarification [2]. In our view three recommendations needed refinement [2]. Weijer and Taljaard [3] have now written a careful response to our commentary. They agree with one of the proposed revisions but not with two others. In this commentary, we will respond to their comments and try to both clarify misunderstandings and stimulate further debate on the ethics of cluster randomized trials (CRTs).

First, we are grateful for the response by Weijer and Taljaard and their clarifications. We especially appreciate their elaboration on the informed consent process in CRTs by adding a second approach to our informed consent model when there are concerns about bias when patients must be recruited after randomization. However, we still disagree on the moral and legal status of the health care worker (HCW) as "research participant" in CRTs. This has implications for the first and second refinements we proposed earlier (see page 1,110, box 1, refinement 3.1 and 3.2) [2] regarding the identification of the research participant.

2. The moral and legal status of Health Care Workers in Cluster Randomized Trials

Regarding the moral and legal status that Weijer and Taljaard assign to HCWs who are involved in CRTs they argue

Conflict of interest: R.v.d.G. is a member of the independent ethics committee to Sanofi. G.v.T., E.O-H., C.M., D.G., and J.v.D. have no conflicts of interest to declare.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

* Corresponding author. Department of Medical Humanities, University Medical Center Utrecht, Utrecht, The Netherlands. Tel.: +31887551347; fax: +31887568099.

E-mail address: r.vandergraaf@umcutrecht.nl (R. van der Graaf).

https://doi.org/10.1016/j.jclinepi.2019.08.005

What is new?

Key findings

- It may not be necessary to protect health care workers as research participants in cluster randomized trials by means of ethical and legal guidance on human subjects research.

What this adds to what was known?

- We elaborated on the argument that health care workers should not be protected by means of ethics guidance documents and laws on human subjects research.

What is the implication and what should change now?

- We stimulate further debate on the moral and legal status of the health care worker as research participant in cluster randomized trials.

in line with the United Nations' International Covenant on Civil and Political Rights (1966) that "All people possess a right to be free of medical or scientific experimentation without informed consent. This applies no less to 'health providers' than to patients in CRTs; their moral status is, we believe, the same" [3]. Weijer and Taljaard [3] accordingly set out that to see HCWs involved in CRTs as professionals who act in line with their duties as employees "ignores the harms that may accrue to employees in research, including the revelation of substandard performance or reputational harms". Accordingly, they "do not agree that standards for informed consent for health providers in CRTs should differ from those for other research participants" [3]. And they argue that "health providers" do not have "an obligation to participate in research" [3]. Finally, our argument that HCWs "should not be allowed to withdraw easily" in their view "undermines health provider autonomy" [2,3].

We agree that people must provide informed consent when they are subjected to "medical experimentation", but the main question is whether we can and should call the way in which HCWs are involved in CRTs is a form of research participation that is equivalent to the way in which healthy volunteers and patients are involved in human subjects research. When a medical research project is conducted, a broad range of professionals is involved. Among these may be physicians, nurses, pharmacists, data scientists, and so on. What morally separates these actors in medical research from patients and healthy volunteers is that the main aim of the CRT is to improve the health and well-being of these actors, not of health professionals. Research may also require time and effort from health professionals (such as communication training or learning how to deliver an intervention), but their mental and physical welfare itself is not targeted. We recognize that the well-being of the HCW may be affected as a consequence of participation, and that potential negative consequences of research on HCW should be minimized. However, because improving their well-being is not the primary target of a CRT, we argue that a different level of protection is warranted. Therefore, we think that the Ottawa Statement should be refined by differentiating between categories of research participants and the level of protection needed.

The Ottawa Statement defines four situations in which a person is a research participant:

1. the intended recipient of an experimental (or control) intervention,
2. the direct target of an experimental (or control) manipulation of his/her environment,
3. with whom an investigator interacts for the purpose of collecting data about the individual,
4. about whom an investigator obtains identifiable private information for the purpose of collecting data about the individual.

There is no explicit mentioning of medical research as a criterion for deciding whether a person is a research participant in the Ottawa Statement. This may explain our different approach to HCWs as research participants in CRTs. We agree that in a CRT HCWs may be the intended recipients of, for example, a prediction rule, and that data may be collected about how well they follow that prediction rule, but we think that the health that is intended to be improved is that of the patients whose care is guided by the predictions of the prediction rule, not that of the HCWs themselves. In line with what we argued earlier, we believe that also in CRTs where patients are indirectly affected and HCWs are the intended recipient, the improved outcome at patient level of an intervention should be the primary objective of this CRT. We think this assumption is also in line with the World Medical Association's Declaration of Helsinki that "the primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments)" [4]. Or, as the authors of the "7-principle framework for clinical research" put it "the overarching objective of clinical research is to develop generalizable knowledge to improve health and/or increase understanding of human biology" [5]. Accordingly, this objective to improve or promote people's health is what renders the study a medical research study for which ethical review and obtaining informed consent is essential and not so much the desired change in behavior of the HCW, which is a mere means to reach health promotion. Therefore, we may classify HCWs as "research participants" but not to the extent that their health is intended to be improved. Depending on applicable laws, this classification may imply that HCWs may not always be legally counted as research participants.

One may object and feel that the desired change in behavior of the HCW is still a secondary objective which renders them (as well as patients) research participants who deserve protection by means of ethics guidance documents and laws on human subjects research. But then it is questionable in what sense these documents will indeed protect them. Weijer and Taljaard mention that HCWs may suffer from reputational damage when participation in a CRT reveals that these HCWs deliver substandard care. Reputational damage is difficult to imagine when results are pseudonymized and analyzed at a group level. Moreover, there is no reason to assume that HCWs who object to participation for conscientious reasons in CRTs or because they do not thrust the experimental intervention are intentionally providing substandard care. Because they are bound by codes of conduct and professional norms, we may expect that HCWs will deliver the care that they were used to provide in line with the current professional standard. For example, guideline 3 of the Declaration of Helsinki states ''The Declaration of Geneva of the WMA binds the physician with the words, 'The health of my patient will be my first consideration,' and the International Code of Medical Ethics declares that, 'A physician shall act in the patient's best interest when providing medical care' [4]. And finally, we do not need a law on human subjects research to ask for their voluntary informed consent. Obviously, HCWs should not be coerced to participate in a CRT, but when physicians and other health care workers prevent that they provide substandard care, as per definition they cannot be coerced to participate. It follows that when department chairs in advance of a proposed CRT know that the willingness to comply with the study protocol for that CRT is low, it is reasonable to assume that those chairs decline participation for their department. In general, chairs of departments will acknowledge that individual physicians remain responsible for maintaining the professional standard. In other words, asking their informed consent to participate will become a form of politeness rather than a means to protect HCWs against potential provision of substandard care. We also think that participation can be reasonably expected from employees in settings where research is one of the main tasks of the institution in which the employee works. For that reason, we wrote that HCWs should not decline too easily when asked to participate, but we realize that in settings where HCWs are not used to research more explanation, why participation in research is essential may be needed from the side of the researchers. In sum, there seems sufficient reason to doubt whether we should pose the administrative burden of having to protect the interests of HCWs on the shoulders of research ethics committees in light of the benefits to be expected by protection of their interests in this way.

3. Implications

Our analysis of the moral and legal status of HCWs in CRTs has implications for two of our claims that worry Weijer and Taljaard. The first is our claim that ''Health care workers ought to be treated differently and have a different moral and legal status than ordinary research participants''. We believe our aforementioned reasoning shows that there is reason to open the debate on whether and what specific protection mechanisms are necessary for HCWs both morally and legally and in particular whether ethical and legal guidance documents on human subjects research are the appropriate means to protect them in CRTs. The administrative burden for investigators of CRTs can then be lowered in jurisdictions where protection of the interests of HCWS by means of laws on human subjects research is not essential.

Our second claim is that ''Patients who are indirectly affected by study interventions ought nonetheless to be considered research participants''. When we agree that the final goal of undertaking the CRT should be the outcome at patient level to improve the well-being of patients and that affecting the behavior of HCWs may be the means to establish an effect in patients, it follows that also patients who are not the intended recipient of the intervention should be considered research participants.

Weijer and Taljaard [3] argue that ''the IMPACT trial does not illustrate well'' our concern that patients who are indirectly affected should be considered research participants. The IMPACT CRT ''hypothesized that implementation of a prediction model for postoperative nausea and vomiting (PONV) would lower the PONV incidence by stimulating anesthesiologists to administer more ''risk-tailored'' prophylaxis to patients'' [6]. We used this trial as an example to argue that the patients in the IMPACT trial are not only research participants because their data were obtained by the investigators (fourth criterion of the Ottawa Statement) but also because they were indirectly affected by the intervention that was targeted at the anesthesiologists and hence that the first criterion should be broadened to include protection for indirectly affected patients [2].

Weijer and Taljaard agree that both the patients and the HCWs in the IMPACT trial should be regarded as research participants because in their view, the intervention was experimental. As regards the IMPACT trial, we may reach the same conclusion about the moral status of the study patients in the IMPACT trial. However, in case of CRTs that test the effectiveness of the implementation of an evidence-based practice, the difference between HCWs as intended recipients and patients as indirectly affected participants may become more meaningful. We think it is helpful to see these patients as research participants in those types of CRTs. At the same time, as we argued earlier, our refinement of the first criterion may imply a substantial increase of the participants who must provide informed consent if all indirectly affected persons have to be counted as participants. Mechanism for waiving informed consent, however, may then be used to waive or modify the consent process. We wrote that if these

patients are not regarded as research participants their informed consent may be too easily ignored [2]. This was not meant to beg the question, as Weijer and Taljaard argue [3], but to ensure that viewing them as research participants ensures that as a general rule, their informed consent is sought and that researchers apply for waivers if, and only if, they feel that it becomes infeasible to ask informed consent.

4. Conclusion

Although HCWs may be regarded as research participants in CRTs, we believe there is sufficient reason to doubt whether the rights and interests of HCWs should be protected by means of ethics guidance documents and laws on human subjects research. Their interests are protected in the first place by professional codes of conduct which ensure that they cannot provide substandard care. Furthermore, protection of HCWs by ethics guidance on human subjects research will create an enormous burden for principle investigators and research ethics committees. Further debate is essential to determine how the interests of HCWs in CRTs can be protected best.

Acknowledgments

Arne Verbout has kindly provided helpful legal insights.

References

[1] Weijer C, Grimshaw JM, Eccles MP, McRae AD, White A, Brehaut JC, et al. The Ottawa Statement on the ethical design and conduct of cluster randomized trials. PLoS Med 2012;9:e1001346.

[2] van der Graaf R, Koffijberg H, Grobbee DE, de Hoop E, Moons KG, van Thiel GJ, et al. The ethics of cluster-randomized trials requires further evaluation: a refinement of the Ottawa Statement. J Clin Epidemiol 2015;68:1108−14.

[3] Weijer C, Taljaard M. The ethics of cluster randomized trials. Response to a proposal for a revision of the Ottawa Statement. J Clin Epidemiol 2019. https://doi.org/10.1016/j.jclinepi.2019.08.006. [Epub ahead of print].

[4] World Medical Association. Declaration of Helsinki. Ethical principles for medical research involving human subjects. 64th WMA General Assembly, Fortaleza, Brazil. 2013. Available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/. Accessed July 11, 2019.

[5] Kappen TH, Moons KG, van Wolfswinkel L, Kalkman CJ, Vergouwe Y, van Klei WA. Impact of risk assessments on prophylactic antiemetic prescription and the incidence of postoperative nausea and vomiting: a cluster-randomized trial. Anesthesiology 2014;120:343−54.

[6] Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA 2000;283:2701−11.