Estimating MEDLINE's identification of randomized control trials in pediatric dentistry

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The purpose of this study was to determine the number of randomized controlled trials in children from 1990-2000 in seven dental disciplines. Sensitive and specific MEDLINE search methodologies were used for upper and lower estimates, capture-recapture corrected those estimates, and hand evaluation refined the estimates. The data indicate that between 602 and 1737 trials were published, and the number per year doubled from 1990 to 2000. These results have implications for clinical decision making, the development of systematic reviews, insurance reimbursement, and teaching.
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INTRODUCTION

With an increasing emphasis on the development of evidence-based clinical decision-making in pediatrics, increasing importance is being placed on the availability of high-quality evidence.[1,2] One reason for this is that access to computer-based communication networks and critically appraised medical information on the Internet can potentially improve clinical decision-making by increasing information availability.[3]

The purpose of this study, therefore, was to estimate the availability of randomized controlled trials in the pediatric dental literature between 1990 through 2000 in seven dental disciplines cited in MEDLINE. Randomized controlled trials, in particular, were sought as they are regarded as the highest level of clinical evidence. High level evidence is a precursor to high level clinical decision making. Further, identification of randomized controlled trials is an initial step in creating a database of clinical trials. Such a database would be an important resource for completing systemic reviews, clinical decision making, insurance reimbursement, teaching and research.

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MATERIALS AND METHODS

Literature Search

A MEDLINE search strategy was developed and implemented to identify the literature in seven dental disciplines: Endodontics, Implant Dentistry, Oral Surgery, Oral Medicine, Orthodontics, Periodontics and Restorative Dentistry[4]. Medical Subject Heading (MeSH) terms, publication type, and truncated text were used for this purpose. For each MEDLINE search strategy, the identified literature was limited to humans, articles written in English, articles on children (<12 years old) and publications from the years 1990-2000 (inclusive). Next, two sensitive and three specific MEDLINE methodological filters developed by Clinical Evidence[5] and The Center for Evidence-Based Medicine[6] were used to identify randomized control trials in the seven dental disciplines. As used here, a sensitive search indicates a search that retrieves the largest number of relevant articles but also includes some irrelevant articles. On the other hand, a specific search indicates a search strategy that identifies a small number of the most relevant articles while excluding the most irrelevant articles and some relevant articles.

Overlapping articles for each of the sensitive and specific searches for the dental disciplines were identified by sequentially: (1) applying the Boolean operator OR to identify the total number of articles; (2) the Boolean operator NOT excluded overlapping articles in each discipline from the six other dental disciplines; (3) the results from step two for each discipline were combined with the Boolean operator OR; and (4) the difference between the results of "OR" search and "NOT and OR" search gave us the resulting overlap.

All literature searches were performed using the Ovid Web Gateway (Ovid Technologies, Inc, NY, NY) Internet interface for MEDLINE (http://gateway.ovid.com).

Table 1a. Number of RCTs found using CE Sensitive Search.

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Total
Oral Medicine	111	112	118	137	167	163	187	210	179	224	119	1727
Orthodontics	102	91	99	114	149	150	170	211	198	166	97	1547
Periodontics	46	51	38	41	63	60	75	80	84	54	28	620
Oral Surgery	21	41	40	44	46	62	69	84	83	82	29	601
Restorative	43	37	35	35	52	51	60	81	72	50	30	546
Endodontics	12	11	7	17	7	12	23	19	17	19	7	151
Implants	1	1	2	1	1	3	1	4	3	4	3	24
Total	336	344	339	389	485	501	585	689	636	599	313	5216

RCTs, randomized controlled trials
CE, Clinical Evidence

Table 1b. Number of RCTs found using CEBM Sensitive Search.

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Total
Orthodontics	58	58	61	81	109	102	116	157	135	115	64	1056
Oral Medicine	57	57	65	74	90	102	100	118	112	146	65	986
Periodontics	33	39	30	25	44	47	56	67	65	36	23	465
Oral Surgery	10	23	21	22	31	38	41	46	49	48	21	350
Restorative	26	28	26	21	38	40	49	61	56	40	18	403
Endodontics	5	9	4	10	3	8	14	11	13	7	4	88
Implants	0	0	2	0	1	3	0	1	3	1	0	11
Total	189	214	209	233	316	340	376	461	433	393	195	3359

RCTs, randomized controlled trials
CEBM, Center for Evidence Based Medicine

A hand examination was done to validate that the studies were randomized controlled trials. Trials were selected randomly using a randomization table.[7] Sixteen articles were randomly selected and read in the seven dental disciplines for all five sensitive and specific searches to determine if the articles were randomized controlled trials.

Analytical Methods

The data obtained was analyzed using GraphPad InStat, GraphPad Software (San Diego California USA). Statistical tests are indicated where used.

Capture-recapture methods[8] were used to estimate the total number of randomized controlled trials: $N = (M+1)(n+1) / [(m+1)-1]$, and variation determined as: $Var(N) = (M+1)(n+1)(M-m)(n-m)/[(m+1)^2(m+2)]$

In these formulations, M is the number of articles identified by search method 1, n is the number of articles identified by search method 2, m is the number of articles identified by both methods, and N is the actual number of articles.

Graphics were prepared using Delta Graph 4.0.5 (SPSS Inc., Chicago IL).

RESULTS

We used two conceptual methods, and three approaches to refine these assessments in determining the number of randomized controlled trials in pediatric dentistry. The two conceptual approaches were sensitive and specific search strategies to determine an upper and lower limit to the number of articles. We then implemented capture-recapture methods to estimate the number that were missed, and identify overlap among the dental disciplines leading to potential over-estimation. Finally, we used hand examination to estimate the actual number of randomized controlled trials.

Over the ten year period from 1990 through 2000, the Center for Evidence-based Medicine (CEBM) and Clinical Evidence (CE) sensitive search strategies identified 3,359 and 5,216 randomized controlled trial articles, respectively (Table 1a, 1b). Among the disciplines the number of randomized controlled trials varied by 64-fold for the CEBM searches, and by 40-fold for the CE searches. Also, the Clinical Evidence searches identified more articles than the Center for Evidence Based Medicine searches ($p = 0.02$, Wilcoxan signed pairs-ranks test). In spite of the differences in search outcome, the ten year number of randomized control trials, by dental discipline, consistently were, respectively: Implants < Endodontics < Oral Surgery < Restorative Dentistry < Periodontics < Oral Medicine < Orthodontics. Interestingly, almost all the disciplines increased by greater than two-fold over the 10-year period.

Because the search strategies and results varied, we assumed that we had missed articles. To refine these numbers, we used capture-recapture methods to generate a

Table 1c. Estimated total # RCTs using Capture-Recapture for sensitive searches from yr=1990-2000

	Sensitive: CEBM + CE	SD	95% CI
Oral Medicine	1739	3.1	6.0
Orthodontics	1548	0.8	1.6
Periodontics	620	0.7	1.3
Oral Surgery	601	1.1	2.2
Restorative	547	1.4	2.8
Endodontics	151	1.1	2.1
Implants	24	1.4	2.8
Total	5231		

RCTs, randomized controlled trials
CE, Clinical Evidence sensitive search
CEBM, Center for Evidence Based Medicine sensitive search

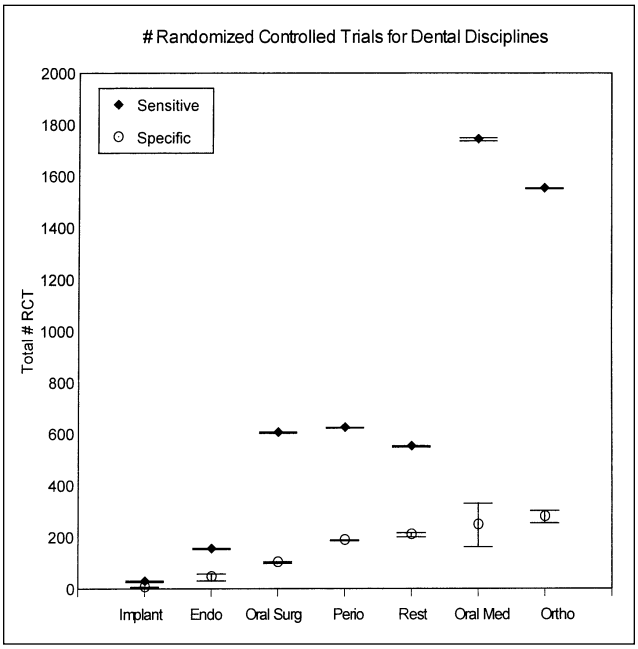

Figure 1. Estimated total number of randomized controlled trials 1990-2000, by discipline, using sensitive and specific search strategies, followed by capture-recapture correction.

Table 2. Results of Handsearching Articles In The Seven Dental Disciplines from yr=1990-2000

	RCT	Not RCT	% RCT
CE Sens	6	10	38%
CEBM Sens	7	9	44%
CE Spec 1	11	5	69%
CE Spec 2	11	5	69%
CEBM Spec	12	4	75%

RCTs, randomized controlled trials
CE1, Clinical Evidence specific search 1
CE2, Clinical Evidence specific search 2
CEBM, Center for Evidence Based Medicine specific search

better estimate of the actual number of articles (Table 1c, Figure 1). The estimated ten year total number of randomized controlled trials for all seven disciplines was 5231 articles. This is slightly larger (0.3%) than the Clinical Evidence search results (5216). A 72 fold range existed between disciplines, and the order was slightly different than that identified in the previous paragraph: Implants < Endodontics < Restorative Dentistry < Oral Surgery < Periodontics < Orthodontics < Oral Medicine

There is also the possibility of overlap in identifying articles among the different dental disciplines, thus leading to an overestimate of the number of randomized controlled trials. To address this we used Boolean operators in combination with our search strategy to estimate this overlap. The results indicated that there were an 18% and a 20% overlap among the dental disciplines for the CE and the CEBM searches, respectively. Applying the average of these (19%) to the results of the capture-recapture (5231) yields a total of 4237 randomized controlled trials.

Finally, we were concerned that the identified articles might not actually be randomized controlled trials. Thus, we randomly selected individual articles examined and classified them (Table 2). The hand examination indicated that only 38% of the identified articles in the CE search were randomized controlled trials, while 44% of the CEBM were. Applying the average of these (41%) to the number of presumed randomized controlled trials identified in the previous paragraph (4237), indicates an upper estimate of 1737 randomized controlled trials in pediatric dentistry published and cited on MEDLINE between 1990-2000.

Using similar methodologies with specific searches we established a lower estimate of randomized controlled trials. Again we used the Center of Evidence Based Medicine (CEBM) and Clinical Evidence (CE) strategies. Over the ten year period, CEBM specific search strategy identified 1016 articles (Table 3a), while the CE strategies identified 970 and 136 in the seven combined dental disciplines (Table 3b, 3c). As with the sensitive searches, among the dental disciplines, the number of randomized controlled trials varied substantially.

Once again, because of the variance among the searches, we were concerned that we had not identified the total number of articles. Using capture-recapture methods this assessment indicated an average among the search strategies of 1022 articles (Table 3d. Figure 1). Next, to adjust for overlap, we again used Boolean operators to combine the searches. There was an average overlap of 17%. Thus the total number of randomized controlled trials was 848.

Finally, we assessed the percentage of randomized controlled trials by hand examination (Table 2). The average of the hand examination indicates that an average of 71% were actually randomized controlled trials.

Table 3a. Number of RCTs found using CEBM Specific Search.

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Total
Orthodontics	10	10	15	16	29	29	31	35	39	28	19	261
Oral Medicine	12	13	15	11	26	30	21	28	21	49	18	244
Restorative	12	14	9	8	21	21	30	27	22	27	6	197
Periodontics	9	19	11	4	21	18	17	30	28	14	10	181
Oral Surgery	2	6	4	8	6	9	11	12	16	15	7	96
Endodontics	1	4	2	1	1	5	6	2	7	4	1	34
Implants	0	0	0	0	0	2	0	0	1	0	0	3
Total	46	66	56	48	104	114	116	134	134	137	61	1016

RCTs, randomized controlled trials
CEBM, Center for Evidence Based Medicine

Table 3b. Number of RCTs found using CE 1 Specific Search.

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Total
Orthodontics	11	10	14	18	29	30	34	38	38	27	20	269
Restorative	13	14	9	7	21	21	29	28	23	27	6	198
Oral Medicine	12	9	12	10	19	20	18	23	15	38	15	191
Periodontics	9	19	11	4	21	18	17	30	27	14	10	180
Oral Surgery	2	6	4	8	6	9	12	12	15	14	7	95
Endodontics	1	4	2	1	1	5	6	2	8	3	1	34
Implants	0	0	0	0	0	2	0	0	1	0	0	3
Total	48	62	52	48	97	105	116	133	127	123	59	970

CE 1, Clinical Evidence specific search strategy 1

Table 3c. Number of RCTs found using CE 2 Specific Search.

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Total
Periodontics	3	7	2	0	4	4	6	5	6	3	0	40
Oral Medicine	1	2	3	4	5	4	6	2	3	5	3	38
Oral Surgery	1	1	2	2	0	2	3	2	3	4	1	21
Restorative	2	0	1	1	3	2	3	3	0	3	0	18
Orthodontics	2	1	0	0	1	3	0	5	3	0	1	16
Endodontics	0	0	0	1	1	0	0	0	0	1	0	3
Implants	0	0	0	0	0	0	0	0	0	0	0	0
Total	9	11	8	8	14	15	18	17	15	16	5	136

CE 2, Clinical Evidence specific search strategy 2

Table 3d. Estimated total # RCTs using Capture-Recapture for specific searches 1990-2000.

	Specific: CE1 + CEBM	Specific: CE1 + CE2	Specific: CE2 + CEBM	Mean	SD	95% CI
Orthodontics	274.3	269	261.0	268.1	6.7	16.6
Oral Medicine	254.7	201	264.4	240.2	33.9	84.3
Restorative	202.1	198	197.0	199.0	2.7	6.7
Periodontics	184.1	180	181.0	181.7	2.1	5.3
Oral Surgery	97.0	95	96.0	96.0	1.0	2.5
Endodontics	35.0	34	34.0	34.3	0.6	1.4
Implants	3.0	3	3.0	3.0	0.0	0
Total	1050.2	980	1036.4	1022.3		

Applying the 71% figure to the 848 number yields 602 randomized controlled trials in pediatric dentistry published and cited on MEDLINE between 1990 and 2000.

Taken together, the specific search strategies indicated an estimated lower limit of 602, while the sensitive search strategies indicated an estimated upper limit of 1737 randomized controlled trials on MEDLINE between 1990 and 2000. These results have some interesting implications.

DISCUSSION

The purpose of this study was to estimate the availability of randomized controlled trials in the pediatric dental literature. Five sensitive and specific MEDLINE search methodologies, and several corrections were used for these estimates. The results indicate that over the 10-year period between 1990 and 2000, a total number of trials between 602 (specific searches) and 1737 (sensitive searches) were published, and that the number of trials published per year doubled. Also of interest, there was significant variation among the dental disciplines, > 50-fold.

As a clinician, high quality clinical decision-making depends on the availability of high quality clinical evidence. Treatment decisions are often based on individual clinical training, clinical experiences, or the clinical experiences of others. This may, or may not be at odds with the best experimental clinical evidence. Interestingly, conclusions about treatment efficacy derived from non-experimental approaches tend to overestimate treatment effects.[9] Ideally, treatment decisions are based on the best evidence. Randomized control trials are considered to be the best available clinical evidence because they best demonstrate causality, best reduce bias and threats to validity (http://cebm.jr2.ox.ac.uk/docs/levels.html).

The results of our study indicate that the number of randomized controlled trial articles pertaining to pediatric dentistry is steadily increasing. This study indicates that between 2 and 10 articles would have to be read per week addressing Implants, Endodontics, Oral Surgery, Periodontics, Restorative Dentistry, Oral Medicine and Orthodontics in order to keep current. In the future, we can expect the total number of articles to increase each year. Given the constantly increasing volume of information, a useful application of this study would involve saving search strategies and updating them regularly to identify important articles.

Given the difficulty and importance of finding all the available studies on randomized controlled trials on which to base sound clinical decisions, this study also suggests the need for secondary journals and information databases that would help facilitate the timely retrieval of high quality literature for high quality clinical making decisions. New dental journals of secondary publication such as Evidence-based Dentistry[11] are being published, which provide summaries of original and review articles with evidence-based conclusions and provide expert commentaries.

Identification of randomized controlled trials relevant to pediatric dentistry is an initial step in creating a register of randomized controlled that would be an important source of information for setting up systemic overviews of the pediatric dental literature which are currently being done in medicine.[12,13] The use of computer-based communication networks and critically appraised medical information on the Internet can help identify randomized control trials and improve clinical decision making by increasing information availability.

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