# Errors of indexing randomized clinical trials in dentistry

## Errori di indicizzazione degli studi clinici randomizzati in odontoiatria

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## Summary

This research checked the capability of PubMed, Embase and Cochrane Library to retrieve randomized clinical trials published in journals of dentistry during 2008. Databases frequently detect and pick out these articles even though they often index as RCT studies which are in-vitro instead.

## Riassunto

Questo studio ha indagato la capacità di PubMed, Embase, Cochrane Library di individuare studi clinici randomizzati pubblicati su riviste odontoiatriche nel 2008. I database individuano frequentemente questi articoli anche se indicizzano spesso come RCT degli studi in-vitro.

## Introduction

The evidence-based medicine (EBM) has emphasized the importance to evaluate the methodological characteristics of studies (Sackett 1997). The Randomised Controlled Trials (RCT) represent today the gold standard in therapy research. In fact, the conclusions of these studies can direct the researchers' choice of therapy directly and indirectly through the systematic review of RCTs. It is therefore very important for the clinician and the researcher to have available instruments which permit to easily identify RCTs from the heap of literature.

Hand-search is currently recognized "*gold standard*" for achieving data of literature. As regards electronic searching, the reliability of database is assessed by means of some indexes of which the ones mainly used are sensibility and precision. The meaning of sensibility being the capacity to spot relevant articles and is measured by the proportion of such articles found among all the articles searched through (for example the proportion of RCTs detected from the total number of RCTs). The precision, instead, represents the number of relevant results given by database in respect of results presented (for example the proportion of real RCTs in the articles found).

Today, some of the databases used in the field of medicine (PubMed, Embase and Cochrane) have filters which allow limiting the researches to only RCTs (Crumley 2005, Herskovic 2007). In the past, some of these studies checked the reliability of these filters for some branches in dentistry (Dumbrigue 2000, Sjogren 2002), however, even today the exact reliability of database commonly used in dentistry is not known. The aim of this study is to evaluate the sensibility and the precision of PubMed, Embase and Cochrane Library to recognize RCTs in dentistry.

A further aim is to check if the formal characteristics (title and abstracts) and methodological characteristics (studies *in-vitro*) of the articles can have an impact on the results.

## Materials and Methods

Three investigating operators (MN, MM, GI) have independently done a research on hard copy journals indexed in the *ISI Web of Knowledge with Impact Factor* 2008 (*Subset Cathegory: Dentistry, Oral Surgery & Medicine*) with the aim of finding all the RCT studies published in these journals during 2008. The clinical randomized studies were considered to be RCTs independently from the experimental scheme (parallel, cross-over, split-mouth, factorial, cluster, etc). Also 'in situ' studies, using patients allocated in a randomized manner, have been considered . Dubious cases have been discussed among the operators to the point of reaching an agreement.

Of the articles found, one investigating operator (TS) recorded the randomization indication in the title and/or abstract.

Once the RCTs of 2008 were gathered, the same three investigating operators (MN, MM, GI) performed researches on PubMed, Embase and Cochrane Library to check their sensibility and precision.

This research took place in August 2010 using filtering limits, such as type of article (journal) and year of publication (yr=2008), to all databases. Also, with PubMed the research was limited to the "*Type of article [Publication Type]: Randomized Controlled Trial*" with Embase it was "*Evidence Based Medicine: Randomized Controlled Trial*", whilst in the case of Cochrane Library the research was limited to "*Publication Type: Randomized Controlled Trial*".

In each research the real and effective RCTs, as well as the studies resulting as 'not RCTs', were identified and were confronted with the list of RCTs which showed up in the hard copy journals.

The articles not resulting RCTs were consulted and one investigating operator (MN) verified if the studies were performed *in-vitro*, for example on extracted teeth.

Statistical Analysis

Three journals, with a total of 947 articles, have been used as proof of reliability to quantify the inter-rater agreement between the three examiners. The K-statistic was calculated for each couple of examinators.

The sensibility of each database was calculated on 'found RCTs / total RCTs'.

Also, for each database was taken into consideration if for the RCTs found and those not found the title or abstract indicated or not 'randomized studies'. Any possible links were tested with Fisher Exact Test.

The precision of each database was calculated using RCT/studies found by database.

The percentage of studies *in-vitro* was calculated on studies found by database which were not RCTs.

## Results

The agreement reached by the investigating operators resulted in elevated readings of k-statistics on a sample of 947 articles.

The comparison of operator 1 against operator 2 obtained one k = 0,98 (standard error =.03), operator 1 against operator 3 one k= 0.92 (standard error 0.03), whilst operator 2 against operator 3 resulted in one k = 0.91 (standard error 0.03).

The journals indexed in cathegory 'Dentistry Oral Surgery & Medicine' in 2008 were 55 over a total of 6479 articles.

The RCTs resulted to be 428, equal to 6.6% of articles published.

Of these 428 RCTs, PubMed and Cochrane Library picked out 397 (sensibility of 92.7%) and Embase detected 349 (sensibility of 81.5%).

Threehundredtwelve RCTs (72.9%) gave either in the title or the abstract the indication of RCT. The RCTs which did not give the indication of RCT in the title or the abstract had a risk of 9.22 [CI95% 4.08; 20.82] p<0.0001, which means that these studies run more than 9 times the risk of not being recognized RCTs by PubMed or Cochrane Library compared to other studies.

The equivalent risk relating to Embase was 3.05 [CI95% 2.07; 4.05] p<0.0001.

Of the 536 articles considered RCTs by PubMed or Cochrane Library only 397 (precisely 74.1%) actually were RCTs whereas 139 articles were really not RCTs. Of these articles as much as 121 (87.1%) were in fact studies *in-vitro*.

Of the 501 articles considered RCTs by Embase, only 349 (precisely 69.7%) actually were RCTs whilst 152 articles were not RCTs. Therefore of these articles as much as 102 (67.1%) were actually studies *in-vitro*.

The results of sensibility and precision of database are listed in Table 1.

Table 1: Sensibility and precision of database

| JOURNAL | Art Tot | RCT | PUBMED/ Cochrane Library | EMBASE | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Found | True | Sens% | Prec% | Found | True | Sens% | Prec% |
| Acta Odontol Scand | 58 | 5 | 6 | 5 | 100 | 83 | 1 | 1 | 20 | 100 |
| Am J Dent | 74 | 19 | 31 | 18 | 95 | 58 | 18 | 11 | 58 | 61 |
| Am J Orthod Dent Ortop | 239 | 16 | 15 | 15 | 93 | 100 | 20 | 15 | 94 | 75 |

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|---|---|---|---|---|---|---|---|---|---|---|
| Angle Orthod | 167 | 8 | 13 | 8 | 100 | 61 | 15 | 8 | 100 | 53 |
| Arch Oral Biol | 164 | 9 | 7 | 6 | 67 | 86 | 6 | 5 | 55 | 83 |
| Aust Dent J | 57 | 1 | 5 | 1 | 100 | 20 | 8 | 1 | 100 | 12 |
| Brit Dent J | 148 | 3 | 5 | 3 | 100 | 60 | 3 | 2 | 67 | 67 |
| Brit J Oral Maxil-lofac Surg | 184 | 6 | 7 | 6 | 100 | 86 | 4 | 4 | 67 | 100 |
| Caries Res | 59 | 17 | 17 | 15 | 88 | 88 | 16 | 15 | 88 | 97 |
| Cleft Pal Cranio-fac J | 90 | 2 | 2 | 2 | 100 | 100 | 2 | 2 | 100 | 100 |
| Clin Imp Dent Relat Res | 33 | 2 | 3 | 2 | 100 | 67 | 3 | 2 | 100 | 67 |
| Clin Oral Implant Res | 163 | 17 | 19 | 17 | 100 | 89 | 14 | 12 | 70 | 86 |
| Clin Oral Invest | 61 | 11 | 10 | 9 | 82 | 90 | 10 | 9 | 82 | 90 |
| Comm Dental Health | 24 | 2 | 2 | 2 | 100 | 100 | 1 | 1 | 50 | 100 |
| Comm Dent Oral Epidem | 63 | 3 | 2 | 2 | 67 | 100 | 2 | 2 | 67 | 100 |
| Dental Materials | 231 | 0 | 7 | 0 | - | 0 | 6 | 0 | - | 0 |
| Dent Mat J | 96 | 1 | 7 | 1 | 100 | 14 | 7 | 1 | 100 | 14 |
| Dental Trauma-tology | 163 | 5 | 5 | 5 | 100 | 100 | 5 | 4 | 80 | 80 |
| Dentomaxillofac Rad | 77 | 0 | 0 | 0 | - | - | 0 | 0 | - | - |
| Eur J Oral Sci | 84 | 4 | 4 | 3 | 75 | 75 | 5 | 3 | 75 | 60 |
| Eur J Orthod | 94 | 12 | 11 | 10 | 83 | 91 | 8 | 7 | 58 | 87 |
| Intern Dent J | 50 | 3 | 3 | 3 | 100 | 100 | 4 | 3 | 100 | 75 |
| Intern Endod J | 136 | 4 | 15 | 4 | 100 | 27 | 15 | 4 | 100 | 27 |
| Int J Oral Maxil-lofac Impl | 120 | 8 | 9 | 8 | 100 | 89 | 9 | 8 | 100 | 89 |
| Int J Oral Maxil-lofac Surg | 200 | 12 | 12 | 12 | 100 | 100 | 12 | 11 | 92 | 92 |
| Int J Paediatric Dent | 74 | 8 | 9 | 8 | 100 | 89 | 9 | 8 | 100 | 89 |
| Int J Period Rest Dent | 58 | 7 | 6 | 6 | 86 | 100 | 6 | 6 | 86 | 100 |
| Int J Prosthodon | 76 | 8 | 5 | 5 | 62 | 100 | 5 | 5 | 62 | 100 |
| J Adhesive Dent | 56 | 3 | 23 | 3 | 100 | 14 | 18 | 3 | 100 | 17 |
| J Am Dent Assoc | 143 | 12 | 12 | 12 | 100 | 100 | 13 | 12 | 100 | 92 |
| J Can Dent Assoc | 56 | 1 | 1 | 1 | 100 | 100 | 1 | 1 | 100 | 100 |
| J Clin Periodontol | 158 | 31 | 29 | 29 | 93 | 100 | 39 | 29 | 93 | 74 |
| J Craniomandibu-lar Pract | 33 | 5 | 5 | 5 | 100 | 100 | 5 | 5 | 100 | 100 |
| J Craniomaxillofac Surg | 65 | 1 | 1 | 1 | 100 | 100 | 1 | 1 | 100 | 100 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| J Dent Res | 181 | 13 | 12 | 11 | 85 | 92 | 12 | 10 | 77 | 83 |
| J Dent | 159 | 17 | 30 | 17 | 100 | 57 | 25 | 14 | 82 | 56 |
| J Endod | 288 | 17 | 33 | 17 | 100 | 51 | 37 | 17 | 100 | 46 |
| J Oral Maxillofac Surg | 408 | 16 | 16 | 16 | 100 | 100 | 9 | 9 | 56 | 100 |
| J Oral Pathol Med | 97 | 1 | 1 | 1 | 100 | 100 | 2 | 1 | 100 | 50 |
| J Oral Rehabil | 121 | 10 | 10 | 8 | 80 | 80 | 9 | 7 | 70 | 78 |
| J Orofacial Pain | 30 | 3 | 3 | 3 | 100 | 100 | 3 | 3 | 100 | 100 |
| J Periodont Res | 96 | 1 | 2 | 1 | 100 | 50 | 2 | 1 | 100 | 50 |
| J Periodontol | 293 | 48 | 48 | 47 | 98 | 98 | 51 | 47 | 98 | 92 |
| J Prosthetic Dent | 145 | 2 | 3 | 2 | 100 | 67 | 3 | 2 | 100 | 67 |
| J Pub Health Dent | 38 | 2 | 2 | 2 | 100 | 100 | 2 | 2 | 100 | 100 |
| Odontology | 11 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Oper Dent | 93 | 8 | 19 | 7 | 87 | 37 | 15 | 7 | 87 | 47 |
| Oral Dis | 103 | 2 | 2 | 2 | 100 | 100 | 1 | 1 | 50 | 100 |
| Oral Micrbiol Immunol | 80 | 5 | 3 | 3 | 60 | 100 | 2 | 2 | 40 | 100 |
| Oral Oncology | 157 | 1 | 1 | 1 | 100 | 100 | 1 | 0 | 0 | 0 |
| Oral Surg Oral Med Oral P | 410 | 16 | 21 | 16 | 100 | 76 | 21 | 15 | 94 | 71 |
| Pediatric Dent | 34 | 5 | 7 | 4 | 80 | 57 | 7 | 3 | 60 | 43 |
| Periodontol 2000 | 35 | 0 | 0 | 0 | - | - | 0 | 0 | - | - |
| Quintessence Intern | 125 | 14 | 15 | 12 | 86 | 80 | 8 | 7 | 50 | 87 |
| Swed Dent J | 21 | 0 | 0 | 0 | - | - | 0 | 0 | - | - |
| | 6479 | 428 | 536 | 397 | 0,927 | 0,741 | 501 | 349 | 0,815 | 0,697 |

## Discussion

Even though RCTs often represent methodological problems in dentistry, today they are the most important studies in therapy (Nieri 2007). In 2008, in the journals indexed in dentistry have been published 428 RCTs. It is possible that this figure increases considerably over the years and that further and ever more accurate information can be passed to clinical practice (Nieri 2009).

The sensibility of database selected to detect clinical randomized studies resulted rather high.

Actually, up to 92.7% of the articles are detected by PubMed whilst Embase detects 81.5%.

The database of Cochrane Library obtain the same results of PubMed. Perhaps there could be some exchange of information between the two database systems able to determine some equality from many points if view. Looking for RCTs in the field of dentistry in PubMed or Cochrane Library does not seem to give substantially different results.

Whilst the sensibility has given good results, the same cannot be said in respect of precision which resulted in 74.1% with PubMed and Cochrane Library and 69.7% with Embase. Therefore it is possible to affirm that many articles indexed RCTs in this database are really not so. It is plausible that the main error made by the indexors is that of blaming the RCT

label of studies which really are randomized but performed *in-vitro*, which means they are not clinical studies or RCTs. In fact more than 85% of the studies indexed erroneously by PubMed or by Cochrane Library to be RCTs are really studies performed *in-vitro* and, even more, on extracted teeth. This percentage is more than 69% with Embase. The precision is a very important characteristic for a database because a researcher expects to find RCTs without having to reduce further the amount of articles in order to eliminate not randomized studies of poor value from EBM's point of view. Correcting this banal error does not seem difficult and in future could increase in a decisive manner the precision of database. In fact not considering the studies *in-vitro* the precision would get to 96% with PubMed and Cochrane Library and 87% with Embase.

To optimize electronic research, the authors of CONSORT indicated to insert immediately in the title or in the abstract methodological terms and clarifications which illustrate without any ambiguity the type of research made, convinced that this detail can facilitate the indexing of RCTs (Moher 2010, Royle 2005, Cook 2007).

Not indicating in the title or abstract of the article that the study performed is an RCT exposes it to an error of indexing with a relevant risk of 9 in the case of PubMed and Cochrane Library. This risk is lower with Embase simply because some articles do not result indexed at all and therefore do not appear in the Embase database.

This study shows some limits, in fact the analysis of only the indexed journals could create a bias because the not indexed journals could turn out to be less attentive in indicating RCTs so that the values of sensibility and precision could be over-estimated. Also, only one recent year (2008) has been analyzed and the indexing of years before could be less accurate and this fact too could have had an impact on overestimating the sensibility and precision of database.

The results achieved, however, refer to dentistry and cannot necessarily be extrapolated to other fields of medicine.

In conclusion, the sensibility of RCTs in dentistry is elevated for commonly used database whilst the precision is low. The indication in the title or abstract of the method of study used and more attention given to indexing the studies *in-vitro* performed on extracted teeth, should increase enormously the values of sensibility and precision of common database concerning dentistry articles and therefore facilitate the sanitary operators' job of rapidly searching for reliable information.

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