De-implementation of low-value care in hip and knee arthroplasty

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Chapter 2

Cell Salvage in Hip and Knee Arthroplasty: A Meta-Analysis of Randomized Controlled Trials

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Abstract

Background: Cell salvage is used to reduce allogeneic red blood-cell (RBC) transfusions in total hip arthroplasty (THA) and total knee arthroplasty (TKA). We performed a meta-analysis to assess the effectiveness of cell salvage to reduce transfusions in THA and TKA separately, and to examine whether recent trials change the conclusions from previous meta-analyses.

Methods: We searched MEDLINE through January 2013 for randomized clinical trials evaluating the effects of cell salvage in THA and TKA. Trial results were extracted using standardized forms and pooled using a random-effects model. Methodological quality of the trials was evaluated using the Cochrane Collaboration's tool for risk-of-bias assessment.

Results: Forty-three trials (5631 patients) were included. Overall, cell salvage reduced the exposure to allogeneic RBC transfusion in THA (risk ratio [RR], 0.66; 95% confidence interval [CI], 0.51 to 0.85) and TKA (RR, 0.51; 95% CI, 0.39 to 0.68). However, trials published in 2010 to 2012, with a lower risk of bias, showed no significant effect of cell salvage in THA (RR, 0.82; 95% CI, 0.66 to 1.02) and TKA (RR, 0.91; 95% CI, 0.63 to 1.31), suggesting that the treatment policy regarding transfusion may have changed over time.

Conclusions: Looking at all trials, cell salvage still significantly reduced the RBC exposure rate and the volume of RBCs transfused in both THA and TKA. However, in trials published more recently (2010 to 2012), cell salvage reduced neither the exposure rate nor the volume of RBCs transfused in THA and TKA, most likely explained by changes in blood transfusion management.

Introduction

Blood loss in total hip arthroplasty (THA) and total knee arthroplasty (TKA) may necessitate allogeneic red blood cell (RBC) transfusion. Concerns regarding the safety of allogeneic RBC transfusions have led to the use of perioperative cell salvage, intended to reduce allogeneic blood use.[1]

Previous meta-analyses of randomized controlled trials concluded that cell salvage is effective at reducing the need for allogeneic RBC transfusion, without adverse impact on clinical outcomes in orthopaedic surgery.[1-3] None of those meta-analyses compared the effectiveness of cell salvage in THA with those in TKA. However, it can be hypothesized that the effects in THA and TKA might be different, given differences in anatomy, size of the wound, and surgical technique. Furthermore, as there is less surrounding tissue that can absorb blood lost in TKA, reinfusion drains are likely to collect blood more effectively in TKA than in THA, leading to a larger reduction in the risk for allogeneic RBC transfusion in TKA

Furthermore, several large randomized controlled trials that have been published more recently indicated that cell salvage did not reduce the need for allogeneic RBC transfusion.[4-6] Various developments in orthopaedic surgery may have resulted in these different outcomes of recent trials. First, there has been a trend toward using more restrictive transfusion thresholds. In the last decade there has been an increased awareness that the traditional transfusion trigger, a haemoglobin concentration of <10 g/dL (~6.2 mmol/L),[7] is no longer tenable because of transfusion risks and escalating costs. Therefore, transfusion in many centres is now based on clinical symptoms, overall patient health, and a more restrictive haemoglobin level of 8 g/dL (~5.0 mmol/L) in uncomplicated cases.[8] Second, the treatment policy in control groups may be different in recent trials, particularly with respect to the routine use of closed suction drainage since Parker et al.[9] showed in 2007 that this was associated with higher transfusion rates in THA and TKA without any effect on the rates of wound infections or hematomas compared with using no drain. Third, changes in the timing of cell salvage potentially affected the outcomes of recent trials. Currently, cell salvage devices can reinfuse blood collected both intraoperatively and postoperatively (i.e., perioperatively), whereas the first cell salvage devices could only reinfuse blood collected during surgery. Finally, surgical techniques might have changed. For example, concerns have been raised about the use of tourniquet control in TKA as complications due to its use can delay recovery.[10] Because of these concerns, more recent studies may not have had routine tourniquet use, leading to lower effectiveness of cell salvage in TKA. All of these developments underline the need to update the available evidence.

The aims of the present study were 1) to assess the effectiveness of cell salvage in reducing allogeneic RBC transfusion in THA and TKA separately, and 2) to examine whether the addition of recent trials changes the conclusions regarding the effectiveness of cell salvage as described by Carless et al.[1] To our knowledge, the meta-analysis by Carless et al. was not only the largest meta-analysis but also the most complete one, as the other meta-analyses only reviewed specific types of cell salvage or patient groups.[2,3]

Materials and Methods

Study selection

All articles involving orthopaedic procedures identified by Carless et al.[1] were retrieved. Next, we searched MEDLINE from January 2009 through January 2013 using the same search strategy as Carless et al. (see Appendix 1). Furthermore, the references of included articles were checked and experts in the field were contacted for additional studies.

Articles were eligible for inclusion if they reported results of randomized controlled trials using cell salvage in THA and/or TKA in adult patients (at least eighteen years old). Studies with a combination of active comparisons were only included if both the intervention and control groups were equally exposed to the active treatment (active treatment plus cell salvage compared with active treatment only), as was done by Carless et al.[1] There were no language restrictions.

Data extraction and outcome measures

Study characteristics and outcomes were extracted for all thirty-five studies involving orthopaedic procedures from Carless et al.[1], using standardized forms, to show the results for THA and TKA separately. If data could not be extracted separately for THA and TKA, the authors of the study were contacted. If they did not respond, the article was placed in the category “not able to split or other orthopaedic procedures.”

Next, the titles of newly identified trials from our search strategy were screened by two reviewers, and full-text articles were retrieved. The reviewers independently selected trials that met the inclusion criteria, with disagreements resolved by consensus. For each selected trial, the reviewers independently extracted the following study characteristics: type of surgery (THA or TKA), transfusion threshold used (none, ≤8.0 g/dL [~5.0 mmol/L] [restrictive], or >8.0 g/dL [~5.0 mmol/L] [traditional]), treatment policy in the control group (no drain, use of closed suction wound drainage after surgery, or another active intervention), timing of cell salvage (intraoperative, perioperative, or postoperative), use

of tourniquet control (in TKA), and primary outcomes (the number of patients exposed to allogeneic RBC transfusion, and the volume of RBCs transfused per patient [with transfusion data expressed in millilitres converted to RBC units by dividing by 300]).

Risk of bias assessment

Included studies were assessed for methodological quality, using the Cochrane Collaboration's tool for assessing risk of bias, by two independent reviewers. The domains assessed were sequence generation, allocation concealment, and blinding[11]. Disagreement was resolved by consensus.

Statistical Analysis

Data were extracted and entered into Review Manager (RevMan) (version 5.2.13; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Dichotomous and continuous data were pooled across trials using a random-effects model. Differences in outcome between the experimental group (receiving cell salvage) and the control group were expressed as a risk ratio (RR) for dichotomous outcomes and as a weighted mean difference (WMD) for continuous outcomes, along with a 95% confidence interval (CI). Thus, an RR of <1 indicates that cell salvage reduces the risk for allogeneic blood transfusion, and a negative WMD value indicates a reduction in the volume of RBCs transfused. If neither the standard deviation nor the standard error of the mean was reported for continuous data, the trial was not included. Differences were considered significant if $p < 0.05$. In addition, data in RevMan were arranged into three groups according to the decade of publication to assess changes in the effectiveness of cell salvage over time.

Subgroup Analysis and Investigation of Heterogeneity

Statistical heterogeneity was examined with the I^2 test. The I^2 test describes the percentage of the total variation across studies that is due to heterogeneity rather than chance (with 0% indicating no observed heterogeneity, and >50% indicating substantial heterogeneity)[11]. Four exploratory analyses of subgroups (defined prior to the study) were performed; these involved the transfusion threshold used, treatment policy in the control group, timing of cell salvage, and use of tourniquet control (in TKA).

Source of funding

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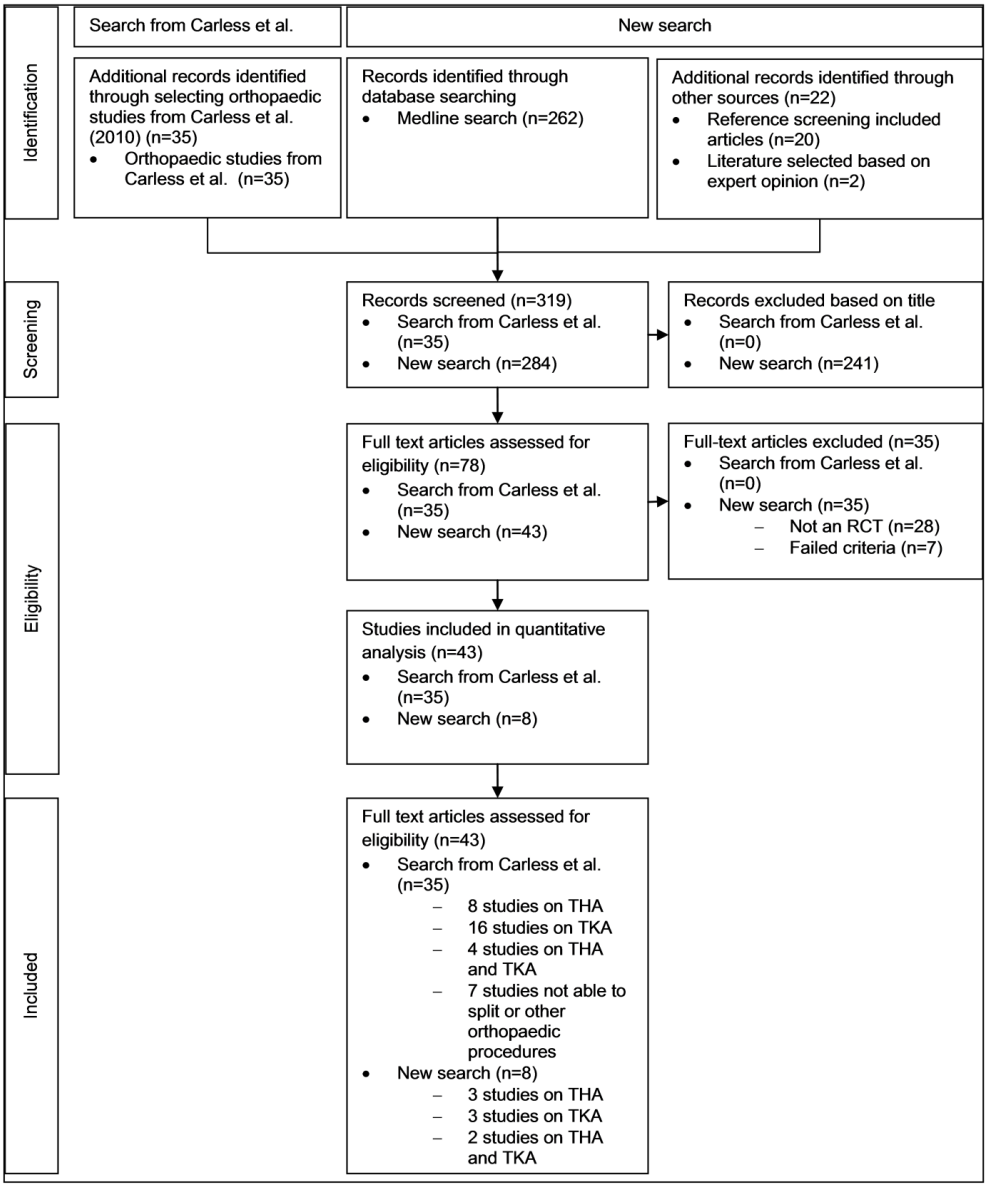

Figure 1: Literature search results

Results

We identified 284 titles in our search: 262 from MEDLINE and twenty-two after checking references and consulting experts (Figure 1). Review of these titles identified forty-three potentially eligible studies. Based on the full articles, eight studies fulfilled the inclusion criteria and were included in addition to the thirty-five studies identified by Carless et al.[1] Of these forty-three included studies (5631 patients), eleven included only THA,[4,12-21] nineteen included only TKA,[5,22-39] six included both THA and TKA,[6,40-44] and seven studies could not be split up or included other orthopaedic procedures.[45-51] Appendix 2 summarizes the characteristics and the risk-of-bias assessment of all included studies.

Risk-of-Bias Assessment

The risk of bias due to inadequate sequence generation was judged to be low in fifteen studies (Table 1). Five studies had adequate allocation concealment (that is, low risk of bias). Three studies were judged to be double-blinded. Recent studies more often seemed to have lower risk of bias (that is, higher quality) compared with studies published before 2010, particularly with respect to sequence generation and allocation concealment.

Table 1: Risk of bias of included studies

		Studies from Carless et al.		New search
	Total, N = 43	Published 1990-1999, n=22	Published 2000-2009, n=13	Published 2010-2012, n=8
Adequate sequence generation				
- Yes, i.e. low risk of bias	15	6	4	5
- No, i.e. high risk of bias	5	2	2	1
- Unclear, i.e. uncertain risk of bias	23	14	7	2
Adequate allocation concealment				
- Yes, i.e. low risk of bias	5	-	-	5
- No, i.e. high risk of bias	11	5	5	1
- Unclear, i.e. uncertain risk of bias	27	17	8	2
Adequate blinding				
- Yes, i.e. low risk of bias	3	1	-	2
- No, i.e. high risk of bias	39	21	13	5
- Unclear, i.e. uncertain risk of bias	1	-	-	1

Effects of Cell Salvage in Orthopaedic Surgery

Figure 2 shows the effect of cell salvage on the RBC exposure rate in orthopaedic surgery from Carless et al.[1]. In THA, cell salvage reduced the RBC exposure rate by 44% (RR, 0.56; 95% CI, 0.38 to 0.82; n = 11) and in TKA by 56% (RR, 0.44; 95% CI, 0.32 to 0.60; n = 18). Cell salvage did not significantly reduce the volume of RBCs transfused in either THA (WMD, −0.97; 95% CI, −1.94 to 0.00; n = 5) or TKA (WMD, −0.42; 95% CI, −0.92 to 0.09; n = 6).

Effects of Cell Salvage in THA

Overall, cell salvage still reduced the RBC exposure rate by 34% (RR, 0.66; 95% CI, 0.51 to 0.85) in THA when recent trials were included, without substantial heterogeneity among studies (I^2 = 50%). However, as shown in figure 3, the date of the study appeared to have an effect, with more recent studies (2010 to 2012) showing no significant effect of cell salvage (RR, 0.82; 95% CI, 0.66 to 1.02), without any heterogeneity (I^2 = 0%).

Overall, cell salvage in THA reduced the volume of RBCs transfused (WMD, −0.67; 95% CI, −1.08 to −0.27; I^2 = 91%). Again, an effect of the study date was observed, with recently published studies (2010 to 2012) showing a nonsignificant reduction in the volume of RBCs transfused (WMD, −0.13; 95% CI, −0.30 to 0.04; I^2 = 39%).

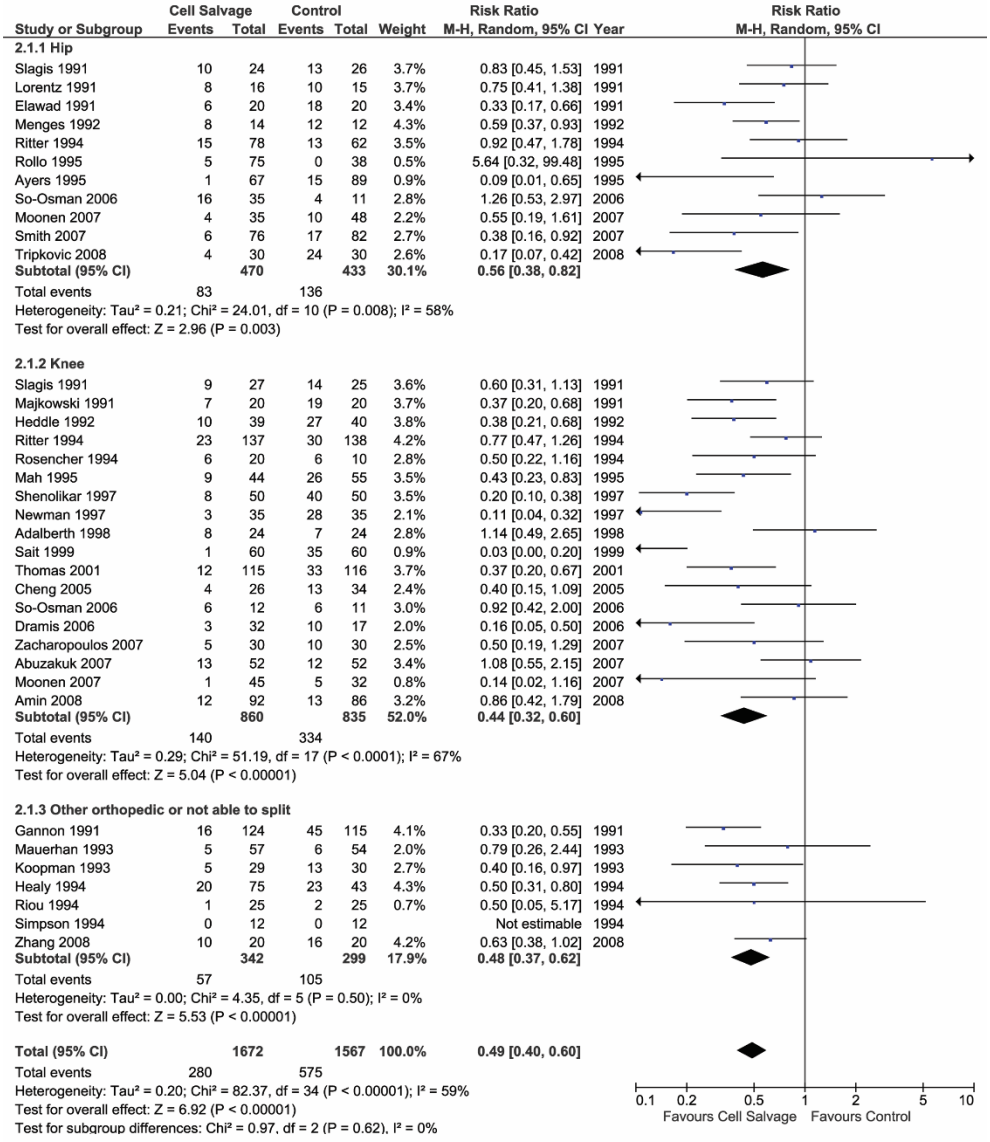

Figure 2: Effects of cell salvage in orthopaedic surgery in studies included in Carless et al: Hip versus Knee Arthroplasty

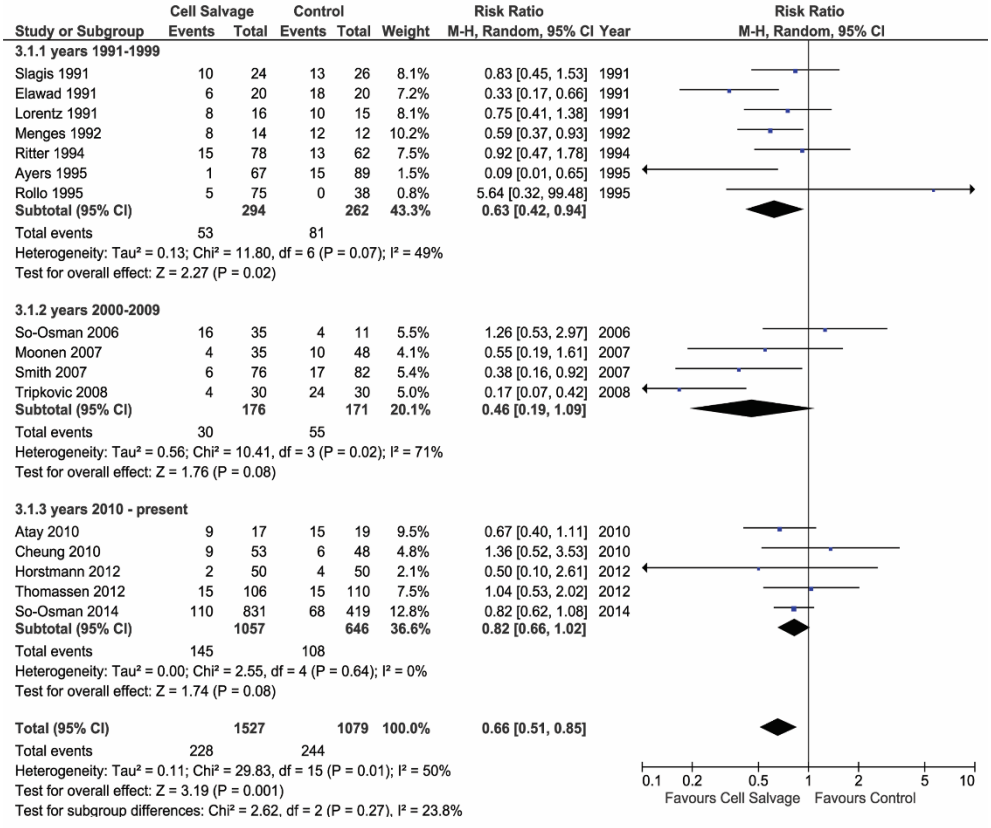

Figure 3: Effects of cell salvage in Hip Arthroplasty over time

Subgroup Analyses

To explain the time period effect described above, exploratory subgroup analyses were performed. Given the number of studies per time period, no further stratification was possible. Therefore, we included all studies from all time periods in the subgroup analyses and assessed 1) whether the effectiveness between subgroups was different, and 2) whether a possible explanatory variable (for example, a more strict transfusion threshold) was more frequently present in recent than in older studies. The variable was considered a possible explanation for a part of the observed change in effectiveness over time only if both criteria were true.

- In studies using a traditional transfusion threshold, cell salvage significantly reduced the RBC exposure rate (RR, 0.57; 95% CI, 0.36 to 0.89; I^2 = 67%; n = 6 [1 recent]) and

the volume of RBCs transfused (WMD, −1.56; 95% CI, −2.16 to −0.95; I^2 = 61%; n = 3 [none recent]). In studies with a more restrictive threshold, cell salvage resulted in a smaller reduction of the RBC exposure rate (RR, 0.72; 95% CI, 0.58 to 0.91; I^2 = 0%; n = 5 [3 recent]) and did not significantly reduce the volume of RBCs transfused (WMD, −0.13; 95% CI, −0.30 to 0.04; I^2 = 39%; n = 3 [all recent]).

- In studies using closed suction wound drainage in the control group, cell salvage significantly reduced the RBC exposure rate (RR, 0.78; 95% CI, 0.62 to 0.98, I^2 = 6%; n = 6 [3 recent]), but not the volume of RBCs transfused (WMD, −0.16; 95% CI, −0.45 to 0.13, I^2 = 61%; n = 4 [2 recent]). In studies using no drain in the control group, cell salvage did not significantly reduce the RBC exposure rate (RR, 0.69; 95% CI, 0.43 to 1.13, I^2 = 45%; n = 5 [2 recent]) or the volume of RBCs transfused (WMD, −1.04; 95% CI, −2.96 to 0.88; I^2 = 98%; n = 2 [1 recent]).
- Intraoperative cell salvage (only applied in one trial) reduced the RBC exposure rate (RR, 0.33; 95% CI, 0.17 to 0.66) and the volume of RBCs transfused (WMD, −2.04; 95% CI, −2.58 to −1.50). Postoperative cell salvage significantly reduced the RBC exposure rate (RR, 0.68; 95% CI, 0.49 to 0.93, I^2 = 55%; n = 13 [4 recent]) and the volume of RBCs transfused (WMD, −0.38; 95% CI, −0.72 to −0.04; I^2 = 86%; n = 6 [3 recent]). Perioperative cell salvage significantly reduced neither the RBC exposure rate (RR, 0.76; 95% CI, 0.58 to 1.00; I^2 = 0%; n = 4 [2 recent]) nor the volume of RBCs transfused (WMD, −0.28; 95% CI, −0.76 to 0.18; I^2 = 34%; n = 2 [1 recent]).

Effects of Cell Salvage in TKA

Overall, cell salvage still reduced the RBC exposure rate by 49% (RR, 0.51; 95% CI, 0.39 to 0.68) in TKA when recent trials were added (Figure 4), with substantial heterogeneity among studies (I^2 = 75%). Again, a time period effect was observed, with more recent studies (2010 to 2012) showing no significant effect of cell salvage (RR, 0.91; 95% CI, 0.63 to 1.31; I^2 = 54%).

Overall, cell salvage in total knee arthroplasty also reduced the volume of RBCs transfused (WMD, −0.33; 95% CI, −0.59 to −0.08; I^2 = 91%). Again, a time period effect was observed, with recently published studies (2010 to 2012) showing a nonsignificant reduction in the volume of RBCs transfused (WMD, −0.32; 95% CI, −0.63 to 0.00; I^2 = 95%).

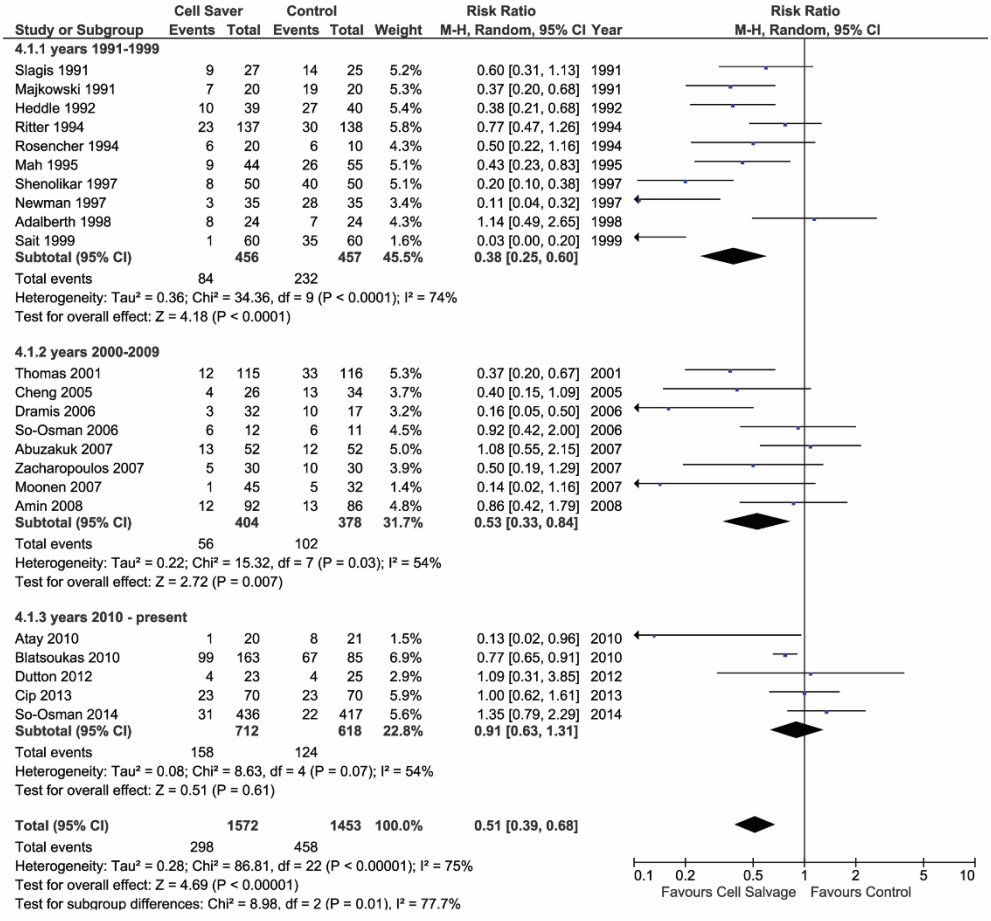

Figure 4: Effects of cell salvage in Knee Arthroplasty over time

Subgroup Analyses

To explain the time period effect described above, exploratory subgroup analyses similar to those for THA were performed.

- In studies using a traditional threshold, cell salvage significantly reduced the RBC exposure rate (RR, 0.54; 95% CI, 0.40 to 0.73; I^2 = 72%; n = 13 [2 recent]) and the volume of RBCs transfused (WMD, −0.60; 95% CI, −1.08 to −0.12; I^2 = 80%; n = 4 [1 recent]). In studies with a more restrictive threshold, cell salvage reduced neither the RBC exposure rate (RR, 0.54; 95% CI, 0.25 to 1.18, I^2 = 74%; n = 5 [2 recent]) nor the

volume of RBCs transfused (WMD, −0.45; 95% CI, −1.07 to 0.18; I^2 = 92%; n = 3 [2 recent]).

- In studies using closed suction wound drainage in the control group, cell salvage significantly reduced the RBC exposure rate (RR, 0.44; 95% CI, 0.27 to 0.72; I^2 = 78%; n = 13 [3 recent]), but not the volume of RBCs transfused (WMD, −0.38; 95% CI, −0.82 to 0.05; I^2 = 90%; n = 5 [1 recent]). In studies using no drain in the control group, cell salvage resulted in a smaller reduction of the RBC exposure rate (RR, 0.56; 95% CI, 0.37 to 0.85, I^2 = 75%; n = 8 [2 recent]), and did not significantly reduce the volume of RBCs transfused (WMD, −0.24; 95% CI, −0.92 to 0.45; I^2 = 96%; n = 3 [2 recent]).
- Postoperative cell salvage significantly reduced the RBC exposure rate (RR, 0.49; 95% CI, 0.37 to 0.66; I^2 = 73%; n = 22 [4 recent]) and the volume of RBCs transfused (WMD, −0.32; 95% CI, −0.55 to −0.08; I^2 = 92%; n = 10 [4 recent]). Perioperative cell salvage resulted in a smaller reduction of the RBC exposure rate (RR, 0.81; 95% CI, 0.68 to 0.97, I^2 = 0%; n = 2 [both recent]) and a reduction of the volume of RBCs transfused (WMD, −0.93; 95% CI, −1.21 to −0.65; n = 1 [recent]).
- In studies performing TKA under tourniquet control, cell salvage significantly reduced the RBC exposure rate (RR, 0.46; 95% CI, 0.33 to 0.65, I^2 = 71%; n = 20 [3 recent]), but did not reduce the volume of RBCs transfused (WMD, −0.22; 95% CI, −0.45 to 0.01; I^2 = 87%; n = 8 [3 recent]). In studies performing TKA without tourniquet control, cell salvage resulted in a smaller reduction of the RBC exposure (RR, 0.78; 95% CI, 0.67 to 0.91; I^2 = 0%; n = 3 [2 recent]) and a reduction in the volume of RBCs transfused (WMD, −0.85; 95% CI, −1.09 to −0.61; I^2 = 0%; n = 2 [1 recent]).

Discussion

Our meta-analysis showed that cell salvage significantly reduces the RBC exposure rate and the volume of RBCs transfused in both THA and TKA, with a larger effect in TKA than in THA based on group averages. However, in trials published more recently (2010 to 2012), cell salvage reduced neither the exposure rate nor the volume of RBCs transfused in both THA and TKA. We therefore conclude that, given changes in blood transfusion management, the effect of cell salvage may have changed over time and it may not be as effective as shown in previous meta-analyses.[1-3] This conclusion seems even stronger if the methodological quality of the studies is considered. Recent studies more often had a lower risk of bias and therefore higher quality of evidence.

Subgroup analyses showed that a more restrictive transfusion trigger (haemoglobin [Hb] ≤8.0 g/dL) was associated with a smaller effect of cell salvage. Cell salvage reduced the exposure rate only in THA and was not effective in TKA. Given that recent trials more

often used this restrictive transfusion threshold, this may partly explain the observed time period effect in effectiveness of cell salvage.

Similarly, using no drain as the standard treatment in the control group was also associated with smaller effects of cell salvage. Cell salvage was no longer effective in THA, and it reduced only the RBC exposure rate in TKA. These results are in line with the meta-analysis of Parker et al.,[9] who showed that routine use of closed suction drainage in THA and TKA was associated with higher transfusion rates and did not have any effect on the rate of wound infections or hematomas compared with no drain use. However, as recent studies did not use 'no drain' as the control treatment more frequently than studies published before 2010, it does not explain the observed time period effect.

Subgroup analyses regarding the timing of cell salvage and use of tourniquet control established no clear reasons for the observed time period effect. Only a few studies, although proportionally more recent studies, performed TKA without tourniquet control. This is in line with the results of the 2009 review by Smith and Hing[10] showing that the use of a tourniquet decreases intraoperative blood loss but could not influence postoperative blood loss in drains or affect transfusion rates.

Some relevant variables were not reported in a sufficient number of trials and could thus not be used in the meta-analysis: preoperative and postoperative haemoglobin levels, the exact timing of haemoglobin measurements resulting in the decision to transfuse or not, and the exact amount of blood given back to the patient, which differs among devices. Therefore, additional research is needed to be able to assess whether cell salvage may have benefit in raising haemoglobin levels for subgroups of patients and to interpret the effect of the timing of haemoglobin measurement and the volume of blood transfused on the effectiveness of cell salvage. Furthermore, we recommend that future studies report the utilized surgical techniques in more detail, enabling future meta-analyses to perform subgroup analyses to determine whether primary outcomes of cell salvage differ by surgical technique.

There are some important limitations of this meta-analysis. First, it included an insufficient number of high-quality studies to permit limiting our analyses to high-quality studies only. However, our risk-of-bias assessment showed that more recent studies seemed to have lower risk of bias compared with studies published before 2010, which strengthens our conclusion that cell salvage may no longer be effective in reducing the RBC exposure rate and the volume of RBCs transfused. Second, only three of the included studies were judged to be double-blinded. Although this is problematic for the quality of the studies, it is probably not possible to further improve blinding procedures given the nature of the intervention. However, as sequence generation and allocation concealment clearly

improved in recent studies, there is lower risk of bias and thus higher quality of evidence in recent studies. Third, the results of this meta-analysis only apply to cell salvage in THA and TKA. Cell salvage may still be effective for other surgical procedures (for example, during cardiac surgery), which could be a topic for further research. In addition, the results only allow us to draw conclusions about the effectiveness of perioperative collection and reinfusion of autologous blood (cell salvage) and not about preoperative autologous blood donation and reinfusion.

Given the results of this meta-analysis, the benefit of cell salvage in clinical practice in uncomplicated patients undergoing THA and TKA is questioned. Further research is needed to be able to definitely answer this question, as current trials have insufficient data on parameters such as haemoglobin levels. The current meta-analysis contributes to this debate by creating awareness among professionals that the effectiveness of cell salvage to reduce transfusion rates is minimized in recent studies, which have lower risk of bias and more often have used more restrictive transfusion triggers.

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Appendix 1: Search Strategy

MEDLINE search strategy

1. cell$ sav$.mp.
2. cell$ salvage.mp.
3. blood transfusion, autologous/
4. autotransfusion$.mp.
5. auto-transfusion$.mp.
6. blood salvage.mp.
7. autovac.mp.
8. solcotrans system.mp.
9. constavac.mp.
10. solcotrans.mp.
11. hemovac.mp.
12. BRAT.mp.
13. fresenius.mp.
14. consta vac.mp.
15. cell saver.mp.
16. dideco.mp.
17. electromedic.mp.
18. electromedics.mp.
19. gish biomedical.mp.
20. haemonetics.mp.
21. orth-evac.mp.
22. pleur-evac.mp.
23. sorenson.mp.
24. reinfusion system.mp.
25. sorin biomedical.mp.
26. or/1-25
27. exp blood transfusion/
28. exp hemorrhage/
29. exp anesthesia/
30. transfusion$.mp.
31. bleed$.mp.
32. blood loss$.mp.
33. hemorrhag$.mp.
34. haemorrhag$.mp.
35. or/27-34
36. 26 and 35
37. randomized controlled trial.pt.
38. controlled clinical trial.pt.
39. randomized controlled trials.sh.
40. random allocation.sh.
41. double blind method.sh.
42. single blind method.sh.
43. or/37-42
44. clinical trial.pt.
45. exp Clinical trials/
46. (clin$ adj25 trial$).ti,ab.
47. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
48. placebos.sh.
49. placebo$.ti,ab.
50. random$.ti,ab.
51. research design.sh.
52. or/44-51
53. comparative study.sh.
54. exp Evaluation studies/
55. follow up studies.sh.
56. prospective studies.sh.
57. (control$ or prospectiv$ or volunteer$).ti,ab.
58. or/53-57
59. 43 or 52 or 58
60. 36 and 59
61. animal/ not human/
62. 60 not 6

Appendix 2: Study characteristics and risk of bias assessment of included studies

Author	Year	Summary of study characteristics									Assessment of risk of bias		
		Participants: Patients undergoing	Type[1]	Interventions		Transfusion trigger			Treatment policy in control group[4]	Tourniquet control	Random sequence generation	Allocation concealment	Blinding
				Description: Intervention (I) and Control (C)	Timing[2]	Yes/ No	Transfusion threshold	Subgroup[3]					
Abuzakuk	2007	Primary cemented total knee arthroplasty	Knee	I: autotransfusion (Bellovac ABT autotransfusion system), n=52; C: standard suction drain (Redivac), n=52	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 1	Yes	Low risk	Unclear risk	High risk
Adalberth	1998	primary total knee arthroplasty	Knee	I: autotransfusion (Solcotrans - Solco Basle UK ltd.)), n=24; Control: no drain, n=24	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 0	Yes	High risk	High risk	High risk
Altinel	2007	bi- or tri-compartmental total knee arthroplasties	Knee	I: autotransfusion (ConstaVac CBCII system), n=16; C: standard care (2 drains for shed blood drainage), n=16	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 1	Yes	Unclear risk	Unclear risk	High risk
Amin	2008	total knee replacement	Knee	I: autotransfusion (Bellovac ABT autotransfusion system), n=92; C: standard vacuum drain, n=86	POST	Yes	Hb < 8.0 g/dl	Trigger 1	Control 1	Yes	High risk	High risk	High risk
Atay	2010	hip and knee arthroplasty	Hip and knee	I: autotransfusion (Transolog), n=17 (hip) and n=20 (knee); C: routine hemovac drain, n=19 (hip) and n=21 (knee)	POST	Yes	Hb < 8.0 g/dl or Hct < 25% and clinical symptoms of anaemia	Trigger 1	Control 1	Yes	Unclear risk	Unclear risk	High risk

Ayers 1995	primary total hip arthroplasty	Hip	I: autotransfusion (Autovac postoperative orthopaedic autotransfusion canister), n=67; C: closed suction drainage system, n=89	POST	No		None	Control 1	N.A.	High risk	High risk	High risk
Blatsoukas 2010	unilateral total knee replacement	Knee	I: 1. autotransfusion (Dideco Compact Advanced and ConstaVac CBCII), n=92; 2. Autotransfusion (ConstaVaC CBCII), n=71; C: no drain, n=85	PERI/ POST	Yes	Hb 9-10 g/dl: 1 unit; Hb 8-9 g/dl: 2 units; Hb 7-8 g/dl: 3 units	Trigger 2	Control 0	No	High risk	High risk	High risk
Cheng 2005	unilateral total knee arthroplasty	Knee	I: autotransfusion (DONOR system), n=26; C: no drain, n=34	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 0	No	Unclear risk	High risk	High risk
Cheung 2010	primary total hip replacement	Hip	I: autotransfusion (Bellovac ABT autotransfusion systemt), n=53; C: no drain, n=48	POST	No		None	Control 0	N.A.	Low risk	Unclear risk	High risk
Cip 2012	total knee arthroplasty	Knee	I: autotransfusion (OrthoPAT), n= 70; C: no retransfusion system, n=70	PERI	Yes	Hb < 8.0 g/dl or signs of anaemia or tachycardia	Trigger 2	Control 1	No	Low risk	Low risk	High risk
Dramis 2006	primary unilateral total knee arthroplasty	Knee	I: autotransfusion (CellTrans system), n=32; C: Standard vacuum drain, n=17	POST	Yes	Hb < 9.0 g/dl or clinical symptoms of anaemia	Trigger 2	Control 1	Yes	Unclear risk	Unclear risk	High risk
Dutton 2012	total knee arthroplasty	Knee	I: autotransfusion (Bellovac ABT autotransfusion system), n=23; C: no drain, n=25)	POST	No		None	Control 0	Yes	Low risk	Low risk	Unclear risk
Ekback 1995	total hip arthroplasty	Hip	I: Autotransfusion (Haemonetics CellSaver 4, Althin model AT 1000 or Shiley/Dideco STAT), n=15; C: no autotransfusion, n=15	PERI	Yes	EVF < 27% (i.e. Hb < 9.2 g/dl)	Trigger 2	Control 1	N.A.	Unclear risk	Unclear risk	High risk

Elawad	1991	primary total hip arthroplasty	Hip	I: Autotransfusion (Electromedic Autotrans AT100) autotransfusion system), n=20; C: no drain, n=20	INTRA	Yes	Hb < 8.5 g/dl	Trigger 2	Control 0	N.A.	Unclear risk	High risk	High risk
Gannon	1991	total hip or total knee replacement	NAS	I: Autotransfusion (Solcotrans), n=124; C: standard suction canister, n=115	POST	Yes	Hb < 9.0 g/dl or by internist based on patients' condition	Trigger 2	Control 1	Yes	Low risk	Unclear risk	High risk
Healy	1994	hip arthroplasty, total knee arthroplasty or spine fusion	NAS	I: autotransfusion (Ortho-Evac system or Solcotrans), n=75; C: standard wound drainage system, n=43	POST	No		None	Control 1	Unknown	Unclear risk	Unclear risk	High risk
Heddle	1992	elective knee arthroplasty	Knee	I: autotransfusion (Solcotrans), n=39; C: standard care (drained blood collected by a Davol suction unit and discarded), n=40	POST	Yes	Hb 8.0-8.9 g/dl: 1 unit; Hb 7.0-7.9 g/dl: 2 units; Hb 6.0-6.9 g/dl: 3 units, Hb 5.0-5.9 g/dl: 4 units	Trigger 1	Control 1	Yes	Unclear risk	Unclear risk	High risk
Horstmann	2012	total hip arthroplasty	Hip	I: autotransfusion (Bellovac ABT autotransfusion system), n=50; C: no drainage, n=50)	POST	Yes	Hb < 6.4/ 8.0/ 9.6 g/dl dependent on ASA classification	Trigger 1	Control 0	N.A.	Unclear risk	Low risk	Low risk
Kirkos	2006	total knee arthroplasty	Knee	I: autotransfusion, n=78; C: standard vacuum drain, n=77	POST	Yes	Hb < 10.0 g/dl	Trigger 2	Control 1	Yes	High risk	Unclear risk	High risk
Koopman	1993	total hip arthroplasty or dorsal lumbo-sacral spinal fusion	NAS	I: autotransfusion (Haemonetics Haemolite-2 system), n=29; C: no autotransfusion, n=30	PERI	Yes	Hct at 30% (i.e. Hb <10.2 g/dl)	Trigger 2	Control 1	N.A.	Unclear risk	High risk	High risk

Lorentz	1991	total hip artrhoplasty	Hip	I: Autotransfusion, n=16; C: standard care, n=15	PERI	Yes	Hb < 9.0 g/dl (operating room, IC); Hb < 10.0 g/dl (other)	Trigger 2	Unknown	N.A.	Unclear risk	Unclear risk	High risk
Mah	1995	elective primary total knee replacement surgery	Knee	I: autotransfusion (Electromedics BT-795), n=44; C: standard care, n=55	POST	Yes	Hb < 10.0 g/dl	Trigger 2	Active	Yes	Low risk	Unclear risk	High risk
Majowski	1991	primary unilateral total knee arthroplasty	Knee	I: autotransfusion (Solcotrans), n=20; C: three standard Redivac drains	POST	Yes	Hb < 9.5 g/dl or if indicated hemodynamically	Trigger 2	Control 1	Yes	Unclear risk	Unclear risk	High risk
Mauerhan	1993	elective primary total hip arthroplasty and total knee arthroplasty	NAS	I: autotransfusion (CBC ConstaVac), n=57; C: standard post-operative collection system, n=54	POST	No		None	Control 1	Yes	Low risk	Unclear risk	High risk
Menges	1992	total hip surgery and pre-operative plasmapheresis	Hip	I: autotransfusion (Autotrans BT 795 P, Dideco system), n=14; C: No autotransfusion, n=12 (both groups also received crystalloids and colloids)	POST	Yes	Hb < 9.0 g/dl or Hct < 28% (i.e. Hb < 9.5)	Trigger 2	Active	N.A.	Unclear risk	Unclear risk	High risk
Moonen	2007	primary total knee arthroplasty or total hip arthroplasty	Hip and knee	I: autotransfusion (Bellovac ABT autotransfusion system), n=35 (hip) and n=45 (knee); C: regular post-operative low-vacuum drainage, n=48 (hip) and n=32 (knee)	POST	Yes	Hb < 8.1/ 8.9/ 9.7 g/dl dependent on ASA classification	Trigger 1	Control 1	Yes	Low risk	High risk	High risk
Newman	1997	unilateral total knee replacement	Knee	I: autotransfusion (Dideco 797 transfusion system), n=35; C: standard Hemovac suction drain, n=35	POST	No		None	Control 1	Yes	Low risk	Unclear risk	High risk

Riou	1994	elective, non-emergency spinal surgery	Other ortho paedic	I: autotransfusion (Solcotrans), n=25; C: postoperative drained blood collected into Solcotrans Orthopedic Plus system but salvaged blood was not considered for reinfusion, n=25	POST	Yes	Hct < 25% (i.e. Hb < 8.5 g/dl)	Trigger 2	Control 1	N.A.	Low risk	Unclear risk	Low risk
Ritter	1994	primary total hip or total knee replacement	Hip and knee	I: autotransfusion (Solcotrans), n=78 (hip) and n=137 (knee); C: no drainage system, n=62 (hip) and n=138 (knee)	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 0	Yes	Unclear risk	Unclear risk	High risk
Rollo	1995	primary total hip arthroplasty	Hip	I: 1. autotransfusion (Haemonetics), n=35; 2. autotransfusion (Solcotrans), n=40; C: no drain, n=38	PERI/POST	No	Based on clinical condition of patient	None	Active	N.A.	Unclear risk	High risk	High risk
Rosencher	1994	knee replacement surgery	Knee	I: autotransfusion (Ortho-Evac system or Solcotrans), n=20; C: no drain, n=10	POST	Yes	Hct at 30% (i.e. Hb <10.2 g/dl)	Trigger 2	Control 0	Yes	Unclear risk	Unclear risk	High risk
Sait	1999	total knee arthroplasty	Knee	I: autotransfusion, n=60; C: standard care without autotransfusion, n=60	POST	No		None	Control 1	Yes	Unclear risk	Unclear risk	High risk
Shenolikar	1997	total knee replacement	Knee	I: autotransfusion (Haemonetics Cell Saver 3), n=50; C: no drain, n=50	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 0	Yes	Low risk	Unclear risk	High risk
Simpson	1994	elective primary total joint arthroplasty	NAS	I: autotransfusion (Solcotrans), n=12; C: closede suction drain, n=12	POST	Yes	Hb < 10 g/dl or Hct < 30% (i.e. Hb < 10.2 g/dl)	Trigger 2	Control 1	Unknown	Unclear risk	Unclear risk	High risk

Slagis											
1991	total hip or knee replacement	Hip and knee	I: autotransfusion (Hemolite cell salver), n=24 (hip) and n=27 (knee); C: Hemovac standard drainage system, n=26 (hip) and n=25 (knee)	POST	No		None	Active	No	Unclear risk	Unclear risk	High risk
Smith											
2007	primary total hip replacement	Hip	I: autotransfusion (ABTrans autologous re-transfusion system), n=76; C: two standard Medinorm vacuum drains, n=82	POST	Yes	Hb < 8.0 g/dl and in symptomatic patients with Hb of 8.0-10.0 g/dl: 2 units	Trigger 1	Control 1	N.A.	Low risk	High risk	High risk
So-Osman											
2006	primary or revision total hip or knee replacement	Hip and knee	I: autotransfusion (DONOR or Bellovac ABT autotransfusion system), n=35 (hip) and n=12 (knee); C: standard closed suction wound drainage, n=11 (hip) and n=11 (knee)	POST	No		None	Control 1	Yes	Low risk	High risk	High risk
So-Osman											
2012	primary or revision total hip or knee replacement	Hip and knee	I: 1. autotransfusion (OrthoPat), n= 412 (hip); 2. Autotransfusion (Donor or Bellovac ABT autotransfusion system), n=419 (hip) and n=436 (knee); C: low vaccum wound drain, n=419 (hip) and n=417 (knee)	PERI/ POST	Yes	Hb < 6.4 for age < 60 years; Hb < 8.1 g/dl for age > 60 years; Hb < 9.6 g/dl in high risk	Trigger 1	Control 1	Yes	Low risk	Low risk	High risk
Thomas											
2001	total knee replacement	Knee	I: autotransfusion (Haemonetics Cell Saver 5), n=115, C: all drainaged blood was discarded, n=116	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 1	Yes	Unclear risk	Unclear risk	High risk
Thomassen											
2012	primary or revision total hip arthroplasty	Hip	I: autotransfusion (Sangvia Blood Management System), n=106; C: regular postoperative low vacuum drain, n=110	PERI	Yes	Hb < 8.5 g/dl or clinical symptoms of anaemia	Trigger 2	Control 1	N.A.	Low risk	Low risk	Low risk

Tripkovic	2008	primary total hip replacement	Hip	I: autotransfusion (BIODREN system), n=30; C: no autotransfusion, n=30	POST	Yes	Hb < 10 g/dl or Hct < 30% (i.e. Hb < 10.2 g/dl)	Trigger 2	Active	N.A.	Unclear risk	Unclear risk	High risk
Zacharapoulos	2007	unilateral total knee replacement	Knee	I: autotransfusion (Gish Orthofuser system), n=30; C: standard wound suction drainage system, n=30	POST	Yes	Hb < 9.0 g/dl	Trigger 2	Control 1	Yes	Unclear risk	Unclear risk	High risk
Zhang	2008	orthopaedic procedures	NAS	I: autotransfusion (Haemonetics Cell Saver 5 system), n=20; C: standard care, n=20	INTRA	No		None	Control 1	N.A.	Unclear risk	Unclear risk	High risk

[1] Type: Hip, knee, hip and knee or not able to split (NAS).

[2] Timing Cell Salvage: POST = postoperative, INTRA = intraoperative, PERI = both intra- and postoperative.

[3] Subgroup: Trigger 1 Hb=<8.0 g/dl; Trigger 2 Hb> 8.0 g/dl

[4] Treatment policy in control group: Control 0 = in control groups no drain is used; Control 1 = in control group standard suction or vacuum drain is used; Active = in control group active treatment (active plus cell salvage versus active comparisons).