# Cumulating Quality of Life Results in Controlled Trials of Coronary Artery Bypass Graft Surgery


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**ABSTRACT:** Many studies evaluating the effectiveness of coronary artery bypass graft surgery allude to the quality of life benefit resulting from surgery. However, no comprehensive empirical estimate of the absolute or relative magnitude of this benefit is currently available. This paper presents a data synthesis of the research literature on bypass surgery to derive such an estimate. It uses follow-up measures of the percent of patients who were angina-free within both the surgical and medical groups of 14 controlled trials to estimate the quality of life benefit following surgery. Results based on the longest reported follow-up period suggest that the chances are approximately 25 to 40% greater that patients will be angina-free if they receive surgery rather than medical treatment. Estimates of benefit are about 15% less in randomized controlled trials compared to controlled trials that used a matching strategy. These results are unlikely to be affected by related factors such as the percentage of patients who crossover from the medical group to the surgical group or the specific method of calculating anginal relief used in this research report. However, differential patient selection may account for the observed design effect.



KEY WORDS: *quality-of-life, data synthesis, meta-analysis, coronary artery bypass graft surgery, angina, controlled clinical trials.*


The evaluation of medical technologies often depends on assessment of quality of life benefits to patients such as freedom from pain, psychological well-being, and physical mobility [1,2]. Quality of life may also be an important consideration for technologies initially thought to be life preserving. Coronary artery bypass graft surgery (CABGS) is a case in point because the procedure may be recommended to relieve the often debilitating angina accompanying coronary heart disease. Randomized trials have not reported a consistent benefit in improved survival and lower mortality for patients re-


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ceiving the surgery [3,4]. Furthermore, the recently completed Coronary Artery Surgery Study (CASS) of patients with "mild" angina included a variety of quality of life measures (e.g., exercise test performance, employment status, recreational status) [5]. While no significant surgical benefits were found for mortality, survival, and myocardial infarction rates [6], many significant benefits on surgical patients' quality of life were found [5]. The assessment of this and other technologies poses a dilemma for the evaluator because most studies do not routinely include quality of life results using comparable measures.

A quality of life assessment based on the existing scientific literature must often rely on proxy variables or more indirect indicators. The most commonly reported indicator of quality of life reported in the CASS and other bypass studies has been the relief from angina pectoris, the often debilitating pain associated with coronary artery disease. CABGS has been presumed to produce significant relief of angina since the first, uncontrolled studies were reported [7,8]. The National Institutes of Health [9] reflected this view in responding to the question, "What is known about the long-term quality of life after coronary artery surgery?" The NIH consensus statement noted,

> The symptom of angina pectoris is reported to be relieved in 80 to 90 percent of the patients undergoing surgery for chronic stable angina.

From a technology assessment perspective, unfortunately, this statement is limited in two major ways. First, it does not quantify the *degree* to which patients could expect their angina to be relieved following an operation. Conceivably, a large majority of patients might have improved only slightly and still have satisfied the letter of this statement. Second, because two courses are open to most patients (surgical or medical treatment), it is impossible for a patient to assess the potential additional benefit involved in undergoing the operation compared to the advantage of staying on a medical regimen. As McPeek, Gilbert, and Mosteller [10] note for most surgical procedures, "The patient's quality of life after the recovery phase matters most in choosing the treatment." Should there be considerable relief from angina associated with medical therapy, the decision to choose surgery becomes even more difficult.

An assessment of the quality of life benefit thus requires comparative data that also reflect the incidence of anginal relief in control groups of patients not undergoing surgery. Such information is especially critical because there are numerous instances in which a major, new surgical intervention was later shown to produce only placebo benefits in pain relief (e.g., gastric freezing, internal mammary artery ligation). A previous review by Buccino and McIntosh [11] did cite evidence from controlled trials of CABGS pertaining to complete relief of chronic angina. However, Buccino and McIntosh's review was based on just four studies, only two of which were randomized clinical trials (RCTs), and was restricted to examining the statistical significance between surgical and medical groups.

The primary purpose of the present research was to derive an estimate of the quality of life benefit for surgical patients in previous controlled trials of CABGS by aggregating the results from the individual studies published in the scientific literature. This study also illustrates both the potential and the

limitations in synthesizing data from published studies to assess an important benefit of most medical research technologies.

The systematic examination of results of multiple clinical trials evaluating the same health intervention is a technique that has been endorsed [12] and utilized for some time [13]. Recently, quantititative procedures, such as meta-analysis, have been applied to cumulate the findings of similar studies [14–17]. These cumulation methods use the results from individual studies to derive a pooled measure of the average magnitude of treatment impact such as an effect size [15] or risk ratio [16]. Furthermore, the procedure allows the reviewer to quantify the contribution of research design or methodology, which is typically impossible within an individual study [18].

## METHODS

### Quality of Life Measure

The outcome measure used in this synthesis was based on the percentage of patients in either a surgical or medical group of a given study who were reported to be angina-free at both entry into the study and the longest reported follow-up period. Choice of the percent of patients who were angina-free as an indicator of life quality was dictated primarily by the frequency with which it was reported in published studies. No other quality of life variable was cited as often. Patients classified as New York Heart Association Type I or as asymptomatic were considered to be angina-free.

### Selection of Studies

Studies were selected from four sources. These included prior reviews [11,19], references from relevant articles, a MEDLARS II search from 1974–1981 using coronary bypass surgery as the keyword, and the table of contents of major medical journals for the past several years. From these four sources 91 studies were identified whose title indicated that some version of CABGS had been tested. Of these 91 studies, 26 were controlled clinical trials that compared results in a surgical and a medical group. Of these 26 studies only 15 reported results on relief of angina and these were examined more closely. Studies were included that had similar (within 2 months) follow-ups in surgical and medical groups. One of the potentially usable studies was excluded because the average follow-up periods for assessment of the percent of patients who were angina-free in medical and surgical groups differed by 13 months. No other exclusion criteria were employed. Thus, selected studies represent the total number of controlled clinical trials available in the period 1970–1983 that had contrasted survival or death in groups of surgical and medical patients with coronary heart disease.

The 14 trials included in this research (see Appendix) were comparable to the 12 excluded trials. Pertinent averages from the included and excluded trials were, respectively: follow-up times (30 months vs. 27 months), percent crossovers of medically treated patients to surgery (14% vs. 9%), year of publication (1977 for both included and excluded studies), distribution of the percent of one, two, and three vessel disease patients (17%, 33%, and 50%

**Table 1** Percent of Angina-Free Patients in Surgical and Medical Groups of Randomized and Nonrandomized Clinical Trials[a]

| | Surgical | | | | Medical | | | | |
|---|---|---|---|---|---|---|---|---|---|
| First author | n/grp. | Entry (E) | Follow-up (F) (Ave. in mos.) | F-E | n/grp. | Entry (E) | Follow-up (F) (Ave. in mos.) | | Difference (F-E)Surgical–(F-E)Medical |
| RCTs | | | | | | | | | |
| CASS | 359 | 25.1 | 41.8<br>60 | 16.7 | 390 | 22.0 | 23.3<br>60 | 1.3 | 15.4 |
| Conti | 70 | 0.0 | 80.0<br>8 | 80.0 | 80 | 0.0 | 41.2<br>8 | 41.2 | 38.8 |
| European | 368 | 0.0 | 37.5<br>60 | 37.5 | 373 | 0.0 | 18.2<br>60 | 18.2 | 19.3 |
| Kloster | 51 | 0.0 | 17.6<br>37 | 17.6 | 49 | 0.0 | 0.0<br>38 | 0.0 | 17.6 |
| Mathur | 55 | 0.0 | 61.8<br>38 | 61.8 | 60 | 0.0 | 6.7<br>38 | 6.7 | 55.1 |
| Seldon | 21 | 0.0 | 42.9<br>4 | 42.9 | 19 | 0.0 | 10.5<br>4 | 10.5 | 32.4 |
| | | | | Ave. (F-E) = 42.8 | | | | Ave. (F-E ) = 13.0 | Average surgical benefit = 29.8 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Nonrandomized trials | | | | | | | | | |
| Bender | 53 | 0.0 | 66.0<br>20 | 66.0 | 35 | 0.0 | 0.0<br>20 | 0.0 | 66.0 |
| Berk | 21 | 0.0 | 90.5<br>14 | 90.5 | 21 | 0.0 | 28.6<br>12 | 28.6 | 61.9 |
| DeMots | 27 | 0.0 | 48.1<br>32 | 48.1 | 19 | 15.8[b] | 0.0<br>32 | −15.8 | 63.9 |
| Hultgren | 52 | 0.0 | 60.0<br>25 | 60.0 | 66 | 0.0 | 21.0<br>23 | 21.0 | 39.0 |
| Matloff | 88 | 0.0 | 80.7<br>15 | 80.7 | 35 | 0.0 | 37.1<br>17 | 37.1 | 43.6 |
| McNeer | 379 | 2.0 | 20.6<br>24 | 18.6 | 402 | 4.0 | 6.5<br>24 | 2.5 | 16.1 |
| Tyras | 119 | 1.7 | 62.2<br>48 | 60.5 | 70 | 17.1 | 27.1<br>48 | 10.0 | 50.5 |
| Vismara | 172 | 5.0 | 42.4<br>39 | 37.4 | 112 | 17.0 | 25.9<br>39 | 8.9 | 28.5 |
| | | | | Ave. (F-E) = 57.7 | | | | Ave. (F-E) = 11.5 | Ave. surgical benefit = 46.2 |

[a]Overall surgical benefit averaged across designs = 39.2.

[b]Three patients who were reported to be angina-free at baseline were not given a group designation. These patients were assumed to be members of the medical group because angina-free patients are more likely to remain on a medical regimen, assuming membership in the surgical group results in little difference in the findings.

vs. 15%, 26%, and 59%), and mortality difference between surgical and medical groups (12% vs. 7%). No statistical tests of the significance of the difference between these averages were conducted due to the small sample size and low statistical power of such tests.

To reduce the likelihood that the same patients had been included in different reports, those studies sharing the same authors were inspected. If study patients came from different medical centers, had mutually exclusive years of enrollment, were of different ages, or had different types of coronary disease, then studies were considered to include different patient groups. Five of the studies shared the same author, and it was not possible to establish whether the same patients were studied or the extent of the possible duplication. However, no two of the studies had the same sample sizes or were simply follow-ups of earlier studies. Thus, it was assumed that no duplicate studies were present.

Because a number of investigators have shown that research design is related to the magnitude of observed treatment benefit for CABGS [17,20], this research also examined results by design category. Two design categories were used: RCTs in which patients were reported to have been assigned to surgical or medical groups by a random process, or nonrandomized trials ("quasiexperiments") [21] which created concurrent controls using nonrandom assignment which involved matching patients with similar histories and other relevant characteristics.

## Data Cumulation Procedure

The studies were coded independently by the authors for number of patients, attrition, and relief of angina; all coding discrepancies were resolved. For each of the two groups in a study—surgery and medicine—a fraction was formed whose numerator was the number of patients who were angina-free and whose denominator was the total number of patients who were assigned to respective groups at the beginning of the study (see Table 1). Surgically assigned patients were not counted unless they actually received CABGS. This resulted in small changes in four of the 14 studies (31 of 390 surgical patients in the CASS study, 27 of 395 in the European study, 1 of 56 in Mathur and Guinn, and 1 of 22 in Berk et al.). These modified totals appear as n/grp in Table 1.

Because the denominator for the follow-up calculations was based on original sample size at entry, estimates were not artifactually increased by the lack of availability of patients at follow-up, exclusions due to medical crossovers, or the number of deaths. Moreover, this makes the data for each group comparable over time so that meaningful comparisons can be made. Entry percents could then be subtracted from follow-up percents within both the surgical and medical groups. Finally, the medical difference was subtracted from the surgical difference, yielding the relative benefit due to surgery. Sample sizes reflecting these rules have been indicated as n/grp for each of the studies in Table 1.

To illustrate these calculations, in Table 1 of the recent CASS report, 22% of medical and 23% surgical patients had no chest pain at entry while the figures were 35% and 58%, respectively, of those still living at the end of 5 years. Recalculating the entry result in the surgical group so that it represents

only those patients assigned to the surgical group actually receiving CABGS yields an adjusted figure of 25.1%. Follow-up results were recalculated in both groups to reflect the number of patients at entry (rather than the total number of surviving patients), thus producing figures of 23.3% (medical) and 41.8% (surgical). The recalculated medical difference was 1.3% (23.3–22.0%) while the recalculated surgical difference was 16.7% (41.8–25.1%). Hence, the net benefit for surgery was 15.4% (16.7–1.3%). (The computational formula appears at the end of the Appendix.) Therefore, each study result represents the difference in degree of complete symptom relief between all surgical patients who received CABGS and all patients assigned to medical groups, including those who may have received surgery.

Typically, one value was reported for the percent of patients who were angina-free and, unless stated otherwise, it was assumed that this result reflected the average follow-up period that was reported. If multiple figures were reported for varying lengths of follow-up, only data coinciding with the longest period of follow-up were coded. Thus, in the CASS example above, follow-up data from 1 and 3 years were also reported, but not included in this analysis.

From these within-study results, the overall, average benefit was calculated by finding the arithmetic average of benefits found in each of the 14 individual studies. The average relative benefit was also calculated for each of two design categories composed of six RCTs and eight nonrandomized trials.

## RESULTS

The average benefit due to surgery was 39.2% across the 14 studies used in this research (see Tables 1 and 2, line 1). That is, the incidence of surgical patients who were angina-free was 39.2% higher, on the average ($p < 0.05$, test for the difference between proportions), than the incidence of angina-free, medical patients. In no case was the percentage of patients who were angina-free in the medical group higher than the percentage of patients who were angina-free in the surgical group at the longest follow-up.

When stratified by design, the average benefit due to surgery was 29.8% in the six RCTs and 46.2% in the eight nonrandomized trials. A Mann-Whitney nonparametric test indicated that this difference approached the usual criterion for statistical significance ($z = 1.61$, corrected for continuity, $p < 0.06$). An alternative parametric analysis of the follow-up results using a pooled or common odds ratio was also performed (as recommended by Yusuf et al. [22]). The odds ratios (and 95% confidence intervals) were 4.42 (3.50, 5.57) and 6.30 (4.91, 8.08) for RCTs and nonrandomized trials, respectively. It should be noted that the comparable Mantel-Haenszel average odds ratios were 4.89 and 9.03 with all ratios from the individual studies indicating a benefit for surgery. The former, average odds ratio, however, was nonhomogeneous indicating a consistent interaction favoring surgery. This result is consistent with previous findings based on mortality and survival outcomes in which nonrandomized trials also overestimated the benefit of surgery relative to the estimates obtained in RCTs [17,20].

The present design effect (see Table 2, Line 1) resulted almost entirely from the discrepancy between the average entry vs. follow-up difference in the

**Table 2** Estimates of Benefit Using Different Analysis Methods

| | RCTs (n = 6) | | | Nonrandomized Trials (n = 8) | | | Nonrand. diff. − RCT diff. (design effect) | Overall surgical benefit averaged across designs |
|---|---|---|---|---|---|---|---|---|
| | Surgery | Medical | Difference | Surgery | Medical | Difference | | |
| 1. Average percent | 42.8 | 13.0 | 29.8 | 57.7 | 11.5 | 46.2 | 16.4 | 39.2 |
| 2. Average based on raw numbers | 33.1 | 11.5 | 21.6 | 41.2 | 7.5 | 33.7 | 12.1 | 27.3 |

surgical groups of nonrandomized trials (57.7%) as compared to the average entry vs. follow-up difference for the surgical groups in RCTs (42.8%). The medical group results were nearly the same for both types of trials. The average entry vs. follow-up difference was 11.5% for the medical groups in nonrandomized trials and 13.0% for the medical groups in the RCTs.

As a check on the accuracy of these findings, results were recalculated aggregating the number of angina-free patients and the total sample size across all studies rather than averaging percents from individual studies. While such pooling is a more controversial aggregation method [23], it does permit studies to be weighted by their sample size. The results were consistent with those found by averaging percents across studies. The overall estimate of subjective benefit decreased from 39.2 to 27.3%, and the magnitude of the design effect dropped slightly from 16.4 to 12.1% (see Table 2, Line 2).

## DISCUSSION

This study illustrates the potential for obtaining quality of life information from the existing scientific literature. It also provides an opportunity to address some of the methodological issues in the assessment of quality of life benefits and to discuss the limitations in cumulating results in controlled clinical trials.

The results of this assessment approach indicate that patients with symptoms of angina who undergo CABGS can expect their chances of becoming angina-free to be about 25–40% (see Table 2) greater than if they had remained on a medical regimen. The direction of benefit was consistent as the percent of patients who were angina-free was always higher in the surgical group for the longest follow-up period that was reported.

The degree of benefit is overestimated by nonrandomized studies that have matched medical and surgical patients rather than randomly assigning them to treatment. This result replicates previous research cumulating objective outcomes [17]. The design effect exceeded conventional levels of significance using recently developed parametric methods [22] for calculating common and average odds ratio statistics, and it approached significance using a less powerful nonparametric test. The chances of a surgical patient remaining angina-free were about 15% greater for those in nonrandomized trials compared to those in RCTs, a 55% increase [(46.2 − 29.8)/29.8].

It is also important to identify a potential source of the different findings in RCTs and nonrandomized trials. Given the very similar results for medical patients in the two types of studies (see Table 1), the design effect is unlikely to be due to differences in the distribution of illness severity among medical patients or in the way anginal relief was measured. Rather, the design effect is most likely attributable to the differences between surgical patients in RCTs and nonrandomized studies.

### Accuracy of the Findings

There is one primary issue that should be examined further in determining the accuracy of the quality-of-life measure reported here (the difference between the percent of patients in a medical or surgical group that were angina-

free), and thus the validity of the estimates found by averaging across studies. The sometimes substantial incidence of crossovers from the medical to the surgical group in RCTs must be considered. Given that crossovers are typically patients with the worst prognosis suffering from rather severe angina [24], it is unlikely that the percent of patients who remained angina-free would be altered in either group. In addition, because medical patients were often dropped from the analysis by the authors of the original studies at the time they crossed over, the number of patients who are angina-free would remain the same. Neither the numerator, the number of patients who were angina-free, nor the denominator, the total number of patients who were assigned to a particular group, would likely be influenced under any of these conditions.[1]

## Design Effect

In the same way that factors having potential impact on the accuracy of quality-of-life measures should be examined, so too should those factors that may contribute to the existence of a design effect. First, any difference in the rate of crossovers between RCTs and nonrandomized trials is unlikely to have influenced the difference in estimates found in the two kinds of designs. The reason is identical to that discussed above in relation to crossovers and the accuracy of the overall difference between life quality in surgical and medical groups, namely that crossovers are very likely to be suffering from severe angina and, therefore, are unlikely to influence the numerator of the statistic used in this research—the number of angina-free patients. Similarly, the denominator of the statistic used would not be influenced because only a small percent of surgical crossovers—see point 3, below—were excluded from the calculations.

Second, because one can expect the recurrence of angina in surgical patients as vessels become occluded again [25], it is possible that a difference in average follow-up periods between RCTs and nonrandomized trials (see Table 1) might explain some of the discrepancy in results. Thus, it is important to determine the comparability of follow-up periods in RCTs and nonrandomized trials. A much shorter average follow-up period in nonrandomized trials would argue against the role of design in producing differential benefit sizes. The average follow-up period is only 7 months shorter in nonrandomized trials compared to RCTs (i.e., 27 vs. 34 months, respectively). Given average follow-ups in RCTs and nonrandomized trials of considerable duration (between 2 and 3 years), this 7 month difference is not likely to be of sufficient magnitude to explain the design effect found in this synthesis.

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[1]A second, less critical issue related to the specific definition of percent angina-free used in this study. Because the denominator used to calculate the percent of angina-free patients was based on the total sample (excepting surgical patients who did not receive CABGS) and not the reduced sample after deaths have been removed, the percent of patients who were angina-free in surgical and medical groups was recalculated and averaged using the number of angina-free patients in the numerator but only the number of survivors in the denominator. This alternative procedure produced results of similar magnitude that led to conclusions identical to those made when the total sample was used in the denominator.

Third, the decision to slightly alter the commonly recommended intention-to-treat principle (patients in the surgical group who did not receive surgery were excluded) [26] could potentially have altered results. However, only 3.3% of the surgical patients were excluded for this reason and all but one of these patients came from an RCT. Had patients who did not receive CABGS been included in the denominator, the estimate of benefits of RCTs would have decreased. Thus, the procedure used above may slightly understate the magnitude of the design effect.

Finally, differences in illness severity between medical and surgical patients and between RCTs and nonrandomized trials might have contributed to the design effect. For example, if one makes the common assumption that patients with triple-vessel disease are more ill and have more angina, then differential selection of patients into either medical or surgical treatments in the studies could bias the results. More of such patients in the medical than in the surgical group would overestimate the effect while an underestimate of the effect would be found with more triple-vessel patients in the surgical than medical group. For five of the six RCTs in which this information was provided, there were 7.0% more patients with triple-vessel disease in the surgical than medical group (47.4% vs. 40.4%). On the other hand, for the three (of eight) nonrandomized trials that reported this information there were 7.3% more patients with triple-vessel disease in the medical than surgical group (60.3% vs. 53.0%). Thus the pattern of this proxy of disease severity suggests that differential patient selection may account for some portion of the design effect.

Selection bias in assigning patients to surgery appears to be the most probable explanation of the design effect found between randomized and nonrandomized clinical trials. Apparently, research that attempts to match groups on their incidence of clinical problems and personal characteristics does not adequately equate groups and thus does not rule out initial differences as an explanation of outcome. For example, in nonrandomized trials, surgical patients and physicians probably played a more active role in choosing the treatment and may thus have been more committed to perceiving it as beneficial while the medical patients were too ill to be considered good risks for surgery.

## Reporting Quality

The validity of these cumulated results depends on the quality of information provided in the original published reports. Recently, there has been some discussion indicating that important information is often unreported [27–29]. The present study was also limited by the information available. There were a number of questions that could not be answered due to the lack of adequately reported information.

One question that could not be addressed concerned the conditions under which the presence of angina was determined. Good research practice would require that those staff who question patients about the extent of their angina be unaware of the treatment each patient received. While this requirement may be difficult to implement, the absence of information in the original studies pertaining to these conditions (only three of the 14 studies described assessment conditions) makes this determination problematic.

It is also possible that patient and physician expectations regarding potential benefits accounted for some unknown portion of the effect attributable to surgery. Such placebo effects ("any effect attributable to a pill, potion, or procedure but not to its pharmocodynamic or specific properties" [30]) are particularly bothersome when subjective measures are involved. The studies assessing CABGS did not include a placebo control group because such a procedure is considered unethical. Consequently, it is not possible to derive a firm estimate for the placebo effect. However, one may examine other, similar treatments to obtain a rough estimate. For example, Beecher [31] noted that placebos accounted on average for 35% of "satisfactory relief" in well-controlled studies of a variety of medical interventions. In particular, he claimed that the placebo effect for surgical relief of angina derived from a subset of these studies dealing with internal mammary artery ligation—a now abandoned procedure—was equal to a 28% difference in "complete pain relief." This is almost identical to the effect found for the CABGS RCTs. This effect is also comparable to the placebo effect reported for psychotherapy [32]. Thus, it is possible that the beneficial effect of CABGS on anginal relief could be due to placebo although its duration of 2 to 3 years makes it less plausible that it accounts for the entire effect found.

Another question concerns the amount of relief from angina due to CABGS. In nine of 14 studies measures taken at entry indicated that all surgical and medical patients displayed symptoms of angina. A small percent of patients in the five remaining studies was angina-free at baseline, and this percent was typically greater (between 2 and 16%) in the medical group. To gauge the effect of this entry difference, one would need to know whether surgical or medical treatment is more or less likely to *sustain* the status of patients who are already angina-free. Because data on individual patients were not available in each study of this synthesis, it was not possible to determine if the entry difference tends to enhance or diminish the benefit of surgery. In any event, the small difference in entry rates would argue that overall results should be minimally affected.

One other problem in examining a medical technology over a period of time is the changes that occur. Wagner [33] has called this "the moving target problem." In the present case there have been major advances in both surgical technique and medical practice. A recent report [34] indicates substantial long-term benefit can now be achieved using comprehensive medical therapy including beta blockers, nitrates, and nitroglycerin. Thus, the present synthesis may overestimate the benefits of CABGS compared to the most recent medical interventions in eliminating the angina associated with coronary heart disease. Again, it is not possible to assess this because the medical treatment actually received by patients was not reported in any of the studies.

There were numerous other difficulties encountered in conducting this research due to poor reporting quality. For example, the actual percentages of anginal relief for the CASS report were not mentioned in the text of the article, but had to be estimated from a figure. Similarly, in the Berk et al. study (see Appendix), information on patients' outcomes and length of follow-up had to be calculated from a table. It was also not possible to report symptom relief in important subgroups (e.g., one, two, and three vessel disease pa-

tients) because these results were not consistently provided in the original studies.

Though the cumulation of study results is necessarily imperfect due to inconsistencies in publication standards, quality of individual studies, and unresolved problems with outcome measures, the approach offers the dual advantages of timeliness and cost-effectiveness. Cumulative results of existing controlled clinical trials can be produced in a much shorter time and at greatly reduced expense when compared to results from a new, multicenter clinical trial. In fact, as illustrated by Chalmers and his colleagues [14], the cumulative results may indicate no further need for a controlled trial [14].

Further research should focus on other quality of life measures besides freedom from angina. The measurement of quality of life is difficult and some measures are particularly troublesome. For example, a follow-up consensus conference on CABGS regarded postoperative employment status as an inappropriate major index of quality of life [35]. This should not deter medical researchers from including appropriate quality-of-life measures, however. As Weinstein [36] has noted:

> . . . to omit quality of life and other intangible considerations because of difficulties in measurement would be irresponsible if these considerations are central to the concerns of the physician, the patient, and the collection of patients and potential patients we call society (p. 311).

Thus, accurate estimates of the relative, subjective benefit of CABGS are vital to informed decisions by individual physicians and patients to recommend and accept surgery. In addition, these estimates are likely to be included in more comprehensive technology assessments. To illustrate, Weinstein and Stason [37] utilized data on degree of symptom relief to estimate the quality-adjusted life expectancy and cost effectiveness of both CABGS and medical treatments. Unfortunately, the medical group data were taken at 2-year follow-up and the surgical group data at 1- and 7-year follow-up in three different studies. Such methodological inconsistencies greatly diminish the validity of any subsequent estimates and indicate clearly the potential need for quality-of-life measures accurately synthesized from previous research.

In summary, the results of this research indicate that those patients who suffer from angina and subsequently receive CABGS are more likely to become angina-free than patients who are treated medically. Estimates of the likelihood of becoming angina-free are approximately 40% greater in the surgical than the medical group. When estimates are based solely on results in RCTs, the degree of benefit is reduced by approximately 10%. These basic findings remain intact when one uses alternative estimates of the percent of patients who are angina-free. Finally, replication of the design effect found in a larger set of studies using a different outcome measure further establishes its importance in the generation of accurate estimates of benefit.

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## APPENDIX

Articles used in data synthesis:

### RCTs

CASS Principal Investigators and their Associates: Coronary Artery Surgery Study (CASS): A randomized trial of coronary artery bypass surgery. Quality of life in patients randomly assigned to treatment groups. Circulation 68:951–960, 1983

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Formula for calculating quality of life benefit (QLB):

$$QLB = \frac{X_2 - X_1}{N_1'} - \frac{Y_2 - Y_1}{N_2},$$

where $N_1'$ = number assigned to surgery minus those not receiving surgery; $N_2$ = number assigned to medical treatment; $X_2$ = number angina-free, surgical group, longest follow-up; $X_1$ = number angina-free, surgical group, entry; $Y_2$ = number angina-free, medical group, longest follow-up; $Y_1$ = number angina-free, medical group, entry.

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