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Randomised controlled trials and publication trends in periodontal research during 1980–2000

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Abstract

Objectives: To study publication trends, as well as the number and proportion of randomised controlled trials covering different areas of periodontal research (RCT-Ps).

Material and methods: The study was based on MEDLINE searches (MeSH terms) for the period 1980–2000. The RCT-Ps (n = 675) were examined for relevance for different areas of periodontal research, journals of publication, and the countries of origin.

Results: In periodontal research the annual number of publications had increased from 162 in 1980 to 440 in 2000. Moreover, clinical trials in periodontal research (CT-Ps) had increased more than 10-fold, and RCT-Ps more than 15-fold. More than 4 out of 10 RCT-Ps covered the areas 'periodontal surgery' and 'gingivitis and plaque treatment or prevention'. More than 6 out of 10 RCT-Ps in total and more than 8 out of 10 RCT-Ps about 'periodontal surgery', were published in two different journals. U.S.A was the most common country of origin of RCT-Ps, contributing to almost 4 out of 10 RCT-Ps during 1988– 2000. **Conclusion:** The annual number of RCT-Ps increased substantially during 1980– 2000, and a few clinical research areas predominated. Future research should give priority to areas where clinical evidence is scarce and where high-quality RCT-Ps are most needed.

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In the past, increased efforts have been made to standardise and to improve the design and quality of clinical trials (Jadad et al. 1996, Begg et al. 1996). A continuously increasing number of publications and new treatment modalities have increased the difficulties in keeping up to date with the latest research and in locating the best evidence for clinical practice. This problem can easily be illustrated by the roughly one million randomised controlled trials (RCTs) conducted in medical research during the past 50 years. Although the field of dental research is somewhat smaller, the situation is equally problematic, with the annual number of RCTs in dental re-

search increasing almost continuously during the recent decades (Sjögren & Halling 2000). Therefore, organisations trying to summarise the current best evidence have been founded, as exemplified by the Cochrane Collaboration (Taubes 1996). The Cochrane Collaboration has its origin in a systematic review initiated in 1976, in Oxford, where Iain Chalmers and colleagues began a search for all RCTs that had to do with pregnancy and childbirth (Taubes 1996). The underlying philosophy of the Cochrane Collaboration might be described as the conscientious, explicit and judicious use of current best evidence, which is also a brief definition of the principles of evidence-based medicine (Sackett et al. 1996). For dental research the evidence is located and systematically reviewed by the Cochrane Collaboration Oral Health Group and the Center for Evidence Based Dentistry, among others (Jokstad 1998). In evidence-based medicine and dentistry, results from well-conducted RCTs are regarded as the 'gold standard' for bringing evidence to clinical practice (Sackett et al. 1996). Sometimes, the evidence from clinical trials is synthesised in a meta-analysis, which is a statistical method for pooling data from several RCTs (Egger et al. 1997). Unfortunately meta-analyses are often misused, criticised and misunderstood (Feinstein & Horwitz 1997). Therefore, it should be emphasised that only data from homogeneous, high-quality RCTs are suitable for pooling together in a meta-analysis (Egger et al. 1997, Egger & Smith 1997). Furthermore, any systematic review or meta-analysis is only as up to date as its latest included reference. Journals of secondary publication (e.g. Evidence Based Dentistry), evidence-based databases and systematic reviews are perhaps the easiest way to locate the clinical evidence, when available (Jokstad 1998, Richards & Lawrence 1998). However, for many treatments and areas of clinical dentistry, systematically reviewed evidence is still scarce (Bader et al. 1999). In clinical periodontology novel treatment strategies are frequently introduced, and the clinicians often have to rely on their own skills for finding the evidence, or on opinions of respected authorities (Richards & Lawrence 1998). For searching publications in dental (and biomedical) research MEDLINE is one of the largest databases. It covers around 4000 journals, is free of charge and easily available via Internet. In a previous study, we investigated the search validity for RCTs in different fields of dental research on MEDLINE and found that MED-LINE was a relatively effective way of locating RCTs about periodontal research (RCT-Ps) (Sjögren & Halling 2002a). Therefore, we conducted this study with the aim of elucidating the annual number and proportion of publications, as well as trends in periodontal research. We also sought to analyse the distribution and origin of RCT-Ps in different areas of periodontal research that were available on MEDLINE.

Material and methods Medline searches

One of the authors (P.S.) searched MED-LINE database (Entrez PubMed, http:// www.ncbi.nlm.nih.gov) for publications (July 2001). Inclusion criteria in the searches were: MeSH term; 'periodontics': publication years; '1980– 2000': and publication types; 'all publications' (i.e. not specified), 'clinical trial' (CT), or 'randomised controlled trial (RCT)': and language; 'English'.

Number and proportion of publications

The total number and proportion of publications in periodontal research,

clinical trials in periodontal research (CT-Ps) and RCT-Ps (MeSH term 'periodontics') were calculated. To test the search validity, the proportion of false inclusions was calculated for the search results of RCT-Ps during 1980–2000. The falsely included RCTs were excluded from further analyses.

Areas in periodontal research covered by RCT-Ps

Abstracts of all RCT-Ps (MeSH term 'periodontics') from 1980 to 2000 were examined for relevance for different areas of periodontal research. All abstracts were examined at least twice by the same author (P.S.). The RCT-Ps were divided to the following domains; bacteriemia 'aerosol and (micro-'antibiotics', biology)', 'diagnostics', 'education and health education', 'flossing and interproximal cleaning', 'full and partial mouth disinfection', 'gingival hyperplasia (non-surgical)', 'gingivitis and plaque (prophylactics, treatment or removal) with mouthwash, gel, dentifrice, etc. (nonantibiotic)', 'NSAIDs (Non Steroid Anti Inflammatory Drugs)', 'peri-implant tissues', 'periodontal surgery', 'scaling and planing (including ultrasonic)', 'subgingival irrigation (nonantibiotic)', and 'tooth brushing (including powered toothbrushes)'. The remaining RCT-Ps were grouped together as 'others'. The annual number of RCT-Ps within each domain was calculated and tabulated together with the publication years.

Journal of publication, journal impact factor and country of origin of RCT-Ps

All RCT-Ps (MeSH term 'periodontics') during 1980–2000 were scrutinised for the journal of publication and tabulated together with the main research areas covered (i.e. the domains, see above). The journal impact factors for year 2000 were obtained via Internet from the ISI journal citation reports (2000 JCR Science Edition). In addition, the RCT-Ps were examined for the country of origin for the years 1988–2000 (for earlier years the country was not routinely given on MEDLINE) and tabulated together with the publication years.

Results

Number and proportion of publications on MEDLINE

The MEDLINE searches gave a total of 6975 hits for publications in peri-

odontal research during 1980–2000, with 991 hits for CT-Ps, and 675 for RCT-Ps (Table 1).

The annual numbers of publications in periodontal research more than doubled during 1980–2000, with a peak in 1996 (Table 1).

CT-Ps and RCT-Ps contributed to 14% and 10%, respectively, of all publications in periodontal research, during 1980–2000. The annual number and proportion of CT-Ps increased more than 10-fold between 1980 and 1994, but decreased between 1996 and 2000 (Table 1). The annual number of RCT-Ps increased more than 15-fold between 1980 and 1994, and remained approximately unchanged between 1994 and 2000 (Table 1).

Areas in periodontal research covered by RCT-Ps

Of the 675 search hits for RCT-Ps during 1980–2000, 42 were false inclusions, belonging to other research areas than periodontal research, leaving 633 RCT-Ps for final analysis. Thus, the proportion of false inclusions for RCT-Ps on MEDLINE was 6% (Table 2).

The most common area covered by the RCT-Ps was 'periodontal surgery' contributing to 24% of the RCT-Ps, followed by 'gingivitis and plaque (non-

Table 1. Annual number of search hits on MEDLINE for clinical trials (CT-Ps) (n = 991), randomised controlled trials in periodontal research (RCT-Ps) (n = 675), and publications in periodontal research in total (n = 6975) 1980–2000. Percentage in brackets

Year	CT-Ps	RCT-Ps	Total
1980	8 (4.9)	4 (2.5)	162
1981	4 (2.7)	3 (2.0)	147
1982	4 (2.5)	2 (1.3)	159
1983	5 (2.8)	2 (1.1)	177
1984	12 (5.3)	7 (3.1)	226
1985	12 (5.0)	9 (3.7)	242
1986	19 (8.2)	8 (3.4)	233
1987	16 (7.6)	14 (6.7)	210
1988	13 (6.2)	7 (3.3)	211
1989	34 (14.3)	12 (5.1)	237
1990	23 (8.3)	14 (5.1)	276
1991	57 (14.6)	37 (9.5)	390
1992	58 (13.9)	36 (8.6)	417
1993	62 (13.1)	51 (10.8)	474
1994	105 (21.8)	66 (13.7)	481
1995	100 (19.6)	66 (13.0)	509
1996	104 (18.5)	73 (13.0)	561
1997	89 (18.1)	66 (13.4)	491
1998	94 (19.3)	69 (14.2)	486
1999	85 (19.1)	67 (15.0)	446
2000	87 (19.8)	62 (14.1)	440

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antibiotic)', and 'antibiotics', with 20%, and 13%, respectively (Table 2). The highest annual number of RCT-Ps about 'periodontal surgery' was seen in 2000, whereas the highest annual numbers of RCT-Ps about 'gingivitis and plaque (nonantibiotic)' were seen during 1993–1995, followed by a 63% decrease between 1995 and 2000 (Table 2). The highest annual number of RCT-Ps about 'antibiotics' was seen in 1998, followed by a more than 50% decrease between 1998 and 2000 (Table 2).

Journals of publication and the journal impact factor

During 1980–2000, 62% of all RCT-Ps were published in the *Journal of*

Clinical Periodontology and the *Journal of Periodontology*, contributing to 32% and 30%, respectively (Table 3). Furthermore, 81% of the RCT-Ps about 'periodontal surgery' were published in these two journals (data not shown). The journal impact factors for the major journals of publication for RCT-Ps are given in Table 3.

Table 2. Frequency distribution of randomised controlled trials in different areas of periodontal research on MEDLINE, 1980–2000 ($n = 633^*$). Cumulative percentage in brackets

Year	Aerosol/ bacteriemia (microbiology) (n = 11)	Antibiotics $(n = 85)$	Diagnostics $(n = 17)$	Education/ health education (n = 16)	Flossing/ interproximal cleaning (n = 15)	Full/partial mouth disinfection (n = 7)	Gingival hyperplasia (non-surgical) (n = 8)	
1980	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (6.7)	0 (0.0)	0 (0.0)	
1981	0 (0.0)	0 (1.2)	0 (0.0)	0 (0.0)	0 (6.7)	0 (0.0)	0 (0.0)	
1982	1 (9.1)	0 (1.2)	0 (0.0)	0 (0.0)	0 (6.7)	0 (0.0)	0 (0.0)	
1983	0 (9.1)	1 (2.4)	0 (0.0)	1 (6.3)	0 (6.7)	0 (0.0)	0 (0.0)	
1984	0 (9.1)	1 (3.5)	0 (0.0)	0 (6.3)	1 (13.3)	0 (0.0)	0 (0.0)	
1985	0 (9.1)	2 (5.9)	0 (0.0)	0 (6.3)	0 (13.3)	0 (0.0)	0 (0.0)	
1986	0 (9.1)	1 (7.1)	1 (5.9)	1 (12.5)	0 (13.3)	0 (0.0)	0 (0.0)	
1987	0 (9.1)	1 (8.2)	0 (5.9)	2 (25.0)	0 (13.3)	0 (0.0)	0 (0.0)	
1988	0 (9.1)	2 (10.6)	0 (5.9)	1 (31.3)	0 (13.3)	0 (0.0)	0 (0.0)	
1989	0 (9.1)	1 (11.8)	0 (5.9)	0 (31.3)	1 (20.0)	0 (0.0)	0 (0.0)	
1990	0 (9.1)	3 (15.3)	1 (11.8)	1 (37.5)	0 (20.0)	0 (0.0)	0(0.0)	
1991	1(18.2)	4(20.0)	1 (17.6)	1 (43.8)	0(20.0)	0 (0.0)	2 (25.0)	
1992 1993	2 (36.4)	6(27.1)	1 (23.5)	0 (43.8)	1 (26.7)	0 (0.0)	0 (25.0)	
1993 1994	4 (72.7) 0 (72.7)	4 (31.8) 10 (43.5)	0 (23.5) 3 (41.2)	0 (43.8) 2 (56.3)	1 (33.3) 1 (40.0)	0 (0.0) 0 (0.0)	0 (25.0) 2 (50.0)	
1994	0 (72.7)	5 (49.4)	1 (47.1)	1 (62.5)	2 (53.3)	1 (14.3)	1 (62.5)	
1995	1 (81.8)	3 (49.4) 8 (58.8)	3 (64.7)	2 (75.0)	3 (73.3)	2 (42.9)	0 (62.5)	
1997	1 (90.9)	6 (65.9)	1 (70.6)	1 (81.3)	0 (73.3)	0 (42.9)	2 (87.5)	
1998	0 (90.9)	13 (81.2)	2 (82.4)	1 (87.5)	1 (80.0)	2 (71.4)	0 (87.5)	
1999	0 (90.9)	10 (92.9)	2 (94.1)	1 (93.8)	2 (93.3)	2 (100.0)	1 (100.0)	
2000	1 (100.0)	6 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (100.0)	0 (100.0)	
	Gingivitis/	NSAIDs $(n=8)$	Peri-implant tissues	Periodontal surgery	Scaling/ planing	Subgingival irrigation	Tooth brushing	Others $(n = 63)$
	plaque							
	(nonentibiotic)	(n - 0)					U	(n - 03)
	(nonantibiotic) (n = 124)	(n = 0)	(n = 17)	(n = 155)	(n=38)	(nonantibiotic) (n = 16)	(n = 53)	(n - 03)
1980	(n = 124) 0 (0.0)	0 (0.0)	(n = 17) 0 (0.0)	(n = 155) 1 (0.6)	(n = 38) 0 (0.0)	(nonantibiotic) (n = 16) 0 (0.0)	(n = 53) 0 (0.0)	1 (1.6)
1981	(n = 124) 0 (0.0) 1 (0.8)	0 (0.0) 0 (0.0)	(n = 17) 0 (0.0) 0 (0.0)	(n = 155) 1 (0.6) 2 (1.9)	(n = 38) 0 (0.0) 0 (0.0)	(nonantibiotic) (n = 16) 0 (0.0) 0 (0.0)	(n = 53) 0 (0.0) 0 (0.0)	1 (1.6) 0 (1.6)
1981 1982	(n = 124) 0 (0.0) 1 (0.8) 0 (0.8)	0 (0.0) 0 (0.0) 0 (0.0)	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) 1 (0.6) 2 (1.9) 0 (1.9)	(n = 38) 0 (0.0) 0 (0.0) 1 (2.6)	(nonantibiotic) (n = 16) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0)	1 (1.6) 0 (1.6) 0 (1.6)
1981 1982 1983	(n = 124) 0 (0.0) 1 (0.8) 0 (0.8) 0 (0.8)	0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) 1 (0.6) 2 (1.9) 0 (1.9) 0 (1.9)	$ \begin{array}{c} (n = 38) \\ \hline 0 & (0.0) \\ 0 & (0.0) \\ 1 & (2.6) \\ 0 & (2.6) \end{array} $	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	1 (1.6) 0 (1.6) 0 (1.6) 0 (1.6)
1981 1982 1983 1984	(n = 124) 0 (0.0) 1 (0.8) 0 (0.8) 0 (0.8) 1 (1.6)	0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$	$ \begin{array}{c} (n = 38) \\ \hline 0 & (0.0) \\ 0 & (0.0) \\ 1 & (2.6) \\ 0 & (2.6) \\ \hline \end{array} $	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9)	$ \begin{array}{c} 1 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 2 (4.8) \end{array} $
1981 1982 1983 1984 1985	(n = 124) 0 (0.0) 1 (0.8) 0 (0.8) 0 (0.8) 1 (1.6) 2 (3.2)	0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $0 (2.6)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9) 0 (1.9)	$ \begin{array}{c} 1 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 2 (4.8) \\ 1 (6.3) \end{array} $
1981 1982 1983 1984 1985 1986	$\begin{array}{c} (n = 124) \\ \hline 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9) 0 (1.9) 0 (1.9)	$ \begin{array}{c} 1 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 2 (4.8) \\ 1 (6.3) \\ 1 (7.9) \end{array} $
1981 1982 1983 1984 1985 1986 1987	$\begin{array}{c} (n = 124) \\ \hline 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9) 0 (1.9) 0 (1.9) 0 (1.9)	$ \begin{array}{c} 1 (1.6) \\ 0 (1.6) \\ 0 (1.6) \\ 2 (4.8) \\ 1 (6.3) \\ 1 (7.9) \\ 2 (11.1) \end{array} $
1981 1982 1983 1984 1985 1986 1987 1988	$\begin{array}{c} (n = 124) \\ 0 (0.0) \\ 1 (0.8) \\ 0 (0.8) \\ 0 (0.8) \\ 1 (1.6) \\ 2 (3.2) \\ 1 (4.0) \\ 1 (4.8) \\ 0 (4.8) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)	(n = 53) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9) 0 (1.9) 0 (1.9) 0 (1.9) 0 (1.9)	1 (1.6) 0 (1.6) 0 (1.6) 2 (4.8) 1 (6.3) 1 (7.9) 2 (11.1) 0 (11.1)
1981 1982 1983 1984 1985 1986 1987 1988 1989	$\begin{array}{c} (n = 124) \\ \hline 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)	$(n = 53)$ $0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 1 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 2 (5.7)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990	$\begin{array}{c} (n = 124) \\ 0 (0.0) \\ 1 (0.8) \\ 0 (0.8) \\ 0 (0.8) \\ 1 (1.6) \\ 2 (3.2) \\ 1 (4.0) \\ 1 (4.8) \\ 0 (4.8) \\ 2 (6.5) \\ 3 (8.9) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)	$(n = 53)$ $0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 1 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 2 (5.7) \\ 1 (7.5)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$ $3 (11.6)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$ $1 (28.9)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)	$(n = 53)$ $0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 0 (0.0) \\ 1 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 0 (1.9) \\ 2 (5.7) \\ 1 (7.5) \\ 1 (9.4)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$ $3 (11.6)$ $4 (14.2)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$ $1 (28.9)$ $2 (34.2)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \end{array}$	$\begin{array}{c} 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 3 \ (37.5) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 0 (5.9)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$ $3 (11.6)$ $4 (14.2)$ $7 (18.7)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$ $1 (28.9)$ $2 (34.2)$ $1 (36.8)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$ $8 (28.3)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994	$\begin{array}{c} (n = 124) \\ \hline 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \\ 15 & (51.6) \end{array}$	$\begin{array}{c} 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 3 \ (37.5) \\ 1 \ (50.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 1 (11.8)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$ $3 (11.6)$ $4 (14.2)$ $7 (18.7)$ $8 (23.9)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$ $1 (28.9)$ $2 (34.2)$ $1 (36.8)$ $5 (50.0)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)4 (81.3)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$ $8 (28.3)$ $8 (43.4)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \\ 4 \ (34.9) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \\ 15 & (51.6) \\ 16 & (64.5) \end{array}$	$\begin{array}{c} 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 1 \ (50.0) \\ 2 \ (75.0) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 1 (11.8) 1 (17.6)	(n = 155) $1 (0.6)$ $2 (1.9)$ $0 (1.9)$ $0 (1.9)$ $1 (2.6)$ $3 (4.5)$ $1 (5.2)$ $2 (6.5)$ $2 (7.7)$ $1 (8.4)$ $2 (9.7)$ $3 (11.6)$ $4 (14.2)$ $7 (18.7)$ $8 (23.9)$ $17 (34.8)$	(n = 38) $0 (0.0)$ $0 (0.0)$ $1 (2.6)$ $0 (2.6)$ $0 (2.6)$ $0 (2.6)$ $1 (5.3)$ $2 (10.5)$ $1 (13.2)$ $4 (23.7)$ $1 (26.3)$ $1 (28.9)$ $2 (34.2)$ $1 (36.8)$ $5 (50.0)$ $2 (55.3)$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)4 (81.3)0 (81.3)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$ $8 (28.3)$ $8 (43.4)$ $5 (52.8)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \\ 4 \ (34.9) \\ 7 \ (46.0) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \\ 15 & (51.6) \\ 16 & (64.5) \\ 12 & (74.2) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 3 & (37.5) \\ 1 & (50.0) \\ 2 & (75.0) \\ 1 & (87.5) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 0 (5.9) 1 (11.8) 1 (17.6) 5 (47.1)	(n = 155) $1 (0.6) (2 (1.9) (0 (1.9) (1.9) (0 (1.9)$	$\begin{array}{c} (n = 38) \\ \hline \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 1 \ (2.6) \\ 0 \ (2.6) \\ 0 \ (2.6) \\ 0 \ (2.6) \\ 1 \ (5.3) \\ 2 \ (10.5) \\ 1 \ (13.2) \\ 4 \ (23.7) \\ 1 \ (26.3) \\ 1 \ (28.9) \\ 2 \ (34.2) \\ 1 \ (36.8) \\ 5 \ (50.0) \\ 2 \ (55.3) \\ 7 \ (73.7) \end{array}$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)4 (81.3)0 (81.3)1 (87.5)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$ $8 (28.3)$ $8 (43.4)$ $5 (52.8)$ $6 (64.2)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \\ 4 \ (34.9) \\ 7 \ (46.0) \\ 6 \ (55.6) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1990 1991 1992 1993 1994 1995 1996 1997	$\begin{array}{c} (n = 124) \\ \hline 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \\ 15 & (51.6) \\ 16 & (64.5) \\ 12 & (74.2) \\ 12 & (83.9) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 1 & (57.5) \\ 1 & (87.5) \\ 0 & (87.5) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 1 (11.8) 1 (17.6) 5 (47.1) 2 (58.8)	(n = 155) $1 (0.6) 2 (1.9) 0 (1.9) 0 (1.9) 1 (2.6) 3 (4.5) 1 (5.2) 2 (6.5) 2 (7.7) 1 (8.4) 2 (9.7) 3 (11.6) 4 (14.2) 7 (18.7) 8 (23.9) 17 (34.8) 14 (43.9) 16 (54.2)$	$\begin{array}{c} (n = 38) \\ \hline \\ 0 & (0.0) \\ 0 & (0.0) \\ 1 & (2.6) \\ 0 & (2.6) \\ 0 & (2.6) \\ 0 & (2.6) \\ 1 & (5.3) \\ 2 & (10.5) \\ 1 & (13.2) \\ 4 & (23.7) \\ 1 & (26.3) \\ 1 & (28.9) \\ 2 & (34.2) \\ 1 & (36.8) \\ 5 & (50.0) \\ 2 & (55.3) \\ 7 & (73.7) \\ 5 & (86.8) \end{array}$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)4 (81.3)0 (81.3)1 (87.5)0 (87.5)	(n = 53) $0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.9) 0 (1.9) 0 (1.9) 0 (1.9) 0 (1.9) 2 (5.7) 1 (7.5) 1 (9.4) 2 (13.2) 8 (28.3) 8 (43.4) 5 (52.8) 6 (64.2) 4 (71.7)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \\ 4 \ (34.9) \\ 7 \ (46.0) \\ 6 \ (55.6) \\ 11 \ (73.0) \end{array}$
1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992	$\begin{array}{c} (n = 124) \\ 0 & (0.0) \\ 1 & (0.8) \\ 0 & (0.8) \\ 0 & (0.8) \\ 1 & (1.6) \\ 2 & (3.2) \\ 1 & (4.0) \\ 1 & (4.8) \\ 0 & (4.8) \\ 2 & (6.5) \\ 3 & (8.9) \\ 13 & (19.4) \\ 8 & (25.8) \\ 17 & (39.5) \\ 15 & (51.6) \\ 16 & (64.5) \\ 12 & (74.2) \end{array}$	$\begin{array}{c} 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 0 & (0.0) \\ 3 & (37.5) \\ 1 & (50.0) \\ 2 & (75.0) \\ 1 & (87.5) \end{array}$	(n = 17) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (5.9) 0 (5.9) 0 (5.9) 1 (11.8) 1 (17.6) 5 (47.1)	(n = 155) $1 (0.6) (2 (1.9) (0 (1.9) (1.9) (0 (1.9)$	$\begin{array}{c} (n = 38) \\ \hline \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 1 \ (2.6) \\ 0 \ (2.6) \\ 0 \ (2.6) \\ 0 \ (2.6) \\ 1 \ (5.3) \\ 2 \ (10.5) \\ 1 \ (13.2) \\ 4 \ (23.7) \\ 1 \ (26.3) \\ 1 \ (28.9) \\ 2 \ (34.2) \\ 1 \ (36.8) \\ 5 \ (50.0) \\ 2 \ (55.3) \\ 7 \ (73.7) \end{array}$	(nonantibiotic)(n = 16)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)0 (0.0)1 (6.3)2 (18.8)0 (18.8)1 (25.0)0 (25.0)2 (37.5)2 (50.0)1 (56.3)4 (81.3)0 (81.3)1 (87.5)	(n = 53) $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $0 (0.0)$ $1 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $0 (1.9)$ $2 (5.7)$ $1 (7.5)$ $1 (9.4)$ $2 (13.2)$ $8 (28.3)$ $8 (43.4)$ $5 (52.8)$ $6 (64.2)$	$\begin{array}{c} 1 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 0 \ (1.6) \\ 2 \ (4.8) \\ 1 \ (6.3) \\ 1 \ (7.9) \\ 2 \ (11.1) \\ 0 \ (11.1) \\ 0 \ (11.1) \\ 1 \ (12.7) \\ 2 \ (15.9) \\ 5 \ (23.8) \\ 3 \ (28.6) \\ 4 \ (34.9) \\ 7 \ (46.0) \\ 6 \ (55.6) \end{array}$

* False inclusion on MEDLINE excluded (n = 42).

Journal	RCT-Ps	JIF
Am J Dent	4	1.452
Am J Orthod Dentofacial Orthop	9	0.757
Aust Dent J	4	0.373
Br Dent J	7	0.822
Clin Oral Implants Res	9	1.680
Clin Prev Dent	10	_
Compendium	8	_
Int Dent J	6	0.419
Int J Oral Maxillofac Implants	4	1.316
Int J Periodontics Restorative Dent	14	0.650
J Am Dent Assoc	7	0.854
J Can Dent Assoc	4	_
J Clin Dent	32	_
J Clin Periodontol	202	1.426
J Dent Res	6	4.438
J Periodontal Res	3	0.946
J Periodontol	189	1.215
J Prosthet Dent	8	0.787
Oral Surg Oral Med Oral Pathol	5	0.865
Periodontal Clin Invest	4	_
Quintessence Int	11	0.712
\tilde{S} cand J Dent Res/Eur J Oral Sci	7	1.808
Spec Care Dentist	4	_

*False inclusions on MEDLINE excluded (n = 42), and journals with < 4 RCT-Ps not listed (n = 76). JIF = Journal impact factor for year 2000. – Indicates not available in ISI journal citation reports.

Countries of origin

The U.S.A. was the most common country of origin of RCT-Ps during

1988–2000, contributing 39% of the RCT-Ps, followed by the UK (11%), Germany (7%), Sweden (6%), and Italy (4%). Of the 39 RCT-Ps that originated

from Germany, 30 were published during 1998–2000 (Table 4).

Discussion

The annual number of publications in periodontal research, CT-Ps and RCT-Ps showed an increasing trend during 1980–2000. A few clinical research areas clearly dominated the RCT-Ps. Furthermore, the *Journal of Clinical Periodontology* and the *Journal of Periodontology* contributed to more than 6 out of 10 RCT-Ps in total, and to more than 8 out of 10 RCT-Ps about 'periodontal surgery'. The U.S.A. was the most common country of origin of RCT-Ps, contributing to almost 4 out of 10 RCT-Ps during 1988–2000.

The MEDLINE database was chosen since it has a world wide coverage of dental research journals and is widely used in the research community. The MEDLINE database is also free of charge and readily available for clinicians over the Internet.

Our aim was to study overall publication trends in periodontal research, not precise publication counts, as the MEDLINE database is constantly changing and because some publications are assigned with faulty MeSH headings, lowering search validity (Sjögren & Halling 2002a, Clarke & Oxman 1999).

Table 4. Countries of origin of randomised controlled trials in periodontal research on MEDLINE, 1988–2000 (n = 587*)

	Year												
Country	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	199	2000
Australia $(n = 5)$	0	0	0	0	0	0	1	2	0	1	0	0	1
Belgium $(n = 19)$	0	0	0	0	0	1	3	3	4	2	3	3	0
Brazil $(n = 5)$	0	0	0	0	0	0	0	0	1	0	0	1	3
Canada $(n = 13)$	0	1	0	0	2	3	4	2	0	0	0	1	0
Denmark $(n = 8)$	0	0	0	0	1	0	4	0	2	0	0	0	1
Finland $(n = 12)$	0	1	2	2	2	3	0	0	0	1	1	0	0
France $(n = 10)$	0	0	0	0	1	1	3	0	0	3	0	2	0
Germany $(n = 39)$	0	0	0	0	0	1	0	1	4	3	10	10	10
Israel $(n = 10)$	0	0	0	1	1	0	2	1	2	1	1	0	1
Italy $(n = 26)$	0	0	0	0	0	1	0	4	7	2	5	2	5
Japan $(n=8)$	0	0	0	1	0	1	1	1	0	0	1	1	2
Norway $(n = 10)$	1	0	0	0	0	1	0	0	1	1	2	2	2
Spain $(n=6)$	0	2	0	0	0	0	1	1	0	1	1	0	0
Sweden $(n = 34)$	2	0	1	1	4	2	2	6	1	4	4	3	4
Switzerland $(n = 16)$	0	0	1	0	0	0	2	1	4	2	3	2	1
Thailand $(n = 4)$	0	0	0	1	0	0	0	2	1	0	0	0	0
The Netherlands $(n = 20)$	0	0	0	2	0	1	3	1	4	0	5	2	2
Turkey $(n = 13)$	0	0	0	0	0	0	3	2	2	4	0	2	0
U.S.A. (<i>n</i> = 227)	3	8	7	16	18	18	25	23	25	27	21	19	17
United Kingdom $(n = 66)$	1	0	1	5	1	10	7	8	9	6	5	8	5
Others** $(n = 27)$	0	0	1	3	1	3	3	2	4	2	3	3	2
Not stated $(n = 9)$	0	0	0	0	2	3	0	0	0	0	1	1	2

*False inclusions on MEDLINE excluded (n = 39). **Countries with three or fewer randomised controlled trials during 1988–2000 were grouped together as 'others'.

In this study we found false inclusions in 6% of the searches for RCT-Ps.

In a previous study we showed that RCTs represented just a fraction of all publications in dental research, and that only one out of 200 dental research publications was an RCT with relevance to the most common activities in general dentistry (Sjögren & Halling 2000).

In the current study, we found that the largest increase in the number of RCT-Ps occurred during the first half of the 1990s. This increase was probably influenced by the debate raised by evidence-based medicine organisations, among others, striving to improve the quality of reporting of clinical trials, highlighted in 1996 by the Consolidation of Standards for Reporting Trials (the CONSORT statement) (Begg et al. 1996), recently revised (Moher et al. 2001).

The journal impact factor is often viewed as a measure of scientific quality (Garfield 1972, 1976). It was recently shown that the quality of RCT reports has no correlation with the journal impact factor (Sjögren & Halling 2002b). In this study the journal impact factors were largely similar for all journals, regardless of the number of RCT-Ps. These findings were not surprising, because the journal impact factor represents the quota of the number of citations of a journal and the number of citable items during the previous 2 years (Garfield 1972, 1976). Nevertheless, it should be emphasised that journals with high impact factors often have a rigorous review process before accepting an article.

Periodontal surgery was the most commonly published research area in the RCT-Ps during 1980-2000. This may reflect the advent of novel technologies for regenerative surgery with enamel matrix proteins and guided tissue regeneration, in combination with an increased interest in treatment modalities with various bone replacement materials (Heijl et al. 1997, Pontoriero et al. 1999, Lekovic et al. 2001). Another, more classic, area of periodontal research that was frequently published in RCT-Ps was different approaches for the prevention or treatment of gingivitis and plaque (nonantibiotic), although the annual number of RCT-Ps in this area showed a marked decrease between 1997 and 2000 (Table 2). Furthermore, different antibiotic regimens for the treatment of periodontal disease were

relatively frequently issued by the RCT-Ps, possibly due to novel antibiotic treatment philosophies lately introduced in periodontal research (van Winkelhoff et al. 1996).

Interestingly, we found that 6 out of 10 RCT-Ps were published in only two different journals. Although a large number of clinical research journals publish substantial amounts of important RCT-Ps, it seems reasonable to suggest that the Journal of Clinical Periodontology and the Journal of Periodontology are of outmost importance for locating RCT-Ps. This is especially true if periodontal surgery is put first, as these two journals covered 8 out of 10 RCT-Ps in this area. In the light of our findings, it seems that a few research areas clearly dominated the RCT-Ps available on MEDLINE.

A number of treatments within periodontal surgery, especially periodontal regeneration with enamel matrix proteins and guided tissue regeneration, were supported by several independently conducted RCT-Ps. This may also be the case for a number of antibiotic treatments, although these often appear to be heterogeneous in trial design (e.g. drug delivery system, outcome measures). Quality assessment of the RCT-Ps was beyond the scope of this study, but would be valuable, especially together with a systematic review. Highquality RCT-Ps, with enough power to evaluate equivalence, about prevention or treatment of gingivitis and plaque (nonantibiotic) are needed to elucidate the most efficient and cost-effective interventions for clinical practice. Other important areas where RCT-Ps were scarce were: the use of different diagnostic methods, treatment of peri-implantitis, possible harmful side-effects of antibiotic treatments, and combinations of regenerative periodontal surgery with fixed or removable prosthodontics (or with implant systems). Moreover, RCT-Ps measuring the perceived health or quality of life would be valuable. Therefore, we suggest that future research should give priority to areas where clinical evidence from RCT-Ps is still scarce, and where high quality trials are needed. The evidence-base for periodontal interventions is of outmost importance. In communities with limited resources, when health care costs need to be reduced, treatments without proper scientific support may be the first to be excluded from a dental health insurance system.

Together, these efforts may lead clinical periodontology towards even more effective and evidence-based treatment strategies. On the microlevel, the ultimate aim should be to reach increased understanding of the best available treatment strategies on an individual patient level, whereas on the macrolevel the aim should be to improve public dental health. Thus, in every unique clinical situation the decisions should be based on the best available research evidence, practitioners' own clinical expertise, and on patient values (Sackett et al. 1996).

Zusammenfassung

Randomisierte kontrollierte Untersuchungen und Publikationstrends der parodontologischen Forschung der Jahre 1980 bis 2000

Ziele: Studium sowohl der Publikationstrends, als auch der Anzahl und des Anteils der randomisierten kontrollierten Untersuchungen (RCT-Ps) auf verschiedenen Gebieten der parodontologischen Forschung.

Material und Methoden: Die hatte Medline Recherchen (MeSH-Terms) der Zeitspanne 1980–2000 zur Grundlage. Die RCT-Ps (n= 675) wurden hinsichtlich ihrer Relevanz sowohl für verschiedene Gebiete der parodontologischen Forschung, als auch für Publikationszeitschriften und die Ursprungsländer untersucht.

Ergebnisse: In der parodontologischen Forschung hat die jährliche Anzahl der Publikationen sich von 162 im Jahr 1980 auf 440 im Jahr 2000 erhöht. Die Anzahl der klinischen Untersuchungen hat sich in der parodontologischen Forschung (CT-Ps) um das mehr als 10-fache erhöht. Die Anzahl der RCT-Ps hat sich sogar um das 15-fache erhöht. Mehr als 4 von 10 RCT-Ps deckten das Gebiet "Parodontalchirurgie" und "Gingivitis sowie Plaqueentfernung oder Prävention" ab. Mehr als 6 von 10 der gesamten RCT-Ps und mehr als 8 von 10 der RCT-Ps über "Parodontalchirurgie" wurden in zwei Zeitschriften publiziert. Die USA waren das häufigste Ursprungsland für RCT-Ps und lieferten während der Jahre 1988-2000 fast 4 von 10 RCT-Ps.

Schlussfolgerung: Die jährliche Anzahl von RCT-Ps zeigte während der Jahre 1980–2000 eine bedeutende Erhöhung und wenige klinische Forschungsgebiete dominierten. Die zukünftige Forschung sollte den Gebieten Priorität geben, auf denen die klinische Evidenz rar ist und wo RCT-Ps von hoher Qualität am dringendsten benötigt werden.

Résumé

Essais contrôlés randomisés et tendances de publication en recherche parodontale durant les années 1980 à 2000

Le but de étude a été d'analyser les tendances

de publication ainsi que le nombre et la proportion d'essais contrôlés randomisés couvrant les différents aspects de la recherche parodontales (RCT-P). L'étude était basée sur des recherches sur MEDLINE (termes MeSH) couvrant la période 1980-2000. Les RCT-P (n=675) ont été examinés pour leur importance dans différentes aires de la recherche parodontale, journal de publication et pays d'origine. Dans la recherche parodontale le nombre annuel de publications a augmenté de 162 en 1980 à 440 en l'an 2000. De plus les essais cliniques en recherche parodontale (CT-P) avaient augmenté de plus de dix fois et les RCT-P plus de quinze fois. Plus de quatre sur 10 RCT-P couvraient la zone de "chirurgie parodontale" et de "traitement de la gingivite et de la plaque dentaire ou prévention". Plus de six sur dix RCT-P au total et plus de huit sur 10 RCT-P à propos de la chirurgie parodontale étaient publiés dans deux journaux. Les Etats-Unis réunissait le plus grande nombre de RCT-P contribuant ainsi à presque quatre dixième des RCT-P. Le nombre annuel de RCT-P augmente continuellement durant l'intervalle 1980-2000 et quelques aires de recherches cliniques sont prédominantes. La recherche future devrait laisser la priorité là où l'évidence clinique est menue et où les RCT-P s'avèrent indispensables.

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