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Letter to the Editor

## Systematic reviews and meta-analyses in minimally invasive surgery




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*I regret letting this wide river  
stream through my fingers  
without sipping a drop of water.*

Giorgos Seferis (1900–1971), Greek poet, Nobel Prize for literature 1963

The number of systematic reviews and meta-analyses in health-care research has dramatically risen through the past decades. A structured scoping search of MEDLINE using PubMed and the search terms ‘systematic review OR meta-analysis’ under the sub-heading ‘surgery’ and the qualifier ‘systematic review’, suggests a tremendous increase of 465% in the number of published systematic reviews from 2005 to 2015. A similar pattern has been demonstrated for randomized trials in the field of minimally invasive surgery.<sup>1,2</sup> Although no systematic relevant data exist, it may be hypothesized that the shift in the proportion of clinical studies to systematic reviews is more modest. These patterns are suggestive of the popularization of evidence-based medicine in surgery.

Systematic reviews are used to inform statements and recommendations of the highest grade in clinical practice guidelines. The value of evidence synthesis has been systematically assessed and the net benefit has been objectively measured with statistical tools. A characteristic example of the scientific merit of meta-analyses refers to the use of intravenous streptokinase in acute myocardial infarction. Cumulative meta-analysis – which is defined as the product of performing a new meta-analysis every time a new trial is added to a series of trials<sup>3</sup> – had demonstrated statistically significant effect by 1973.<sup>4</sup> Another 34500 patients were subsequently enrolled in 25 studies and conclusive evidence was reached only when the results of mega-trials became available.<sup>4</sup> While similar impressive paradigms are numerous, the value of systematic reviews in the reduction of various systematic errors associated with individual studies is inarguable.<sup>5</sup> Adherence to a protocol limits the introduction of bias associated to authors' personal beliefs and perceptions. A systematic literature search ensures encompassing the greatest amount of available evidence

and allows for small study effects to be explored. The pluralism of trials provides a multifaceted view of clinical outcomes, extenuates falsely inflated intervention effects and provides more precise effect sizes and interval estimations. Furthermore, plotting of effect sizes facilitates assessment of heterogeneity across trials, whereas individual patient meta-analysis and advanced meta-analysis methods allow for exploration of sources of heterogeneity and the effect of patient, treatment and study characteristics on intervention outcomes.

The importance of systematic reviews in informing clinical decision-making and the increasing trend in the number of systematic reviews has prompted researchers to evaluate the quality of this volume of evidence. The PRISMA (Preferred Reporting Items in Systematic reviews and Meta-Analyses) guidelines are the result of a worldwide initiative of a group of review authors, methodologists, clinicians and medical editors to improve the quality of systematic reviews and promote transparent and unbiased reporting.<sup>6</sup> The PRISMA tool is a checklist of 27 components considered to be essential for transparent reporting. Together with its counterpart document for randomized controlled trials, the CONSORT (Consolidated Standards of Reporting Trials) checklist, PRISMA is now being actively endorsed by the International Committee of Medical Journal Editors and several medical journals now require conformation to these guidelines as a prerequisite for submission of a systematic review.<sup>7</sup> Recommendations for the conduct and reporting of scholarly work are available for virtually every study design and have been summarized by the EQUATOR (Enhancing the QUALity and Transparency Of health Research) network.<sup>8</sup> The Penelope program is a pilot online tool, which uses decision-tree software to guide authors in finding the appropriate quality assessment tool for their work and improve their compliance with reporting guidelines.<sup>9</sup> Since systematic reviews are recognized as important evidence-based health care resources and serve as references for clinical guidelines, clear guidance on the methodology of systematic reviews is crucial.

Since the launch of publically and commercially available meta-analysis packages, statistical synthesis of individual trials' outcomes is accessible to everyone. However, meta-analysis is more than a combination of data to produce a summative result. A systematic review involves the principles of scientific research: defining a clear hypothesis, performing a systematic and versatile assessment of data, and using novel ideas and integrative models for the investigation of an area of interest. This concept encompasses the development of a pre-specified protocol, a systematic literature search, structured item abstraction, the use of valid and appropriate statistical tools, and the ability to assess the results under the prism of the trial-level data. There is a considerable

background of evidence supporting each step of this approach.<sup>10,11</sup> A recent systematic review of the quality of meta-analyses in the field of surgery suggests considerable room for improvement.<sup>12</sup>

The scientific merit of systematic reviews has two dimensions: methodological and reporting quality.<sup>6,13</sup> Components related to the methodological approach of the review and analysis process, such as the comprehensiveness of the literature search, the appropriateness of the statistical synthesis methods and the assessment of risk of bias, define methodological quality. Reporting quality of a systematic review refers to adequate reporting of every step of this process, enabling consumers – physicians, policymakers, clinical guidelines committees – to assess the methodology and to replicate the work, as part of a quality assurance process.<sup>14</sup>

The application of evidence synthesis in the field of minimally invasive surgery is somewhat unique. Many other fields of medicine are supported by reliable evidence, which has been accumulated throughout the years. Laparoscopic techniques constitute an emergent field of surgery, the first operations having been performed in the 1980's.<sup>15</sup> Synthesis of methods in this field is of specific importance, since the results of major randomized trials became available in the past decade. Cumulative analyses of randomized trials have identified clinical outcome differences, which were not evident in individual studies.<sup>16–18</sup> The specific importance of systematic reviews and meta-analyses in laparoscopic surgery dictates a thorough qualitative assessment of primary sources and a meticulous work on the methodology and reporting quality of evidence synthesis.

Synthesis of evidence in minimally invasive surgery may not be representative of the general practice due to selection bias in observational studies, i.e. patients with less co-morbidities may be more frequently selected for a minimally invasive procedure. Furthermore, advanced minimally invasive procedures even in a randomized setting may be performed more frequently by experienced laparoscopic surgeons and open procedures by less experienced surgeons or surgeons in training, thereby limiting comparability of the study arms and external validity of the outcomes. Adequate reporting is a cornerstone in the assessment of the quality of evidence provided by RCTs and ultimately in the evaluation of the confidence on outcomes of evidence synthesis.

The rise in the number of systematic reviews and meta-analyses does not necessarily result in improvement of scientific evidence, as much of this work will remain unexploited due to poor quality. Failure to comply with scientific principles of conduct and reporting scholarly work results in wasted time and efforts. Disregarding these principles is like letting a river stream through our fingers without drinking a drop of water.

## Disclosures

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## Conflicts of interest

None.

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