Comparison of cemented and uncemented fixation in total hip replacement

A meta-analysis

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Background   The choice of optimal implant fixation in total hip replacement (THR)—fixation with or without cement—has been the subject of much debate.

Methods   We performed a systematic review and meta-analysis of the published literature comparing cemented and uncemented fixation in THR.

Results   No advantage was found for either procedure when failure was defined as either: (A) revision of either or both components, or (B) revision of a specific component. No difference was seen between estimates from registry and single-center studies, or between randomized and non-randomized studies. Subgroup analysis of type A studies showed superior survival with cemented fixation in studies including patients of all ages as compared to those that only studied patients 55 years of age or younger. Among type B studies, cemented titanium stems and threaded cups were associated with poor survival. An association was found between difference in survival and year of publication, with uncemented fixation showing relative superiority over time.

Interpretation   While the recent literature suggests that the performance of uncemented implants is improving, cemented fixation continues to outperform uncemented fixation in large subsets of study populations. Our findings summarize the best available evidence qualitatively and quantitatively and provide important information for future research.

The success of total hip replacement (THR) and the frequency in which it is performed are largely due to the development of the cemented low-friction arthroplasty (Charnley 1960); its survival rate of 80% at 25 years (Berry et al. 2002, Callaghan et al. 2004) remains unsurpassed. The improved survival of circumferentially coated uncemented cups and stems that allow bone to grow into or onto the prosthesis (Zicat et al. 1995, Kim et al. 1999, Della Valle et al. 2004, Sinha et al. 2004,) has supported their growing use in the United States, despite the higher costs (Agins et al. 1988, Barber and Healy 1993, Clark 1994, Mendenhall 2004). In 2003, an estimated two-thirds of all primary THRs were performed with uncemented fixation (Mendenhall 2004). This contrasts with some European countries such as Sweden, which have adopted these newer uncemented technologies more cautiously and have much lower revision rates (Malchau et al. 2002, Kurtz et al. 2005).

Both cemented and uncemented implants are heterogeneous groups with many factors that can influence survivorship, such as geometry, materials, surface finishes, and bearings. Moreover, study-specific factors including surgical approach, expertise of the surgeon, and study design may add to baseline differences between studies. In order to summarize the best available evidence on the relative success of cemented and uncemented fixation in THR from comparative studies, we conducted a systematic review of the literature and a meta-anal-

ysis. We concentrated specifically on the impact of cemented versus uncemented fixation on revision rates.

Material and methods

Search strategy and selection criteria

We performed a comprehensive search of Medline (1966–2005), BIOSYS (1990–2005), Embase (1993–2005), Web of Science (1990–2005), and the Cochrane Library (2005, issue 5) for articles published in English and those published in other languages. The reference list of each comparative study was manually examined to find additional relevant studies. Finally, additional studies were identified by contacting experts in the field and manufacturers of implants.

Inclusion criteria were established a priori to minimize any possible selection bias. The objective was to identify all studies including information on: (1) THR performed for any reason other than acute fracture, (2) controlled comparison of cemented vs. uncemented fixation, and (3) outcome as measured by survival to time of revision surgery for any reason. All randomized controlled trials and comparative observational studies with a control group were included. The following were excluded: (1) studies that included revision cases, (2) studies including cancer or tumor cases, (3) animal studies, (4) studies containing previously published data, (5) studies that did not report any revision events, and (6) case reports. Initial screening of articles was performed by one of us (SM). Two reviewers (SM and KJB) then independently assessed each of the studies for eligibility for inclusion. If the title or the abstract was judged by either reviewer to be potentially eligible, the full article was examined. Any disagreements were resolved by consensus.

Data extraction and synthesis

Data were extracted by one of us (SM) and checked for accuracy by a second investigator (KJB). Information retrieved from each study included survivorship estimates, study design, participants, implants and methods of fixation employed, definition of outcome measures, study setting, number of surgeons, statistical methods employed, factors that were used to match or stratify patients, patient characteristics, sample size and follow-up duration, withdrawal or censorship data, and potential sources of conflict of interest. Failure events were described as any revision surgery for removal or exchange of (A) either cup, stem or both, or (B) one specific component. We performed stratified analysis on key components of study design (i.e. randomized vs. non-randomized studies, age range, and definition of failure event) and regression analysis (meta-regression) on aggregate measures of patient characteristics within studies, in assessing whether study outcomes varied systematically with these features (Colditz et al. 1995). Reporting was carried out in line with QUOROM (Moher et al. 1999) and MOOSE (Stroup et al. 2000) guidelines.

Statistics

Differences in survival and standard error were derived from reported survival analysis estimates or from reported differences in the proportion of revised THRs. We performed meta-analysis using inverse-variance weighting (Sharp and Sterne 1998) to calculate fixed and random effects summary estimates. The convention in reporting results here is that summary estimates greater than zero favor uncemented fixation and those less than zero favor cemented fixation. Between-study heterogeneity was assessed using a Chi-square statistic (Lau et al. 1997) and the more conservative random effects estimate was reported. Studies performing multiple comparisons on the same treatment group or not specifying whether there was patient overlap between such repeated comparisons could result in a potential loss of independence. In such cases, adjustments were made to the weighting of studies using a previously described method for conservatively inflating variance estimates (Jordan et al. 2002, Enanoria et al. 2004).

We used subgroup analysis to explore heterogeneity potentially caused by discrete factors identified a priori. These included study design (randomized vs. non-randomized), study site (registry vs. single institution), component followed (cup versus stem), and patient age range (≤ 55 versus > 55 years of age). We also tested the hypothesis that certain groups of implants that have performed poorly in observational studies could influence
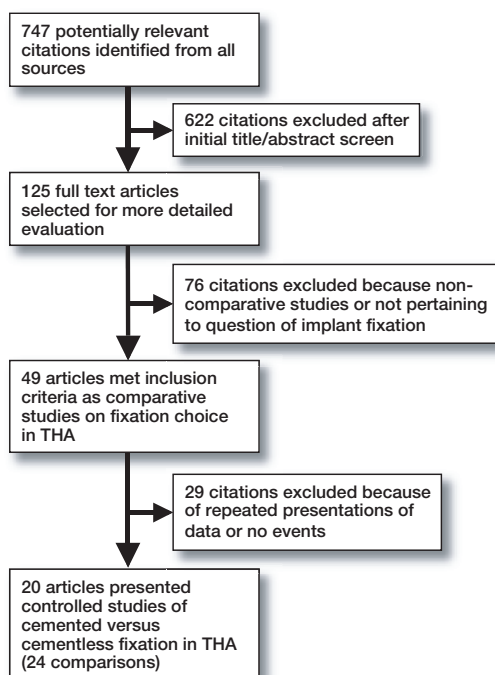
Figure 1. Flow diagram showing details of the literature search, including articles excluded at each stage of the review.

summary estimates, such as titanium stems and screw-fit or macro-ingrowth cups (Robinson et al. 1989, Tompkins et al. 1994, Rorabeck et al. 1996b, Kubo et al. 2001, Aldinger et al. 2004, Fink et al. 2004, Grant and Nordsletten 2004). Sensitivity analysis was performed to assess the contribution of each individual comparison to the summary estimate. Meta-regression was used to evaluate the association between study results and year of publication, duration of follow-up, and characteristics of the study sample including sample sex ratios and average age. A p-value of less than 0.05 was considered significant. Potential for publication bias was evaluated with the use of Egger's test for funnel plot asymmetry (Egger et al. 1997). All analyses were performed using STATA 8.2 (Stata Corporation, College Station, TX).

Results

Of the 747 citations identified after literature searches, 20 studies (reporting 24 comparisons) met our inclusion criteria (Figure 1). Study char-

acteristics and survival estimates are summarized in Tables 1 and 2. When all 24 comparisons were pooled (Table 3), no significant benefit to either fixation method was found among subgroups defined by study setting (registry- or multiple center-based vs. those from single institutions), study design (randomized and non-randomized studies), or failure definition (type A: either component or both, vs. type B: specific component failure). All subsequent analyses were performed within subgroups defined by failure definition.

Type A failure definition: revision of cup or stem, or both

The forest plot (Figure 2) represents the pooled estimate showing no significant overall advantage of one fixation method over the other. The seven comparisons that did not restrict analysis to patients less than or equal to 55 years of age favored cemented fixation by 4% and differed significantly from the group of two studies that did (Table 4). Sensitivity analysis did not show a significant result with omission of any single study. Meta-regression did not show any significant associations between duration of follow-up, year of publication, age, or sex ratio and the outcome estimate. The Egger test for funnel plot asymmetry did not reveal any evidence of publication bias ($p = 0.2$).

Type B failure definition: revision of cup or stem specifically

10 studies compared cemented and uncemented stems, and 5 compared cemented and uncemented cups; all were non-randomized. From the Norwegian registry (Havelin et al. 2000), uncemented stem and cup survivorship estimates were calculated by combining data on both hydroxyapatite-coated and porous-coated designs. There was significant heterogeneity present and the pooled estimate shown in Figure 3 shows a difference in survival probability that does not significantly favor either fixation method. In the analysis of subgroups (Table 4), several important sources of heterogeneity were discovered. Subgroup analysis differentiating studies using a titanium stem in the cemented group from those reporting use of a stainless steel or cobalt chrome cemented stem demonstrated that the former favored uncemented fixation whereas the latter favored cemented fixation, and the dif-

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Table 1. Characteristics of the studies included (n = 20)

Study Authors, year	Location	Study design [a]	Follow-up (years)	Implant compared [b] Cemented	Cementless
Wykman et al. 1991	Sweden	RCT	4.2	Charnley LFA	HP-Garches
Reigstad et al. 1993	Norway	RCT	5	Landos Titane	Zweymuller Endler
Laupacis et al. 2002	Canada	RCT	6.3	Mallory-Head	Mallory-Head
Havelin et al. 2000	Norway	MCC	11	Multiple	Multiple
Lucht 2000	Denmark	MCC	3	Multiple	Multiple
Puolakka et al. 2000	Finland	MCC	10	Multiple	Multiple
Malchau et al. 2002	Sweden	MCC	10	Multiple	Multiple
Zimmerman et al. 2002	USA	MCC	1	Multiple	Mutiple
Krismer et al. 1991	Austria	SCC	6	RM cup	Müller cup
Freeman and Plante-Bordeneuve 1994	UK	SCC	7	NR	NR
Weidenhielm et al. 1995	USA	SCC	7	Exeter-CPT	PCA
D'Lima et al. 1998 Volkman et al. 1999	USA	SCC	6	Harris Precoat cup	Harris-Galante Porous Model Munchen
Emerson et al. 2002	USA	SCC	7.5	Mallory-Head Interloc titanium	Mallory-Head circum-ferential porous coat
Guerra et al. 2003	Italy	SCC	10	AnCA cemented	AnCA HA
Gaffey et al. 2004	USA	SCC	15	Charnley all-polyethylene	Harris Galante 1
Clohisy and Harris 2001	USA	MP	11	CAD/ Harris all-polyethylene cup	Precoat/Harris-Galante 1&2
Goetz et al. 1994	USA	MP	6	Harris Precoat	Harris-Galante
Kim et al. 2003	USA	BL	9.3	Elite	Profile
Knessl et al. 1989	Switzerland	BL	7	Muller/Enler	Zweymuller/Enler

[a] RCT: randomized controlled trial; MCC: multicenter cohort study; SCC: single-center cohort study; MP: matched-pair cohort study; BL: bilaterally controlled cohort study.
[b] In the case of multicenter studies with multiple implant combinations tested, the reader is referred to the primary sources for a complete list; NR: not reported.
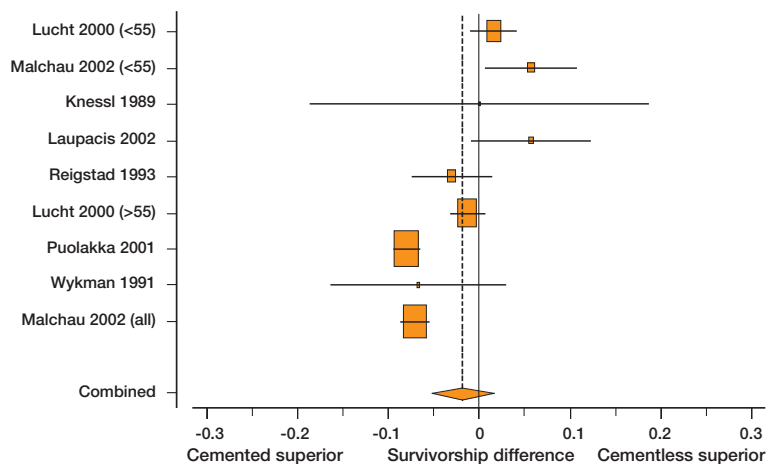

Figure 2. Forest plot of cemented vs. uncemented fixation survivorship difference for type A studies (where failure is defined as revision of either or both components). Shaded boxes represent study-specific estimates with area proportional to sample size and attached horizontal lines representing 95% CIs. The diamond at the bottom represents combined random effects estimate. Positive numbers (> 0) favor uncemented implant fixation and negative numbers (< 0) favor cemented implant fixation. The Danish registry reported on by Lucht et al. (2000) is entered twice because of stratification of results of patients into age groups of ≤ 55 years and > 55 years, but does not require adjustment of weights because the comparisons are independent.

Table 2. Comparisons of fixation strategies and comparative survivorship results

Failure Definition	Study (first author and year)	Sample size Cemented	Cementless	Average age [a] Cemented	Cementless	Difference in survivorship proportion (95% CI)
Type A: either component or both						
	Laupacis 2002	124	126	64	64	0.03 (-0.02–0.08)
	Wykman 1991	90	90	67.4	64.8	-0.04 (-0.11–0.03)
	Lucht 2000	NR [b]	NR	≤ 55	≤ 55	0.01 (-0.01–0.04)
	Lucht 2000	NR	NR	> 55	> 55	-0.01 (-0.03–0.00)
	Malchau 2002	76391	2744	NR	NR	-0.07 (-0.08–0.06)
	Puolakka 2001	4069	5519	NR	NR	-0.08 (-0.09–0.06)
	Reigstad 1993	60	60	65	64	-0.03 (-0.07–0.01)
	Malchau 2002	2588	1004	< 55	< 55	0.04 (-0.01–0.08)
	Knessl 1989	60	60	60	60	-0.02 (-0.10–0.07)
Type B: specific component survival						
	D'Lima 1998	100	100	71	52	-0.01 (-0.04–0.02)
	Emerson 2002	102	78	70	55	0.12 (0.06–0.18)
	Freeman 1994	38	89	67	53	0.04 (-0.05–0.13)
1. Stem	Guerra 2003	599	608	NR	NR	-0.02 (-0.03–0.00)
	Laupacis 2002	124	126	64	64	0.07 (0.05–0.10)
	Havelin 2000	2849	5912	< 60	< 60	0.08 (0.06–0.09)
	Kim 2003	50	50	47.3	47.3	0.00 (-0.05–0.05)
	Goetz 1994	41	41	61	57	-0.06 (-0.14–0.01)
	Weidenhielm 1995	85	66	62.6	66.9	-0.12 (-0.19–0.04)
	Zimmerman 2002	174	85	72.4	75.3	0.07 (0.04–0.09)
2. Cup	Gaffey 2004	471	120	65.7 [c]	62.6	0.07 (0.05–0.09)
	Havelin 2000	2849	3341	<60	<60	-0.03 (-0.04–0.01)
	Krismer 1991	263	160	62.9	57.3	-0.06 (-0.11–0.01)
	Volkmann 1999	329	169	70	58	-0.04 (-0.07–0.01)
	Clohisy 2001	45	45	61	62	-0.02 (-0.09–0.05)

[a] For the purposes of meta-regression analysis, studies that only specified an age range (i.e. ≤ 55 or < 60, versus > 55 or > 60) were assumed to have mean ages of 50 for the younger group and 70 for the older group.
[b] NR: not reported.
[c] Sample-weighted average of 15- and 25-year Charnley stem cohorts.

Table 3. Results of meta-analysis

Studies	No. of comparisons	Pooled difference [a] in survivorship proportion (95% CI) [b]	Hypothesis test for subgroup difference [c]
All studies	24	-0.005 (-0.031–0.022)	None
Registry/multi-institution-based studies	8	-0.002 (-0.046–0.042)	p = 0.5
Single institution-based	16	-0.006 (-0.040–0.027)	
Randomized studies	4	0.016 (-0.054–0.086)	p = 0.3
Non-randomized studies	20	-0.009 (-0.037–0.020)	
Failure type A	9	-0.018 (-0.052–0.016)	p = 0.2
Failure type B	15	0.003 (-0.031–0.036)	

[a] Inverse variance weighted meta-analysis reporting random effects estimates given test of heterogeneity p-value < 0.2 in all cases.
[b] Negative numbers favor cemented fixation whereas positive numbers favor uncemented fixation.
[c] Z-test for significant difference in summary estimate of survival difference, using standard normal distribution with 1 degree of freedom.

Table 4. Meta-analysis by selected subgroups (95% CI)

Failure definition	Studies	Subgroup definition	Number of comparisons	Pooled difference [a] in survivorship (95% CI) [b]	Hypothesis test for subgroup difference [c]
Type A: either component or both					
	Laupacis et al., Reigstad et al., Wykman et al.	Randomized studies	3	-0.010 (-0.076–0.057)	
					p = 0.4
	Knessl et al., Lucht et al., Malchau et al., Puolakka et al.	Non-randomized studies	6	-0.021 (-0.061–0.019)	
	Lucht et al., Malchau et al.	Patients ≤ 55	2	0.031 (-0.008–0.069)	p = 0.004
	Knessl et al., Laupacis et al., Reigstad el al., Lucht et al., Puolakka et al., Wykman et al., Malchau et al.	Age unrestricted	7	-0.038 (-0.069– -0.007)	
Type B: specific component					
	D'Lima et al., Emerson et al., Freeman et al., Goetz et al., Guerra et al., Havelin et al., Kim et al., Laupacis et al., Weidenhielm et al., Zimmerman et al.	Stem only	10	0.013 (-0.032–0.059)	
					p = 0.2
	Clohisy et al., Gaffey et al., Havelin et al., Krismer et al., Volkman et al.	Cup only	5	-0.018 (-0.073–0.038)	
	Krismer et al., Volkman et al.	Threaded or macro-ingrowth cup	2	-0.054 (-0.090– -0.018)	p = 0.02
	Clohisy et al., Gaffey et al.	Micro-ingrowth or ongrowth cup	2	0.031 (-0.056–0.12)	
	Emerson et al., Laupacis et al.	Titanium cemented stem	2	0.12 (0.051–0.19)	p < 0.001
	Goetz et al., Weidenhielm et al., D'Lima et al., Guerra et al., Kim et al.	Stainless steel or cobalt chrome	5	-0.051 (-0.098– -0.004)	

[a] Inverse variance weighted meta-analysis reporting random effects estimates given test of heterogeneity p-value < 0.2 in all cases.
[b] Negative numbers favor cemented fixation whereas positive numbers favor uncemented fixation.
[c] Tests for significant difference in summary estimate of survival difference, using standard normal distribution with 1 degree of freedom.

ference between the two was statistically significant. For comparisons of cups using a threaded or macro-ingrowth implant with those using a micro-ingrowth or on-growth uncemented design, the former favored cemented fixation whereas the latter did not, and the difference between subgroups was significant. Sensitivity analysis revealed that omission from the pooled analysis of the study of cup survival by Gaffey et al. (2004) (Figure 4) resulted in a shifting of the pooled estimate towards favoring cemented fixation. Meta-regression showed year of publication to be associated with improved survival of uncemented implants relative to cemented implants (Figure 5). The Egger test for funnel plot asymmetry did not reveal any evidence of publication bias (p = 0.5).

Discussion

We have summarized the best evidence from comparative studies on the use of cemented vs. uncemented fixation in THR. 20 studies comparing cemented and uncemented fixation in THR met the criteria for inclusion in this systematic review. While meta-analysis did not demonstrate overall superiority of either method of fixation as measured by a difference in survival, subgroup analysis of the type A comparisons not restricted to young patients (less than or equal to 55 years of age) demonstrated a statistically significant survival advantage with cemented fixation. Among type B studies, a linear association between survival difference and year of publication was found, with uncemented fixa-
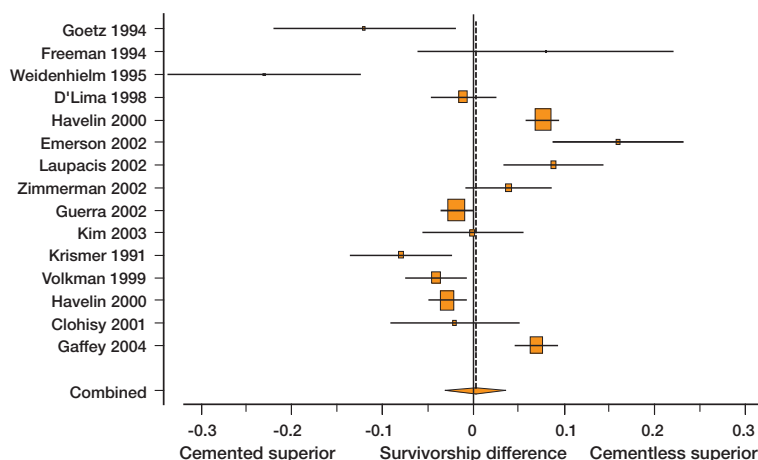
Figure 3. Forest plot of cemented vs. uncemented fixation survivorship difference for type B studies (where failure is defined as revision of a specific component—cup or stem). Shaded boxes represent study-specific estimates with area proportional to study size and attached horizontal lines representing 95% CIs. The diamond at the bottom represents combined random effects estimate. Positive numbers (> 0) favor uncemented implant fixation and negative numbers (< 0) favor cemented implant fixation.
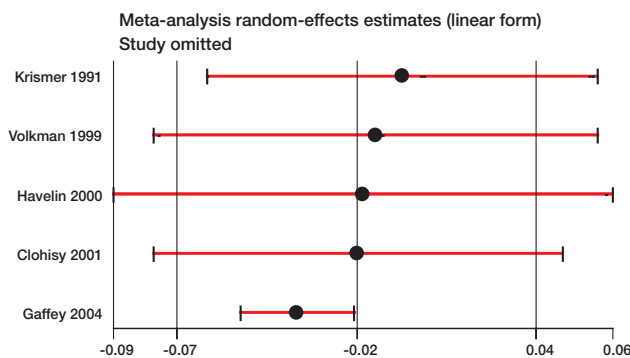

Figure 4. Sensitivity analysis of pooled estimate of type B studies (where failure is defined as revision of a specific component—the cup) to omission of each individual study. Positive numbers (> 0) favor uncemented implant fixation and negative numbers (< 0) favor cemented implant fixation.

tion outlasting cemented comparators after 1995. Poor performance by cemented titanium stems and threaded and macro-ingrowth cups were found to lead subgroup estimates to favor uncemented stems and cemented cups in their respective subgroups. These findings offer important lessons for future investigations.

This analysis suggests that cemented fixation gives favorable results at the population level, though some caution in drawing inferences is advisable. These results may have limited generalizability to the United States or other countries where cemented fixation is performed much less frequently, where THR is performed at an earlier mean age (Lucht 2000, Puolakka et al. 2000, CDC 2002, Malchau et al. 2002), or where the population is not as socially or demographically uniform. Moreover, young patients suffer from higher failure rates (Berry et al. 2002, Malchau et al. 2002) and pose a dilemma in the choice of implant and fixation method. Lower revision rates with uncemented fixation at 8–10 years in patients who are 50 years old or younger (Capello 1990, Xenos et al. 1995, Kronick et al. 1997, Fink et al. 2004) has
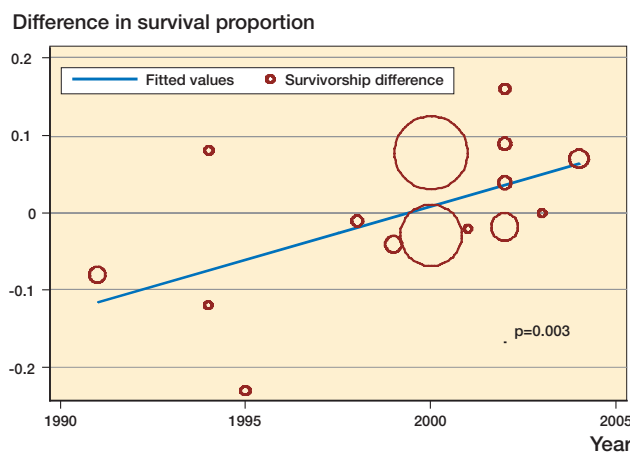
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Figure 5. Scatter plot of study estimate of the difference in survival probability vs. year of publication with superimposed regression line. Y-axis values greater than zero favor uncemented fixation and the area of each circle is proportional to the sample size of the study. Slope = 1.4% per year (95% CI: 0.5–2.3)

encouraged optimism. The 7% difference between the population level (age unrestricted) and younger subgroup estimates (Table 4: –0.038 vs. 0.031) means that prospective studies should be designed to compare the best available cemented implants against the best available uncemented implants without pooling all age groups, because results are likely to differ between groups.

Improvement in relative performance of uncemented fixation in recent years was found among type B studies. This is consistent with data from numerous uncontrolled studies (Zicat et al. 1995, Kim et al. 1999, Della Valle et al. 2004, Sinha et al. 2004). A study on the survival of more modern uncemented cups by Gaffey and colleagues (2004) compared to the results from a historical cemented control group has provided some of the strongest evidence to this effect at 15 years of follow-up. That study is the most current of the 5 specifically addressing cup survival, and the only one to favor uncemented fixation, which may explain why its omission in the sensitivity analysis (Figure 4) led to a significant shift in the summary estimate of survival difference to favor cemented fixation. The study by Gaffey et al. (2004) was designed to assess the importance of implant fixation with cemented vs. uncemented technique, and part of the difference in survival may be mediated through impact on wear rates. Uncemented fixation has been found to increase wear rates, which can lead

to early failure (Tanzer et al. 1992, Xenos et al. 1995, McCombe et al. 2004). Improvements in polyethylene production, alternate bearing surfaces, and other design features may have contributed to the relatively improved survival of uncemented implants. Further studies will be necessary to confirm these assertions.

Cemented stems of titanium and threaded macro-ingrowth cups explain some inconsistency in the results of studies that were included in the meta-analysis. For series of cemented titanium stems, numerous authors have reported loosening rates of 10–49% at 3–5 years (Robinson et al. 1989, Tomp-kins et al. 1994, Rorabeck et al. 1996a). We found cemented fixation to be inferior when titanium stems were used and superior when a stainless steel or cobalt-chrome stem was used. Similarly, threaded macro-ingrowth cups have performed poorly with loosening rates of 25–55% at 10–15 years of follow-up (Kubo et al. 2001, Aldinger et al. 2004, Grant and Nordsletten 2004.). When these implants were tested against cemented cups, cemented cups outperformed them by 5%, whereas studies comparing porous-coated Harris-Galante I/II cups to cemented polyethylene cups moved the difference in survival in the direction of favoring uncemented fixation by 9%. The World Medical Association Declaration of Helsinki (World Medical Association 1997) requires that new treatments be tested against the best known current standard. We found

that control groups have not always been selected with regard to the best available treatment or standard of care. Future comparative trials should avoid these past mistakes and use systematic reviews and comprehensive summaries of implant performance from the implant registries, with long-term follow-up in selecting comparator groups.

4 randomized controlled trials assessing hybrid fixation (cementation of one component and uncemented fixation of the other) were excluded because they either only focused on polyethylene wear rates and component loosening or had inadequate follow-up to detect any failures resulting in revision (Godsiff et al. 1992, Karrholm et al. 1994, Onsten et al. 1998, McCombe and Williams, 2004). With respect to failure defined as revision of either or both components (type A), only the Danish and Swedish registries presented data on hybrid fixation as distinct from purely cemented or uncemented fixation and this was judged inadequate for independent subgroup meta-analysis. Thus, the hybrid fixation method was only assessed indirectly through analysis of studies comparing individual component failures.

While the majority of studies that were included were non-randomized and subject to significant bias and confounding, the potential for bias is not restricted to non-randomized studies. Of the 3 randomized controlled trials, only Laupacis et al. (2002) documented proper randomization techniques and concealment of allocation, and discussed reasons for exclusion or non-participation. Loss to follow-up or non-response during data collection are also important sources of selection bias. Lack of attention to this problem was seen among both randomized and non-randomized studies in this review. Of the 3 randomized studies that mentioned the reasons for their exclusion and censoring, only Laupacis et al. provided the type of flow chart and accounting for withdrawals that the CONSORT statement (Altman 1996) requires in documentation of randomized controlled trials. Such clear and transparent reporting of all features related to validity of such trials ought to be enforced in orthopedic journals, as it is in many high-impact medical journals (Altman 1996, Moher et al. 2001a, b).

Definition of a failure event in studies of implant survival is fraught with inconsistencies. While we attempted to use estimates based on revision undertaken for any reason—because this is less subjective than "aseptic loosening" or "mechanical failure"—the propensity for differential misclassification and resulting bias is present. This is because the decision to undertake a revision is influenced by the opinions of the surgeon and the patient. Moreover, this is not an adequately sensitive definition of all clinical failures. Revisions are occasionally performed on well-fixed implants without evidence of infection or mechanical failure, and many radiographically loose or symptomatic implants never come to be revised. Reporting of health-related quality of life and functional outcome in addition to standardized reporting of failure events in survival analyses will improve the accuracy and comparability of clinically relevant outcomes in future research. Randomized studies using radiostereometry (Mjöberg et al. 1986, Karrholm et al. 1994), a highly sensitive and specific computerized radiographic technique for quantifying implant migration and wear, may become useful surrogates in the future for detecting early failure and exposing fewer patients to new technologies that are potentially dangerous.

The studies reviewed here have shown that failure events in THR are rare, and that long-term follow-up is required to generate meaningful estimates of difference in survival probability. It is not uncommon for an implant being studied to be removed from the market or replaced by a new version before the scheduled endpoint of a trial, as was the case for the Mallory-Head prosthesis (Biomet, Warsaw, IN) used by Laupacis et al. (2002). This can make clinical trials costly, logistically challenging, and in the end, potentially irrelevant. Some authors assert that national registries ought to be the research study design of choice to provide timely and relevant outcomes data to guide clinical practice, as it has in Scandinavia (Maloney and Harris 1990, Maloney 2002, Howard et al. 2004), and the results of this study underscore the need for this powerful tool for improvement of patient outcomes. Randomized clinical trials will, however, continue to be valuable when: (1) the question of relative superiority has been narrowed down to a few seemingly equivalent choices of fixation or implants, and a specific target population has been identified

under which the experiment could be undertaken with equipoise; or when (2) the development of validated surrogate markers for early failure (such as radiostereometry) allows smaller sample sizes and shorter duration in the testing of a new strategy against an established control.

Several limitations in our work are important to note. In any systematic review or meta-analysis, there may be publication bias, incomplete ascertainment of studies, and errors in data extraction. The studies included in this review represent a diversity of designs, patient populations, surgical implants and approaches, and methods for assessing their efficacy. We believe that restricting our analysis to randomized studies alone would have ignored most of the comparative evidence on the subject. Also, certain potential predictors of outcome—such as race, rehabilitation program, and activity level—could not be explored, due to very limited information on these variables among the studies that were included. We did not find any statistical evidence of funnel plot asymmetry to suggest publication bias. We attempted to minimize errors in data extraction through cross-checking of all quantitative information by two of the authors. We used all sources of data that we could identify from a comprehensive literature search, without any restriction regarding language, to find studies for inclusion. Given the limitations in the published literature on this topic, the methods used in this systematic review and meta-analysis had limited bias and they explored sources of heterogeneity to the greatest degree possible.

In conclusion, the published evidence suggests that cemented fixation still has superior survival among large subgroups of populations studied, and that survival of uncemented implants continues to improve. The effect on analyses of relative benefit from the use of suboptimal control groups (such as those with cemented stems of titanium and threaded cups) emphasizes the need for more uniform standards in the selection of control groups in future trials. Further research and improved methods are necessary to better define specific subgroups of patients in which the relative benefits of cemented and uncemented implant fixation can be more clearly demonstrated.

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