Progress in medicine has been made in the past primarily through the clinical experience of physicians and uncontrolled observations. With the advent of medical journals, knowledge dissemination and much of medical progress had been made possible through clinical reports and meticulous observations on cases or series of cases. This was true for many medical breakthroughs, including the initial paper by Burrill Crohn, Leon Ginzburg and Gordon Oppenheimer, who described their observations of a mere 14 surgical patients with 'regional ileitis', which later became known as Crohn's disease. However, in recent decades, the controlled clinical trial gained primacy as the holy grail of evidence-based medicine, and observational studies similarly became subject to stricter and preferably comparative statistical methodology in the forms of population-based studies, prospective cohorts or retrospective case-control studies. This trend, towards comparative and preferably controlled research methodology as the prevailing dogma, has led to case reports falling out of favour with the medical scientific community touting its potential caveats of chance associations and susceptibility to many uncontrolled confounders. Coupled with the fact that case reports may create less citation potential, which is necessary for a journal impact factor and citation index standing, case reports and case series have also found it increasingly difficult to be published. Indeed most leading gastroenterology journals, JCC included, now generally refrain from publishing case reports or small case series.

Does this mean there is no place for the case report anymore? Is there still a case for the small case series? We believe case reports or case series still have important role in advancing medical knowledge, one that is often not possible through controlled clinical trials or even through population-based studies. Clinical trials, population-based epidemiological investigations and even large case-control studies can only investigate the designated associations they set for themselves, but are rarely useful for recognising a novel association per se. Moreover, certain sub-populations are deliberately excluded from clinical trials, making them inapt to disclose associations of therapeutic interventions with certain co-morbidities or specific patient characteristics. Thus, rare and often unexpected associations are even nowadays first revealed by case report/s.

One such publication significantly impacted on our medical practice and has saved many lives, by describing a modestly sized case series of patients with tuberculosis following anti-TNF therapy, which was spurred by a single case encountered by Professor Joseph Keane in his Irish hospital [Keane J, personal communication]. Some cases may be so striking so as to correspond to what may be dubbed as the ‘parachute rule’, i.e. even a single case of jumping out of a plane and landing safely with a parachute is enough evidence to make a controlled trial of parachutes redundant. Similarly, some
associations are so unlikely, that even a single case report may indicate a genuine need to alter medical practice or to consider novel biological phenomenon. Such was the report in JCC several years ago of fatal disseminated BCGosis in a newborn who was exposed to infliximab in utero, implying that these babies may be at risk if given live-attenuated vaccines after birth. Of great importance also was the report of progressive multi-focal leukoencephalopathy following natalizumab treatment in a single Crohn’s disease patient. When striking enough, a single case report may even indicate a previously unrecognised biological process or phenomenon of high importance, such as the recently reported case of human neoplasia actually caused by invasive transformed cancer cells from a colonising tapeworm. For these and other rare events, the ability of the human mind to pick up extremely unique perturbances of knowledge surpasses the ability of statistics to identify them, despite present well-designed clinical trials or population-based studies.

However, to enhance the validity of a single case of a rare event, accruing even a handful of similar such cases will support the purported association. With this understanding in mind, the Collaborative Open Network For Extremely Rare cases (CONFER) project was initiated by the European Crohn’s and Colitis Organization (ECCO) in 2012. ECCO CONFER Cases is an initiative to continuously identify, assemble and report together rare inflammatory bowel disease (IBD) cases or rare cases of IBD-associated diseases and complications of clinical relevance.

The four categories of topics usually covered by the CONFER activities are: rare infections, uncommon drug beneficial effects or side effects, rare IBD manifestations and infrequent disease associations [neoplastic, infectious etc.]. By joining forces with the many members and supporters of ECCO, a joint report of all similar such cases can result in a case series including more significant numbers of patients which will advance our knowledge about these uncommon patients, which would otherwise be reported as single case reports or not reported at all. ECCO CONFER was launched with the realisation that if a particular IBD event is so rare as to be encountered only once by one out of 100 IBD experts during their career, than joining forces by the ≥3 000 members of ECCO may result in 30 such cases being identified, to enhance the scientific robustness of the report.

Since its launch, ECCO CONFER has operated according to a structured protocol. A call is made once a year through the official ECCO website and via email also to all ECCO Members, to propose CONFERS case projects. Two to four cases are selected by the CONFER steering committee once a year, and the proposing investigator then acts as the primary investigator and develops his/her case into a CONFER case project with the steering committee. When the title of the CONFER case project is decided, a call is subsequently made to all ECCO members inviting those who have encountered a similar case to contribute their case to the CONFER case series and become co-investigators for the particular project. This call is followed by several reminders if needed. All received cases are joined into a case series by the primary investigator and prepared for publication. So far, three ECCO CONFER projects were successfully completed and have already been published in JCC: investigating the occurrence of cerebrovascular events in patients treated with anti-TNFs; the association of Cogan’s autoimmune auditory disorder with IBD; and the association of optic neuritis with biologic drugs. A minority of CONFER projects did not find sufficient numbers of cases and it was decided not to continue with submission and eventual publication as a CONFER project, and to allow the investigator to report his/her interesting case independently.

IBD-logy remains a big challenge for all physicians who are active clinicians and work with patients and their daily problems. Progress in our understanding of this disease aetiology and its therapy relies upon well-designed clinical trials and systematic comparative studies. However, the clinical importance of clinical observations in individual patients should not be underestimated. Medicine is an art in practice which is driven by human ethics, philosophy of life, technology and experimental data but also by pioneers who had the ability to observe and report significant data on individual patients. Uncontrolled observations of uncommon events can still result in unravelling disease aetiology, improving diagnostic strategies and enriching therapeutic outcomes. We believe there is still room for educated, careful, uncontrolled observations of uncommon clinical events or associations. Their rarity and nature call for collaborative reporting efforts spanning hundreds of doctors, to yield the best possible evidence.

We believe that ECCO CONFER and other similar initiatives have proven and will continue to prove the value and contribution of case reports to medical knowledge, even in a medical world reigned by group-comparative statistics.

In addition, through this manuscript, we would like also to strongly encourage and warmly invite further submissions to the CONFER committee.

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Conflict of Interest

None.

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