**Critical appraisal of studies of intervention**

This document summarizes the most important aspects when evaluating a randomized controlled trial, in terms of methodology, statistics, and results analysis and reporting.

The critical appraisal of any studies, and in particular of RCTs, is difficult and time-consuming. It requires good knowledge in research methodology. This document will help you formulate clear questions to assess the internal validity and external validity of the paper, to detect weaknesses or on the other hand strengths of the paper, to report any real (or potential) bias, to understand the limitation of the study, so that you can have a clear and sound understanding of the paper and its conclusion at the end of the analysis.

A full analysis of a RCT study will take you probably at least two hours. You will gain time and efficiency following this “guide”.

This template applies to all sorts of RCT designs, including non-inferiority, parallel, crossover, and factorial, double-blind, double dummy, cluster, N-of-1, paired, withdrawal, adaptive and pragmatic trials.

**This critical appraisal template of a RCT study has been several divisions, each concerning a specific topic:**

1. **You will study and report the background of the study, and if the research question is clear and answerable with the study design, i.e. a RCT**
2. **You will report the main findings/results of the study**
3. **You will evaluate the internal validity of the study**
   1. **You will evaluate and report your assessment of the methodology and statistics used**
   2. **You will evaluate and report how results are reported and presented**
   3. **You will evaluate the potential bias in the study and which measure were taken to decrease their impact on the validity of the results**
4. **You will evaluate the external validity of the study, including generalizability and applicability**
5. **You will evaluate if the study is presented in a clear and transparent manner, including the figures and table. You will also assess if adverse effects were effectively recorded and correctly reported**
6. **And finally, you will come to a global conclusion regarding the validity of the study, and if you can implement its findings in your own clinical setting**

Several lectures in the EBM course complement this critical appraisal of RCT.

This critical appraisal document is based on the following documents:

- [Consort 2010 checklist](../literature%20references/CONSORT%202010%20Checklist.pdf) of information to include when reporting a randomized trial

- [Gosall N, Gosall G. The Doctor’s guide to critical appraisal](https://www.amazon.com/Doctors-Guide-Critical-Appraisal-5th/dp/1784140090), 4th Edition. Pastest Ltd Edt. Cheshire, England, 2015

- [Straus SE et al. Evidence-based Medicine. How to practice and teach EBM](https://www.elsevier.com/books/evidence-based-medicine/straus/978-0-7020-6296-4). 3rd Edition. Elsevier, England, 2005

- [Pyrczak F. Evaluating Research in academic journals](https://www.routledge.com/Evaluating-Research-in-Academic-Journals-A-Practical-Guide-to-Realistic/Pyrczak-Tcherni-Buzzeo/p/book/9780815365662). A practical guide to realistic evaluation. Routledge Edts, New-York 2017

- [Motulsky. Biostatistique. Une approche intuitive.](https://livre.fnac.com/a6076083/Harvey-J-Motulsky-Biostatistique) De Boeck Edts, Bruxelles, Belgique, 2010

- [Elwood M. Critical appraisal of epidemiological studies and clinical trials](https://global.oup.com/academic/product/critical-appraisal-of-epidemiological-studies-and-clinical-trials-9780199682898?cc=ch&lang=en&). 4th Edition. Oxford University Press, 2017

- [Wang D, Bakhai A. Clinical trial. A practical guide to design, analysis and reporting.](https://books.google.ch/books/about/Clinical_Trials.html?id=zgx_YTHny5sC&printsec=frontcover&source=kp_read_button&hl=en&redir_esc=y#v=onepage&q&f=false) Remedica, London, 2006

- [Simpson A. Epidemiologie appliquée. Une initiation à la lecture critique en sciences de la santé.](https://www.cheneliere.ca/10328-livre-epidemiologie-appliquee-3e-edition-une-initiation-a-la-lecture-critique-en-sciences-de-la-sante.html) TC media livre, Montréal, 2017

- [BMJ critical appraisal checklists](https://bestpractice.bmj.com/info/toolkit/ebm-toolbox/critical-appraisal-checklists/)

**Title of the paper, first author, Journal:**

*Please report here the citation of the paper.*

**Why did you chose such paper?**

*Please report here why you have chosen such paper. Were you looking for some information regarding a patient?*

**1. Introduction / research question / background**

**1.1. Is the research question, or the objectives of the study, clearly stated in the study?**

Having a good hypothesis, and an answerable question, is probably the most critical step in any study. Not all questions can be answered with a RCT design study. A clear and well documented research question will also help readers to locate the appropriate study, and researchers to perform secondary studies, such as systematic reviews and meta-analysis.

*Please answer here below if the research question has been clearly formulated in the study report.*

*You will often find this answer at the end of the introduction section. Ideally, the title should also indicate clearly the hypothesis and research question.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “goal” or “objective”.*

**1.2. Did the authors perform a thorough literature search?**

Often, funding agencies require the authors to perform a full literature review, to assure that the questions has not been answered already ([paper](../literature%20references/lit%20searching%20for%20identification%20of%20a%20problem.pdf)). This should prevent replicating studies unnecessarily. This would otherwise not only bring very little new information, but and especially would deny patients in the placebo arm to benefit from an already known effective treatment.

Many systematic reviews and / or meta-analysis have unfortunately shown that many RCTs were performed when the answer to the research question was already known ([paper](../literature%20references/cumulative%20meta%20analysis%20for%20grant%20submission.pdf)).

However, this does not need to be a systematic review, but it should comprehensive enough to demonstrate that the authors understand the subject around their research question, and did not miss an important piece of information.

*Please answer here below if the authors performed and reported a thorough literature search.*

*You will find this information in the introduction section. A quick look at the references might also indicate the thoroughness of the literature search.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “background”.*

**2. Results in brief**

*Please report here in 3 to 5 sentences the main reported findings of the study.*

*This section will then lead you to evaluate in section 3 to 5 the internal and external validity of the study, so that you can share your conclusions with the audience in section 6 after your have completed a thorough assessment of the paper.*

**3. Methodology / internal validity analysis**

Good research methodology is of the utmost importance for ensuring an appropriate internal validity of the paper. You will explore and verify the following points here below.

**3.1. Has the study been registered?**

Registration of the study allow readers and researchers to clearly expose the research question(s), research hypothesis, the main and secondary outcomes, and the Statistical Analysis Plan, before the beginning of the study.

Registration increases transparency, and prevents, or at least decreases, the risk of post-hoc analysis with subsequent spurious findings, which often prove wrong in the future ([paper](../literature%20references/registration%20of%20RCT%20syst%20rev%20meta%20analysis.pdf)).

RCT can be registered in many websites. [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/home),

*Please respond here below if the study has been registered, and if yes in which database.*

*Registration data can be found at the end of the abstract, or in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “registration”.*

**3.2. Was the Institutional Review Board approval obtained?**

An approval to conduct research, and especially randomized controlled trials, should be obtain each and every time from a research ethic committee. Ideally, the approval number/ identification should be available.

*Please respond here below if the study has been reviewed by an ad-hoc research committee.*

*Institutional Review Board approval can be found in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “IRB” or “Intistutional Review Board” or “research ethic committee”.*

**3.3. Did the authors calculate the required sample size? Did the authors report the values of α and β values for calculating the required sample size?**

Calculation of an ideal sample size is important to avoid recruiting too many patients, potentially putting them at risk of adverse effects or subjecting them unnecessarily to a placebo treatment, when an effective active treatment has been found. On the other hand, recruiting too few patients will result in a low and insufficient power.

Sample size calculation is based on α, β and Δ.

α (Alpha) is the probability of Type I error in any hypothesis test–incorrectly rejecting the null hypothesis. β (Beta) is the probability of Type II error in any hypothesis test–incorrectly failing to reject the null hypothesis. Δ is the expected difference between groups, based on previous studies or on a pilot study.

*Please respond here below if the authors reported the required sample size for their chosen α and β values.*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “sample size”.*

**3.4. Are inclusion and exclusion criteria clearly reported?**

If inclusion criteria are too strict, this will greatly threaten the generalizability of the findings. On the other hand, if inclusion criteria are too loose, it might lead to no difference between groups because of a dilution effect. The same principle applies to exclusion criteria.

*Please explain below if inclusion and exclusion criteria for participants are well reported. Please comment if you think inclusion and/or exclusion criteria are not appropriate and might hamper the generalizability of the findings.*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “inclusion” or “exclusion” or “population” or “sample” or “sampling”.*

**3.5. Did the authors properly randomize their subjects?**

Randomization is extremely important to avoid confounding factors, and to decrease biases, such as selection bias. Central pharmacy randomization by telephone is an accepted valid randomization technique. Modern techniques include stratified and covariate adaptive randomization.

*Please answer below if randomization is appropriate.*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “randomiz/sation”.*

**3.6. Was the randomization process well concealed?**

Concealment is as important as randomization, and often forgotten (or poorly delt with). Methods for blinding should be clearly reported. Proper randomization but poor concealment can lead to many biases, including performance bias.

*Please answer if patients and physicians (and other health care workers involved in the research) were properly blinded throughout the study?*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “concealment”.*

**3.7. Were the participants in each arm assessed equally?**

Each participant, regardless of the treatment he or she is receiving, should undergo the same care and same assessment, at the same time.

*Please answer if both arms (and more) were investigated in a similar manner (same exams? Same frequency? Same timing?).*

*You will often find this answer in the method section, eventually in the result section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “assessment”.*

**3.8. Compared to the experimental drug, what was the comparator drug?**

The choice of a comparator drug is very important. Currently, the best available care should be used instead of a placebo drug. In the absence of any available and recognized treatment, placebo can be used. Care should be used to make sure that the comparator was used in an adequate manner, ie make sure the dosage is appropriate and not too low (absence of efficacy) or too high (adverse effects).

*Which comparator has been used in the paper? Is it a faire comparison?*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “placebo” or “comparator”.*

**3.9. Did the authors used a non-inferiority, equivalence, or superiority trial design?**

These different trial designs will give different responses. Non-inferiority trials are more common than equivalence. Its goal is to demonstrate that a new treatment is no less effective than an existing one. In equivalence and non-inferiority trials, the conclusion depends upon the value of ∆ chosen as the maximum acceptable difference.

*Please state hereunder if the trial is a non-inferiority, an equivalence, or a superiority trial.*

*You will often find this answer in the method section. The title should ideally also describe the design of the trial.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “non-inferiority” or “equivalence” or “superiority”.*

**3.10. Did the authors assess for participant compliance in the RCT? If yes, how?**

Poor compliance, to the investigational drug, can lead to a (severe) underestimation of the efficacy of the trial drug. Participant compliance should ideally be assessed throughout the trials, for all arms.

Different methods exists to assess participant compliance in RCTs. According to the drug under study, blood or urine levels can estimate the degree of compliance of the participants. Participants can also be asked to fill a daily diary, or bring back their boxes with, eventually, the remaining drugs.

Finally, if compliance is poor, a separate analysis between good and bad compliers could be indicated, to distinguish between efficacy and effectiveness of the drug under investigation.

*Did the authors assess for compliance in their study? How?*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “compliance”.*

**3.11. Is a flow chart for participants, from enrolment to final analysis, reported?**

According to the Equator CONSORT guidelines, a clear flow chart of the participants should be reported. It should include all eligible participants, included participants, and finally patients who completed the study and were analysed. This will also help the investigators to analyse the final effect of the drug in a Per-Protocol Analysis, and in an Intention-to-Treat analysis.

*Did the authors report a participant flow chart?*

*You will often find this answer in the result section or in a separate figure.*

*To help you locate your answer in the manuscript, you can search the document in the figures.*

**3.12. Is the duration of the follow-up long enough to capture (rare) adverse effects?**

Too often, the surveillance (follow-up) of the participants terminate at the end of the study, or very soon after. A short surveillance time, in a highly selected participant population, without (or with very few) comorbidities or drug interaction, will not capture rare adverse effects. Although inherent to the design of RCTs, this should be mentioned in the limitation section.

*Did the authors report how long were the participants followed up after termination of the study?*

*You will often find this answer in the method section or discussion section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “adverse effect”.*

**3.13. Did the authors follow the CONSORT guidelines?**

CONSORT guidelines, published by the EQUATOR network, help researchers in their methodology, avoid many biases, and increase transparency and reproducibitliy for future research.

*Did the authors followed the CONSORT guidelines (or any equivalent good practice guidelines)?*

*You will often find this answer in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “CONSORT”.*

**3.14. Were all the analysis reported in the paper planned beforehand? Or did the authors perform any post-hoc analysis? If yes, is it clearly reported a post-hoc analysis?**

Post-hoc analysis, although tempting, carry a (very) high risk of “chance” finding, i.e. some results might be accidently positive, but often become negative when investigated primarily in a subsequent study. Investigators should avoid post-hoc analysis. However, post-hoc analysis can sometime lead to new findings, when confirmed in subsequent studies. Post-hoc analysis should then be clearly reported as such in the paper.

*You can find this information in the data that were published in the register before the study started. If the study has not been registered, record this answer a NO. If the study has been registered, but if the outcome of interest has not been registered, record this answer as NO, at least for the outcome of interest. If the study has been registered, and the post-hoc analysis are clearly presented has exploratory findings, then answer YES.*

*You will often find this answer comparing the pre-planned investigation reported in the trial registry with the analysis performed in the published paper.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “post-hoc” or “exploratory”.*

**3.15. Are those patients who were in the study but subsequently excluded from the analysis due to loss of follow-up or other reasons clearly described and accounted for in the calculation of outcomes? Was the analysis performed on the basis of intention-to-treat (ITT) (effectiveness) or by per protocol (PP) (efficacy)? Or both?**

Participants in a RCT not always complete the study. They might leave the study for personal reasons, because of death, or moving, or because of severe adverse effects, to mention a few.

Loss to follow-up patients might distort the estimate, and can compromise the study’s validity. Loss to follow-up sometimes leads to overestimates of treatment effects and sometimes to underestimates. As a rule of thumb, loss to follow up < 5% is often considered as acceptable.

Ideally, analysis should be then performed in a Per-Protocol and in an Intention-to-Treat manner. In a Per-Protocol analysis, only participants completing the study, with valid data, are included in the final analysis. In an Intention-to-Treat, all included participants are analysed, provided they have a minimum data at the end of the study.

*Please describe here if the authors performed a PP analysis and also an ITT analysis. If not, do you estimate that the other analysis should have been performed? Why?*

*Please report here the number of participant’s loss to follow up in each and every trial arm.*

*You will often find this answer in the method section or in the result section, or as well in tables describing the analysis.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “Intention-to-treat” or “per protocol”.*

**3.16. Did the authors perform multiple comparisons? If yes, did they adjust for multiple comparisons (Bonferroni, Holm, Sidak adjustments)?**

Multiple comparisons are tempting. However, they carry a high risk of false positive finding. If α is set-up at 5%, on average, 5 tests out of 100 tests will be positive in that study, but negative in subsequent studies.

Authors should avoid multiple comparisons. The number of comparisons should be defined before the analysis. There exist many statistical methods to adjust for multiple comparisons.

*Did the authors performed more than 10 comparisons? If yes did they report a risk of false discovery rate? Or family wise error? Or did they adjust for multiple comparisons?*

*You will find the answer in the method section, or in the legends of the result tables.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “multiple” or “bonferroni”.*

**3.17. How did the authors account for missing values?**

Missing values can threaten the internal validity of a study. Researcher should report the number of missing values, and any statistical methods used (or not) to account for missing values.

*Please report here if researchers mention the number of missing values. Please report here if the researchers describe the missing values or not (missing at random, missing completely at random, not missing at random). Finally, please report here if the authors used any statistical method such as imputation to account for missing values.*

*You will find the answer most likely in the method section, or in the result section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “missing”.*

**3.18. If there is an interim analysis or early stopping, did the authors provide a clear reason and an ad-hoc statistical analysis?**

Stopping a trial early, before enrolling all previously planned participants, is difficult. It should be based on solid and robust statistical analysis.

*Did the authors stop the trial early? If yes, please report why (serious adverse effect? Futility?)*

*You will find the answer in the method section or result section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “early” or “stop” or “adaptive”*

**3.19. Is the statistical analysis plan available?**

Statistical analysis plan should ideally be published, to increase transparency and avoid multiple comparison or post-hoc analysis.

*Did the authors published their statistical analysis plan?*

*Statistical analysis plan can be found the method section, or in the supplementary material, or in the trial registry.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “statistical analysis plan”.*

**3.20. For binary outcomes, did the authors report both absolute and relative effect size?**

The true effect size of an intervention is more important than the mere p value, which can be low but clinically insignificant if the number of enrolled participants is really high. For every important outcome, the authors should report at least a confidence interval, so that the reader can better evaluate the possible true impact of an intervention.

*Please report here if confidence intervals or effect size is reported for the outcomes of interest.*

*You will find the answer in the results section, maybe in the results tables or figures, or in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “effect size”.*

**3.21. In case of multiple outcomes, did the authors clearly distinguish primary vs secondary outcomes?**

In a RCT, primary and secondary outcomes should be clearly defined. Primary outcome should be limited to a minimum number, ideally a single one. Conclusion should be based primarily on the outcomes of the primary outcome. Secondary outcomes should be kept to a minimum. Primary and secondary outcomes should be pre-specified.

*Please describe below if primary and secondary outcomes are clearly defined and reported as such. Please report if conclusions are based on secondary outcomes only.*

*You will find answers to this question in the method section.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “outcome”.*

**3.22. Did the authors report composite outcomes? If yes did they report for both the composite outcome AND their individual components?**

When event rate is really low, it might be difficult to obtain statistically valid information with a RCT. In rare instance, a composite outcome might be indicated. However, this should be pre-planned.

*Please describe below if the authors used a composite outcome as a primary outcome. Please report below if the authors not only report the composite outcome altogether, but also the individual outcomes of the composite outcome.*

*To help you locate your answer in the manuscript, you can search the document using the keyword “composite”.*

**3.23. Biases in RCT**

RCT can be fraught with many biases, from their inception (selection bias, sampling bias, allocation bias), to their completion, analysis (reporting bias, ascertainment bias) and even publication (publication bias).

Here below is a list of the most common biases encountered in published RCTs ([Cochrane training Chapter 8: Assessing risk of bias in a randomized trial](https://training.cochrane.org/handbook/current/chapter-08)) (accessed 20.01.2023).

At the very minimum, you should make sure that the authors took all preventative measures to avoid the following biases:

* **Selection bias** occurs when there are systematic differences between groups. For example, if groups are not comparable on key demographic factors, then between-group differences in treatment outcomes cannot necessarily be attributed solely to the study intervention. RCTs attempt to address selection bias by randomly assigning participants to groups – but it is still important to assess whether randomization was done well enough to eliminate the influence of confounding variables.
* **Performance bias** refers to systematic differences between groups that occur during the study. For example, if participants know that they are in the active treatment rather than the control condition, this could create positive expectations that have an impact on treatment outcome beyond that of the intervention itself. Ideally, participants and investigators should remain unaware of which group participants are assigned to. Of note, this is more easily achieved in medication trials, where the medication and the placebo appear identical, than in psychotherapy trials.
* **Detection bias** refers to systematic differences in the way outcomes are determined. For example, if providers in a psychotherapy trial are aware of the investigators' hypotheses, this knowledge could unconsciously influence the way they rate participants' progress. It is crucial that psychotherapy RCTs address this by utilizing independent outcome assessors who are blind to participants' assigned treatment groups and investigators' expectations.
* **Attrition bias** occurs when there are systematic differences between groups in withdrawals from a study. It's common for participants to drop out of a trial before or in the middle of treatment, and researchers who only include those who completed the protocol in their final analyses are not presenting the full picture. Analyses should include all participants who were randomized into the study (intention to treat analysis), and not only participants who completed some or all of the intervention.

**3.24. Are the raw data available? if yes, in a repository? Online? On request?**

Many Journals or funding agencies, such as the Swiss National Fund, require researchers to deposit raw data of their research in publicly accessible repositories.

*Did the authors deposit their raw data in an accessible repository?*

*You will find this information in the appendix section.*

**3.25. Conflict of interest. Are the conflicts of interest well described?**

Authors might have conflict of interest when performing research. Although this does not automatically preclude them from conducting the research, a transparent declaration will help.

*Is there any conflict of interest declared? Do you think that some conflict of interest might have impacted the analysis of the data or its reporting? If yes, in what sense?*

*You will find this information in the appendix section.*

**3.26. How was the study funded?**

Funding research is very important. It should be done in a transparent manner. Funding agencies should have no access in data analysis and manuscript writing.

*Is the funding of the research clearly reported? Is the role of the funding agency clearly stated?*

*You will find this information in the appendix section.*

**3.27. Authorship?**

Each author should contribute significantly to the research and/or manuscript writing. Guest authorship (authorship with no significant contribution) or ghost authorship (authorship not disclosed) are prohibited.

*Did authors significantly participated to the research and/or manuscript writing?*

*You will find this information in the authorship declaration, often required by Journal, in the appendix section.*

**4. Results presentation / discussion / adverse effects reporting / analysis**

**4.1. How do you feel confident are you in the results? P value(s) vs confidence intervals (CI)? Did the authors report only p values or also confidence intervals? Is the effect size also reported. For binary outcomes, and if appropriate, is the Number Needed to Treat (NNT) and eventually the Number Needed to Harm (NNH) reported?**

*Please answer below if confidence intervals are reported for the outcomes of interest. When applicable, did the authors report the NNT or NNH?*

**4.2. Were reported outcomes “hard” endpoints (death, recurrence of disease, ICU admission) or surrogate markers (laboratory change)?**

*Please answer below if the reported outcomes of interest, especially in the primary outcomes, are “hard” endpoints, or surrogate markers.*

**4.3. Were reported outcome “patient related outcome(s)”? or “patient related experience”?**

*Please answer below if the authors also report “patient related outcomes” or not.*

**4.4. How were adverse effects collected? And reported? How long was the surveillance after trial termination to detect (late) adverse effects?**

*Please answer below if adverse effects were prospectively collected and reported.*

**4.5. Does the title of the paper represent the main findings of the paper?**

Ideally, the title should include the study type, the intervention, and the population of interest. This will help readers and systematic review researchers to correctly identify (and not miss) a paper of interest. A poor title might read: an investigation of adolescent depression and its implication. A better title could read: Gender differences in the expression of depression by early adolescent children of alcoholics (from Pyrczak F. Evaluating Research in academic journals. A practical guide to realistic evaluation. Routledge Edts, New-York 2017, p13.

***Please report here is the title of the paper is adequate and describe well the research that has been conducted***

*You will find the answer by reading the title of the paper*

**4.6. Is the abstract well presented? In a structured manner? Does it convey the main results of the paper?**

Most Journals now request a short and structured abstract, containing the following sections: background, methods, results, and conclusion).

*Are the details in the abstract consistent with the results section in the manuscript? Is all the information that is in the abstract present in the text? Are the most important findings reported with their confidence intervals? Conclusion: Are statements supported by results from this study? Is there any spin?*

*You will find the answer in the abstract.*

**4.7. Did the authors discuss about their findings, including but not limited to limitations?**

Every study, even the best ones, have some limitation, this for numerous reasons.

*Did the authors mention the limitations of their studies?*

*You will find this information in the discussion section, often at the end of the discussion, before the conclusion.*

**4.8. Figures and tables.**

Not all figures and tables are necessary.

*Please report here if you think all figures and tables are necessary.*

Figures can be misleading, with truncated y axis for instance ([Truncating the Y-Axis: Threat or Menace?](../../../../../truncated%20y%20axis.pdf)).

*Please report here if you think the figure(s) are representing the results in an exact, faithful and trustworthy manner.*

**4.9. Is the conclusion faithful to the results?**

Are the authors interpreting the results correctly, without any “spin”? Over-emphasizing some results, or some specific aspects of the findings, to make them more favorable, is misleading. This “distortion” of the reality is called “spin” ([see ref. paper for spin in OBGYN RCTs](../../../../../spin%20in%20RCT%20in%20OBGYN.pdf)).

*Please report here your (personal) evaluation.*

*You will find the answer by comparing the results (especially the effect size, the number needed to treat, the number needed to harm, the absolute risk reduction) with how the the authors describe their findings, and conclude the paper*

**4.10. Is the writing, the grammar, of good quality?**

*Please report here your (personal) evaluation.*

**5. Generalizability / external validity analysis**

**5.1. Generalizability**

Is the population in the research study similar to yours in term of sex, age, ethnicity, comorbidities, stages of current disease, etc…?

*Please answer here to the question.*

**5.2. Applicability / implementation**

Do I have all the required knowledge and workforce and material to implement the findings of the study in my local population of interest?

*Please answer here to the question.*

**6. Conclusions**

**6.1. Does the study provide new information or is it a confirmation / validation of previous work?**

This is a personal evaluation. You should base your answer what has been already been published in the literature regarding the specific topic.

*Please state here in a sentence if this study provide new information.*

**6.2. Internal validity of the study?**

This is a personal evaluation. Your answer should reflect a general appreciation of section 2, especially sample size calculation, randomization, and correct statistical analysis including no (or clearly explained) exploratory analysis, no (or corrected) multiple comparisons, and ITT analysis.

No or poor / inappropriate randomization, no (or poor) concealment, exploratory analysis and no ITT analysis in case of significant participant loss to follow up should raise doubt about the internal validity of the study.

*Please state here in a sentence if the internal validity of the study is appropriate.*

**6.3. Do issues exist about ethics and research standards?**

Every RCT should be approved by an appropriate body, often an institutional review board. In your view, is this study ethical?

*Please state here if, in your view, this research is ethical or not.*

**6.4. Are the findings relevant to clinical practice?**

Finally, all findings in RCTs should help the patient, throughout the world.

*Please state here if you think that the study is valid, externally transportable, and applicable in you patient population.*