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3 **Off-pump versus On-Pump Coronary Artery Bypass Grafting:**  
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5 **A Systematic Review and Meta-Analysis of Propensity Score Analyses**  
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41 **Disclosure**

42  
43 Concerning relations with industry, Jochen Börgermann (as the principal investigator)  
44  
45 and Oliver Kuss conducted a randomized trial to compare off-pump versus on-pump  
46  
47 coronary artery bypass grafting which was sponsored in part by a grant from Medtronic,  
48  
49 Düsseldorf, Germany. There was no external funding of the project reported here and all  
50  
51 authors report no further conflicts of interest.  
52

53 **Word count** (excluding abstract and references): **2693**  
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3 **Ultramini-abstract**  
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5 Our systematic review of propensity score analyses to compare off-pump and on-pump  
6 surgery in coronary artery bypass grafting finds off-pump surgery superior in all of the  
7 assessed short-term outcomes. This advantage was statistically significant and clinically  
8 relevant for most outcomes, especially for mortality, the most valid criterion.  
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3 **Abstract**  
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5 **Objectives:** Despite numerous randomized and nonrandomized trials on off- and on-  
6 pump coronary artery bypass grafting, it remains open which method is superior. Patient  
7 selection and small sample sizes limit the evidence from randomized trials; lack of  
8 randomization limits those from nonrandomized trials. Propensity score analyses are  
9 expected to improve on at least some of these problems. We aimed to systematically  
10 review all propensity score analyses comparing off- and on-pump coronary artery  
11 bypass grafting  
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21 **Methods:** Propensity score analyses comparing off- and on-pump surgery were  
22 identified from eight bibliographic data bases, citation tracking, and a free web search.  
23  
24 Two independent reviewers abstracted data on eleven binary short-term outcomes.  
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28 **Results:** 35 of 58 initially retrieved propensity score analyses were included, accounting  
29 for a total of 123,137 patients. The estimated overall odds ratio was <1 for all outcomes,  
30 favouring off-pump surgery. This benefit was statistically significant for mortality [odds  
31 ratio: 0.69, 95%-CI: 0.60-0.75], stroke, renal failure, RBC transfusion ( $p < 0.0001$ ), wound  
32 infection ( $p < 0.001$ ), prolonged ventilation ( $p < 0.01$ ), inotropic ( $p = 0.02$ ) and IABP support  
33 ( $p = 0.05$ ). The odds ratios for myocardial infarction, atrial fibrillation, and re-operation for  
34 bleeding were not significant.  
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45 **Conclusions:** Our systematic review and meta-analysis of propensity score analyses  
46 finds off-pump surgery superior to on-pump surgery in all of the assessed short-term  
47 outcomes. This advantage was statistically significant and clinically relevant for most  
48 outcomes, especially for mortality, the most valid criterion. These results agree with  
49 previous systematic reviews of randomized and nonrandomized trials.  
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3 **Introduction**  
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5 Coronary artery disease (CAD) is still the most frequent cause of death in industrialized  
6 countries. In middle-aged cohorts, CAD has a prevalence of about 20%. More than  
7 50.000 patients undergo coronary artery bypass grafting (CABG) in Germany annually.  
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12 There is a trend to higher patient age and an increasing prevalence of comorbidities(1).  
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14 Today's surgical standard involves coronary revascularization with heart-lung machine  
15 support and cardioplegia-induced cardiac arrest, the so-called on-pump technique.  
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18 While this technique is routinely used, there are still morbidity and mortality risks,  
19 attributed to a systemic inflammatory response and to atheromatous macroembolization.  
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22 Because of these adverse side effects, the standard technique has been challenged in  
23 recent years by the emerging off-pump technique, which avoids the use of  
24 cardiopulmonary bypass and cardioplegia. The question which method is superior is one  
25 of the most hotly debated and polarizing issues in cardiac surgery(2).  
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31 Due to the public health as well as the economic impact of this question, a large number  
32 of randomized clinical trials (RCTs) were conducted. Most of them are summarized in  
33 systematic reviews(3;4). These systematic reviews show a trend towards an advantage  
34 of off-pump surgery in terms of the clinically relevant post-operative outcomes mortality,  
35 stroke and myocardial infarction. The observed effects are not always found to be  
36 statistically significant, mostly due to limited sample sizes.  
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47 In addition to these RCTs, a number of nonrandomized trials have been conducted. The  
48 respective data were also collected in a systematic review(5). It is commonly agreed that  
49 results from observational studies should not be used for making treatment  
50 recommendations. Nonrandomized studies, however, avoid two important deficiencies  
51 of RCTs. First, RCTs are frequently conducted in highly selected patients groups(6),  
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3 enrolling patients that are younger and healthier than the average patient(7). Second,  
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5 and this is of special concern in cardiac surgery, clinically relevant outcomes are only  
6  
7 rarely observed. That is, RCTs intended to find differences between treatments require  
8  
9 large sample sizes to detect differences between those rarely occurring outcomes. For  
10  
11 example, a study designed to detect a post-operative mortality reduction from 3% to 2%  
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13 with 80% power and 5% type I error would require more than 8000 patients. This  
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15 number should be compared to the sample size of the largest RCTs published up to  
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17 now(8), which included 388 patients. The number of patients included in the largest  
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19 systematic review of RCTs to date was 5537 (from 66 trials)(4). Therefore, not even the  
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21 largest systematic reviews on this topic would have enough power to find the postulated  
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23 difference in post-operative mortality.  
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29 Lack of randomization is of course the reason for distrusting observational studies as a  
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31 basis for treatment recommendations. Randomization ensures that all relevant (known  
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33 and unknown) prognostic and risk factors are balanced across treatment groups. In  
34  
35 observational studies, we have to rely on statistical methods like stratification, matching,  
36  
37 or multivariate adjustment to adjust for baseline differences in treatment groups.  
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41 A very promising technique for this adjustment is the so-called propensity score method,  
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43 which, if conducted with matching on the propensity score, achieves a kind of pseudo-  
44  
45 randomization. This ensures that at least the known and measured prognostic factors  
46  
47 are balanced. The propensity score method, proposed as early as in the 1980s(9), has  
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49 only recently been applied to clinical research, but sees increasing use, especially in  
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51 cardiology and cardiac surgery(10). Moreover, there are indications that the propensity  
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53 score method is statistically superior to the standard methods for multivariate  
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3 adjustment(11;12), especially when the number of events is low as in coronary artery  
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5 bypass grafting(12).  
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8 In the following we report on a systematic review and a meta-analysis comparing off-  
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10 pump and on-pump coronary artery bypass grafting explicitly including only propensity  
11  
12 score analyses.  
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## 14 15 16 **Methods**

### 17 18 **Search strategy**

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21 Searches were conducted independently by two persons (OK, biostatistician; BvS,  
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23 medical student) in the first week of February, 2006. Our search strategy was three-fold:  
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25 First, we searched the literature data bases MEDLINE, EMBASE, ACP Journal Club,  
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27 CCTR (Cochrane Central Register of Controlled Trials), CDSR (Cochrane Database of  
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29 Systematic Reviews), DARE (Database of Abstracts of Reviews of Effects), EBM  
30  
31 Reviews, and Web of Science for the keywords "Propensity" and "Off-Pump". Second,  
32  
33 we analysed the citations of six methodical papers(9;13-17) on propensity score  
34  
35 analysis via Web of Science (<http://www.isiknowledge.com>) as there is evidence that  
36  
37 failure to use citation tracking may cause bias due to overlooked studies(18). Third, we  
38  
39 searched the open web-based scientific data bases Google scholar  
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41 (<http://scholar.google.com>), Scirus (<http://www.scirus.com>), and Vivísimo clustering  
42  
43 (<http://vivisimo.com>), also with the keywords "Propensity" and "Off-Pump". Finally, we  
44  
45 checked the references of all available papers. Meeting abstracts and unpublished  
46  
47 reports were included. Authors of meeting abstracts were contacted by email for  
48  
49 additional information on the described studies. There were no restrictions on language  
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51 or time of publication.  
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5 **Data collection and management**  
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7 Full text versions of all initially retrieved publications were read independently by two  
8 reviewers (OK, BvS). Data were abstracted into a self-developed CRF, which had been  
9 tested in a small pilot review encompassing five studies. The data collected by both  
10 reviewers were entered in a data base and disagreements were located by automatic  
11 comparisons. Agreement between reviewers was checked on a previously selected  
12 subgroup of abstracted items (inclusion of study, high risk population, type of propensity  
13 analysis, reporting of confounders in the PS model). All disagreements on abstracted  
14 data were resolved by consensus and by discussion with a third reviewer (JB).  
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28 **Inclusion criteria**  
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31 Studies were included into the meta-analysis if they reported a comparison of at least an  
32 off-pump with an on-pump group and made use of a propensity score analysis for  
33 comparing treatments. Especially randomized controlled trials, observational studies  
34 without a propensity score analysis, and systematic reviews with no new original data  
35 were excluded. For inclusion, studies also had to provide at least one of the binary  
36 clinical outcomes mortality, stroke, myocardial infarction, atrial fibrillation, renal failure,  
37 inotropic support, RBC transfusion, wound infection, re-operation for bleeding, IABP  
38 support or prolonged ventilation. We considered only short-term or in-hospital outcomes,  
39 respectively. Studies with mere experimental outcomes were excluded. We always kept  
40 the outcome definitions of the original researchers. Double publications were removed,  
41 but we included data from the same study populations if these populations did not  
42 completely overlap in the propensity score analyses.  
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3 **Statistical methods**  
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5 For descriptive purposes we report absolute and relative frequencies for categorical  
6 variates. We used the odds ratio (OR) to describe treatment effects. From studies using  
7 regression adjustment or stratification in the propensity score analysis, we extracted the  
8 ORs with the corresponding confidence intervals directly from the text. In studies with a  
9 matched propensity score analysis, we used the absolute numbers of events and  
10 calculated ORs with confidence intervals with standard methods. Studies with zero  
11 events were corrected by the “reciprocal of the opposite treatment arm” method(19). In  
12 one study a relative risk (RR) was used to describe the treatment effect. As ORs and  
13 RRs are approximately equal for rare outcomes, we equated this RR with an OR.  
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16 For combining ORs from different studies, the random effects inverse-variance  
17 method(20) was applied, that is, ORs from the individual studies were combined as  
18 weighted averages. The random effects method, as compared to the fixed effects  
19 method, was chosen because it allows heterogeneous treatment effects between  
20 studies, and is slightly more conservative. However, as a sensitivity analysis we also  
21 present the fixed effects estimates. All calculations were performed with log-transformed  
22 ORs and results were retransformed for presentation. Though it is well known that the  
23 inverse-variance method has deficiencies, we emphasize that it is the only method  
24 applicable with our approach where absolute numbers of events are only available in  
25 cases of matched PS analyses. To facilitate interpretation of results, we also computed  
26 summary NNTs (number needed to treat with off-pump surgery to avoid one additional  
27 event) for each clinical outcome. NNTs were derived from the combined ORs using the  
28 ideas of Zhang and Yu(21). The required baseline risk data were calculated from the  
29 studies which reported a matched propensity score analysis, since absolute frequencies  
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3 are only available in these cases. To assess heterogeneity between studies, we  
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5 performed the standard test for homogeneity (based on Cochran's Q)(20), and also the  
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7 recently proposed  $I^2$  statistic.  
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10 Meta-regression on location of study (Northern America vs. others), type of PS analysis  
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12 (matching vs. non-matching), population risk (high risk vs. standard risk), volume per  
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14 year (defined as the number of patients divided by the length of the observation period,  
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16 but only in single centre studies), and percentage of off-pump patients in the general  
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18 study population (not necessarily equal to this percentage in the PS population) was  
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20 conducted to judge the influence of these factors on heterogeneity. For this meta-  
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22 regression, all outcomes were combined in a single data set, and the analysis was  
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24 adjusted for correlated (within study) outcomes by using a random effects model(20).  
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28 All statistical estimates are given with their 95% confidence intervals. The study data  
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30 base was programmed in Microsoft® ACCESS, all statistical analyses were conducted  
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32 with SAS®, 9.1.2. (SAS Institute Inc., Cary, NC, USA)  
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## 38 **Results**

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40 The initial search yielded 58 publications, 39 (66%) were found in the described  
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42 literature data bases, 8 (14%) by citation tracking, and 11 (19%) in the open scientific  
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44 data-bases.  
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48 35 of the initial 58 publications (60%) were included in the final analyses (table supp 2),  
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50 24 (69%) from the described literature data bases, 3 (9%) from citation tracking, and 8  
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52 (22%) from the open scientific data bases (Figure 1). Five publications were excluded  
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54 because they did not compare an off-pump with an on-pump group, 6 because they  
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56 made no or wrong use of the propensity score method; 4 were systematic reviews  
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3 without new original data. In 6 publications, no information was given on the prespecified  
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5 outcomes, and in 1 publication results from the PS analysis were given only narratively.  
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7 One publication was removed because of double publication.  
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10 Table 1 provides an overview of the included studies: Sixteen (46%) studies were  
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12 conducted in Europe, the remaining in Northern America. Authors of 19 (54%) PS  
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14 analyses reported on a high-risk population. The 35 studies account for a total of  
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16 123,137 observations, 49,718 (40.4%) procedures were conducted off-pump. In the  
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18 online supplement we give the estimated odds ratios for the single studies numerically  
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20 (table supp 1) and graphically (figure supp 1).  
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24 Table 2 reports the results of the meta-analyses for the specific outcomes. For all eleven  
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26 outcomes we find an estimated odds ratio below 1 in favour of off-pump surgery. This  
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28 effect is highly significant ( $p < 0.0001$ ) for the outcomes mortality, stroke, renal failure,  
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30 and RBC transfusion, significant for wound infection ( $p < 0.001$ ), prolonged ventilation  
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32 ( $p < 0.01$ ), IABP (0.01) and inotropic ( $p = 0.02$ ) support, and borderline significant for re-  
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34 operation for bleeding ( $p = 0.06$ ). Insignificant odds ratios near 1 are observed for  
35  
36 myocardial infarction and atrial fibrillation. Estimates from the fixed effects model  
37  
38 differed only slightly from the random effect estimates. Heterogeneity of studies for the  
39  
40 different outcomes varied widely. A very large heterogeneity was found for the outcomes  
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42 inotropic support and RBC transfusion, and large heterogeneity for re-operation and  
43  
44 atrial fibrillation. All other outcomes showed at most moderate or no heterogeneity.  
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50 In meta-regression, heterogeneity of treatment effects could not be explained by the  
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52 location of study (Northern America vs. Europe,  $p = 0.33$ ), type of PS analysis (matching  
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54 vs. non-matching,  $p = 0.99$ ), population risk (high risk vs. standard,  $p = 0.65$ ), volume per  
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3 year (p=0.55), or percentage of off-pump patients in the general study population  
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5 (p=0.25).  
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## 9 **Discussion**

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11 Our systematic review and meta-analysis of PS analyses finds off-pump surgery  
12 superior to on-pump surgery with respect to all of the assessed short-term outcomes.  
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14 This advantage was statistically significant and clinically relevant for most outcomes,  
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16 especially for the most valid outcome of mortality. This study is the first that  
17 systematically collected evidence only from propensity score analyses, a statistical  
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19 technique for analysing nonrandomized trials that finds increasing use in cardiac surgery  
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21 and that is especially suited for situations with rare outcomes.  
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28 Of course, our results have to be compared to the existing knowledge on the topic, and  
29 especially to previous meta-analyses of randomized (3-5) and nonrandomized trials  
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31 (5)(Figure 2). It should be noted that there is only a small overlap (n=7) of our studies  
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33 and the observational studies included in the Wijeyesundera et al.(5) review. As such, our  
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35 results can be considered roughly independent of the results of Wijeyesundera et al.  
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37 Compared to the randomized trials we find our results not contradicting their results, our  
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39 estimates being well within the confidence intervals of estimates from randomized trials.  
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41 Of course, confidence intervals from RCTs are larger, reflecting smaller sample sizes.  
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43 We also expect randomized trials to be performed in selected populations, and certain  
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45 differences between RCTs and our PS analyses are not surprising. Compared to  
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47 previous nonrandomized trials, there is agreement in most of the outcomes. But we also  
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49 find a non-overlapping confidence interval for stroke, and only succinct overlapping  
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51 intervals for atrial fibrillation and RBC transfusion. It should be noted, however, that  
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3 large sample sizes in both the Wijeyesundera et al. review as well as in our study  
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5 guarantee small confidence intervals, and not all significant differences can be  
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7 considered clinically relevant.  
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10 Our systematic review, which is the first to explicitly include only propensity score  
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12 analyses, also contributes to the body of methodical knowledge. Only about 70% of the  
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14 studies were found in the standard literature data bases. This underlines the importance  
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16 of a free web search and, especially important for PS analyses, citation tracking of  
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18 classical papers describing the method of propensity score. We were not surprised by  
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20 the results of our meta-regression on the influence of type of PS analysis. Although  
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22 current guidelines favour the use of matching(22) we found no differences between  
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24 studies using matching and those using other techniques for adjusting for the propensity  
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26 score. This was already stressed in the initial PS paper by Rosenbaum and Rubin(9).  
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28 However, and somewhat contrary to common perception, we found no differences in  
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30 effects from high risk and low risk populations.  
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36 Any systematic review and meta-analysis is vulnerable to publication bias, that is, the  
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38 selective reporting of trials depending on study results. Funnel plots were proposed to  
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40 graphically assess publication bias. We drew funnel plots for all our outcomes. All plots  
41  
42 indicated no publication bias (see figure supp 2). Moreover, as the comparison between  
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44 off- and on-pump in CABG is such a hotly debated issue(2), we expect most (or  
45  
46 hopefully all) of the studies to be submitted and published, as predicted by Sedrakyan et  
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48 al(3).  
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52 Our study has some limitations. We only reported short-term outcomes; especially data  
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54 on graft patency or revascularization rates are missing. This is problematic because new  
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56 evidence suggests that the on-pump technique may result in better graft patency(23).  
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3 Graft patency data were omitted because they are rarely reported, and frequently  
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5 patients are lost to follow-up.  
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8 It is tempting to speculate why most of the CABG procedures are still performed on-  
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10 pump. Off-pump surgery is technically more demanding than the on-pump technique  
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12 performed under cardioplegic arrest. Only a small number of centres train their staff in  
13  
14 the former technique. Therefore, off-pump surgery is part of just a limited number of  
15  
16 surgeons' armamentarium. This contrasts with the experience in other centres, e.g.  
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18 Emory University in Atlanta, where more than 80% of surgical revascularizations are  
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20 performed off-pump(24). In countries such as Japan or India, the percentage is >  
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22 50%(25). Authors from these countries have demonstrated that an off-pump program  
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24 can be established without risk and with good patient outcomes. As we show in our  
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26 paper, the evidence remains ambiguous at this time. This is also reflected in the  
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28 American Heart Association's scientific statement paper(2). Lack of a compelling  
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30 indication is certainly a significant reason for not abandoning the standard technique in  
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32 favour of one that is highly challenging.  
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38 To finally conclude, current evidence from nonrandomized trials of any design suggests  
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40 that off-pump coronary artery bypass grafting is superior, at least with respect to short-  
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42 term outcomes. This finding is in line with the collected evidence from the present  
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44 randomized trials. In the future large ongoing randomized trials, among them the  
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46 CORONARY trial from Canada (4700 patients planned, expected end of recruiting  
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48 phase: May 2014, ClinicalTrials.gov Identifier: NCT00463294) and the ROOBY trial  
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50 (26)(2200 patients planned, expected end of recruiting phase: November 2008) will  
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52 contribute to the definite answer. Long-term follow-up of patients from current trials will  
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54 provide additional evidence.  
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3 **Acknowledgements**  
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5 We are grateful to Lena Minning, Mareike Kunze, and Jörn Klauke (Institute of Medical  
6  
7 Epidemiology, Biostatistics, and Informatics, Faculty of Medicine, University of Halle-  
8  
9 Wittenberg, Halle (Saale), Germany) for designing and programming the study data  
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3 **Figure legends**  
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6 Figure 1: Flow diagram of initially retrieved and eventually included studies  
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11 Figure 2: Results from previous meta-analyses of randomized trials (RCT), observational  
12 studies (OBS), and our propensity-score analyses (PS) for all our pre-specified  
13 outcomes. For the meta-analyses of RCTs we give the result from the most recent meta-  
14 analyses. Results are given as Odds ratios with 95% confidence intervals, in cases  
15 where the previous meta-analyses reported relative risks, we recalculated the OR by  
16 using the formula of Zhang and Yu(21).  
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Table 1: Included studies

Study	Observation period	Location of Study	of Study centres (No.)	Are the patients from a high-risk group (as reported from the authors)? If yes, which risk	Average patient age	PS analysis population		General population
						Gender (% male)	Proportion of Off-Pump Patients (%)	Proportion of Off-Pump Patients (%)
Ascione 2002	04/96-04/01	England	1	Overweight (BMI ≥ 25)	63.0	79.5	23.7 (674/ 2844)	23.7 (674/ 2844)
Ascione 2003	04/96-08/02	England	1	Severe LV dysfunction (EF < 30%)	65.3	90.4	29.6 (74/ 250)	29.6 (74/ 250)
Boening 2003	01/98-12/01	Germany	1	No	65.5	--	42.6 (72/ 169)	20.5 (133/ 650)
Calafiore 2003a	11/94-12/01	Italy	1	No	64.4	83.2	50.0 (961/ 1922)	--
Calafiore 2003b	11/94-12/01	Italy	1	EuroSCORE ≥ 6	70.1	71.7	50.0 (510/ 1020)	--
Calafiore 2005	11/94-12/01	Italy	1	No	62.6	86.1	50.0 (597/ 1194)	--
Chukwuemeka 2005	00/95-00/03	Canada	1	Preoperative renal dysfunction	70.3	64.4	25.0 (146/ 584)	5.5 (158/ 2869)
Frankel 2005	01/98-06/02	USA	1	No	--	--	50.0 (2141/ 4282)	41.2(3646/ 8843)
Grunkemeier 2002	00/98-00/00	USA	9	No	66.5	73.1	31.8 (990/ 3110)	15.0 (1194*/ 7955)
Ivanov 2006	00/96-00/02	Canada	1	No	--	--	50.0 (503/ 1006)	4.5 (514/ 11368)
Karthik 2003	04/97-03/02	England	2	Non-elective CABG	65.0	72.4	50.4 (417/ 828)	48.1 (1813/ 3771)
Karthik 2004	04/97-03/02	England	2	Peripheral vascular disease	65.6	79.4	50.0 (211/ 422)	48.1 (1813/ 3771)
Lamy 2005	03/01-12/02	Canada	14	No	64.6	--	50.0 (1233/ 2466)	49.5 (1657/ 3350)
Lee 2006	07/99-01/04	Canada	1	No	--	--	50.0 (165/ 330)	48.1 (290/ 603)
Lu 2005	04/97-04/03	Great Britain	1	LMS disease	65.7	80.5	21.6 (259/ 1197)	21.6 (259/ 1197)
Mack 2004a	00/99-00/01	USA	4	Multivessel disease	--	--	50.0 (5774/ 11548)	41.9 (7283/ 17401)
Mack 2004b	01/98-03/02	USA	82	Women	68.8	0.0	50.0 (3688/7376)	19.4 (4250/ 21902)
Magee 2002	01/98-07/00	USA	2	Multivessel disease	--	--	33.3 (1606*/4818)	23.5 (1983/ 8449)
Magee 2003	01/99-12/00	USA	--	More than two grafts	68.0	68.6	50.0 (16937/33874)	8.8 (17969/ 204602)
Meco 2004	--	Italy	--	Age > 75	--	--	65.5 (78/ 119)	--
Oo 2003	04/97-09/02	England	1	EuroScore ≥ 6	71.4	72.6	50.4 (196/ 389)	--
Pandey 2005	04/97-09/02	England	1	No	61.9	80.8	50.0 (360/ 720)	17.4 (987/ 5679)
Patel 2002a	04/97-05/01	England	2	No	62.0	78.1	48.0 (1117/ 2327)	48.0 (1117/ 2327)
Patel 2002b	04/97-03/01	England	4	No	62.8	79.1	7.7 (843/ 10941)	7.7 (843/ 10941)
Sabik 2002	01/97-06/00	USA	1	No	66.0	69.5	50.0 (406/ 812)	13.0 (481/ 3712)
Saunders 2004	00/96-00/02	USA	1	Functional mitral regurgitation	--	--	50.0 (127/ 254)	20.6 (222/ 1078)

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6	Seif 2005	00/93-00/04	USA	1	No	--	--	25.0 (1913/ 7641)	--
7	Sharony 2004	06/93-10/02	USA	1	Atheromatous Aortic disease	73.0	68.8	50.0 (245/ 490)	28.5 (281/ 985)
8	Srinivasan 2004	04/97-09/02	England	1	Diabetes	65.2	77.0	19.6 (186/ 951)	19.6 (186/ 951)
9	Stamou 2002	06/94-12/00	USA	1	No	--	--	50.0 (1670/ 3340)	22.3 (2320/ 10389)
10	Stamou 2004	10/98-06/01	USA	1	No	--	--	50.0 (1833*/ 3666*)	44.6 (2477/ 5554)
11	Stamou 2004	10/98-06/01	USA	1	No	--	--	50.0 (1833*/ 3666*)	44.6 (2477/ 5554)
12	Stamou 2005	01/00-12/00	USA	1	Parsonnet score $\geq$ 20 points	71.0	48.3	61.4 (315/ 513)	61.4 (315/ 513)
13	Stamou 2006	01/00-10/03	USA	2	Non-elective CABG	--	--	50.0 (2013/ 4026)	36.3 (2273/ 6260)
14	Weerasinghe 2005	01/01-11/03	England	3	Multivessel disease	64.5	73.7	40.0 (817/ 2041)	40.0 (817/ 2041)
15	Williams 2005	01/98-09/03	USA	1	No	63.5	69.8	11.3 (641/ 5667)	11.3 (641/ 5667)
16									

17 \*: Numbers estimated from the text

Table 2: Results of meta-analyses

Response	Number of Studies (Patients)	OR [95%-CI] p-Value, REM	p-value Homogeneity	I <sup>2</sup> (%)	NNT [95%-CI]	OR [95%-CI] p-Value, FEM
Mortality	28 (100,066)	0.69 [0.60-0.75] p<0.0001	0.18	14	189 [155, 251]	0.70 [0.65-0.76] p<0.0001
Stroke	22 (55,290)	0.42 [0.33-0.54] p<0.0001	0.16	16	104 [90, 132]	0.49 [0.41-0.58] p<0.0001
Myocardial infarction	14 (35,951)	0.97 [0.73-1.30] p=0.86	0.06	32	2685 [254, -229]	0.91 [0.74-1.11] p=0.35
Atrial fibrillation	11 (29,343)	0.92 [0.80-1.05] p=0.20	0.01	51	79 [33, -143]	0.85 [0.80-0.91] p<0.0001
Renal failure	17 (38,866)	0.60 [0.51-0.70] p<0.0001	0.21	11	82 [67, 110]	0.59 [0.53-0.66] p<0.0001
Inotropic support	7 (6,153)	0.59 [0.38-0.90] p=0.02	p<0.0001	82	8 [5, 41]	0.65 [0.56-0.75] p<0.0001
RBC transfusion	8 (16,685)	0.36 [0.25-0.54] p<0.0001	p<0.0001	91	9 [7, 13]	0.49 [0.44-0.54] p<0.0001
Wound infection	13 (33,030)	0.59 [0.45-0.77] p<0.001	0.97	0	314 [235, 553]	0.59 [0.45-0.77] p<0.0001
Re-operation for bleeding	14 (39,480)	0.76 [0.57-1.02] p=0.06	<0.01	50	195 [107, -2753]	0.69 [0.59-0.81] p<0.0001
IABP support	7 (9,703)	0.60 [0.41-0.89] p=0.01	0.18	10	245 [164, 904]	0.57 [0.43-0.76] p<0.001
Prolonged ventilation	6 (8,675)	0.71 [0.56-0.89] p<0.01	0.32	0	116 [77, 312]	0.74 [0.61-0.90] p=0.002

Figure 1

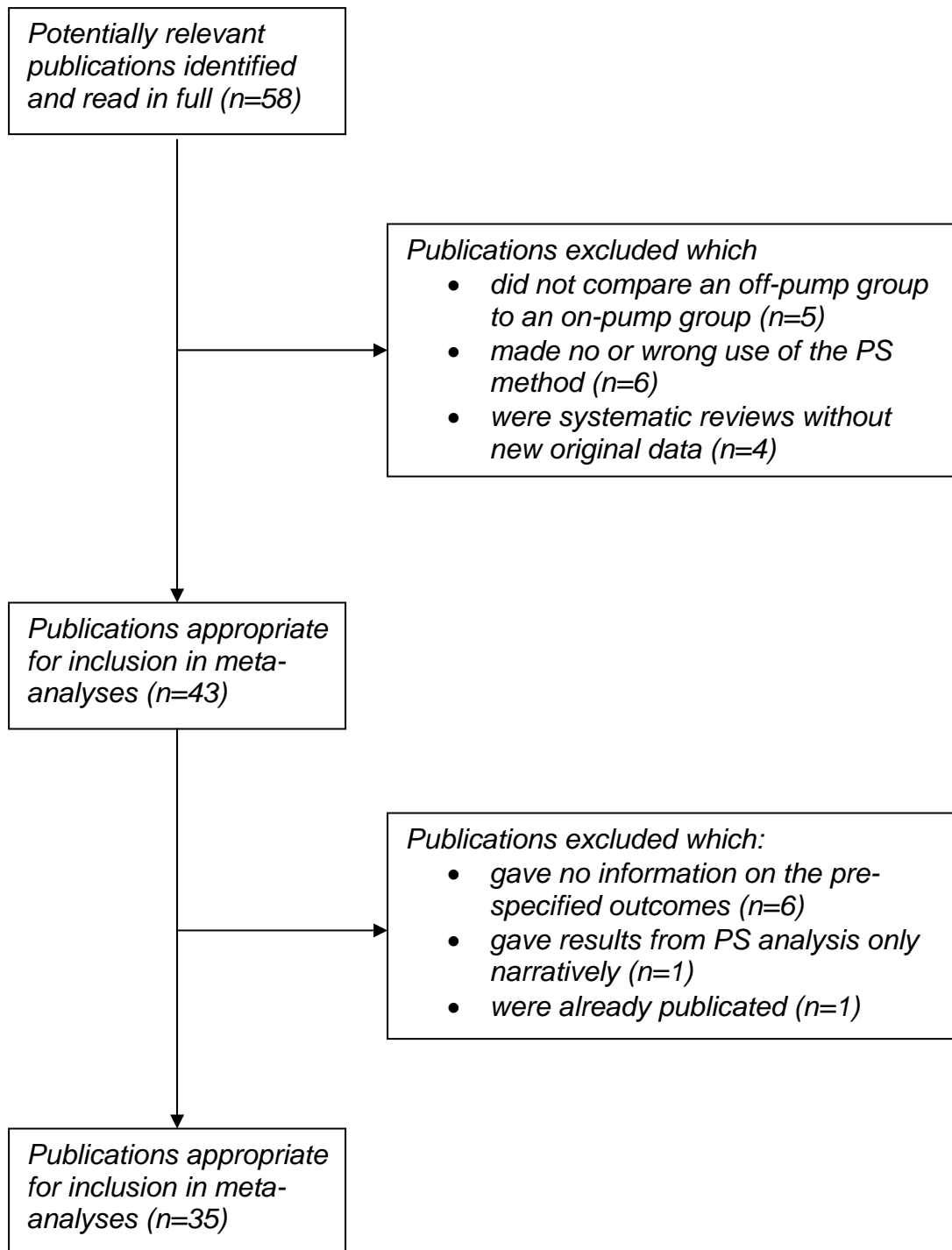
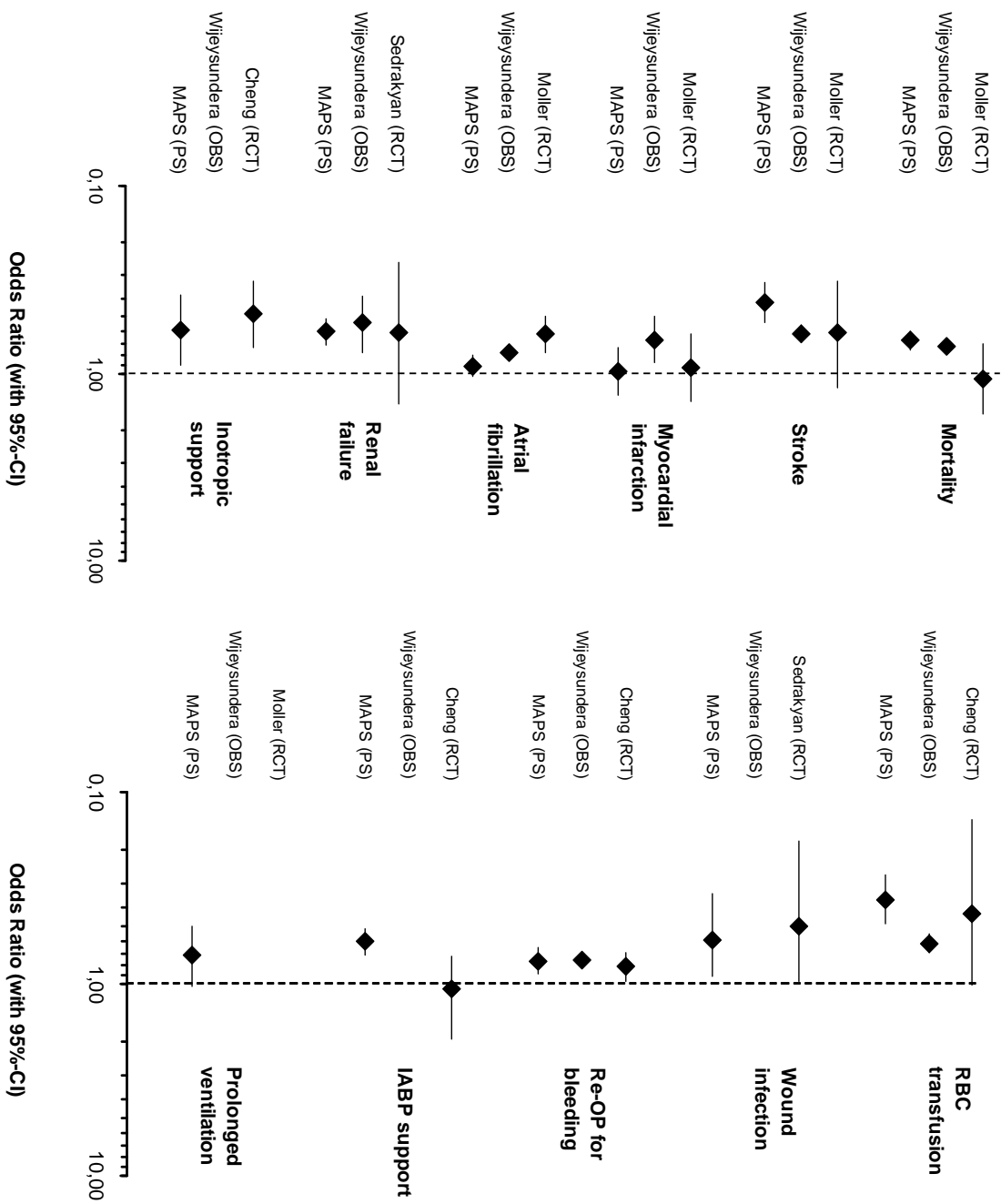


Figure 2



## SUPPLEMENTAL MATERIAL

**Table supp 1:** Results from the single studies. Given are the odds ratios [with 95%-CI] and the relative weights (in %), with which the respective studies was weighted in the overall random effect (RE) or fixed effect (FE) estimator

Mortality			
Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.37 [0.18-0.77]	2.29	1.32
Ascione 2003	1.45 [0.51-4.17]	1.15	0.63
Boening 2003	2.74 [0.24-30.9]	0.23	0.12
Calafiore 2003a	0.41 [0.21-0.79]	2.77	1.63
Calafiore 2003b	0.52 [0.28-0.96]	3.04	1.82
Calafiore 2005	0.63 [0.24-1.64]	1.38	0.77
Chukwuemeka 2005	0.90 [0.24-3.31]	0.76	0.41
Ivanov 2006	0.71 [0.22-2.26]	0.96	0.52
Karthik 2003	0.83 [0.36-1.93]	1.76	0.99
Karthik 2004	0.98 [0.35-2.75]	1.20	0.66
Lamy 2005	0.90 [0.48-1.69]	2.96	1.76
Lu 2005	0.95 [0.41-2.18]	1.77	1.00
Mack 2004a	0.54 [0.43-0.68]	12.35	13.25
Mack 2004b	0.81 [0.63-1.04]	11.39	11.29
Magee 2002	0.53 [0.32-0.83]	4.73	3.07
Magee 2003	0.83 [0.72-0.96]	17.83	35.88
Meco 2004	0.09 [0.01-0.83]	0.28	0.15
Oo 2003	0.57 [0.21-1.56]	1.26	0.69
Pandey 2005	0.39 [0.12-1.27]	0.94	0.51
Patel 2002b	0.59 [0.31-1.12]	2.86	1.69
Sabik 2002	0.50 [0.09-2.73]	0.45	0.24
Saunders 2006	0.87 [0.30-2.47]	1.16	0.64
Sharony 2004	0.54 [0.29-1.03]	2.86	1.70
Srinivasan 2004	0.53 [0.18-1.55]	1.10	0.60
Stamou 2004	0.63 [0.50-0.83]	11.08	10.72
Stamou 2005	0.48 [0.23-0.98]	2.29	1.32
Stamou 2006	0.81 [0.57-1.15]	7.48	5.67
Williams 2005	0.53 [0.22-1.24]	1.66	0.93



### Stroke

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Calafiore 2003a	0.26 [0.09-0.80]	4.21	2.68
Calafiore 2003b	0.18 [0.05-0.63]	3.48	2.14
Calafiore 2005	1.25 [0.33-4.69]	3.12	1.89
Chukwuemeka 2005	0.00 [0.00->100]	0.00	0.00
Grunkemeier 2002	0.37 [0.17-0.77]	7.64	5.86
Ivanov 2006	0.11 [0.01-0.87]	1.37	0.77
Karthik 2003	0.36 [0.08-1.53]	2.56	1.51
Karthik 2004	0.09 [0.02-0.50]	2.19	1.27
Lamy 2005	0.49 [0.23-1.06]	7.43	5.63
Lee 2006	0.14 [0.02-1.13]	1.33	0.74
Lu 2005	0.17 [0.02-1.31]	1.35	0.75
Mack 2004a	0.64 [0.48-0.85]	18.56	40.44
Oo 2003	0.17 [0.03-0.93]	1.94	1.11
Pandey 2005	0.00 [0.00->100]	0.00	0.00
Patel 2002a	0.24 [0.08-0.74]	4.16	2.64
Patel 2002b	0.26 [0.09-0.70]	4.77	3.12
Sabik 2002	0.60 [0.14-2.51]	2.68	1.59
Sharony 2004	0.27 [0.09-0.84]	4.09	2.59
Srinivasan 2004	0.15 [0.02-0.96]	1.56	0.88
Stamou 2002	0.56 [0.33-1.00]	11.09	10.69
Stamou 2006	0.60 [0.33-1.08]	10.28	9.35
Williams 2005	0.78 [0.33-1.87]	6.19	4.37

### Myocardial infarction

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	2.29 [0.91-5.76]	6.59	4.86
Ascione 2003	1.61 [0.71-3.85]	7.38	5.79
Boening 2003	1.01 [0.22-4.66]	3.05	1.77
Calafiore 2003a	0.66 [0.30-1.48]	7.83	6.39
Calafiore 2003b	0.76 [0.33-1.76]	7.51	5.96
Calafiore 2005	1.51 [0.42-5.36]	4.14	2.57
Chukwuemeka 2005	1.13 [0.43-2.94]	6.27	4.52
Karthik 2003	0.72 [0.26-1.98]	5.79	4.02
Karthik 2004	0.96 [0.24-3.92]	3.55	2.12
Lamy 2005	2.09 [1.18-3.69]	11.18	12.74
Mack 2004a	0.58 [0.40-0.85]	14.80	29.60
Patel 2002b	0.81 [0.44-1.51]	10.42	10.89
Sabik 2002	0.60 [0.14-2.51]	3.38	2.00
Srinivasan 2004	0.68 [0.31-1.48]	8.11	6.78

### Atrial fibrillation

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.73 [0.51-1.04]	7.95	3.25
Ascione 2003	0.85 [0.39-1.87]	2.45	0.67
Calafiore 2003a	0.64 [0.49-0.84]	10.61	5.70
Calafiore 2003b	0.79 [0.56-1.12]	8.25	3.47
Karthik 2003	1.30 [0.89-1.88]	7.51	2.95
Karthik 2004	1.39 [0.84-2.30]	5.03	1.63
Lu 2005	1.11 [0.81-1.53]	9.03	4.08
Mack 2004a	0.79 [0.73-0.87]	17.64	54.44
Pandey 2005	1.03 [0.73-1.45]	8.43	3.60
Seif 2005	0.91 [0.78-1.07]	15.05	16.89
Srinivasan 2004	1.21 [0.85-1.72]	8.06	3.32

### Renal Failure

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.90 [0.44-1.85]	4.20	2.50
Ascione 2003	0.70 [0.28-1.79]	2.64	1.50
Calafiore 2003a	0.80 [0.31-2.03]	2.61	1.48
Chukwuemeka 2005	0.81 [0.22-2.96]	1.42	0.77
Karthik 2003	0.44 [0.22-0.90]	4.34	2.60
Karthik 2004	0.59 [0.26-1.34]	3.31	1.92
Lamy 2005	0.23 [0.08-0.69]	2.00	1.11
Lu 2005	0.92 [0.42-1.98]	3.66	2.14
Mack 2004a	0.50 [0.41-0.61]	22.42	32.79
Mack 2004b	1.07 [0.64-1.78]	7.48	4.99
Oo 2003	0.35 [0.14-0.89]	2.66	1.51
Pandey 2005	0.61 [0.25-1.48]	2.83	1.62
Sabik 2002	0.00 [0.00->100]	0.00	0.00
Sharony 2004	0.66 [0.23-1.88]	2.10	1.17
Srinivasan 2004	0.38 [0.16-0.94]	2.88	1.64
Stamou 2006	0.52 [0.37-0.72]	13.57	11.63
Weerasinghe 2005	0.69 [0.56-0.85]	21.87	30.64

### Inotropic support

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.81 [0.63-1.03]	16.71	35.80
Ascione 2003	0.22 [0.08-0.56]	9.33	2.29
Boening 2003	1.33 [0.71-2.47]	12.92	5.57
Chukwuemeka 2005	1.27 [0.87-1.85]	15.59	15.35
Lu 2005	0.49 [0.35-0.69]	15.93	18.78
Oo 2003	0.35 [0.21-0.59]	14.11	8.11
Pandey 2005	0.33 [0.23-0.49]	15.42	14.10

### RBC transfusion

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.40 [0.30-0.52]	12.98	13.27
Calafiore 2003b	0.59 [0.42-0.81]	12.63	9.26
Frankel 2005	0.50 [0.39-0.58]	13.38	25.49
Oo 2003	0.12 [0.07-0.22]	10.72	3.06
Pandey 2005	0.15 [0.10-0.23]	11.93	5.56
Sabik 2002	0.64 [0.48-0.84]	12.97	13.05
Srinivasan 2004	0.21 [0.14-0.32]	12.02	5.88
Williams 2005	0.80 [0.66-0.99]	13.36	24.42

### Wound infection

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.83 [0.42-1.66]	14.96	14.96
Ascione 2003	0.84 [0.16-4.55]	2.52	2.52
Boening 2003	1.00 [0.00->100]	0.01	0.01
Chukwuemeka 2005	0.86 [0.18-4.16]	2.82	2.82
Karthik 2004	0.50 [0.11-2.33]	3.03	3.03
Lu 2005	0.73 [0.33-1.61]	11.25	11.25
Mack 2004a	0.54 [0.31-0.97]	21.33	21.33
Mack 2004b	0.50 [0.21-1.17]	9.78	9.78
Pandey 2005	0.41 [0.19-0.92]	11.17	11.17
Sabik 2002	0.12 [0.02-0.99]	1.63	1.63
Sharony 2004	0.50 [0.04-5.53]	1.22	1.22
Srinivasan 2004	0.65 [0.29-1.42]	11.20	11.20
Williams 2005	0.56 [0.23-1.34]	9.10	9.10

### Re-operation for bleeding

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.56 [0.28-1.10]	8.50	5.12
Ascione 2003	0.50 [0.10-2.50]	2.66	0.92
Boening 2003	0.44 [0.04-4.33]	1.44	0.46
Frankel 2005	0.80 [0.53-1.24]	12.10	13.26
Karthik 2003	1.72 [0.73-4.04]	6.68	3.27
Karthik 2004	1.03 [0.27-3.95]	3.58	1.33
Lu 2005	1.39 [0.63-3.07]	7.30	3.82
Mack 2004a	0.46 [0.35-0.60]	14.39	32.94
Pandey 2005	0.56 [0.23-1.36]	6.45	3.08
Patel 2002b	1.45 [0.90-2.31]	11.41	10.78
Sabik 2002	0.69 [0.26-1.84]	5.67	2.52
Sharony 2004	0.12 [0.02-0.98]	1.69	0.55
Srinivasan 2004	0.74 [0.25-2.23]	4.85	2.00
Stamou 2006	0.70 [0.50-1.00]	13.29	19.94

### IABP support

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.39 [0.14-1.15]	10.73	7.49
Ascione 2003	1.59 [0.57-4.55]	10.96	7.69
Boening 2003	0.01 [0.00->100]	0.04	0.02
Karthik 2003	0.44 [0.21-0.96]	17.03	14.37
Lu 2005	1.07 [0.52-2.18]	18.33	16.16
Oo 2003	0.48 [0.19-1.23]	12.85	9.52
Stamou 2006	0.46 [0.30-0.71]	30.06	44.74

### Prolonged ventilation

Study	OR [95%-CI]	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.86 [0.67-1.10]	47.62	59.46
Karthik 2003	0.58 [0.31-1.08]	12.10	9.38
Lamy 2005	0.61 [0.36-1.04]	16.24	13.18
Lu 2005	0.83 [0.43-1.61]	10.94	8.39
Oo 2003	0.36 [0.15-0.86]	6.54	4.79
Srinivasan 2004	0.52 [0.22-1.26]	6.55	4.80

**Table supp 2:** List of included papers

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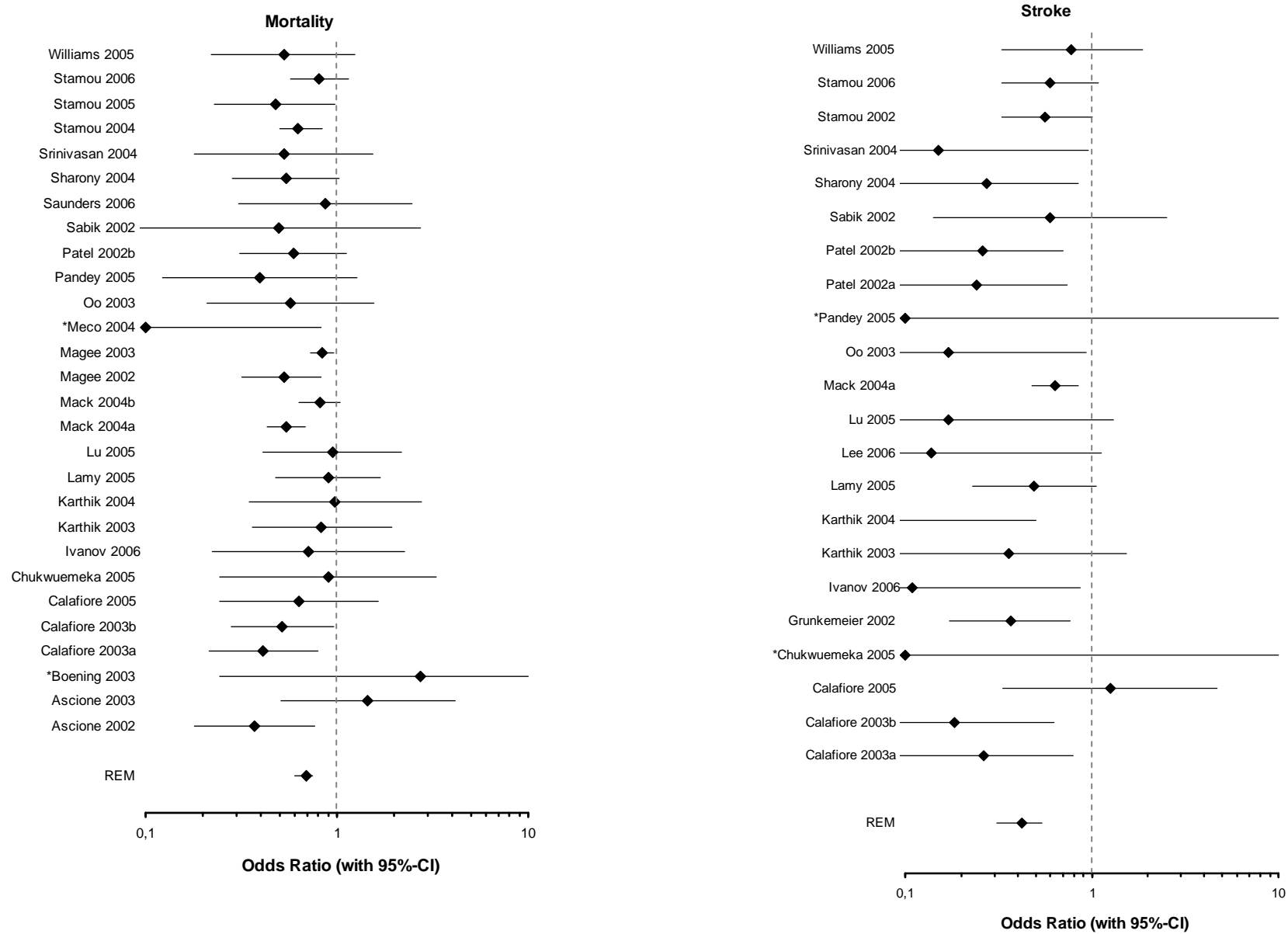
Weerasinghe A, Athanasiou T, Al Ruzzeh S, Casula R, Tekkis PP, Amrani M, Punjabi P, Taylor K, Stanbridge R, Glenville B. Functional renal outcome in on-pump and off-pump

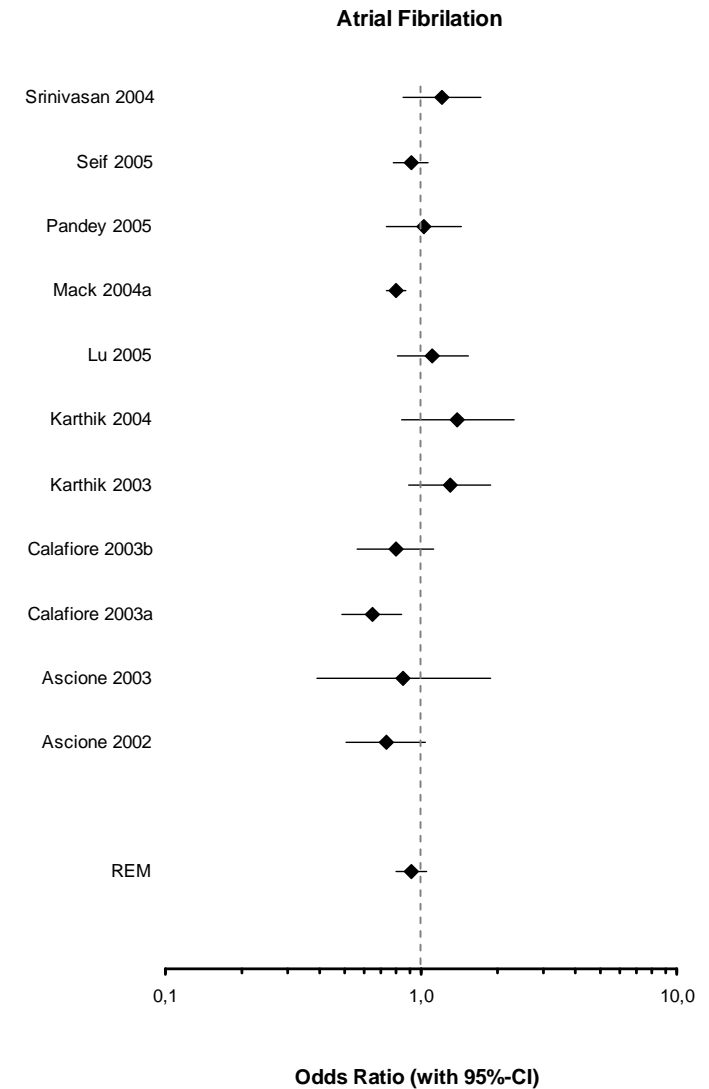
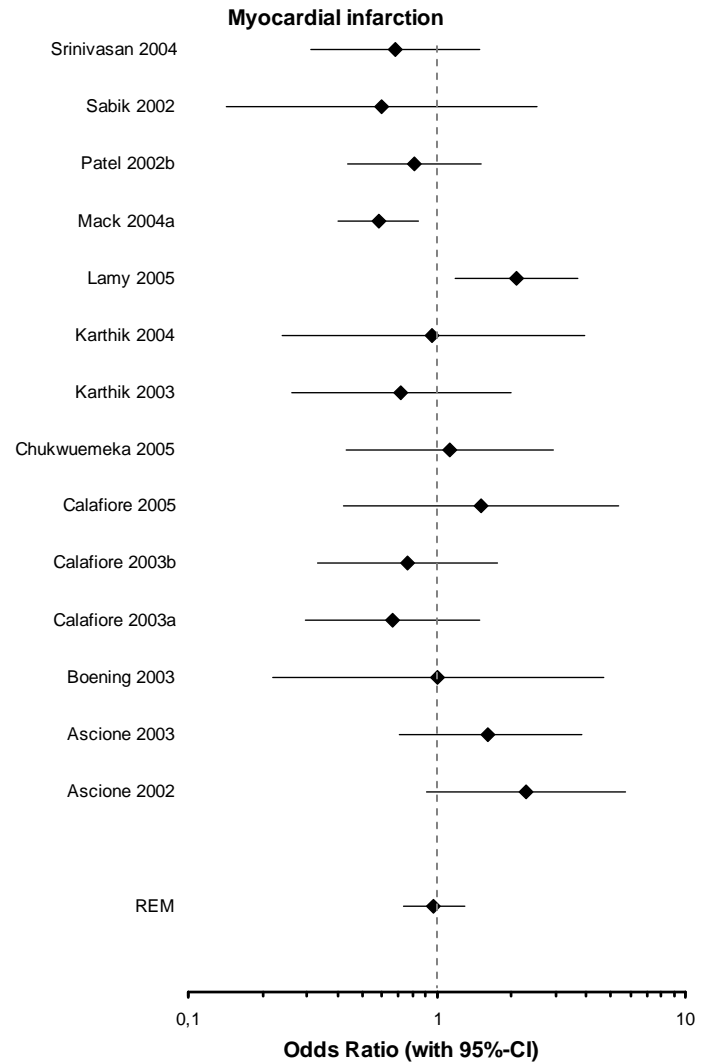


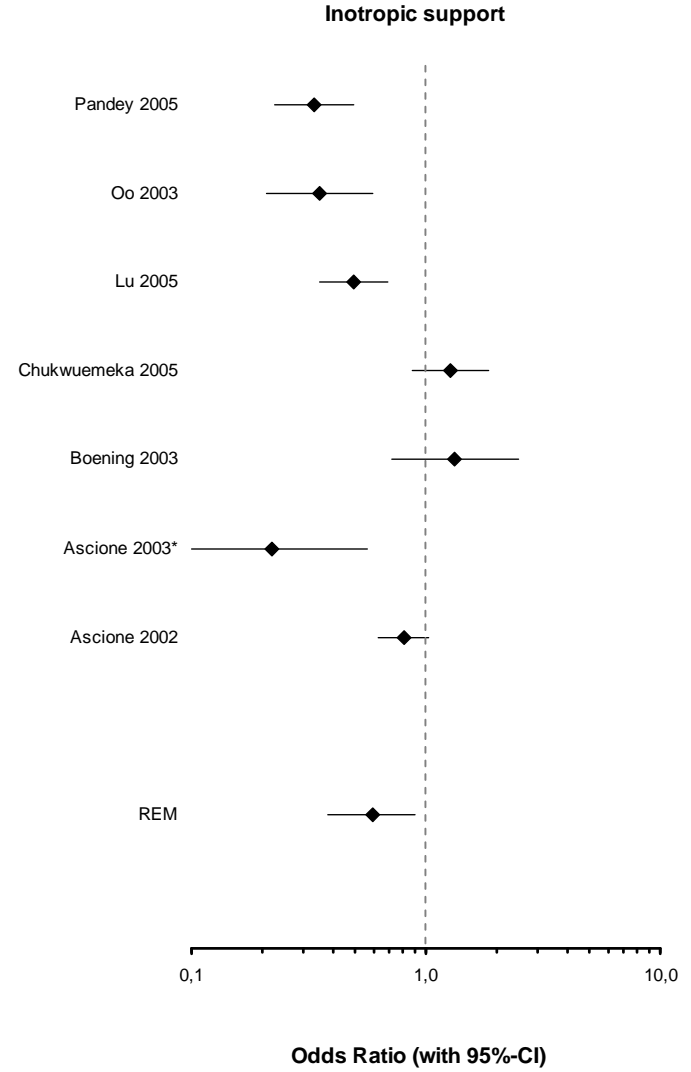
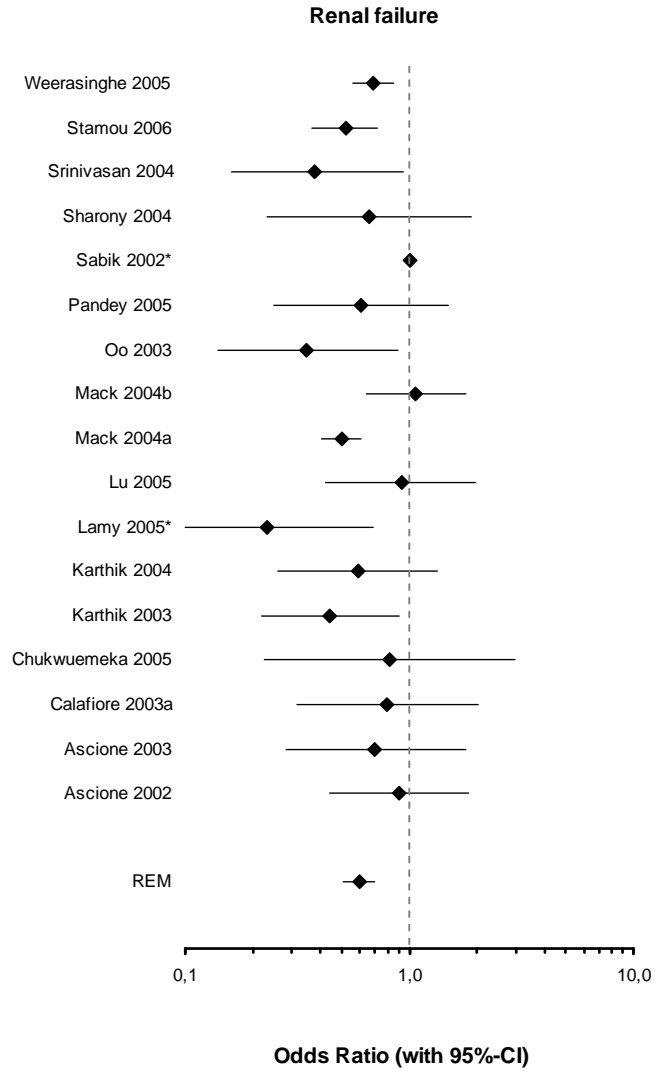
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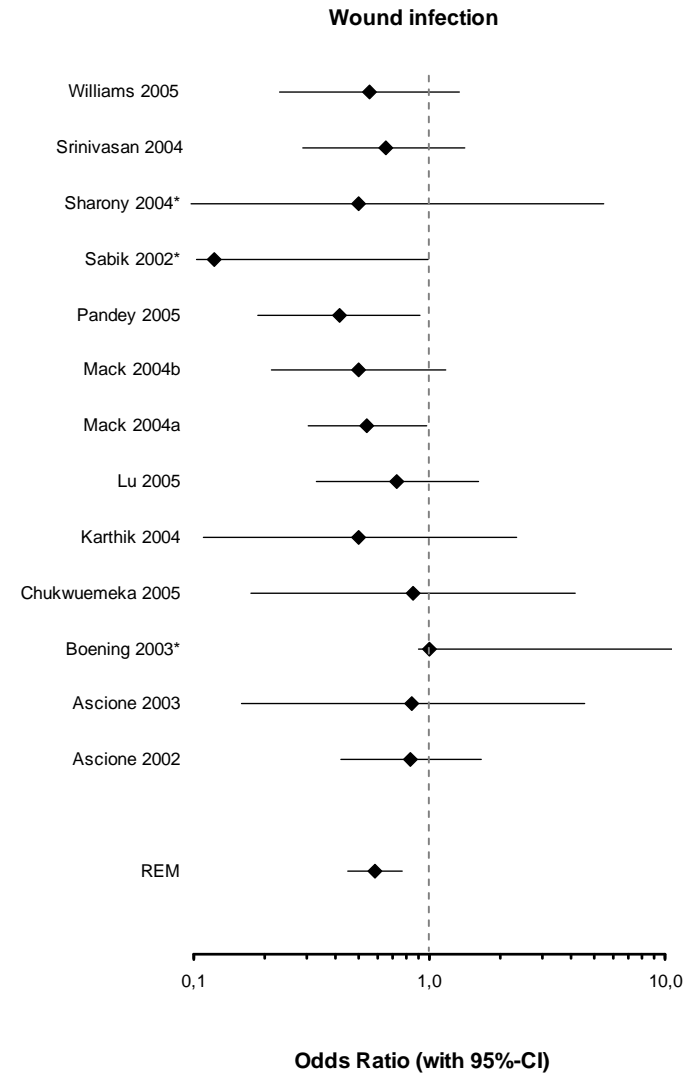
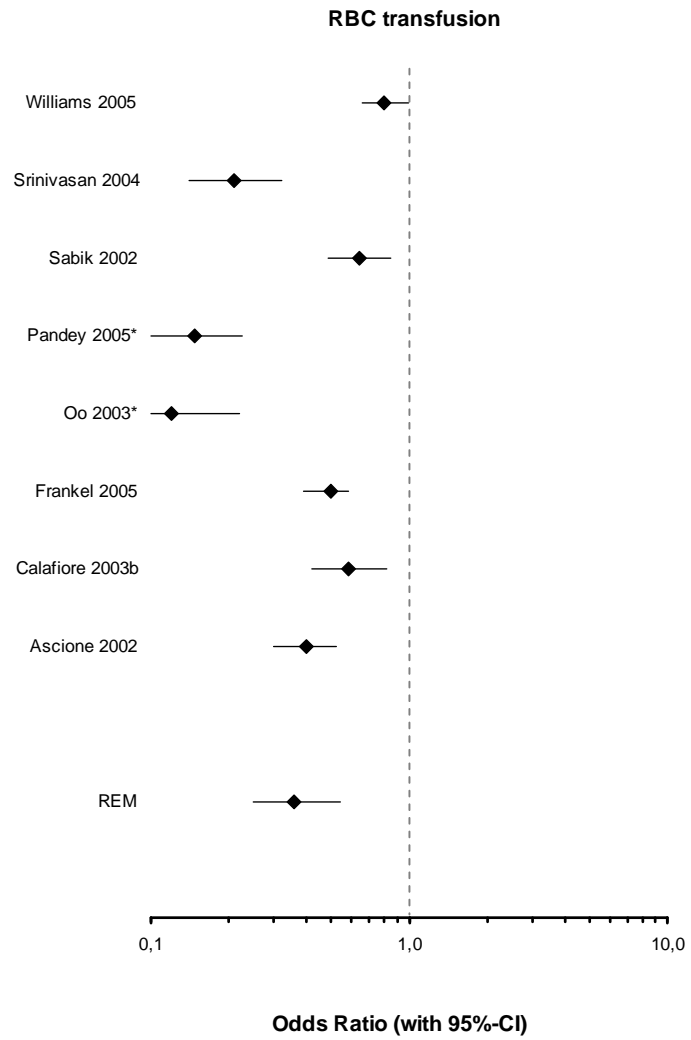
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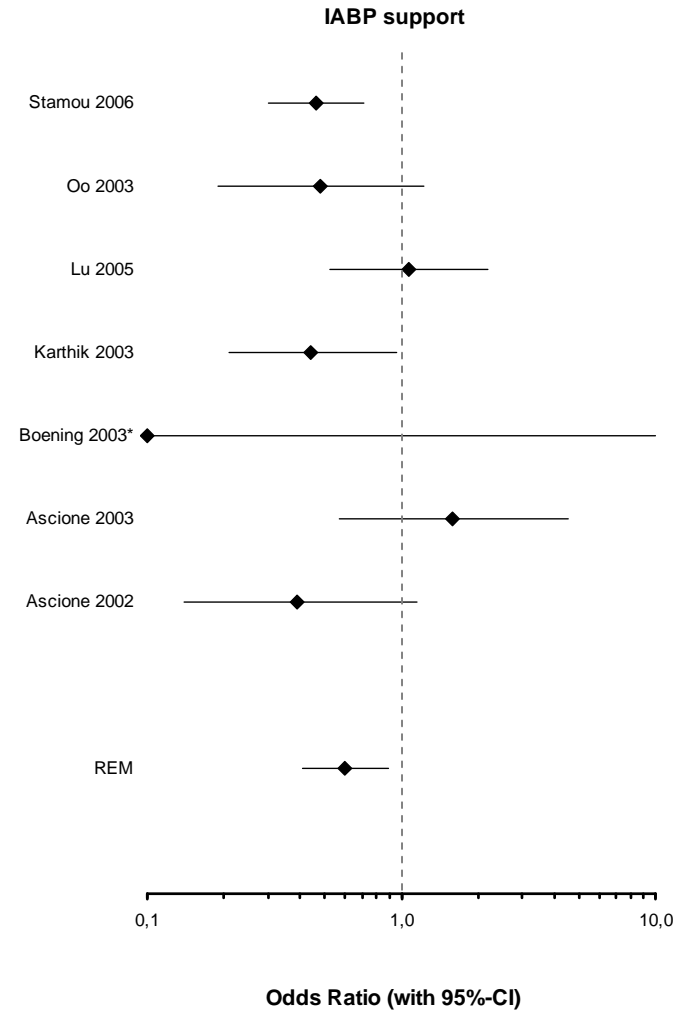
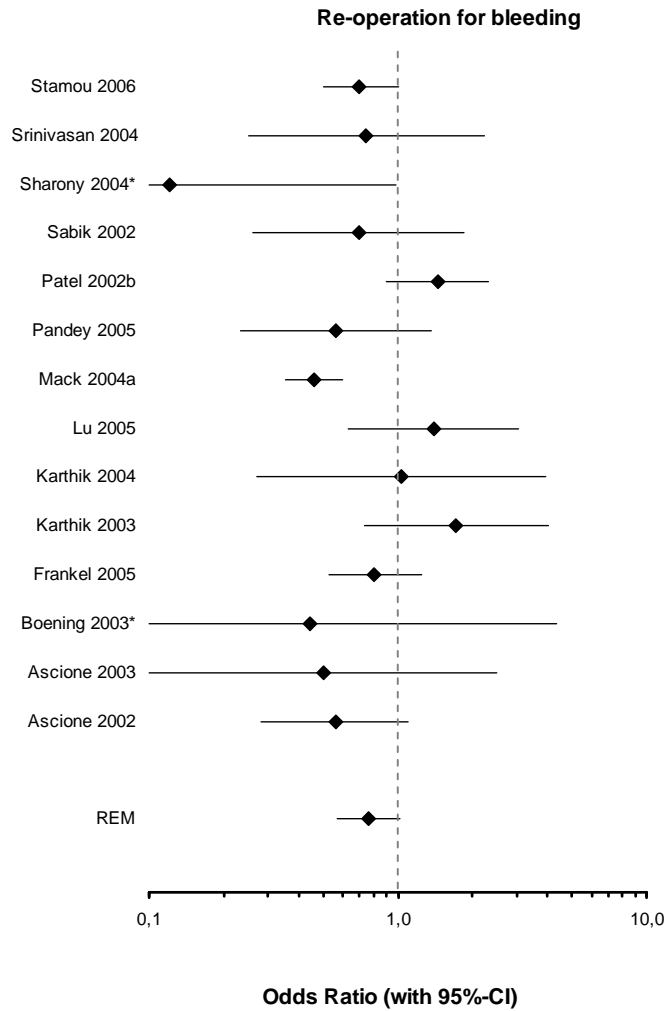
**Figure supp 1:** Forest-plots for all outcomes. To enhance readability, x-axes are only drawn from 0.1 to 10. Confidence intervals having values outside this range are marked by an asterisk(\*).











### Prolonged ventilation

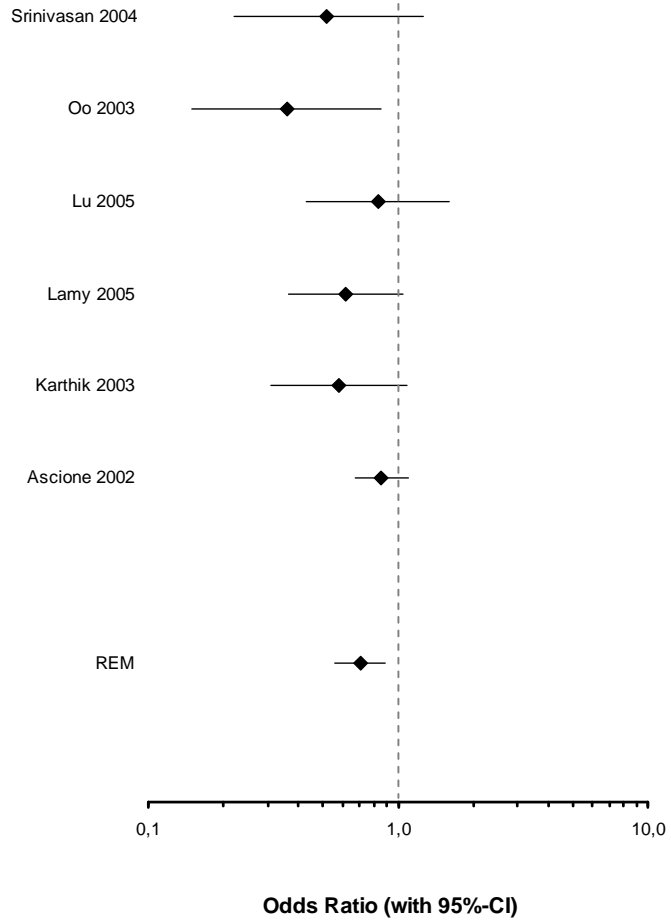
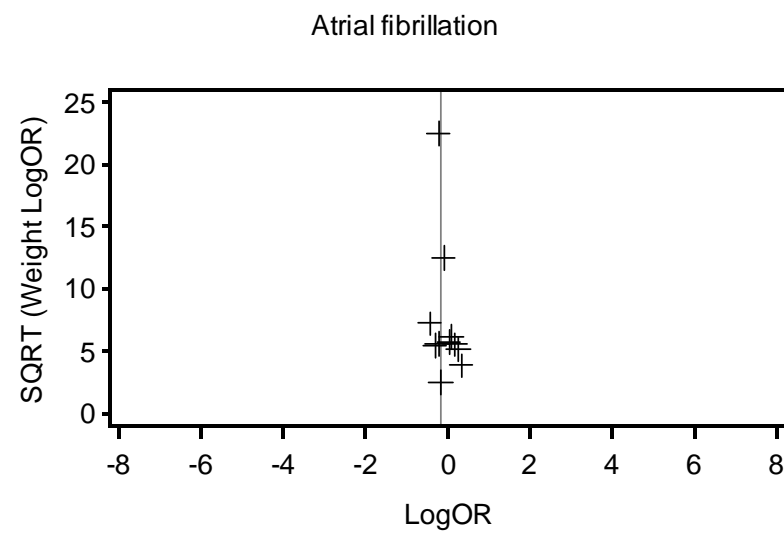
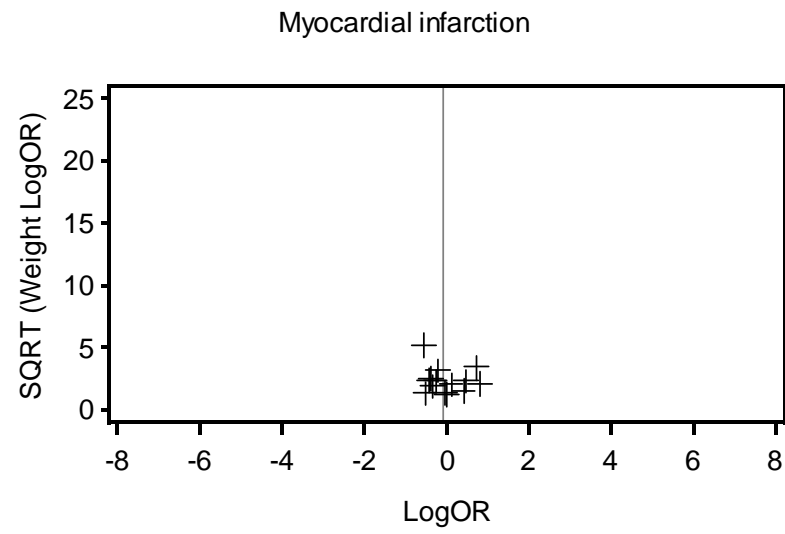
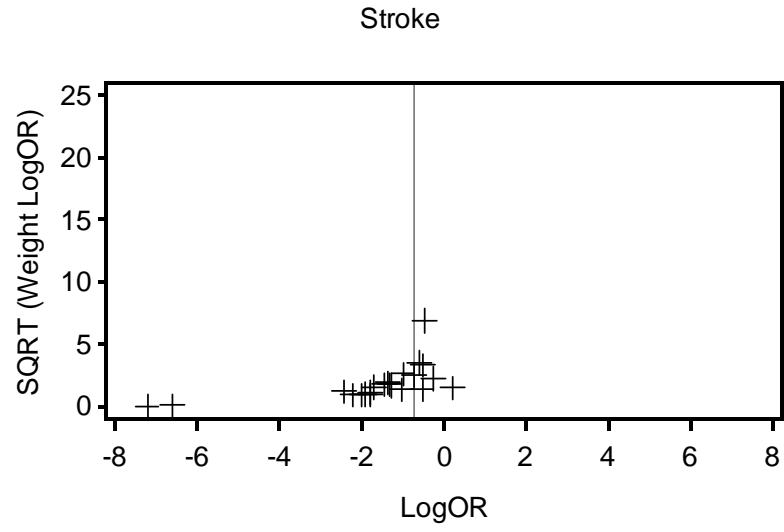
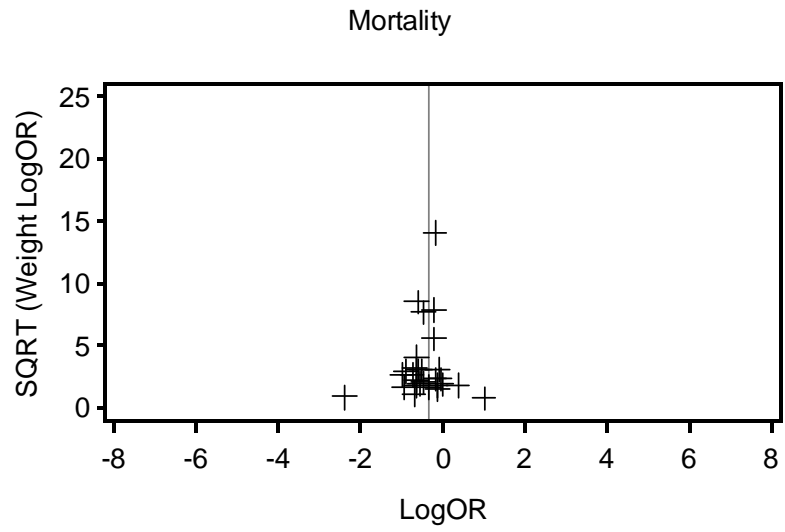
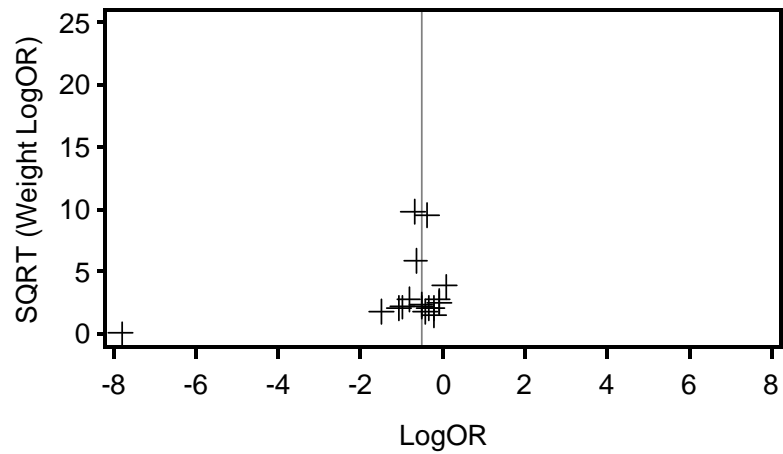


Figure supp 2: Funnel-plots for all outcomes

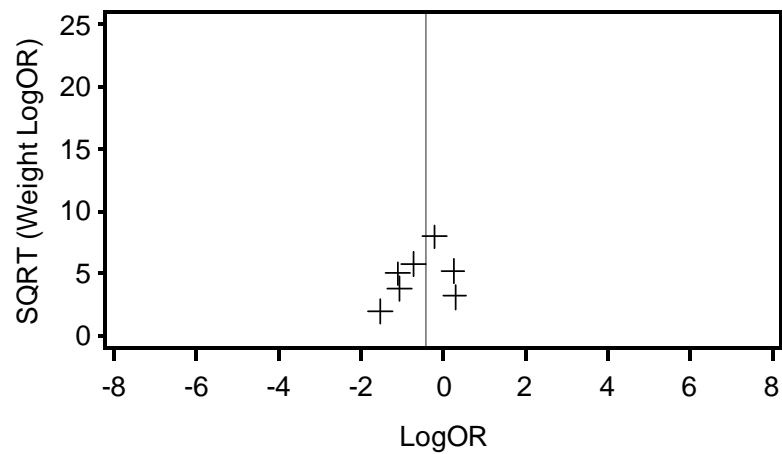




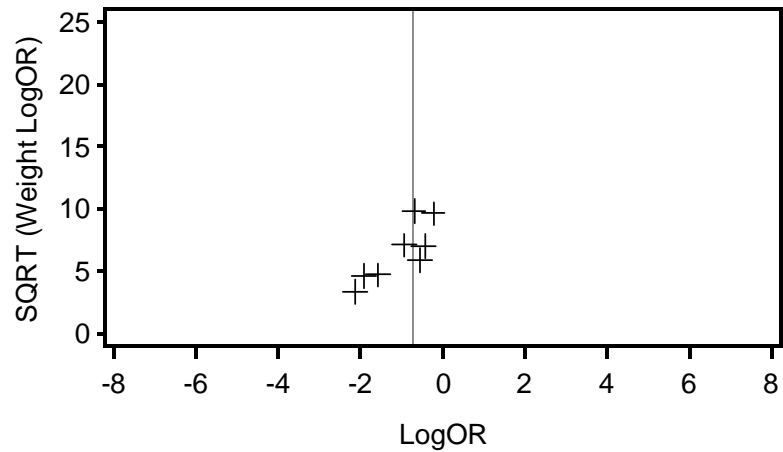
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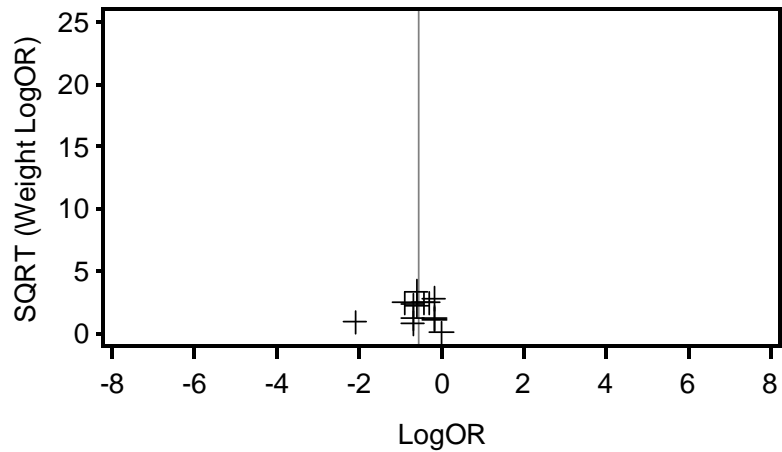
Inotropic support



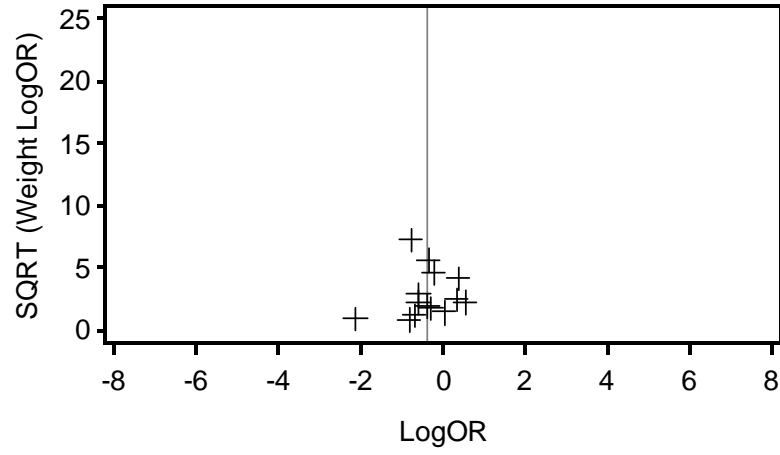
RBC transfusion



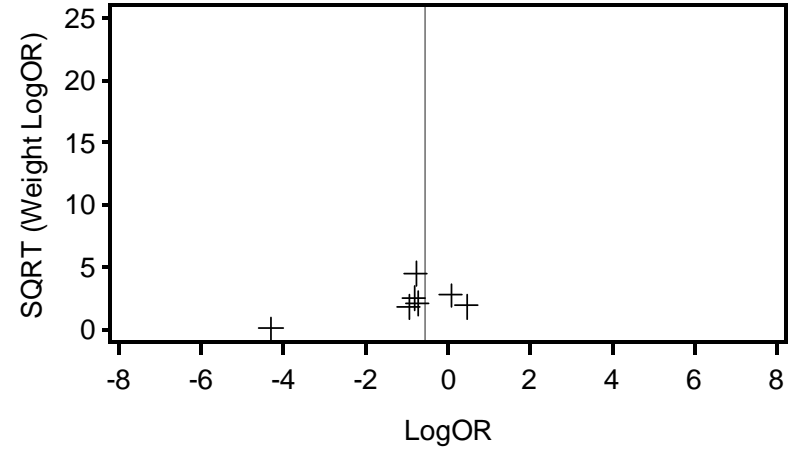
Wound infection



Re-operation for bleeding



IABP support



Prolonged ventilation

