Case reports: More than enough evidence

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Case reports, unlike randomized trials, are simply records of what actually happened – in the office, the clinic, or the hospital. They are chance events that we seek to understand and explain. They are fairly easy to write up, and do not require a lab, a research budget, or an administrator: "All you need," wrote one of my medical students, "is a patient and an observation."[1] Randomized trials, on the other hand, are carefully choreographed research enterprises that seek to answer specific questions about medicines or treatments under carefully controlled conditions. Randomized trials may be ingeniously constructed, but they are not creative. Case reports are fresh, speculative, hypothetical, and innately creative because they must try to explain the unexpected. The observations and hypotheses brought forth in case reports and case series supply many of the questions that randomized trials seek to answer. Case reports are exploratory; randomized trials are confirmatory. The case report vindicates the role of chance in the advance of knowledge.

Case reports have been dismissed by many as a weak form of evidence, little more than clinical oddities written up by dilettantes working at the fringes of medicine. It is true that some case reports are probably one-off aberrations that will never happen again. Others, however, are sentinel events, harbingers of something new and important. There is novelty at the fringes of medicine, where we find uncharacterized syndromes, new tests and technologies, bizarre drug reactions, innovative surgical approaches, new hypotheses, and unexpected connections. Case reports live and thrive on the fringes – and the fringes are very close to the cutting edge. The first use of data from a wrist activity tracker to safely cardiovert a patient with new atrial fibrillation in the ER was described in a recent case report.[2] The early successes of circulating tumor DNA testing (the "liquid biopsy") have been documented in several case reports,[3] and genomic case studies of exceptional cancer responders have led to increased survival for significant subpopulations of patients with the same mutations.[4] Case reports also play a critical role in understanding and treating new diseases and epidemics, such as toxic shock syndrome, AIDS, SARS, West Nile virus, Ebola, and Zika. A 2014 case report by Kreuels et al, *A case of severe Ebola virus infection complicated by gram negative septicemia*,[5] meticulously documents the natural history of Ebola virus infection, describes an effective treatment regimen using general ICU measures, and gives basic principles – the vital importance of aggressive IV hydration, the use of ultrasound to assess the adequacy of hydration, and the need to monitor for signs of superimposed bacterial infection using lab testing – that can improve the odds of survival. Practical management points are a strong suit of case reports.

In addition to its function in discovery and innovation, the case report has an essential role in personalized medicine. The interactions of multiple co-morbid conditions, drugs, and sociodemographic factors in any one patient are too complex to be studied in randomized controlled trials, which must be reductionist in order to study treatments in large populations. It follows that randomized trials, while helpful for many patients, cannot be applied to all; for this reason, RCTs have been described as "imprecision medicine."[6] Individual case reports, which allow for almost unlimited complexity, can be used in n-of-1 trials to identify the variables that might suggest favorable response to a drug or treatment. These results can then be generalized to groups with similar characteristics. This type of inductive or "specific-to-general" research approach is the future of personalized medicine, and it ties in perfectly with the case report.

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If you have an interesting case and want to publish it, my advice is that you a find a medical student or resident to work with you as a co-author. Trainees bring energy, imagination, and fresh knowledge of the basic sciences to the project. They love to hypothesize, and often can find ingenious and plausible explanations for the case report findings. They need help with organization and editing (they tend to put too much extraneous information in their case descriptions) and have to be careful not to overstate their conclusions. The back-and-forth process of drafting the manuscript and then responding to peer review is a great opportunity for extended mentoring, and can sometimes lead to ongoing research and writing partnerships. Finally, the published case report serves as tangible evidence of teaching for faculty co-authors who aspire to academic promotion.[7] I have co-published 15 case reports with medical students and residents, and I feel strongly that these collaborations represent some of the best and most productive teaching I have ever done.

Despite the protests of the acolytes of evidence-based medicine and the impact factor, case reports are important. They give practical guidance in the management of complex patients. They identify new diseases and key sentinel events. They provide a venue for novelty and new technologies. They generate hypotheses that can be tested in clinical trials. They help teach medical trainees to write and think like scientists, and experienced physicians to be better mentors and teachers. When it comes to case reports, there is more than enough evidence to proceed.

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