Research Integrity in trying times: a scenario on the presentation and dissemination of information

Background

It has been 10 months since the origin of the global health crisis caused by the comma virus pandemic. This virus can affect nearly every organ system in the body. Patients are also more prone to other infections, especially the potentially fatal lucor fungal disease. Formerly a rare infection, the lucor-commavirus double infection is increasingly reported all over the world, disproportionately affecting those in tropical regions.

Myra Nair (MN) is a postdoctoral researcher studying fungal pathogens in the Molecular Biology lab at the KL University in Belgium. Hailing from Synd, a hotspot of commavirus-lucor infections, she is keen on studying the pathogenesis of this infection. Her mentor, Professor Ignace Janssen (IJ), is an authority in the field. MN has developed a hypothesis that a drug deferixin, which lowers iron levels in the blood, would be useful to prevent this double infection.

Issue 1

MN presents her hypothesis to IJ, outlining the current knowledge. In in-vitro and animal models, the growth of the lucor fungus is markedly inhibited by deferixin. Only two Randomized Control Trials (RCTs) on humans exist, conducted prior to the pandemic on small patient groups with severe co-morbidities (n=20 and 12). Both studies found the drug to be ineffective, but concluded that this could be due to the small sample size and the severely ill patients. In human trials studying non-lucor fungal infections, deferixin showed modest positive results. MN reasons that though the RCTs have shown no effect, further trials are warranted since the commavirus-lucor infections constitute an unprecedented situation, and since the drug is highly effective in-vitro.

IJ is very interested in developing MN's idea. He encourages MN to promptly write a proposal for funding application, which he revises. When MN reads the approved version prior to submission, she realizes that IJ has removed most of the information on the two RCTs. When she points this out, IJ explains that they require the funds immediately, and that omitting this information is inconsequential as the drug could save lives. Besides, he argues, the RCTs were performed in a completely different cohort and are thus not relevant to their study. MN, though reluctant, agrees because she trusts IJ's experience and is keen on starting the research.

1. a. Questions for researchers

1. Is it problematic or questionable to not include all information on funding proposals? Why?
2. What values and virtues play a part in this context?

3. How can an early stage researcher such as MN respond to this kind of situation? Could she bring up her concerns with another person or body without jeopardizing the project?

1. b. Questions for Research Administrators

1. Does the non-inclusion of possibly relevant information in the funding proposal constitute research misconduct?

2. What are the institutional safeguards that could help prevent this practice?

1. c. Questions for RIOs and RECs

1. During health emergencies such as the pandemic, timely research could be hugely impactful. Do ethics review procedures and safeguards change in this situation?

2. Do ethical standards for research protocols change in emergency situations?

Issue 2

The proposal is accepted and approved swiftly by the review board. With IJ's colleague Dr. Olivier Peeters (OP), an infectious diseases specialist, and MN's Syndian colleague Qabiz Rahim (QR), a biostatistician, they plan a multicenter randomized control trial. Proportionate to the incidence of the lucor-commavirus infections, most of the participants will be Syndians.

The trial proceeds as planned, and in four months, the team has the preliminary results. Of 60 patients with commavirus-lucor infections treated with deferixin, there were only 3 fatalities whereas 12 of the 60 in the control arm succumbed to the illness. Those treated with deferixin also had shorter hospitalizations, with the results confirmed as being statistically significant. IJ, MN and OP realize the importance of this breakthrough, and are eager to publicize the results. OP is bent on submitting a manuscript as quickly as possible, and they do so in two days to a high-impact factor journal. Because QR could not be reached via telephone or e-mail during this time, they have not informed him about the submission, though he is included as an author.

2. a. Questions for researchers

1. What are the ethical principles that guide collaborations in research?
2. In this instance, practical difficulties have prevented timely and effective communication. What are possible ways in which this could be avoided?

2. b. Questions for Research Administrators

1. Effective communication between collaborators is crucial throughout the course of the research, but sometimes challenging. This can be especially true in the case of international collaborations. Are there ways in which research administrators can encourage open and timely communication between collaborators?

Issue 3

The mean review time for the journal is 4 weeks. OP insists that they not delay communicating the information to the medical community. Consequently, IJ, MN and OP upload the unreviewed manuscript in a pre-print server, a practice which is allowed by the journal.

The pre-print article immediately receives instant attention, not only from medical practitioners worldwide but also on social media and news outlets. Within a week, deferixin is incorporated into the treatment guidelines of many countries, including Synd. Consequently, there is a huge demand for deferixin, and it is being prescribed indiscriminately. Patients who routinely require deferixin for other conditions are faced with drug shortages and unaffordable prices.

3. a. Questions for researchers

1. As part of the collaboration, should QR have been specifically informed about the manuscript being pre-printed? Is this a different context from publication?
2. Is it ethically acceptable to publicize non peer-reviewed information? What could be the reasons for and against doing so?

3. Are there any precautions that the authors could have taken while uploading the pre-print version?

4. What are the responsibilities of researchers when they convey their findings to the scientific community, and to the general public? What are the values that should guide this? Should the research team have anticipated the far-reaching effects of their publication on the situation in Synd and other countries?

3. b. Questions for Research Administrators

1. Are there ways in which research administrators can monitor or influence how research results are communicated?

3. c. Questions for RIOs and RECs

1. By publishing a pre-print (unreviewed) article, do the authors violate the European Code of Conduct for Research integrity?

2. Are there other relevant guidelines (for instance, from the WHO) that offer guidance on how information should be communicated, especially in a pandemic situation?

Issue 4

10 days after the pre-print was uploaded, the authors receive the peer reviewers' feedback. Three reviewers point out a serious flaw: the datasets do not reflect the attributes used to randomize participants. The randomization appears faulty, with fewer seriously ill patients in the deferixin arm, which accounts for the lower mortality observed. The findings of the entire study are cast into doubt.

IJ, MN, and OP immediately retract the manuscript from the pre-print server stating the reason for retraction. However, it has already been widely shared and cited. On reviewing the randomization tables, IJ finds that the faulty randomizations have occurred in the Syndian centres. He claims that QR is solely accountable, though this was not indicated in the manuscript. QR

denies any responsibility, pointing out that he was not informed about the submission or the pre-print.

4. a. Questions for researchers

1. What are the best practices concerning retraction of research manuscripts? Do the researchers' responsibilities end with the retraction?
2. In the submitted manuscript, QR's specific role as part of the research team was not mentioned, leading to ambiguity about the attribution of responsibility. Are there standardized ways of acknowledging contributors' roles?
3. To what extent do you think each researcher, or each team in a collaboration is responsible for the whole research project?
4. Does the degree pf overall responsibility for the project change based on the seniority or designation of the researcher?

4. c. Questions for RIOs and RECs

1. The ECCRI states that "all partners in research collaborations take responsibility for the integrity of the research." In practice, to what extent is this true, especially in the context of international and interdisciplinary research?

References:

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Suggested Resources:

Committee on Publication Ethics (COPE) Retraction Guidelines: https://publicationethics.org/node/19896

Embassy theme page on Inaccurate representation of Results in the Media: https://embassy.science/wiki/Theme:1f1c45e8-e91d-4eb4-b252-23e319d34f78

European Code of Conduct on Research Integrity: https://www.allea.org/wp-content/uploads/2017/05/ALLEA-European-Code-of-Conduct-for-Research-Integrity-2017.pdf

International Bioethics Society and the World Commission on the Ethics of Scientific Knowledge and Technology: Statement on COVID-19: ethical considerations from a global perspective: https://unesdoc.unesco.org/ark:/48223/pf0000373115

Position of the European Network of Research Ethics Committees (EUREC) on the Responsibility of Research Ethics Committees during the COVID-19 Pandemic: http://www.eurecnet.org/documents/Position_EUREC_COVID_19.pdf

Standard Operating Procedures for Research Integrity (SOPs4RI) toolbox: Publication and Communication: https://sops4ri.eu/tool_category/publication/

Trust in Science and Changing Landscapes of Communication: https://www.allea.org/wp-content/uploads/2019/01/ALLEA_Trust_in_Science_and_Changing_Landscapes_of_Communication-1.pdf

University of Michigan Research Administrators' Toolkit: Communications Best Practices : https://orsp.umich.edu/sites/default/files/resource-download/communications-best-practices.pdf

WHO Ethical standards for research during public health emergencies: Distilling existing guidance to support COVID-19 R&D: https://apps.who.int/iris/bitstream/handle/10665/331507/WHO-RFH-20.1-eng.pdf?sequence=1&isAllowed=y

WHO Guidance for Managing Ethical Issues in Infectious Disease Outbreaks: https://apps.who.int/iris/bitstream/handle/10665/250580/9789241549837-eng.pdf?sequence=1&isAllowed=y