The reporting quality of abstracts of randomized controlled trials on Ginkgo biloba

Tintinger, Marie

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SCHOOL OF MEDICINE

MARIE TINTINGER

THE REPORTING QUALITY OF ABSTRACTS OF RANDOMIZED CONTROLLED TRIALS ON GINKGO BILOBA

Diploma thesis

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Prof. Darko Modun, MD, PhD

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LIST OF ABBREVIATIONS

ROS - reactive oxygen species

PAF - platelet activating factor

MAPK - mitogen-activated protein kinase

EBM - evidence-based medicine

RCT - randomized controlled trial

Met – Metformin

GKB – Ginkgo biloba

HbA1c - Blood glycated hemoglobin

BMI - body mass index

WC - waist circumference

VAI - visceral adiposity index

MS – Multiple sclerosis

POD – postoperative delirium

IOP – intraocular pressure

ADR – adverse drug reaction

1. INTRODUCTION

1.1. Ginkgo biloba

Ginkgo biloba is an herbal nutritional product, which is considered to be one of the most common herbs used in the world (1). For decades, it has played a major role in the treatment and prevention of many diseases, especially in the area of traditional Chinese medicine (2). The extracts from the leaves can be converted into tea but also into tablets or liquids as they do in the more western medicine (3).

It is thought that ginkgo biloba exerts cognitive enhancing effects and plays a role in conditions including confusion, memory loss, headache, and anxiety. Moreover, it is presumed, that it may mitigate tinnitus, dizziness, or vertigo. Ginkgo biloba decreases blood viscosity leading to improved inner ear and cerebral blood flow and causes an improvement of mitochondrial function and energy metabolism which when impaired, contribute to the pathogenesis of these disorders (2).

In a study published in 2018, patients with sub-chronic or chronic tinnitus were enrolled in a double-blind randomized controlled trial. Over a period of 12 weeks, patients in the intervention group had to take pills consisting of EGb 761. It was proven, that loudness, annoyance, and the overall suffering of the patients was reduced by the therapy (4). The herbal product is most often used as an extract instead of in its pure form. The widely used Ginkgo biloba extract (EGb 761) is a standardized extract with most toxic ginkgolic acids removed (5).

It takes a complex procedure to extract the therapeutically important constituents from the dried leaves of the Ginkgo biloba plant (3). The leaf extracts are prepared from dried ginkgo leaves and are mixed with an acetone-water mixture or other convenient solvents. Comprised in the process is the enrichment of components which are preferred and the elimination of substances which are unwanted. The synthesis of EGb761 requires a 27-step extraction process, and the liquid extract is dried to give one extract from approximately 50 parts raw ginkgo leaves (6).

EGb 761 consists of two major groups of substances, the flavone glycosides (flavonoid fraction 22-27%) and the terpene lactones (terpenoid fraction 5-7%). The latter consist of bilobalide and ginkgolides A, B, C. Bilobalide has been shown to have a stabilizing effect on mitochondria, which could lead to a decrease of reactive oxygen species (ROS) production. Although ROS are products generated during normal metabolism, they can be harmful when they are produced in excess. They can lead to the induction of oxidative

modification of cellular macromolecules, can cause the inhibition of protein function and promote cell death (7).

Ginkgolide B seems to have an antagonistic effect on platelet activating factor (PAF), which is a mediator produced my many different cells. It functions in exerting numerous physiological mechanisms involved in inflammation (8). Additionally, it induces neutrophil degranulation and platelet aggregation, having an increasing effect on microvascular permeability. With its protective action against cerebral hypoxic damage and its contribution to increasing cerebral metabolism, it makes it a possible contributing factor in neuroprotection (3,5). Especially in the peripheral vascular system, the effects become apparent. Among these is an improvement of the blood circulation which has a positive influence on intermittent claudication, a complication of peripheral arterial disease (9).

The flavone glycosides act as cation-chelators, enzyme-inhibitors, and antioxidants/free radical-scavengers. Their oral bioavailability is poorly but they still seem to have a major contribution to the effects of EGb761 (6). Whether or not they are able to cross the blood-brain barrier in significant concentrations, remains uncertain (5). Their polyphenol structure is thought to be responsible for their antioxidant properties. Especially the two constituents, quercetin and myricetin, cause an effective inhibition of the oxidation of tert-butyl hydroperoxide. The flavones may also exert an anti-apoptotic function by, amongst various other things, inducing oxidation. Modulation of certain proteins involved in intracellular apoptotic signaling cascades such as the mitogen-activated protein kinase (MAPK) cascade may contribute to the glycosides´ anti-apoptotic effects (10).

1.2. Evidence based medicine

Originally, evidence-based medicine (EBM) was developed in the early 1990s and primarily focused on guidelines for clinical practice, the creation of systematic reviews and critical assessment of scientific work. EBM has become an essential basis for today's clinicians to scrutinize and evaluate scientific data, in order to be able to implement the newest and most qualitative research into every day's clinical practice. Its contribution to improving the quality of research by disclosing problems arising from already existing research lead to a constant development of better research (11). EBM requires a clear portrait of relevant clinical questions, an in-depth examination of the question's literature, a thorough evaluation of the available evidence and applicability of the findings to the clinical situation (10).

Among many study designs, a hierarchy of evidence subsides in which randomized controlled trials hold the highest quality of evidence as seen in Figure 1 (11). The hierarchy ranks from simple observational methods at the bottom to more advanced study types. There is a decreasing risk of bias as one goes up the pyramid (12).
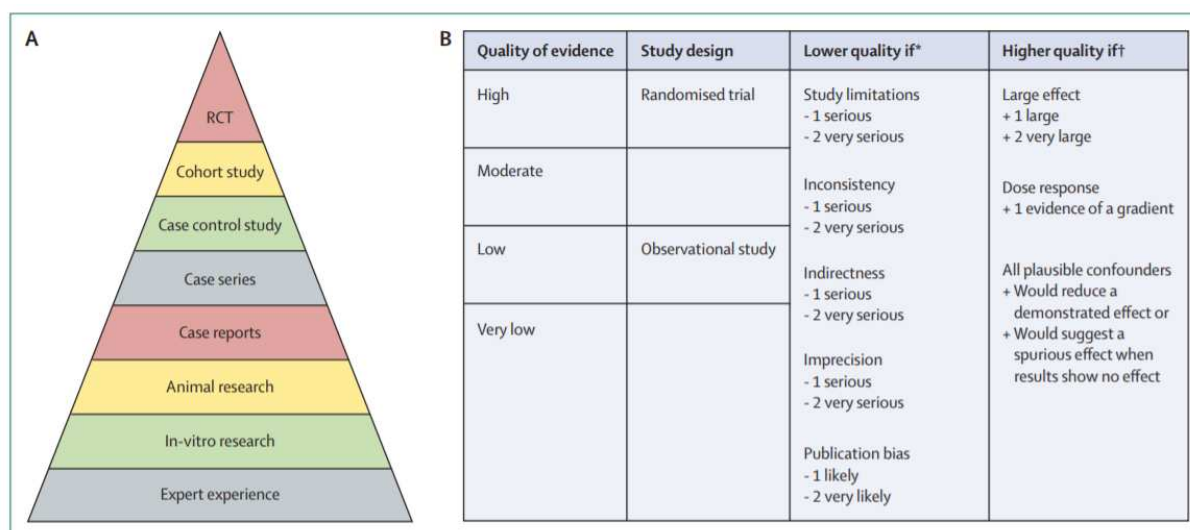

Figure 1. Hierarchy of evidence (11).

1.3. Randomized controlled trials

The gold standard for determining the safety and efficacy of a treatment are randomized controlled trials (RCTs), which belong to the group of cohort studies. They can compare new treatments with already existing standard treatments and prove their ascendancy. Providing the highest level of evidence by avoiding and controlling many possible sources of bias, RCTs can ascertain whether a coherence in cause-effect relation between treatment and outcome exists (13-15). In the process, a study population which is appropriate for the treatment tested, is defined. To establish recruitment of qualified patients, clear inclusion and exclusion criteria need to be constructed. Demographic characteristics, disease state, and maybe even comorbidity and comedication are factors in which study subjects must be equal (13).

The contestants are randomly allocated into two groups of which one of them, the experimental group, is going to receive the new treatment and the other group, the control group, either the gold standard treatment or a placebo (14). An association between any

differences in the results and the treatment effect can only be made if the groups are structurally equivalent, which is precipitated by randomization reducing confounding (13).

In the field of research, there is a big potential for errors to happen. Bias, a confounding factor, and chance are one of the main ones which should be considered. In order to minimize these systematic errors, it is important to accomplish a well-designed RCT. Many features need to be considered to reach this goal. Essentially, there is a need to identify whether the hypothesis being tested matches the sample to be studied, so a generalization of any results can be made. Moreover, a sufficient number of recruits is required to detect a clinically important difference between the regimens. In most cases, the studies should be masked so the patients and/or the trialists remain unaware of which treatment was given (15).

Its purpose is the reduction of "performance bias", which is a result of differences in outcome, that can occur when the intervention or allocation is known. This bias may manipulate the estimated effect of the intervention. Randomization is one of the key features, having an influence on the quality of the study. It should completely be based on chance. It aids in the reduction of "selection bias" and "allocation bias" (14-17).

The former can lead to a systematic error in an association or outcome when a systematic difference between groups or individuals and the population of interest occurs (18). Allocation bias is a part of selection bias. Per definition, allocation bias originates from a systematic difference in the assignment of participants to the treatment and control group, respectively. If investigators predict or know which intervention the respective participant is expected to get, this type of bias can occur. It can influence the investigators approach toward participants and affect the process of allocation into the different study groups. By that, subjects with good prognoses, meaning that good outcomes and treatment responses can be assumed, can be assigned to a certain group (19).

It is almost not avoidable that some participants would not finish the study, be it because of withdrawal, non-compliance, or misdiagnosis. This can lead to a deviation of baseline factors between the two groups which would make randomization redundant in the first place. Therefore, analysis of the results should be based on an "intention to treat". This strategy ensures that all patients in their respective groups are analyzed as a whole, whether they did or did not complete the study. Another contributor to the reduction of systematic errors in RCTs is the statistical power. It is the competence of a study to recognize "a difference between the two groups when such a difference exists" (20).

1.4. Consort for reporting randomized controlled trials

The CONSORT statement is a set of recommended instructions for reporting randomized trials and is based on evidence (21). It was initially developed in 1996 and renewed 5 years later. The positive impact on the quality of reporting randomized controlled trials could be seen but were not as promising as expected due to many other inadequate trial reports. Based on new evidence and experience over several years, in 2010 the updated CONSORT 2010 was released. The paper includes a 25-item checklist, presented in a table and a flow diagram. Its focus lies on parallel, two-group randomized controlled trials. Conscientious adherence by authors to the checklist ensures accuracy and integrity of reporting (22).

CONSORT contributes to improve the reporting by providing instructions to authors and facilitating critical appraisal. Furthermore, it can be used by peer reviewers and editors in the identification of potentially biased results and those which are difficult to interpret. The statement focuses on the internal and external legitimacy of trials (23). As the main CONSORT Statement rests upon the standard two-group parallel design, it has been extended in order to cover other design aspects, interventions and data. Many different extensions to the Statement exist but the aim of this work was to focus on the quality of reporting in abstracts, which was created due to the lack of adequate and high-quality abstracts (21).

Readers of scientific papers and journal articles often base their assessment of the addressed clinical trials on the information given in the abstract. Many health professionals all over the world can only gain access to abstracts and not full articles and base their decisions solely on the information gathered from abstracts. Hence it is important for abstracts to be constructed in a sufficiently detailed, clear, and transparent way (24).

The list presented in Table 1. provides authors with essential items when reporting the primary results of a randomized trial in any conference abstract or journal (21).

Table 1*: Items to include when reporting a randomized trial in a journal or conference abstract

Item	Description
Title	Identification of the study as randomized
Authors *	Contact details for the corresponding author
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)
Methods	
Participants	Eligibility criteria for participants and the settings where the data were collected
Interventions	Interventions intended for each group
Objective	Specific objective or hypothesis
Outcome	Clearly defined primary outcome for this report
Randomization	How participants were allocated to interventions
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment
Results	
Numbers randomized	Number of participants randomized to each group
Recruitment	Trial status
Numbers analysed	Number of participants analysed in each group
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision
Harms	Important adverse events or side effects
Conclusions	General interpretation of the results
Trial registration	Registration number and name of trial register
Funding	Source of funding

*This item is specific to conference abstracts.
doi:10.1371/journal.pmed.0050020.t001

1.5. Checklist items

TITLE

Identification of the study as randomized

Example*. "Ginkgo Biloba Extract EGb 761 ® Versus Pentoxifylline in Chronic Tinnitus: A Randomized, Double-Blind Clinical Trial"* (25).

AUTHORS

Contact details for the responding author

Example: *"Department of Otorhinolaryngology, University Hospital Kralovske Vinohrady, Šrobárova 50, 10034, Prague, Czech Republic. klara.prochazkova@gmail.com. "(*25).

TRIAL DESIGN

Description of the trial design (e.g. parallel, cluster, non-inferiority)

Example: *"For both treatment group`s* (25).

METHODS

Participants: Eligibility criteria for participants and the settings where the data were collected

Example*: "(Sixty T2DM patients were recruited); (The patients, currently using Met)"* (26).

Interventions: Interventions intended for each group

Example: "The patients, currently using Met, were randomly grouped into those treated with either GKB extract (120 mg/day) or placebo (starch, 120 mg/day) for 90 days. Blood glycated hemoglobin (HbA1c), fasting serum glucose, serum insulin, body mass index (BMI), waist circumference (WC), insulin resistance, and visceral adiposity index (VAI) were determined before (baseline) and after 90 days of GKB extract treatment." (26).

Objective: Specific objective or hypothesis

Example: "To determine whether Ginkgo biloba extract (ginkgo) improves cognitive function in persons with multiple sclerosis (MS)." (27).

Outcome: clearly defined primary outcome for this report

Example: "Main outcome measure: all-cause mortality at 180 days" (28).

Randomization: How participants were allocated to interventions

Example: "Eighty elderly patients undergoing tumor surgery at Zhejiang Cancer Hospital and complicated with postoperative delirium (POD) between June 2013 and July 2016 were randomly divided into treatment group (group A) and control group (group B) according to the random number table method." (29).

Blinding (masking): Whether or not participants and the settings where the data were collected were blinded to group assignment

Example: "GiBiEx is a multicentre randomized clinical trial, placebo controlled, double blinded, which compared subjects randomized to twice-daily doses of either 120-mg of IDN 5933 (also known as Ginkgoselect®Plus) or to placebo for a 6-months period." (30).

RESULTS

Numbers randomized: Number of participants randomized to each group

Example: "A total of 35 patients with mean age 63.7 (6.5) years were randomized to the ginkgo biloba extract-placebo (n = 18) or the placebo-ginkgo biloba extract (n = 17) sequence." (31).

Recruitment: Trial status

Example: "A futility analysis was performed because of slow accrual." (32).

Numbers analysed: Numbers of participants analysed in each group

Example: "A total of 35 patients with mean age 63.7 (6.5) years were randomized to the ginkgo biloba extract-placebo (n = 18) or the placebo-ginkgo biloba extract (n = 17) sequence." (31).

Outcome: For the primary outcome, a result for each group and the estimated effect size and precision

Example: "A total of 28 patients (80.0%, 14 in each group) who completed testing did not differ at baseline in age, sex, visual field mean deviation, contrast sensitivity, IOP, or blood pressure. Changes in visual field and contrast sensitivity did not differ by treatment received or sequence (P > 0.2 for all). Power to have detected a difference in mean defect as large as previously reported was 80%." (31).

Harms: Important adverse events or side effects

Example: "A total of 28 adverse events were reported: 11 in the ticlopidine-alone group and 17 in the ticlopidine/Ginkgo biloba group. The adverse events judged to be possibly related to ticlopidine in the ticlopidine-alone group were epigastric discomfort (2 cases), diarrhea (1), skin eruption (1), and a feeling of being cold (1) or hot (1). The adverse events judged to be related to ticlopidine or Ginkgo biloba in the ticlopidine/Ginkgo biloba group were epigastric discomfort (2), diarrhea (2), nausea (2), and headache (1)." (33).

Conclusions: General interpretation of the results

Example:" In this small group of healthy Korean men, the addition of a single dose of Ginkgo biloba extract did not prolong the bleeding time and was not associated with additional antiplatelet effects compared with the administration of ticlopidine alone. The coadministration of Ginkgo biloba extract with ticlopidine was not associated with any significant changes in the pharmacokinetic profile of ticlopidine compared with ticlopidine administered alone." (33).

Trial registration:

Example: "URL: http://www.clinicaltrials.gov. Unique identifier: NCT02135939." (34).

Funding:

Example: "The present study was supported by grants" (35).

2. OBJECTIVES

To analyze Ginkgo biloba RCT abstracts publicly available on PubMed using the CONSORT checklist.

3. MATERIALS AND METHODS

This study was conducted as a cross-sectional evaluation of publicly available RCT abstracts including Ginkgo biloba. A PubMed search for all RCTs on Gingko biloba was performed. The search strategy used the term 'Gingko biloba' and the term 'randomized controlled trial' as article type. Inclusion criterion was the availability of abstracts, as the search engine found several article titles without available abstracts on PubMed and in English language. The search was carried out in January 2020. To assess the reporting quality of analyzed abstracts, the 16 item CONSORT checklist for abstracts was used.

The following abstracts´ data were analyzed: article title, year of publication, journal name, journal impact factor and quartile of the category in the year the article was published (data from the Journal citation reports, Web of science). If the journal was cited in several Web of Science categories, the category with the higher quartile value was chosen for this study.

Furthermore, data such as randomization in the title, contact of the corresponding author, trial design (not reported, parallel group, cluster randomized, crossover, factorial, superiority, equivalence, noninferiority, combination and other), participants (no clear description of eligibility criteria, clear description e.g. setting and participants, clear description of only patients and clear description of only setting), intervention (no clear description, clear description of dose, route, duration etc.), objective (no specific aim, objective or hypothesis addressed and specific aim, objective or hypothesis addressed), outcome (no clearly defined primary outcome for this report and clearly defined primary outcome for this report), randomization (not clearly described method for assigning participants to intervention and not clearly described method for assigning participants to intervention), blinding (not reported whether anyone was blinded and reported who was blinded), number (not reported number of participants in each group and reported number of each group), number 2 (not reported number of participants analyzed and reported number of participants analyzed), outcome (not reported or reported), harms (not reported or reported), conclusion (not reported or reported), trial registration (not reported or reported) and funding source (not reported or reported).

The abstracts´ data were exported into a spreadsheet using Microsoft Office Excel 2016, and a descriptive statistical analysis was performed. Results are presented as median, whole numbers and proportions. The statistical analysis was performed using MedCalc software for Windows (v.11.5.1.0, MedCalc Software, Ostend, Belgium).

4. RESULTS

The search carried out in January 2020 on PubMed resulted with 309 abstracts which included Ginkgo biloba. Out of 309 identified abstracts, 62 were excluded (Figure 2). Forty-eight of the excluded abstracts were published in the period from 1980 to 1996, and there is no available data of journal impact factors and quartiles for this period. In summary, a total of 247 abstracts fulfilling the eligibility criteria were included in this study.
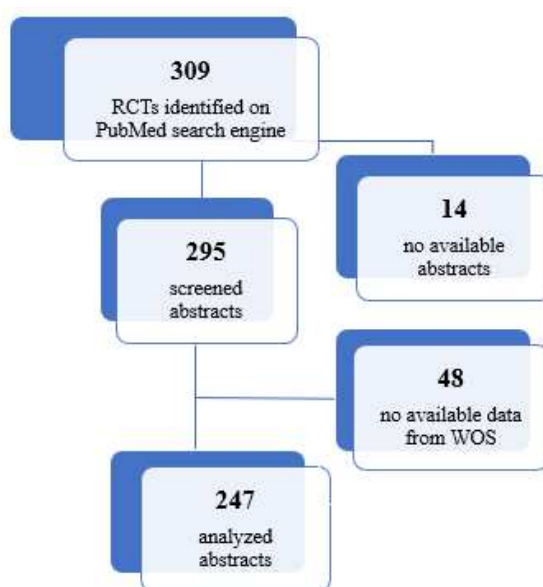

Figure 2. Diagram flow of the abstract's analysis

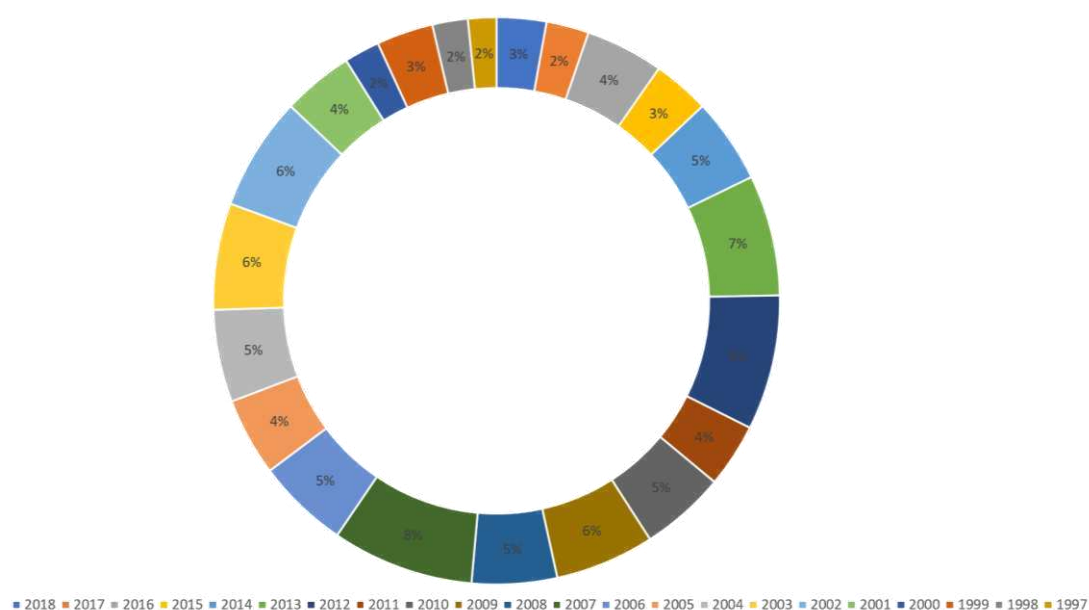Figure 3 shows the distribution of Ginkgo biloba abstracts by the year the study was published.

Figure 3. Distribution of abstracts during the examined period

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Furthermore, the abstracts were published in 150 different journals. Moreover, the majority of articles (17, 6.88%) were published in Zhongguo Zhong Xi Yi Jie He Za Zhi and Human psychopharmacology: Clinical and Experimental (11, 4,45%). Journals that most frequently published Ginkgo biloba articles are presented in Table 1.

Table 1. Journals with the largest proportion of Ginkgo biloba publications

Journal name	Number of articles	Years of publication
Zhongguo Zhong Xi Yi Jie He Za Zhi. (English name Chinese Journal of Integrated Traditional and Western Medicine)	17	2002, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2014, 2016
Human psychopharmacology: Clinical and Experimental	11	2002, 2004, 2006, 2007, 2016
Pharmacopsychiatry	6	2001, 2003, 2012
Neurology	5	2008, 2012, 2013, 2014
Psychopharmacology	5	2000, 2004, 2005, 2006
Phytotherapy research	4	1999, 2005, 2008, 2010
JAMA	4	1997, 2002, 2008, 2009
Nutrients	3	2016, 2017, 2018
Acta ophthalmologica	3	2001, 2007, 2018
BMC complementary and alternative medicine	3	2014, 2016, 2018
European archives of otorhinolaryngology	3	2001, 2016, 2017
Chinese journal of integrative medicine	3	2009, 2014
International journal of geriatric psychiatry	3	2008, 2011, 2014
British journal of clinical pharmacology	3	2005, 2007, 2014
Journal of psychiatric research	3	1997, 2007, 2012
Journal of alternative and complementary medicine	3	2000, 2005, 2009
Arzneimittelforschung	3	1998, 1999, 2007
Wiener medizinische Wochenschrift	3	2002, 2004, 2007
Nutritional neuroscience	3	2001, 2006

The median value of all journals impact factor was 1.818 and the journal with the highest impact factor included in this study was JAMA (year 2002 16.586, year 2008 31.718 and year 2009 28.899). Figure 4 shows the distribution of the journals according to Web of Science quartile values.
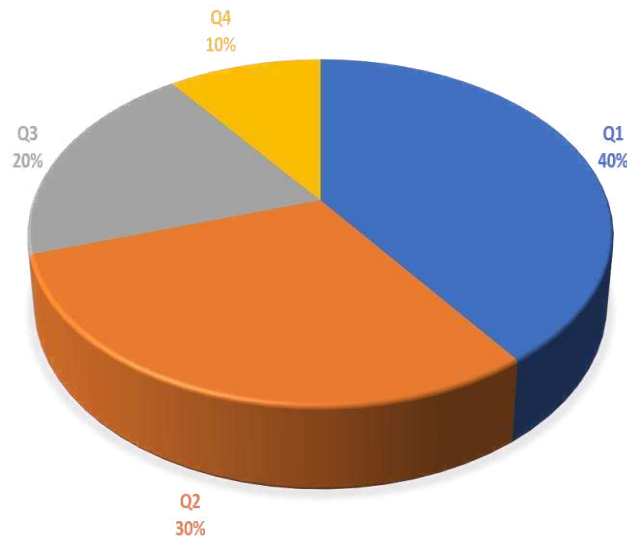
Figure 4. Distribution of quartiles of the published Ginkgo biloba articles

The CONSORT items trial registration and funding source were absent in the majority of analyzed abstracts. Moreover, these items were presented in only one abstract which account for 0.4% of all the analyzed abstracts. Item randomization was included only in two of the analyzed abstracts (0.8% of all the abstracts). Another item of CONSORT checklist which was least likely to be reported was harms. The possible harms of RCTs were reported in only 24 (9.72%) of the abstracts.

Furthermore, 77 (31.17%) abstracts reported number of participants which were analyzed and 79 (31.98%) reported number of participants in each of the study group. Only 80 (32.39%) of the abstracts included randomization in the title. Blinding was reported in 120 of the abstracts (48.58%) and contact of the corresponding author was included in 134 (54.25%) abstracts.

Outcome was reported in 155 of the abstracts (62.75%) and intervention in 182 of the abstracts (73.68%). Furthermore, most reported items were as follows: participants (207, 83.81%), trial design (224, 90.69%), conclusion (234, 94.74%), primary outcome and objective (both 237, 95.95%).

The median value of all the abstracts was 8 (95 confidence interval 8-9). Only one abstract, published in the journal *Lancet Neurology*, contained all the CONSORT items. The median values of all the journals categorized by quartiles is presented in Table 2.

Table 2. Median values of CONSORT checklist items across different quartiles

Journal quartile (Q)	Median
1	8
2	9
3	8
4	8
not indexed in WOS	9

5. DISCUSSION

The results of this study suggest that publicly available Ginkgo biloba RCT abstracts were not following the 16 item CONSORT abstract guidelines. Interestingly, only one out of 247 analyzed abstracts included all the needed items. This study was published in the journal Lancet Neurology (impact factor 23.917) in 2012.

Moreover, the least frequently reported items were trial registration and funding. A study on the correlation between industry funding and the reporting quality of large long-term weight loss trials, published in 2009, showed that on average, industry funded studies are associated with an higher odds ratio, supporting the hypothesis that the absence of the item `funding` has an influence on the overall quality of a study (36).

Ginkgo biloba has played a major role in the treatment and prevention of many diseases for thousands of years, especially in the area of traditional Chinese medicine (2). In 2019, an analysis of individual case safety reports including Ginkgo biloba and cardiac arrhythmias in the World Health Organization global database Vigibase, evaluating 162 reports from 18 countries, was performed. According to this analysis, the database did not contain any reports from China, which lead to the under-reporting of adverse drug reactions (ADR). This absence of reports could be due to differences in indications of use, but most probably reflects differences in the identification and/or reporting of ADR`s (37).

Since the majority of articles were published in Zhongguo Zhong Xi Yi Jie He Za Zhi, a Chinese journal, this finding could indicate why only 24 out of 247 abstracts reported the item harms. Since founding, a Chinese policy was introduced, establishing a better combination of Chinese and Western Medicine in China regarding reporting in clinical, research, prevention, and teaching experience. The implementation of this integrated Chinese and Western medicine lead to an increased international use of this herbal product, making it a top-selling herbal medicinal product, particularly in Europe but also in other western countries (38).

Zhongguo Zhong Xi Yi Jie He Za Zhi was founded in 1981 and is considered a representative of the Integrated Traditional and Western medicine, which explains why most articles included in this study, were published in this paper. From 1981 to 2000, there was a steady increase of published articles with a maximum in the year 2000 (39).

While analyzing the 247 abstracts, the majority of all articles, were shown to have been published in the year 2000. Human Psychopharmacology: Clinical and Experimental was the second most common journal with 4.45% cited articles. In 2019, it is reported to have had an impact factor of 2.112 and to have been cited in four `web of science` categories:

clinical neurology, pharmacology and pharmacy, psychiatry, and psychology, all of which are in the third quartile (40).

Our study did not observe differences between the median values of the CONSORT checklist between journals of different quartiles. Surprisingly, even the journals which are not indexed in Web of Science had a median value of 9. Furthermore, journals indexed in Web of Science had the median values as follows; Q1 8, Q2 9, Q3 8 and Q4 8. It was expected that more valuable and adequately written abstracts would be published in superior journals. However, the results of this study do not support this hypothesis.

The first limitation of this study is that it only included results of the PubMed search engine. There is a possibility that using other search engines (for instance Scopus) would result in a higher number of Ginkgo biloba abstracts. Another limitation is the presence of other guidelines for publishing and writing abstracts but this study including only the 16 item CONSORT checklist. However, as there is a lack of high quality conducted and published RCTs on herbal supplements, Ginkgo biloba among others, this study should encourage further researchers to use guidelines in reporting of the studies.

6. CONCLUSION

1. In total 247 Ginkgo biloba abstracts fulfilling the eligibility criteria were included in this study.

2. The majority of articles (17, 6.88%) were published in Zhongguo Zhong Xi Yi Jie He Za Zhi,and Human psychopharmacology-clinical and experimental (11, 4,45%).

3. The least frequently reported items were trial registration and funding (0.4%).

4. The most frequently reported items were primary outcome and objective (both 95.95%).

5. The median value of all the abstracts was 8 (95 confidence interval 8-9).

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8. SUMMARY

Objectives: The aim of the study was to analyze Ginkgo biloba RCT abstracts publicly available on PubMed using the CONSORT checklist.

Materials and Methods: A PubMed search for all RCTs on Gingko biloba was performed. The search strategy used the term 'Gingko biloba` and the term 'randomized controlled trial' as article type. Inclusion criteria was abstract`s availability. The search was carried out in January 2020. To assess the reporting quality of analyzed abstracts, the 16 item CONSORT checklist for abstracts was used. The following abstract`s data were analyzed: article title, year of publication, journal name, journal impact factor and quartile of the category in the year the article was published. Furthermore, data such as randomization in the title, contact of the corresponding author, trial design, participants, intervention, objective, outcome, randomization, blinding, number, number 2, outcome, conclusion, trial registration and funding source were evaluated.

Results: The PubMed search resulted with 309 abstracts which included Ginkgo biloba, out of which 62 were excluded. Forty-eight of the excluded abstracts were published in the period from 1980 to 1996, and there is no available data of journal impact factors and quartiles for this period. The median value of all journals impact factor was 1.818 and the journal with the highest impact factor included in this study was JAMA (year 2002 16.586, year 2008 31.718 and year 2009 28.899). The most reported items were as follows: participants (207, 83.81%), trial design (224, 90.69%), conclusion (234, 94.74%), primary outcome and objective (both 237, 95.95%). The median value of all the abstracts was 8 (95 confidence interval 8-9). Only one abstract, published in the journal *Lancet Neurology*, contained all the CONSORT items.

Conclusion: Based on the 16 items of CONSORT for abstracts**,** the quality of reporting randomized controlled trial abstracts on Ginkgo biloba is low. This lack of reporting quality means a loss in reproducibility and the assumption of an overall decreased quality of the respective paper.

9. CROATIAN SUMMARY

Naslov: Kvaliteta sažetaka randomiziranih kontroliranih kliničkih istraživanja biljke Ginkgo biloba

Metode: Obavljena je PubMed pretraga svih randomiziranih kontroliranih kliničkih istraživanja biljke Gingko biloba. Strategija pretraživanja koristila je termin "Gingko biloba" i pojam "randomizirano kontrolirano kliničko istraživanje" kao vrstu članka. Kriteriji za uključivanje bili su dostupnost sažetaka. Pretraživanje je obavljeno u siječnju 2020. Za ocjenu kvalitete izvješćivanja analiziranih sažetaka korišten CONSORT dokument koji sadrži 16 stavki. Analizirani su sljedeći dijelovi sažetaka: naslov članka, godina izdavanja, naziv časopisa, čimbenik odjeka časopisa i kvartil kategorije u godini u kojoj je članak objavljen. Nadalje, ocjenjivani su podaci poput randomizacije u naslovu, kontakta dopisnog autora, dizajna istraživanja, sudionika, intervencije, cilja, ishoda, randomizacije, zasljepljivanja, broja ispitanika, broja analiziranih ispitanika, ishoda, zaključka, registracije istraživanja i izvora financiranja.

Rezultati: PubMed pretraga rezultirala je s 309 sažetaka koji su uključivali Ginkgo biloba, od kojih su 62 izuzeta. Četrdeset i osam isključenih sažetaka objavljeno je u razdoblju od 1980. do 1996. godine, a za to razdoblje nema dostupnih podataka o čimbenicima odjeka i kvartila u časopisu. Srednja vrijednost faktora utjecaja svih časopisa bila je 1.818, a časopis s najvećim čimbenikom odjeka u ovom istraživanju bio je JAMA (godina 2002. 16.586, godina 2008. 31.718 i godina 2009. 28.899). Najviše dostupnih stavki CONSORT liste bilo je kako slijede: sudionici (207, 83,81%), pokusni dizajn (224, 90,69%), zaključak (234, 94,74%), primarni ishod i cilj (oba 237, 95,95%). Medijan vrijednost svih sažetaka bila je 8 (interval pouzdanosti 8-9). Samo je jedan sažetak, objavljen u časopisu Lancet Neurology, sadržavao sve stavke CONSORT liste.

Zaključak: Na temelju 16 točaka CONSORT-a za sažetke, kvaliteta izvješćivanja randomiziranih kontroliranih sažetaka na Ginkgo biloba je niska. Ovaj nedostatak kvalitete izvješćivanja znači gubitak obnovljivosti i pretpostavku općeg smanjenja kvalitete odgovarajućeg rada.

10. CURRICULUM VITAE

Personal information

Name: Marie Tintinger

Date and place of birth: November 17th, 1996, Saarlouis, Germany.

Citizenship: German

Address: Im Steinecken 18, 66798 Wallerfangen, Germany.

E-mail: marietintinger@freenet.de

Education:

10/2014 - 07/2020 University of Split School of medicine, Split, Croatia.

10/2018 - 07/2019 Erasmus, University of Erlangen-Nuremberg, Erlangen, Germany

08/2006 - 07/2014 High School Diploma, Robert-Schuman Gymnasium, Saarlouis, Germany.

Languages:

German (mother tongue)

English (C1)

French (B1)

Croatian (A2)