

June 7, 2021

***A reaction to the editorial “Meta-Analyses and Systematic Reviews: JBJS Policy Revisited.”***

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**NEXT study group NEXT study group: R. Babst, F.J.P. Beeres, J.N. Doornberg, R.H.H. Groenwold, M. van Heijl, M. Hogervorst, R.M. Houwert, F.F.A. IJpma, M.M.E. Knobe, M.C. Kruyt, L.P.H. Leenen, S.M. Muijs, F.C. Oner, B.J.M. van de Wall**

Dear editors,

We would like to comment on the revisited JBJS policy on meta-analyses and systematic reviews as captured in the editorial of the 103th issue.

First of all, we applaud the decision to increase the relevance and efficiency of systematic review projects by the principle that before undertaking such a project, similar review studies should be identified and only repeated if substantial new evidence can be expected. Also, the additional search in trial registries for unpublished data will be a great improvement as such data have the tendency to represent less favourable results. However, we have severe concerns about the new policy that meta-analyses and systematic

reviews should only include results of randomised controlled trials (RCTs).

Although RCTs are considered the highest level of evidence to establish the effects of medical treatments, many have pointed at the serious shortcomings of this design, especially for surgical research. These generally stem from the highly artificial conditions that have to be imposed on the surgical practice to fit into the design. As a consequence, the obtained results are often not representative or limited to a specific subgroup for a short time frame, thus limiting the applicability of trial results in daily practice. At the same time meta-epidemiological research has shown that non randomized observational studies of surgical interventions can be of high quality with low risk of bias too [1]. Therefore, it seems unwise to discard the results of non-randomized studies.

The strength of including observational studies in systematic reviews and meta-analyses is that all available evidence on a given topic is presented to the readers including the real-world variety of study populations and long-term outcome effects. In such reviews, data of RCTs and observational studies can be presented separately which allows readers to draw their own conclusions. On top of that, for each study, the quality can be appraised using available methodology (such as the MINORS criteria, the ROBINS-I tool, or the Cochrane Risk of Bias assessment tool), to provide readers with key information to appraise the validity of the included studies (RCTs and observational).

Our study group published several systematic reviews and meta-analyses including observational data for (orthopaedic) trauma [2-5]. These studies show the added value of including observational evidence: including more studies leads to larger sample sizes, which allows for more detailed investigation of subgroup effects. What is more, observational studies appear to be more representative of daily practice, e.g., in terms of patient and surgeon characteristics. Provided that the included observational studies are of sufficient quality, their results complement those of RCTs.

The most frequently named limitation in observational studies is the impossibility to correct for confounders such as surgical team, local preference and population characteristics. However, especially in orthopaedic trauma, which treatment a patient receives depends on which hospital he or she happens to visit, mimicking a random process. As a result, a comparison of ‘surgical schools’ is a recognized but seldom exploited natural experiment [6]. For example, ribfixation is incorporated in several hospitals in the Netherlands while other hospitals still favour non-operative treatment for patients with multiple rib fractures [7]. One could argue that this variation allows for an unprecedented natural experiment, that may be more valid than any RCT as inclusion of patients in such trials is subject to surgeons’ bias: “I am not including this patient, because she needs surgery”.

Our NEXT (Natural Experiment) study group aims to take advantage of such –undesired- high variability in surgeons’ treatment preferences by comparing similar prospective cohorts with identical patient characteristics, with the sole difference: the local –biased- differing treatment protocols [8].

A recent review of the Canadian Orthopedic Trauma Society (COTS) showed that from developing an idea to publishing the RCT takes about 10 years [9]. From developing a research question to publishing the results of a study is a much faster process for observational studies. While RCTs are ongoing, patient care should be improved based on the full scope of available evidence, including observational studies.

Instead of making a distinction between randomised and non-randomised study designs, in our opinion the leading principle to include the results of a study in a systematic review or meta-analysis should be the quality of a study, including for example data quality, representativeness of daily practice (patients and surgeons), low attrition rates, and comparability of treatment groups. Different study designs should be regarded as complementary to each other when evaluating surgical interventions and initiatives to improve the design of observational studies should be welcomed. To enable the full potential of the existing literature both RCTs and observational studies should be included in systematic reviews and meta-analyses.

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Disclaimer: e-Letters represent the opinions of the individual authors and are not copy-edited or verified by JBJS.

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Conflict of Interest: None Declared

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## Article Author Response

10 June 2021

### *Article Author(s) to Letter Writer(s)*

Dear Drs. Houwert and van de Wall,

Thank you for your recent letter in response to our recent editorial, which updates our policies for Meta Analyses and Systematic Reviews. I believe you have mis-read the editorial. We state that Meta Analyses should include data from high quality randomized trials. We use the term Systematic Reviews for analyses which include data from observational trials. There is little in your letter that is in conflict with our updated policy. Thank you again for writing.

Sincerely,

Marc Swiontkowski, MD

Editor in Chief

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## **E-Letter Writer Response**

24 June 2021

### *Letter Writer(s) to Article Author(s)*

Dear Dr. Swiontkowski,

Thank you for your response. We are pleased to understand that there may be a misunderstanding and that our position on the value of non-randomized studies in surgery is not in conflict with the Journal's policy. However, we do believe that the recommendation to only include RCTs that are sufficiently homogenous in meta-analyses, will be interpreted by the readers as a recommendation to not include non-randomized studies and de facto devaluation of observational research.

Even after reading your explanation that systematic reviews can contain observational studies, the impression remains that data from observational studies should not be used in a pooled (meta) analysis. The point that we would like to make is that multiple study designs can be combined very well in pooled analyses (meta-analyses), provided that the studies are of sufficient quality. In our opinion, the decision to incorporate studies should not be based on design, but rather on the methodological quality. That way, the large amount of available (high level) evidence from non-randomized studies, which is the dominant study type for surgical research, can be used for what it is generated: scientific advancement.

By acknowledging non-randomized studies as a valuable tool for scientific research including meta analyses, this research strategy will also be stimulated and consequently, important surgical research questions can be answered faster and more efficient. We truly believe that the JBJS readership and in the end the patients will benefit from such an approach.

Sincerely and on behalf of the NEXT study group,

Marijn Houwert, Bryan van de Wall, Rolf Groenwold and Moyo Kruyt

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## **Article Author Response**

1 July 2021

*Article Author(s) to Letter Writer(s)*

Dear NEXT Study Group,

Thank you for your input. I believe the message of the editorial is clear and is not in conflict with your perspective.

Sincerely,

Marc Swiontkowski, MD

Editor in Chief