

International Guidelines - Effects causing different recommendations

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The mission of the international network of guidelines is “to promote excellence and helps our members to create high quality clinical practice guidelines that foster safe and effective patient care”¹. By July 2017 6396 documents from 96 organizations originating from 82 countries were included into the network as mentioned on the homepage². It can be regarded as an excellent initiative to provide such an information for the user but the question remains, if the recommendations in the guidelines are as valid as they are expected to be.

Recommendations in guidelines are based on evaluable data from studies, publications, reviews and meta-analysis. All resource might be influenced and biased by several factors but the most important influence on a conclusion drawn from an investigation is the quality of the study.

In 2006 Cunningham et al.³ published the data of the MAGIC trial in the *New England Journal of Medicine*. The trial investigated the question if perioperative chemotherapy vs surgery alone for resectable gastroesophageal cancer can improve the outcome.

The study recruited from 1994 to 2002 503 patients from 6 countries which were operated

upon by 129 surgeons. A standardized resection technique was not demanded and a D2 lymphadenectomy was only performed in 41% of the patients.

Beside the long recruitment period and the low annually resection rate of participating surgeons the publication revealed several changes in the protocol like the exclusion from 59 patients from the Netherlands (after three years) or the inclusion of patients with distal esophageal cancer (after five years). Whereas in 1994 a 15% 5-year-survival improvement (power 90%) has been estimated it was changed in 1996 to a 10% 5-year-survival improvement (power 70%)⁴.

Although the quality of the MAGIC trial is questionable the study has been cited in several international guidelines (Germany, UK, ESMO, USA Canada, Japan) as a reference for the application of perioperative chemotherapy in patients with gastric cancer. However, the conclusion drawn from the MAGIC trial varies within the different guidelines tremendously. Whereas the German guideline emphasizes a perioperative chemotherapy in patients with T3 N0/+ or T4 N0/+ the Canadian guideline also includes patients with a T1 N2/3 and T2 N+ stage while the Japanese guideline is not recommending

perioperative chemotherapy in any tumor stages⁵. Coming back to the question why studies of minor quality can be published in well recommended journals later influencing therapeutic strategies by guideline recommendations, one has to reflect possible influences and bias on publications such as reporting positive results, recommendation of the authors or the institution, relationship to the editorial board, sponsors and others. Ben Goldacre describes in the book “Bad Pharma” published in 2013⁶ extensively the driving forces on publications and the success of the pharma industry introducing new drugs or new regimens into therapeutic strategies.

For scientists it is unacceptable that studies with major mistakes are published and even worse are not corrected or retracted after a critical analysis. Allison et al. describes in his article “A tragedy of errors” published in Nature 2016⁷ his experience with authors and editors after confronting them with substantial or invalidating errors. His conclusion is: robust science needs robust corrections.

This correction would also be necessary for the mentioned example recommending perioperative chemotherapy in patients with gastric cancer.

Looking again into details our group⁸ analyzed the review of Diaz-Nieto et al (Cochrane Library 2013)⁹ on the influence of post-surgical chemotherapy vs surgery alone for resectable gastric cancer. Manzini et al.⁸ selected 4 out of 34 papers with the highest weights on the final result (survival) and identified several inconsistencies influencing the validity of the papers using the CONSORT-checklist. The new meta-analysis after exclusion of the 4 papers was still in favour of a postoperative chemotherapy after gastric resection. The next meta-analysis was done after exclusion of those 8 studies showing a statistical significant benefit for postoperative chemotherapy. Finally a meta-analysis of 26 studies with no statistical benefit for post-operative chemotherapy was performed resulting in the surprising result “benefit for the chemotherapy”.

In conclusion it can be assumed that Cochrane reviews can show substantial deficits that can only be detected by careful analysis of the underlying publications.

We therefore have to support our colleagues in the

critical reading of publications or reviews because so called evidence based recommendations can be influenced by many factors (study design, study population, selection criteria, objectiveness, relationships to journals, dependence/independence of guideline contributors, financial support...) in order to reach our goal: safe and effective patient care.

Competing interests

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