affordable healthcare, to help address the differences in spending that underlie the injustices highlighted in the study by Obermeyer et al.⁸. And although social scientists and ethicists have called for such transformations^{13,14}, many health practitioners and researchers continue to lack proficiency in the basic terminologies and concepts of racial justice. These competencies need to be required for medical licensing and accreditation.

A radically socially conscious approach is needed to eliminate subtle but widespread discrimination. We urge each reader to take action in their institution today and, with continued vigor in the upcoming months and years, to induce a true culture shift that would stop algorithmic design from perpetuating

inequities. For this, systemic education of health practitioners and investigators on issues of racial justice is needed, as well as standards for anti-racist development and analysis of research.

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References

- Hardeman, R., Medina, E. & Boyd, R. N. *Engl. J. Med.* **383**, 197–199 (2020).
- Cooper, H. & Fullilove, M. J. *J. Urban Health* **93**, 1–7 (2016).
- Benjamin, R. *Race After Technology: Abolitionist Tools for the New Jim Code* (John Wiley & Sons, 2019).
- Eubanks, V. *Automating Inequality: How High-Tech Tools Profile, Police, and Punish the Poor* (St. Martin's Press, 2018).
- O'neil, C. *Weapons of Math Destruction: How Big Data Increases Inequality and Threatens Democracy* (Broadway Books, 2016).
- Vyas, D.A., Eisenstein, L.G. & Jones, D.S. N. *Engl. J. Med.* <https://doi.org/10.1056/NEJMms2004740> (2020).
- Noor, P. *Br. Med. J.* **368**, m363 (2020).
- Obermeyer, Z., Powers, B., Vogeli, C. & Mullainathan, S. *Science* **366**, 447–453 (2019).
- Benjamin, R. *Science* **366**, 421–422 (2019).
- Forscher, P. S., Lai, C. K. & Axt, J. R. et al. *J. Pers. Soc. Psychol.* **117**, 522–559 (2019).
- Noble, S. *Algorithms of Oppression: How Search Engines Reinforce Racism* (NYU Press, 2018).
- Boyd, D. & Crawford, K. *Inf. Commun. Soc.* **15**, 662–679 (2012).
- Benjamin, R. *Sci. Technol. Human Values* **41**, 967–990 (2016).
- Powers, M. & Faden, R. *Social Justice: The Moral Foundations of Public Health and Health Policy* (Oxford University Press, 2006).

Competing interests

The authors declare no competing interests.

The ethics of deferred consent in times of pandemics

In the current COVID-19 pandemic, many researchers are applying to research ethics committees for deferred-consent procedures for protocols that aim either to test treatments or to obtain tissue or samples from research participants. However, the deferred-consent procedure has not been developed for pandemics. In this Comment, we interpret existing guidance documents and argue when and under which conditions deferred consent can be considered ethically acceptable in a pandemic.

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Currently, several COVID-19 studies allow the inclusion of patients in their protocols on the basis of the so-called ‘deferred consent’ or Exemption from Informed Consent procedure used in emergency-care research settings. For example, the RECOVERY protocol, in which patients are randomly assigned to various treatment arms (among others, dexamethasone), states “Due to the poor outcomes in COVID-19 patients who require ventilation (>90% mortality in one cohort), patients who lack capacity to consent due to severe disease (e.g. needs ventilation), and for whom a relative to act as the legally designated representative is not immediately available, randomisation and consequent treatment will proceed with consent provided by a treating clinician (independent of the clinician seeking to enrol the patient) who will act as the legally designated representative. Consent will then be obtained from the patient’s personal legally designated representative (or directly

from the patient if they recover promptly) at the earliest opportunity”¹.

However, deferred-consent procedures have not been developed for pandemics, and in the past decade there has been increasing debate on the ethical acceptability of this procedure^{2–4}. Whether the inclusion of these procedures in a study is acceptable deserves further scrutiny.

What is deferred consent?

The deferred-consent procedure has been developed for two types of emergency-care settings: clear-cut cases in which patients are incapable of providing informed consent, such as seizures, sepsis, shock and severe traumatic brain injuries; and a ‘gray area’ of emergency-care situations in which the ability of patients or their representatives to provide voluntary informed consent and to understand the information may be diminished, such as in the case of respiratory distress, depression or acute myocardial infarction⁵.

In a deferred-consent procedure, at the time of the experimental intervention, the patient is incapable of providing informed consent and their legal representative is incapable of providing consent or is not available. Consent for continuation of trial enrollment and data collection is obtained only when the patient is capable of providing informed consent or the representative is available, which renders the consent ‘deferred’.

Several documents legislate the right for those carrying out the trial to use deferred consent^{6–10}, but by and large they have in common the following:

- the research participant suffers from an emergency condition that needs immediate treatment;
- this condition renders the participant incapable of giving informed consent;
- an attempt has been made to obtain informed consent from the participant’s legal representative;

- the study cannot be conducted in a population that has not developed the condition under study;
- informed consent to remain in the study is obtained from the participant or the legal representative as soon as possible;
- the treatment under investigation is considered to be potentially beneficial for the participant;
- the research participant has not objected in advance to research participation;
- the research cannot be conducted without the option of deferred consent;
- the risks of receiving the intervention are minimal, at least in comparison with the standard treatment of the research participant; and
- the research ethics committee has approved the deferred-consent procedure.

Some guidance documents have additional requirements, such as the need for community engagement, the maximum time of enrollment without informed consent from the participant or the representative, and the use of advance directives before participants become incapable of giving informed consent.

At the same time, deferred-consent procedures are also debated. For example, one of the questions is which alternatives exist when a conventional informed-consent process in an emergency-care situation is impossible^{2–4}. In particular, patients who fall into the ‘gray area’ may be able to understand aspects of the study that could be explained in a modified informed-consent procedure, which could be done instead of the use of merely waivers or deferrals of consent⁴.

Deferred consent and COVID-19

In the context of COVID-19, respiratory distress is the prime symptom of COVID-19, and the condition of a patient may deteriorate soon after they are admitted in a relatively stable condition at the emergency department. In the intensive care unit, the treatment of patients with COVID-19 consists mainly of ventilator support with supportive case measures.

Additional experimental anti-viral or anti-inflammatory medications may be added to this standard treatment, and these are assumed to be most effective when administered as soon as possible after symptom onset¹¹. In many settings, additional medications are provided mainly within the context of clinical trials¹¹.

In the case of COVID-19, patients may be intubated early after admission, which makes it impossible for them to provide consent. The fact that this is happening as

part of a pandemic, such as COVID-19, makes contacting the legal representative much more complicated. They might not be immediately available because they may not be allowed in the intensive care unit because of lack of protective equipment, because they are in self isolation or because travel is not recommended. If the legal representative cannot be physically present to sign papers, organizing informed consent remotely is an alternative but can be logistically difficult, which may cause delays.

Because of such foreseen complications, for some COVID-19 studies, several protocols have included deferred-consent procedures. However, we believe that in practice, there are very few situations in which deferred consent will be needed or is warranted. In our experience, only a few patients need immediate intubation, and in most cases, successfully contacting a remote legal representative does not lead to a life-threatening delay in the provision of care. In many COVID-19-related studies there is a ‘therapeutic window’ (Clinical Trial Regulation 35)⁶ for obtaining informed consent. Patients may be coherent when they are admitted to a COVID-19 ward. In these COVID-19 wards, patients can sign an informed-consent document preemptively, for inclusion at a later time when their condition deteriorates and authorization is no longer possible, or they may be pointed to potential COVID-19 studies and express their interest in participation, such as by means of an advance directive (e.g., Council for International Organizations of Medical Sciences guideline 16)⁷.

Moreover, as has been seen with hydroxychloroquine, which has been widely used as a possible treatment for COVID-19 but has been shown to cause substantial toxicity without any current proven benefit^{12,13}, some of these experimental treatments may worsen symptoms and put the patient at higher risk than if they were receiving supportive care only. If this is known in advance, the minimal-risk requirement for acceptance of deferred consent cannot be met.

We argue that as long as researchers and sponsors have an opportunity to enroll patients in advance of intubation, such as admission to a COVID-19 ward, a deferred-consent procedure in a pandemic should not be regarded as acceptable.

However, in the case of observational studies investigating COVID-19, such as obtaining blood to determine viral load and collecting inflammation-related parameters in patients who are severely ill, we believe that the requirements that need to be met for deferred consent may be too stringent.

Obtaining these data in the context of an ongoing pandemic can be of major importance for quickly learning about the disease, which immediately affects the treatment of subsequent patients¹⁴. It poses a minimal risk to patients but has no direct benefit for these patients either. We think the following conditions should apply when collection of tissues or samples with a deferred-consent procedure is proposed:

- (a) for studies with a therapeutic intent, it is not possible to enroll patients in advance of intubation;
- (b) there is no way to obtain samples (and the related data) other than through the use of a deferred-consent procedure;
- (c) the study cannot be done with competent patients (e.g., when this leads to bias in sample collection) or incompetent patients are needed to obtain the sample (subsidiarity);
- (d) all other conditions for deferred consent are fulfilled; and
- (e) applicable ethical and legal procedures for data collection are followed, such as protection of confidentiality of the personal data collected and mitigation of risks to privacy¹⁵.

These conditions may be relevant only to this very unique situation of a pandemic that presents a new pathogen for which no vaccine or effective treatment is available, for which it may be of the utmost importance to collect real-time data and samples to guide treatment decisions and to understand this emerging disease. In these cases, deferred consent should be allowed under the conditions that we have outlined. □

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References

1. Randomised Evaluation of COVID19 Therapy (RECOVERY). <https://www.recoverytrial.net/files/recovery-protocol-v6-0-2020-05-14.pdf> (2020).
2. Johnson, L. R. & Siddaiah, R. *Br. Med. J.* 351, h4609 (2015).
3. Olsson, A. et al. *Trials* 21, 246 (2020).

4. Dickert, N. W. et al. *Am. J. Bioeth.* **5**, 7–17 (2020).
5. Baren, J.M. <https://improvinghealthcare.mehp.upenn.edu/ethics-policy-covid19/intersection> (2020).
6. The European parliament and the Council of the European Union. Clinical Trials -Regulation (EU) No 536/2014. https://ec.europa.eu/health/human-use/clinical-trials/regulation_en (2014).
7. Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). *International Ethical Guidelines for Health-related Research Involving Humans* (CIOMS, 2016).
8. European Medicines Agency. <https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice> (2016).
9. World Medical Association. <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/> (2013).
10. US Food and Drug Administration. Code of Federal Regulations Title 21 §50.24. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.24> 2019.
11. Cardone, M., Yano, M., Rosenberg, A. S. & Puig, M. *Front. Immunol.* <https://doi.org/10.3389/fimmu.2020.01131> (2020).
12. Torjesen, I. *Br. Med. J.* **369**, m2263 (2020).
13. Mahévas, M. et al. *Br. Med. J.* **369**, m1844 (2020).
14. Henry, B. M., Santos de Oliveira, M. H., Benoit, S., Plebani, M. & Lippi, G. *Clin. Chem. Lab. Med.* <https://doi.org/10.1515/cclm-2020-0369> (2020).
15. EUR-Lex. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02016R0679-20160504&from=EN> (2016).

Competing interests

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