Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Leaks of Clinical Trial Data and Research Integrity

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On April 16, 2020, STAT news reported that of 113 patients with severe coronavirus disease 2019 (COVID-19) treated with remdesivir in a clinical trial at the University of Chicago, most got better within 6 days and only 2 died.[1] These data did not come from a press release, abstract presentation, preprint source, or peer-reviewed publication. Rather the information was obtained from a leaked video recording of an internal discussion that the lead investigator of the trial, Dr Kathleen Mullane, had with her colleagues. The news report had an immediate positive effect (12% increase) on the stock price of Gilead Sciences, the manufacturer of remdesivir.[2] Although investors, the lay press, and the public derived hope from the report, it is far from clear whether the leaked information accurately reflects the overall results of this large multicenter trial, and, more importantly, whether any conclusion can be reached from this trial without an appropriate control group. This incident is extremely troubling because it threatens research integrity and patient welfare that such medical research is intended to advance. In this perspective, we outline steps that must be taken to prevent such occurrences in the future.

First, from personal experience, it is very common for academic groups to informally discuss results of ongoing trials. These discussions take place within an institution as well as with colleagues from other institutions. Some are simple one-line statements from a principal investigator to colleagues that a certain number of patients given a new drug have responded to therapy. Sometimes the presentations can be more detailed, with remarks on the type of adverse events or on the dosing schedule. From one standpoint, these informal updates on ongoing trials convey investigator enthusiasm with a newly active therapy. It leads to better accrual. On the other hand, in today's world, investigators must recognize that their every word may be recorded, every slide photographed, and every presentation filmed, with or without their consent. Everyone has access to powerful recording technology on their mobile devices. Investigators must assume that any discussion of ongoing trial results, even among friends, is being recorded. That realization is the first step to prevent similar leaks.

Second, these discussions happen mainly in trials without a control group, or in open-label randomized trials. In such trials, investigators are aware of the specific treatment that a patient is receiving. In new drug trials for cancer, tumor response can be objectively measured, and so the investigator has a good idea of the effect of the agent on the tumor. But tumor response may not reflect whether a patient is deriving true clinical benefit (improved survival or quality of life).[3] Responses seen in one institution may also not reflect the true effect across sites in a multicenter trial. Thus, investigators must be disciplined enough to curb their enthusiasm and recognize that their assessment of whether a drug is beneficial could be wrong and that it is not wise to discuss preliminary data with anyone. This is even more of a concern in cases such as COVID-19 in which we do not have a measurable surrogate end point similar to tumor response in cancer. Improvement in clinical condition can occur as part of the natural history, and in this case it is impossible to be confident of a causal association between remdesivir and recovery without a control group.

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Third, investigators must be aware of legal consequences. Leaked information can affect the value of a company stock price when such information is made public.[2] If the leak is not made public by the media, or reaches the wrong hands, it could lead to insider trading. Already, investigations by the Securities and Exchange Commission have been called for.[4] Investigators typically act in good faith and with the goal of disseminating seemingly exciting information early with their colleagues. However, they need to recognize that good intention is neither an excuse nor a defense if legal contracts or disclosure agreements are compromised.

Finally, leaks threaten research integrity. Patients need us to identify the right treatments and make the right decisions. Early peeks at the data jeopardize future conduct of the research in question. They may lead to differences in the types of patients who are subsequently accrued to the trial, excluding some and including the ones that are felt (likely erroneously) to benefit the most. Leaks such as the one involving remdesivir may slow accrual to randomized controlled trials because patients (or their representatives) now feel that they should receive the active treatment and may be reluctant to be randomized. Once leaks start, they do not stop. Within a week of the initial leak we now have results of a randomized trial of remdesivir "accidentally" posted on a World Health Organization website that have been obtained and published by the press.[5] This leak found that remdesivir was not beneficial, and, as expected, had the opposite effect on the company stock price.[6] The hopes of patients swung from one extreme to another, and faith in the integrity of clinical trials has been affected. COVID-19 is an unprecedented crisis. In our haste to find answers mistakes will happen. But we must use the opportunity to learn from these mistakes and ensure that they are not repeated. No more leaks.

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