

RULES AND GUIDELINES FOR SUBMISSION OF ARTICLES REPORTING ORIGINAL RESEARCH

There is no doubt that original research has always been, and remains, the cornerstone of scientific thought throughout the world. The reporting and publication of the results of original research is a final and, according to modern thinking, necessary stage of scientific activity. It is the quality of the description of the research, (from the planning stages to the discussion of results), that determines its credibility and, perhaps, the prospects of its future use for the formulation of new hypotheses and decision-making. These rules and guidelines are designed to help authors prepare high-quality manuscripts. The situation relating predominantly to research on medical interventions (medicine, medical devices, organizational activities, etc.) are discussed, but rules and guidelines are universal and can be used when describing research aimed at other objectives, (in epidemiology, for example).

OBLIGATORY CONDITIONS FOR ACCEPTING MANUSCRIPTS FOR CONSIDERATION

- 1. The conformity of the research theme with the remit of the journal.** The journal publishes original research results (including systematic reviews), clinical observations, literary reviews and informational messages, a substantial part of which is dedicated to pediatrics, i.e. “preservation and restitution of child health from birth to 17 years, inclusive”.
- 2. Approval of the manuscript’s originality.** According to the journal editors, the criterion of the manuscript’s originality lies in the fact that neither the paper itself nor one of its significant fragments (including tables, figures) has been published previously. They check the originality of the manuscript, applying the “Anti-Plagiarism” system, as well as conduct a free search using public search engines. However, in exceptional cases, the editorial board reserves the right to publish results of previously published research of both domestic and foreign authors. This can be due to the importance of the received data and the need for their distribution among members of the professional community.
- 3. The presentation of the structured manuscript.** The manuscripts containing research results *must* include a structured abstract (see the relevant “Rules and guidelines for preparation of structured abstracts”) and the following sections: Background, Methods, Results, Discussion, Conclusion, Sources of Financing, Conflicts of Interest, References and Contacts. Each of the sections must be prepared according to the guidelines stated below. If the necessary information is not available, the corresponding subsections can be left blank.

Table 1. **Obligatory** elements of the manuscript reporting original research

I. ARTICLE TITLE
II. STRUCTURED ABSTRACT
III. BACKGROUND
IV. METHODS 4.1. Plan (design) of the research 4.2. Conformity criterion 4.3. Research facilities 4.4. Research period 4.5. Description of the medical intervention 4.6. Research findings 4.6.1. The main research finding 4.6.2. Additional research findings 4.7. Subgroup analysis 4.8. Methods of findings' registration 4.9. Ethical expertise 4.10. Statistical analysis 4.10.1. Principles of sample size calculation 4.10.2. Methods of statistical data analysis
V. RESULTS 5.1. Research participants 5.2. Main research results 5.3. Additional research results 5.4. Undesirable phenomena
VI. DISCUSSION 6.1. Resume of the main research results 6.2. Discussion of the main research results 6.3. Limitations of the research 6.4. Brief practical implications
VII. SOURCE OF FINANCING
VIII. CONFLICT OF INTEREST
IX. ACKNOWLEDGEMENTS
X. REFERENCES
XI. CONTACTS

ELUCIDATION OF SOME ISSUES DEALING WITH THE PREPARATION OF MANUSCRIPTS CONTAINING ORIGINAL RESEARCH RESULTS

I. TITLE

The title of the article must be clear, without ambiguous language, and be as brief as possible. We recommend that authors adopt the following principles when creating the title of the manuscript:

- identify research participants (healthy, sick people) or the studied phenomenon,
- determine a studied intervention (including any formulated retrospectively),
- indicate the research findings (the final result of the study featured),
- formulate the plan (design) of the research, mentioning the following attributes: temporal characteristics [retrospective, prospective], the principle of group or comparable group formation (randomized, case-control type, etc.), the condition of the control group (controlled, uncontrolled).

The title of the manuscript should not contain acronyms (exceptions are possible).

II. STRUCTURED ABSTRACT

See the file “Rules and guidelines for submission of abstracts of manuscripts reporting original research”.

III. BACKGROUND

When preparing this section, authors are advised to stick to the following principles:

- briefly describe the significance of the problem:
 - a) its scale (prevalence, morbidity, etc.),
 - b) indirect effects (social, economic);
- define the resolved and unresolved aspects of the problem, with an analysis of previously published data.

When determining the scale and indirect effects, authors can take into account previous, current and/or predicted tendencies. When formulating assumptions, authors are advised to proceed from the evidential hierarchy, focusing primarily on the results of systematic reviews, then on the results of randomized trials or major epidemiological studies, and, only in the absence of such, on the results of quasi experimental and non-comparative studies, and then expert opinion. Special attention should be paid not only to already known facts within the scope of the researched problem, but also to unresolved issues. It is the latter that determine the relevance of the research – a key factor for decision making on the appropriateness of further manuscript reviewing. The BACKGROUND section *must* be ended with the definition of research objectives. When formulating research objectives, it is recommended that the author use the elements of the research question, in particular to indicate: a) target population, b) planned intervention (if any), c) the availability of the comparable group, d) evaluation findings.

IV. METHODS

Ideally, a detailed description of this section should be made prior to the research. It is obvious that this information determines the course of the research, the conditions of its implementation and the analysis of the results obtained. The only exception is the data describing changes in the research protocol taking place after its initiation. If this information is available, it is necessary to mention not only the fact of the research protocol change, but also the reasons for it.

Generally, this section must give an idea of the plan (design) of the research, its participants and venue, its period, prospective medical intervention (if it is planned), methods for the evaluation of research results and the way in which research hypotheses were tested.

All the subsections mentioned below should be presented in the text of the manuscript, regardless of the availability of the information necessary for their completion.

4.1. Plan (design) of the research

Authors are asked to define the plan of the research in accordance with one of the possible variants (Tables 2, 3). *The minimum requirement* is to specify whether the research was controlled (if there were two or more planned groups), and, if it was controlled, whether it was randomized.

When describing randomized trials, authors should adhere to the standards of reporting the results of randomized controlled studies (CONSORT; <http://www.consort-statement.org/consort-2010>).

with different interventions?													
Between subjects of one group during research period?	+/-	+/-	-	+	-	-	-	-	-	-	-	+	-
What criteria were used for division of research subjects into groups:													
Hidden randomization?	+	-	-	-	-	-	-	-	-	-	-	np	np
Division on the basis of given criteria?	-	+	-	-	-	-	-	-	-	-	-	np	np
In accordance with other reasons?	-	-	+	+/-	-	-	-	-	-	-	-	np	np
Age?	-	-	-	-	-	-	+	-	-	-	-	np	np
Territorial belonging?	-	-	+/-	+/-	+/-	+/-	+/-	np	np	np	np	np	np
Treatment method selection?	-	-	-	+/-	+/-	+/-	-	-	-	-	+/-	np	np
Participants' wish?	-	-	-	+/-	+/-	+/-	-	-	-	-	+/-	np	np
Based on some outcomes?	-	-	-	-	-	-	-	+	+	+	+/-	np	np
What stages of the research were prospective:													
Selection of research subjects?	+	+	+	+/-	+	-	+/-*	+	-	-	-	+/-	+/-
The evaluation of the initial state and division into intervention groups?	+	+	+	+/-	+	-	+/-*	+	-	-	-	np	np
Results evaluation?	+	+	+	+/-	+	+/-	+/-	+	-	-	-	+/-	+/-
Hypothesis formulation?	+	+	+	+	+	+	+	+	+	+/-	+/-	+/-	np
What variable was considered to evaluate the group comparability:													
Intervention factors (factors connected with evaluation outcomes)?	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-	-	np
The evaluation of group differences at the beginning of the research?	+/-	+/-	+/-	+	+/-	+/-	+/-	-	-	-	-	-	np

Note. (+) – this characteristic distinguishes this plan of the research, (-) – this characteristic is not a distinctive indicator of this plan of the research, (+/-) – it is impossible to unambiguously evaluate the significance of this characteristic for the definition of the research plan, (np) – this characteristic is not applied for the definition of the research plan.

RCR – randomized controlled research; QRCR – quasi randomized controlled research; NRCR – non-randomized controlled research; CRBC – controlled research accompanied by observations before the beginning and upon completion (of the study); PCS – prospective cohort study; RCS – retrospective cohort study; HCR – historically controlled research; CCCS – cohort (embedded) “case-control” study; CCS – case-control study; CS – crossover study; ISC – initial state control study (with a “before-after” plan); CSs – case series.

4.2. Conformity criteria

The availability of information on the criteria of conformity with the research conditions (inclusion, non-inclusion and exclusion criteria) is necessary for obtaining a clear view of the external generalizability of the research findings¹ and their practical implementation, for example, in customary clinical practice.

It is necessary to enumerate in detail, and, in case of need, to describe (for example, by specifying threshold values for quantitative characteristics) the previously (prior to the research) formulated criteria of inclusion and non-inclusion in the study. These groups of criteria should not duplicate one another. For example, if the inclusion criterion is “aged 7-12”, then the non-inclusion criterion cannot be set as “aged < 7 and > 12”.

Conformity criteria may include not only the socio-demographic and clinical factors, but also the organizational background in which the research has been conducted (for example, the inclusion of hospitalized patients only, or day patients only, or pupils, but only during the educational process, etc.).

Often one has to face the fact that authors do not specify some criteria on the basis of their own beliefs about their irrelevance. For example, the research can include the patients hospitalized on weekdays, but due to some organizational reasons it cannot include those who has been hospitalized on weekends or holidays. The main reason for the need to mention this criterion (as well as similar ones) is the fact that we can know nothing about its significance. If the value of these (or similar) factors is confirmed, this would seriously limit the external generalizability of the research results stated above. In this

¹ *Generalizability* is an opportunity to apply the research results to the target population, for example, on all patients with a particular diagnosis included in a study.

regard, it is *advisable* to distinguish between previously formulated and situational (applied due to the real-time research facilities) conformity criteria.

Conformity criteria must be supplemented by the description of the criteria of exclusion from the research (if any, both previously formulated and situation applied).

4.3. Research facilities

It is obvious that research results depend to a large extent on research facilities. That is why authors should provide detailed information on the venue of the research (hospital, clinic, children's comprehensive, specialized institution, unorganized child population, etc.), indicating the location and departmental affiliation of the centre taking part in the research. If the research has been conducted on the basis of several centres, each of them should be described. Along with the venue for the research, authors should clarify some specific factors (social, economic, cultural) that can influence the external generalizability of the research findings. These factors can include the participation of children from poor families or from certain religious communities, children with an adverse social environment, etc.

4.4. Research period

One obligation when describing the results of the prospective research is to present information on a) the planned duration of inclusion in the study, b) duration of the observation period, c) a description of all intermediate checkpoints. If planned time intervals have occurred during the research, this fact should be mentioned.

In case of retrospective studies, the period of retrospection should be indicated.

4.5. Description of the medical intervention

Description of the studied medical intervention must be in as much detail as possible. It is necessary to describe doses for subsequent application, their titration period, their means of introduction and the duration of the medical intervention, as well as the conditions of its termination. In terms of surgical interventions, the peculiarities of preoperative preparation and the surgery itself, including anesthesia and post-operation patient management, should also be described. All changes in the planned medical intervention occurring during the study should be mentioned.

References to "the standard therapy" conducted in terms of customary clinical practice are not enough. However, a detailed description of the patients' treatment (in comparable groups with the results of statistical analysis) should be presented in the RESULTS section.

4.6. Research findings

4.6.1. The main research finding

The main finding is a previously selected and eventually established research result arising from the influence of a medical or other intervention, risk factor, etc. Depending on conditions, the research findings can be both the most significant for the studied problem (for example, the number of fatal outcomes), and other surrogate characterizing (often minor) features (for example, the number of leukocytes per blood volume unit as a marker of inflammation). The "one study – one hypothesis – one main finding" principle is grounded, generally accepted and, in this regard, must be the basis, both during the planning of the research, and while describing its results. The main research finding can not only refer to the effectiveness of the medical intervention. In some cases, it can deal with the criterion of its safety. However, in both cases, the main research finding must be described as specifically and unambiguously as possible. It should be added that the expected data on the main research finding are used to calculate the sample size that is sufficient for achieving the statistical criteria used for testing the research hypothesis.

4.6.2. Additional research findings

Additional findings are research results that allow the analysis of other effects or mechanisms relating to the medical intervention. For example, the clinical profile of a disease's so-called "hard endpoints" (deaths, life-threatening clinical behaviour, severe complications) can be chosen as the main research finding. At the same time, additional research findings can be used (and described in the manuscript) for an evaluation of the patient's quality of life. Similarly, a biochemical indicator can be used in clinical practice for monitoring the clinical course, and another indicator can be used for the evaluation of the effects of the intervention, the applicability of which is under examination. Both the main and additional research findings must be previously (prior to the beginning of the study) formulated. The number of additional research findings is not limited, but authors should take into account that, depending on the data, the number of additional findings for a piece of research usually varies from two to four.

4.7. Subgroup analysis

Subgroup analysis is conducted when it is necessary to evaluate the effects of a medical intervention, or the influence of other factors in various subgroups formed on the basis of sex, age, and clinical and other characteristics. Ideally, the criteria used for the formation of subgroups should be a) determined before the beginning of the research and b) grounded. However, even in terms of such a strict approach, the analysis of the effects of the intervention in subgroups is a source of bias. In this subsection, authors are advised to describe the criteria used for the formation of subgroups on which additional analysis (for example, of the effects of the intervention) will be carried out. It is advisable to accompany this information with links to references confirming the validity of this analysis.

4.8. Methods for registration of findings

It is necessary to describe all the methods and tools used for the registration of the main and additional research findings, and the description must be substantial, i.e. connected with a specific research finding. It is enough just to mention extensively used methods and tools, noting who, and in what time-frame, and using what facilities, has already applied them. Executors can be both the co-authors of the manuscript, and also contracted external co-executors, as well as laboratories (regardless of the details of ownership). The methods and tools that have no evidence base in literature (the original methodology) or there is lack of evidence (the experimental methodology) should be described in more detail. If this information is available, it is advisable to specify the link to the literary source in which the reliability of the method or tool has already been tested. The applicability of the original (author) methods and tools must be demonstrated, (if it is not the purpose of the research), by a brief description of their sensitivity and of the reproducibility of the results. It is also advisable to provide such information while determining research findings based on subjective (medical, expert) evaluations.

The editorial board does not consider research in which the evaluation of the main research findings has been conducted using invalid original methods and tools.

4.9. Ethical expertise

In accordance with the guidelines of WAME (The World Association of Medical Editors), "Before conducting all research on people, as well as research involving medical histories and human body tissues, it is necessary to obtain written confirmation of the research verification and permission issued by the officially formed supervisory committee (institutional supervisory board or Ethics Committee) ... If the research is not subject to such an evaluation, confirmation by the relevant Committee is required" ... By following these guidelines, it is *obligatory* for authors to provide information on the verification protocol results by the Ethics Committee of any level, by a) citing its resolution in this section, b) specifying the document's ID, c) indicating the date of its signing, and d) citing the official name of the Ethics Committee. The journal editorial board reserves the right to request, from authors of manuscripts, the provision of a copy of the Ethics Committee's resolution on the research permit.

4.10. Statistical analysis

4.10.1. Principles of sample size calculation

The need for the sample size calculation (for both comparative and non-comparative studies) is for scientific, ethical and financial considerations. However, one should mention that Russian researchers rarely use this element of planning. The journal editorial board asks authors:

- to describe the procedure of sample size calculation in detail, or
- to provide another sample size justification (if any), or
- to specify that the sample size has not been calculated.

4.10.2. Methods of statistical data analysis

The WAME's guidelines define the general principle of this subsection as follows: "Describe statistical methods in sufficient detail to enable a prepared reader having access to the original data to evaluate their suitability for solving the research problem and verifying the results".

When completing this section, authors should:

- specify the format of the quantitative data presentation: the arithmetic mean (standard deviation), median (25; 75 percentile), 95% confidence interval, etc.;
- describe the statistical criteria used for data analysis, by clearly identifying the criteria used for the quantitative and qualitative data analyses, as well as the criteria used for the analysis of the source characteristics' values, and for the analysis of their changes in the course of the research;
- mention the statistical software package (including the developer and the country of origin) used.

V. RESULTS

Authors should remember that the description of the results obtained should not be accompanied by their discussion, or by reference to the results of other studies and formulation of conclusions. This information *should be* provided in the DISCUSSION section.

5.1. Research participants

In this section, (rather than in the METHODS section, as often happens), authors should provide a description of the studied sample, that should include:

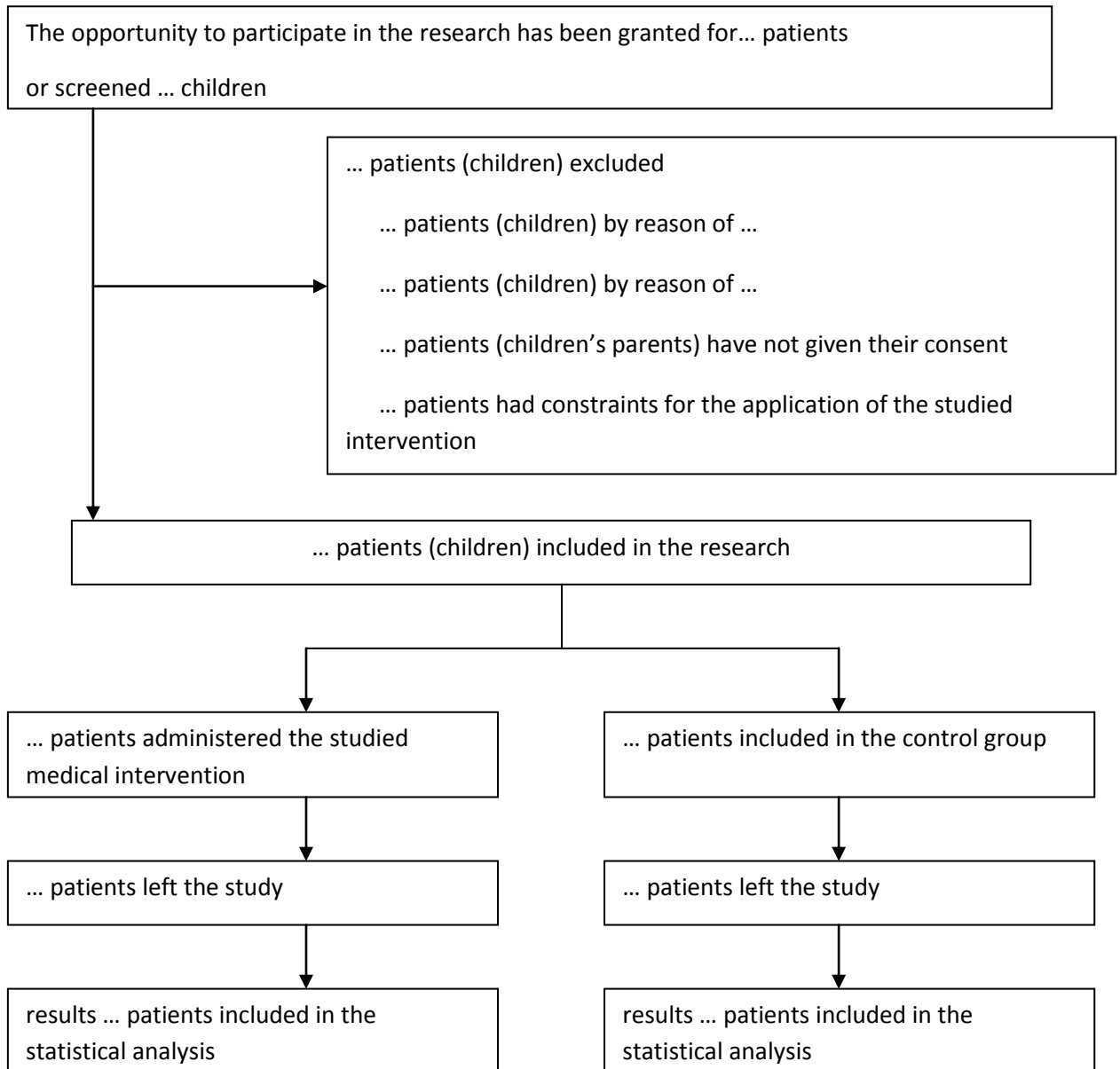
- the presentation of the research scheme,
- the description of the initial characteristics of research participants.

The authors of the manuscript are *highly recommended*, (and this is obligatory for research with a complicated plan (design) or which is conducted in three or more stages), to submit the research scheme in the form of linked blocks containing information on the number of patients screened (for example, the number of patients hospitalized during the research period), the number of patients included in the research (divided into comparable groups), the number of patients who have the medical product or service, the number of patients taking part in the research, and the number of participants included in the analysis (Fig. 1). In addition, it is necessary to specify the reasons why the patients screened have not been included in the research, and why excluded participants have stopped their participation.

As a rule, the description of research participants includes sample characteristics such as sex, age, indicators of physical development, and clinical and anamnestic signs. This information helps editors (and, subsequently, readers) to develop a clear view of the studied group. The description of the whole sample will give an idea of the breadth of the interpretation of the research results (i.e. what the external generalizability of the results is). The description and a comparative statistical analysis of the studied groups indicate their comparability and, therefore, specify whether the research results are a

consequence of the medical intervention, risk factors and phenomena studied. When comparing the groups, the presentation of some characteristics can be required, particularly characteristics whose relationship with the effects of medical interventions or the course of diseases is well-known.

Figure 1. The research scheme (possible option)



5.2. Primary Findings

The main research results *must* include a description of the main result and the results of the statistical data analysis related to it. However, it is not enough to rely only on the “p” value (that must be submitted to within three decimal places). It is necessary to determine the magnitude of the effect (change), representing it not only in the form of averages (arithmetic mean, geometric average or median), but also with point estimates, with the interval estimates describing the data spread (standard deviation, percentiles) or characterizing the reliability of point estimates (confidence intervals). In controlled research including groups having incomparable initial characteristics, the description of the

main research result *must be* supplemented with an analysis of the effect of detected differences, with an adjustment made using multicentric study methods (for example, regression analysis).

The description of the main research results can be conducted using two principles. The basic principle lies in the analysis of the main research results using all of the participants, regardless of whether there has been a complete or partial fulfillment of the protocol (the so-called *intention-to-treat* procedure). The analysis of the medical intervention results based only on the participants who have fully fulfilled the research protocol (*per-protocol* analysis principle) can supplement the basic calculations only.

5.3. Additional findings

The practice of comparing “everything with everything”, which has already spread and taken root in Russian authors’ publications, is invalid and, in some cases, leads to significant errors. That is why the description of additional research results may include only those findings that have been described by the authors in the section “Additional research findings” (see METHODS). As stated above, reference to previously formulated additional findings represents a fair research and publication practice.

This subsection may include the results of the evaluation of the effect of the medical intervention on the subgroups. The analysis *must be* limited only to those subgroups listed (with a brief justification) in the “Subgroup analysis” subsection (see METHODS).

5.4. Adverse events

It is necessary to identify all undesirable phenomena occurring during the research. Undesirable phenomena include any medical events (any diseases, injuries, unplanned operational interventions, etc.) whose connection with the medical intervention (preventative, diagnostic, therapeutic or any other) cannot be ruled out. In addition, any absence of undesirable phenomena should be mentioned. If a record of undesirable phenomena of the medical intervention has not been made, then authors *should* underline this fact.

VI. DISCUSSION

The journal editorial board encourages the use of a structured format by authors when discussing the research results. However, the discussion should not lead to a “justification” of the results obtained. The main purpose of this section is the discussion of both the advantages and possible disadvantages, including biases and limitations, of the research. The proposed variant for structuring is presented below.

6.1. Resume of the primary findings

6.2. Discussion of the primary findings

A discussion of the results related to the hypothesis (the main purpose) of the research should be carried out, in the context of previously known data, opinions and theories, including additional research results and subgroup analysis results. If necessary, authors should discuss the key mechanisms of the implementation of the medical intervention effects.

6.3. Limitations

Discussion of research results *must be* accompanied by an analysis of factors that can affect the research findings significantly. These limitations can be assigned to each stage of the research, starting with its justification and the methods used, and ending with the interpretation of results, (the magnitude of effects, applicability of research results where there are changes in conditions for its use, etc.). The limitations associated with research methods can be regarded as the most substantial: conditions of its course, sample size, evaluation tools used, etc.

6.4. Brief practical implications

It is reasonable to give a brief justification for the clinical and/or scientific use of research results. However, authors should resort to overgeneralizations with great care, and not unreasonably insist on the applicability of research results in other, or broader, conditions of clinical or scientific practice.

VII. SOURCE OF FINANCING

Authors should indicate the source(s) of research financing (if any), specifying, for example, the following: "The research has been carried out with the financial support (financing) ...".

VIII. CONFLICTS OF INTEREST

Authors should identify any so-called conflicts of interest, such as conditions and facts that can misrepresent (evidently or hypothetically) research results, (for example, finance provided by interested individuals and companies, their participation in the discussion of research results, manuscript writing, etc.). Where such conflicts are absent, it is necessary to use the following statement: "The authors of this article confirm that there are no conflicts of interest to report".

IX. ACKNOWLEDGEMENTS

Authors have an opportunity to acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials (consultation, technical assistance, translations, etc.).

X. REFERENCES

References can include only published data, opinions and theoretical reflections. The journal editorial board does not limit authors in the number of cited sources. However, it will object to the use of an unreasonably large number of references on, for example, well-known issues or issues researched in a large number of studies and providing ambiguous results. The use of a large number of references when describing the results of a systematic review is an exception. In general, authors are advised to use no more than three references for each statement. However, each authors' statement, except the best-known ones, must be accompanied by references to information sources. Authors should avoid self-citation, except in cases where it is necessary (for example, if there are no other data sources):

Examples of references to journal or journal articles.

- Yank V, Rennie D. Excerpts from the United States Renal Data System 2007 annual data report. *Am J Kidney Dis.* 2008; 51(1, Suppl. 1):1–320.
- Fedoseenko MV, Namazova-Baranova LS. Pneumococcal infection: a real threat to children. How to protect oneself? *Pediatric pharmacology.* 2010;7(1):114–7.

Example of references to Internet sources.

- who.int [Internet]. Maternal, infant and young children nutrition. WHA65.6 [updated 2012 May 26; cited 2012 Sep 15]. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_R6-en.pdf.

Example of references to books.

- Khaitov RM. *Immune system physiology.* Moscow: VINITI RAS; 2005. 375 p.

The text of the manuscript should contain references. Number the references (numbers in square brackets) in the list in the order in which they appear in the text.

XI. CONTACTS

The article should contain the contact details of the author responsible for correspondence (with the editorial board, reviewers, readers), including full name, academic degree and rank, position, organization department and full organization name (of the main place of employment), work postal address (with postal code), e-mail address, office phone number and mobile phone number (required for operational communication with the author, but not included in the published version of the manuscript). If there are co-authors of the article, the full name and organization name (the main place of employment) should be specified.

References used for preparation of the set of rules and guidelines:

1. Moher D, Schulz KF, Altman DG. Unified standards for the presentation of the results of randomized controlled trials (CONSORT): updated guidelines for improving the quality of reports of randomized controlled trials. *The international journal of medical practice*; 2001. Available from: <http://www.mediasphera.aha.ru/mjimp/2001/4/r4-01-1.htm>.
2. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c869. doi: 10.1136/bmj.c869.
3. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals [updated December 2013]. Available from: <http://www.icmje.org/icmje-recommendations.pdf>.
4. *Epidemiological dictionary*. John M. Lust (ed.) (4th edition). Moscow; 2009. 316 p.
5. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions* [Internet]. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. Available from: www.cochrane-handbook.org.
6. Saygitov RT. The effectiveness of editorial activities while preparing the manuscripts containing original research results: the results of blind randomized controlled study. *Current Pediatrics*. 2010;9(6):5-15.