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Nullius in Verba

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Surgery, like other fields of medicine, has not been spared from a number of phenomena. Although it is natural to perceive these as recent trends, our awareness of these phenomena can be traced back to 1979; when Cohen L. and Rothschild H. claimed that even if current medical progress is extraordinary, the path has often been directed by overwhelming acceptance of popular but unproven ideas. These were called bandwagons of medicine. Some of these ideas were proven valid later, but more often they were abandoned and replaced by a new bandwagon. Preventing bandwagons from taking off in medicine must result from efforts at different levels. Innovators must constrain their self-interest, and drive towards achieving fame and success; recognizing instead the need to establish evidence for their ideas. New models for therapy must be weighed carefully and assessed in the balance of available published evidence before they are used on patients. Multimedia should not mislead patients, representing certain approaches as the "best" treatment, approaches which are actually the "latest" treatment, and lacking sufficient evidence. Physicians must learn that the process of development in medicine is slow and disregard the stimulus to accept the potentially plausible that remains unproven.[1]

Several articles in the literature claiming to be are publishing the "first" case, or the "largest" series to date. According to a PubMed search, carried out in August 2022, there over 400,000 such cavalier claims, appearing in 11,000 articles in the past two decades alone. Further, among the most common conclusions in over 40,000 articles in PubMed is the assertion that a procedure is "safe and feasible". This latter phenomenon has interestingly started in parallel with the beginning of a high volume of articles on laparoscopic surgery circa three decades ago. The fact that "safe and feasible" is neither part of the aim of the study nor of the methodology in most articles makes the conclusion absurd. Further, this conclusion has nothing to do with well-established safety outcome trials.

According to E. J. Huth, such publications would flunk the "who cares test"![2]: a question every academic, technical or professional writers have to ask themselves:

"Who cares about what I am writing?" Of course, if the answer is "No-one", the topic or the style of writing, etc. needs to be adapted or the writing should be stopped. Most authors think that their paper merits the attention of far more readers than it is likely to receive. This trait can lead to tactically poor decisions in writing the paper and selecting an appropriate journal. Decisions based on such questions can be crucial for prompt publication. Selecting the journal is also important to reach the appropriate audience (investigators, practitioners or technicians) and readers interested in the topic.[3]

In fact, first-in-human studies are an event reportable to the IDEAL (Idea Development Exploration Assessment Long-term). Ideal is a collaboration developed in an effort at maximizing patient safety. IDEAL proposes a recommendation for the assessment of surgery based on numerous steps of a surgical development process, parallel to the use of registries and prospective databases. In a step-up approach, a report of a new technique should be registered and, further, a case series implemented. The next step would be a prospective development study for early technique modifications and an evaluation before a trial starts. These protocols must be registered publicly. After a pre-trial has supported enough data for compiling a power-analysis, a pilot randomized trial can be started. Alternatively, an interrupted time series can be implemented, if a randomized controlled trial is not feasible. Finally, an established method needs to be monitored by prospective databases for the analysis of the outcome and the identification of rare and late events.[4]

Moreover, safety outcome trials and feasibility studies are well-defined entities by the FDA Medical Policy Council and by the UK National Institute Health Research,[5] respectively. For different purposes, early feasibility studies, first-in-human studies, traditional feasibility studies, and pivotal studies are available, each requiring adherence to a strict. Early feasibility studies for an early clinical evaluation and for a proof of principle must be justified by an appropriate benefit-risk analysis and adequate patient protection. In a first-in-human study a device for a specific indication is evaluated for the first time in humans. The traditional feasibility study is a clinical investigation that is used to gather preliminary safety and effectiveness information on a near-final or final device to plan a pivotal study. A pivotal study is a clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified, intended use. The number of patients in this study is statistically determined by a power analysis.[6]

Furthermore, B. Millat made us aware of the feasibility hazards that studies may present: worsened risk-benefit ratio, no valuable information provided to patients and surgeons. As an example, Millat claimed that just the fact that an operation can be done by a laparoscopic approach does not mean that the operation has to be done in every patient. Operations such as laparoscopic cholecystectomy or laparoscopic anti-reflux surgery have been dramatically increasing due to questionable indications. This lowers the risk-benefit ratio, as complications in healthier and younger patients with only a relative indication weigh more than in severely ill patients. Furthermore, feasibility studies likely come from a center of expertise without any external validation. Specific results and a selected patients collective, in addition to withdrawing cases within the surgeon's individual learning curve, led to a generalization of the results. Often, the excellent results of a feasibility study cannot be replicated in a large multi-center study. The efficiency of a surgical concept must by validated by comparison with an adequately defined control group and statistical tests.[7] *Exempli gratia* of disingenuous phenomena inundating the colorectal literature include bandwagon effect, spin, and deceiving analyses.

Although bandwagons are known to all cultures familiar with carnival festivals, the term was popularized in the United States by Dan Rice, a clown who in 1848 entered politics to support the Taylor campaign. Rice would have said "jump on the bandwagon."[8] The bandwagon phenomenon was first defined in 1950 by economist Leibenstein as the desire of individuals to embrace something in order to conform to people they wish to be associated with in order to be fashionable.[9]

Returning to the field of surgery, the most infamous bandwagons probably were: phlebotomy, frontal lobotomy, prophylactic tonsillectomy, and radical mastectomy. Bandwagons share a few patterns: They offer simplified one-size-fits-all solutions to complex clinical conditions, an inability of others to reproduce similar results, and they are in unison with the prevailing zeitgeist. Rikkers, in his 2002 presidential address to SSAT (The Society for Surgery of the

Alimentary Tract) described the bandwagon effect as it pertains to surgery. Bandwagons are processes or movements, that are defined as a current trend that attracts adherents by its timeliness, vigor, and novelty as well as amassing power or influence by the internal unit of a group. Medical bandwagons are defined as the overwhelming acceptance of unproven but popular ideas and lead to inappropriate therapies for a large number of patients. The answers to the question of why bandwagons occur frequently are manifold. Those who propagate these bandwagons, can be driven by: potential economic gain, feeding the ego, academic advancements, or improved reputation among funding agencies, peer reviewers of manuscripts, or patients themselves. These and other factors can lead to a framework for eventual bandwagons. Rikkers stated that two key components are helping to avoid bandwagons in medicine. First, clinical decisions should be based on the best available evidence and, second, we should encourage independent and critical thinking in ourselves.[10]

In the specific case of colorectal surgery, there are at least five such cases currently ongoing. These are as follows: laparoscopic lavage of perforated colon, laparoscopic "ventral" rectopexy, stapled hemorrhoidopexy (PPH), watch & wait for rectal cancer, and transanal TME (total mesorectal excision). However, it must be acknowledged that legitimate clinically relevant concerns have been in place preceding the advent of these five bandwagons.

Colon perforation generally requires emergency surgery when associated with peritonitis. Reasons for the perforation can be iatrogenic or spontaneous but, most commonly, colonic perforation occurs secondary to malignancy or in patients with diverticulitis.[11] Perforation due to diverticulitis has an increasing prevalence up to 3.8 in 100,000[12] and an intra-operative mortality of about 8%.[13] The most frequent site of the perforation is the sigmoid colon in colonic cancer but also in acute diverticulitis patients. Recently, laparoscopic lavage has been introduced for the treatment of perforated diverticulitis with peritonitis, even though it is known that the clinical presentation of peritonitis can also be caused by an underlying perforated carcinoma. Thus, it is possible, even likely, that a certain percentage of perforated colon cancer patients has been undergoing laparoscopic lavage. Analyzing three RCTs[14-16] has shown that colorectal cancer patients were lavaged in every tenth case. This leads to delay in diagnosis and treatment initiation of a median of two months in these RCTs. This is important as a perforation of colon cancer is mostly seen when the disease is in an advanced stage, without previous treatment. The reason for the delay is that laparoscopic lavage aggravates the infection due to faecal content and tumor cells and leaves the cancer undiagnosed.

An analysis of the National Cancer Database including over 180.000 patients showed that waiting time of more than 6 weeks between diagnosis and surgical procedure was associated with higher 30-day and 90-day mortality, as well as a lower 5-year overall survival.[17] Further, a meta-analysis including seven studies showed that delayed resection of colorectal cancer was associated with a poorer overall and also disease-free survival.[18] To summarize, the existing literature highlights that diagnosis should not be delayed and the interval between diagnosis and surgical procedure should be as short as possible to improve patient outcomes. In addition, lavage itself has the potential to spread tumor cells in the abdominal cavity and can therefore accelerate tumor progression in patients.

Approaches to the management of full-thickness rectal prolapse (FTRP) have been the subject of discussion for more than 100 years. The literature illustrates a disproportionate abundance of surgical techniques, which include those directed at obliteration of the pouch of Douglas, and suspension of the rectum by various means. Regarding the latter operation, Carrasco.[19] reported in 1934 suturing the rectum to the sacrum. This concept that went down into the literature as posterior rectopexy because the rectum was suspended by sutures placed onto the sacrum. The addition of a mesh to attach the rectum to the sacrum was proposed by Wells,[20] who employed a polyvinyl alcohol sponge in 1959, whereas Ripstein[21] used Teflon in 1965. Meanwhile, Lloyd-Davies described in 1949 a rectopexy technique where the rectum was sutured to the vaginal wall: it was called anterior.[22] In 1960 Deucher called the same procedure ventral rectopexy.[23] On the basis of this brief historical flashback, the reader may easily understand that neither the use of mesh nor the term ventral are new in the literature of rectopexy for FTRP. Moreover, the adjectives posterior and ventral made no reference to where the rectum was suspended: the sacrum and the vagina, respectively. In

more recent years, the reader can encounter publications that utilize the adjective "ventral" rectopexy, albeit the rectum is still suspended with mesh *posteriorly* to the sacrum.[24] The bandwagon that followed resulted in a number of studies have claiming improvement in terms of constipation rates following "ventral" rectopexy. Nonetheless, such studies consist of small case series with short follow-up,[25] as well as retrospective studies with large loss to follow-up.[26] In 2015, D'Hoore et al. claimed a decrease in obstructed defecation from a preoperative 54% rate to a 15% rate after "ventral" rectopexy. Nonetheless, the study was retrospective with just one third of the patients having the diagnosis of FTRP, no validated functional evaluation scores, and non-systematic follow-up.[27] In 2016, a double blind RCT led by Laurberg concluded that there was no difference in rates of obstructed defecation between posterior and ventral rectopexy both performed laparoscopically at one-year follow-up.[28]

The search for alternatives to hemorrhoidectomy for grade III and IV internal hemorrhoids has been motivated by the need to reduce postoperative pain with its associated disability as well as its potential long-term sequelae. A few procedures have been proposed as an alternative to address such concerns while trying to keep an eye on the recurrence rates observed following excisional surgery. Among the innovative techniques are dearterialization and stapled hemorrhoidopexy (PPH), both non-excisional technique that are aimed at addressing postoperative pain and its disability. The latter technique was invented and popularized by Longo in Vienna, Austria. Subsequent to stapled hemorrhoidopexy grabbing headlines, Mortensen implemented a single-center randomized trial (RCT) at St. Mark's Hospital in the year 2000 involving professor Nyström P. from Sweden as independent assessor of the trial clinical outcomes. The RCT was prematurely terminated due to persistent anal pain and fecal urgency for up to 15 months in 31 percent of the patients having been randomized to stapled hemorrhoidopexy.[29] Although no direct causality could be established, muscle incorporation in the doughnuts was associated with adverse outcomes. Mortensen went the extra mile using histopathology to further elucidate the potential drawbacks of this technological innovation. A prospective cohort of consecutive patients underwent stapled hemorrhoidopexy at John Radcliffe Hospital during the same year. The main findings of the study pointed at the internal sphincter (rather than the rectal wall) as the muscle having been excised by the stapler.[30]

Any bandwagon effect involving cancer care has obviously undergone a great deal of scrutiny (as is appropriate) given the concern deriving from any deviation from the standard of care. The so-called Watch & Wait for rectal cancer is no exception. Professor Nahas, chair of colorectal surgery at the State University of Sao Paulo delivered a lecture on this topic at the State University of New York, Stony Brook in 2012. His contribution is of great relevance given his position as successor to Professor Habr-Gama, who is the first proponent of the Watch & Wait policy. In essence, Watch and Wait suggests that chemoradiation alone would lead to "clinical complete response". Indeed, the first obstacle is the definition of such ca oncept: absence of residual mass or ulcer; residual scar with negative biopsies; sustained for at least 12-month follow-up; negative radiological studies? With regard to the last definition, it must be noted that the accuracy of most imaging tests carried out after chemoradiation does not exceed 60%.[31] The next obstacle is the fact that clinical response does not predict pathology response. A retrospective study of 488 stage 2 rectal cancer patients concluded that 75% of patients with "clinical complete response" still had residual cancer cells in biopsy.[32] Similarly, a prospective study of stage 3 rectal câncer patients reported the following correlation between clinical and pathological response: sensibility 24%; specificity 56%; PPV 19%; NPP 61%.[33] A systematic review of 30 publications including 650 patients having undergone Watch & Wait after chemoradiation from 1990 to 2011 identified 18 publications by Habr-Gama and 12 by other authors. This critical appraisal concluded that the 4.6% locoregional recurrence, 96% overall and 72% disease-free survival reported by Habr-Gama could not be reproduced by any other authors.[34] In conclusion, methodologically speaking "Wait and Wait" policy has been based exclusively on retrospective observations from a cases series. The main obstacles to "Wait and Wait" policy remain: arbitrarily chosen time to assess response, a lack of standard criteria to define clinical/pathological response, potential for a mismatch between clinical response and pathologic response, inaccuracy of imaging studies in predicting pathologic complete response, and that pathologic complete response in the rectal wall does not predict tumor sterilization of the regional lymph nodes.

Trans-anal excision of rectal cancer (taTME) was developed by Volkmann R. et al in 1878.[35] The rationale behind taTME was based on the concern for involved circumferential margins and incomplete quality of the total resorectal excision in obese males with low rectal cancer and bulky mesorectum in a narrow pelvis. In fact, the shortcomings of laparoscopic access to pelvic in low rectal cancer have been confirmed by two recent RCTs which concluded that laparoscopic resection is inferior to open surgery,[36, 37] nevertheless, it is questionable that taTME is the solution rather than robotic TME. Valid concerns about taTME are the following: taTME often results in a very low anastomosis, regardless of tumor location, with unnecessary organ loss and potential morbidity and functional disadvantages of the coloanal anastomosis.[38] The International taTME registry reports that 38% of 720 patients underwent taTME for tumors located at 10 cm (up to 13 cm) from the anal verge with a 5-cm distal resection margin.[39] Further, in 2019, taTME was abandoned in Norway due to an increased rate of new patterns of local recurrences, that occurred shortly after taTME and presented multifocal.[40] Further concerns are several reported urethra perforations and laceration of the internal iliac veins. This could be a problem, that several that surgeons are unfamiliar with the anatomy of a bottom–up view and the attempts to carry out the dissection entirely from below.[41] To conclude, so far, taTME has presented more disadvantages than advantages, which is why we predict that taTME will not be established as technique of choice for low-rectal cancer patients compared to robotic TME.

Spin represents a troubling factor for naïve readers as it consists of bias leading to unwarranted interpretation of results with potential for harm. Although the concept was mentioned by Altman D.G.,[42] we owe it to Abe Fingerhut who stated a loud and clear definition: "interpreting statistically non-significant results for the primary outcomes as demonstrating treatment equivalence". Ways to avoid any spin are clearly to gain knowledge in the used clinical research method and the necessary tools. Further, diagnostic tests, the validity of the methodology, risk analysis, sufficient and adequate power analysis have to be known and implemented. It is important especially for the reader to distinguish between statistical and clinical significance. If no valid comparison can be made or a study is underpowered, no conclusion can be drawn. One of the important tasks of journal editors and peer-reviewers is to ensure that the article is adherent to publishing and writing guidelines without any spin.[43]

A lot more subtle and quite complex is the topic of deceiving analyses unintentionally misleading the readers. To mention a few: McNamara fallacy, Neyman's bias, Concorde fallacy, etc. To go into detail, Neyman, was a statistician who established the concept of hypothesis testing in research, and became well-known for excluding various ill patients resulting in a divergence of the estimated association between outcome and exposure.[44] Voluntary registries are particularly at risk for Neyman's bias.[45] Next, Robert McNamara, was a US Secretary of Defense during the Vietnam War and became connected to a bias of making decisions on the basis of only one data set while ignoring any further data. The excessive focus on event rates without any adjusting for loss to follow-up can cause the McNamara fallacy.[46] Another bias is the Concorde fallacy which was initially called sunk-cost fallacy. It can occur when the funding of a project is continued even when it has become clear that it has no future. An example for medicine would be, when authors are advocating for a surgical procedure despite overwhelming evidence against it.[47]

Conclusion

Nullius in Verba (Latin, nothing in the words) was the motto of the London Royal Society of Medicine back in 1660. The motto was encouraging scientists, as well as the society, not to publish any manuscripts before the results had been proven to be reproducible. Today, the question remains where the surgical literature stands in that regard.[48]

Conflict of interest

The authors report no conflicts of interest relevant to this work.

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