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[Intervention Review]

Perioperative blood transfusions and recurrence of colorectal cancer

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ABSTRACT

Background

The improvement of renal allograft survival by pre-transplantation transfusions alerted to the potential detrimental effect of transfusions in cancer treatment.

Objectives

This meta-analysis evaluates the role of perioperative blood transfusions (PBT) on colorectal cancer recurrence. This is accomplished by updating the results of a previously published meta-analysis (Amato 2006) to December 2009.

Search methods

Papers were retrieved using Medline, EMBASE, the Cochrane Library, trials web-based registries, or the CCG Database. The search strategy was: {colon OR rectal OR colorectal} WITH {cancer OR tumor OR neoplasm} AND transfusion. The publication bias was balanced by reviewing the proceedings of international congresses.

Selection criteria

Patients undergoing curative resection of colorectal cancer (classified either as Dukes stages A-C, Astler-Coller stages A-C2, or TNM stages T1-3a/N0-1/M0) were included if they had received blood products within one month of surgery. Excluded were patients with distant metastases and studies with short follow-up or no data.

Data collection and analysis

A specific form was used for data collection. Data was cross-checked, using the most recent publication in case of repetitive ones. Papers' quality was evaluated using the method by Evans and Pollock. Odds ratios (OR, with 95% confidence intervals) were computed for each study, and pooled estimates were generated by RevMan (version 5). When available, data were stratified for risk factors of cancer recurrence.

Main results

Updating the previous review through December 2009 identified 41 additional papers, for a grand total of 278 references. Two-hundred and forty-two of them were excluded because they analyzed survival (n=27), were repetitive (n=29), letters/reviews (n=71) or had no data (n=115). Thirty-six studies on 12,127 patients remained included: 23 showed a detrimental effect of PBT; 22 used multivariable analyses, and 14 found an independent PBT effect. Pooled estimates of PBT effect on recurrence in randomised studies yielded an OR of 1.42 (95% CI, 1.20 to 1.67) against transfused patients. Stratified meta-analyses confirmed these findings also by site and stage of disease, regardless of timing, type, and in a dose-related fashion, although heterogeneity was detected. Data on surgical techniques was not available for further analysis.

Authors' conclusions

This updated meta-analysis confirms the previous findings and supports the association of PBT on the recurrence of curable colorectal cancers. However, since heterogeneity was detected and the effect of surgical technique could not be assessed, a causal relationship cannot still be claimed. Carefully restricted indications for PBT seems necessary.

PLAIN LANGUAGE SUMMARY**Does perioperative blood transfusion affect the recurrence rate of potentially curable operations for colorectal cancer?**

This review include 36 studies, identified from 278 references retrieved until December 2009, and report a moderate association between colorectal cancer recurrence and perioperative transfusions, with an OR of 1.42 (95% CI, 1.20 to 1.67). Similar estimates are present in several subgroup meta-analyses, as well as in meta-analyses stratified for known risk factors. These findings support carefully restricted indications for perioperative blood transfusions in colorectal cancer patients operated for cure, and continue to await the results of studies addressing the role of surgeon-related risk factors on the need for transfusion and disease recurrence.

BACKGROUND

It is well established that renal allograft survival is improved by blood transfusions before transplantation, with a dose-response relationship between the number of transfused units and long-term allograft survival rates (Opelz 1973; Opelz 1978; Sanfilippo 1984). However, the exact mechanisms of the host immunomodulation remain unclear (Terasaki 1984). Prompted by the identification of this lasting immunosuppressive effect, in 1981 Gantt expressed concern about the possible adverse effects of transfusions in patients being treated for cancer (Gantt 1981). Within one year, the first experimental study showing tumor growth promotion by allogenic blood transfusion was published (Francis 1981) and, shortly after, the first retrospective report linking perioperative blood transfusions (PBT) to colorectal cancer recurrence appeared in the same journal (Burrows 1982). Following these early reports, several other studies have been published in the literature, with conflicting results as to the verification of the working hypothesis, that is that PBT, by decreasing the mechanisms of cancer immune surveillance, is responsible for increased colorectal cancer recurrence.

OBJECTIVES

The objective of this review is to evaluate the recurrence rates of colorectal cancer for patients operated with curative intent and receiving perioperative blood transfusion (PBT), compared to the same type of patients not receiving PBT. We want to evaluate the hypothesis that PBT result in increased colorectal cancer recurrence in these patients, as indicated by some papers in the literature, although at variance with others. Furthermore, a meta-analysis can lead to a better estimation of the transfusion effect (if any), and to a minimization of the type-II statistical error, due to small sample sizes in some of the reported studies.

METHODS

Criteria for considering studies for this review

Types of studies

We will consider both randomised controlled trials (RCTs), prospective cohorts and retrospective surveys.

Types of participants

Patients treated either by colonic resection, anterior resection of the rectosigmoid, or abdominoperineal excision of the rectum with curative intention; disease classified as either Dukes stages A to C, Astler-Coller stages A to C2, or TNM stages T1-3a/N0-1/M0; a negligible proportion (<5%) or absence of patients treated with adjuvant therapy.

We will exclude studies considering patients with distant metastases at surgery; studies with follow-up less than six months; studies in which crude recurrence rate or disease-free survival were not indicated; and studies in which control patients received some blood components

Types of interventions

Any amount of blood products given to the patients is considered a transfusion. The type of blood component used in each study will be searched consistently throughout, in order to identify a specific

effect, if any. The perioperative period included one month before and after the operation, comprising surgery.

Types of outcome measures

The primary outcome will be colorectal cancer recurrence, measured either as crude recurrence rate or, when this is not available, its actuarial estimate (i.e., 1 - disease-free survival). Survival or mortality will be recorded and qualitatively discussed, but not quantitatively assessed in this meta-analysis, since it is less temporally related and less biologically associated with PBT.

Search methods for identification of studies

A search of the literature published between January 2005 and December 2009 will be conducted by scanning the Index Medicus, searching MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), the controlled trials register at www.controlled-trials.com, and the CCG Specialised Register. The following MESH terms and search strategy will be used: {colon OR rectal OR colorectal} WITH {cancer OR tumor OR neoplasm} AND transfusion.

The bibliographies of the retrieved articles will be examined thoroughly to identify further eligible studies. The tendency not to publish negative trials will be balanced by an inspection of any retrieved proceedings of international congresses of surgery. There will be no language restrictions.

The newly collected studies will be integrated with the studies identified by the previous Cochrane systematic review on this subject matter (Amato 2006) which, conversely, was an update of a published meta-analysis (Amato 1998).

Data collection and analysis

Also for this updated review, the authors analysed data on the primary outcome published in English (or with an English abstract) between January 2005 and December 2009, using the Cochrane methodology and software.

As suggested by the Meta-Analysis Cooperative Group, the present review will consider both RCTs, prospective cohorts and retrospective surveys, since its aim is mostly "hypothesis-generation". To guarantee the Cochrane high standards, however, separate analyses will be conducted for these types of studies, and their results compared.

A specific data extraction form will be used to help gather all necessary information. Data extraction will be cross-checked by two reviewers (AA and MP) separately, and differences resolved. When several papers described the results of the same study, only the most recent publication will be considered.

Quality assessment of the included trials will be performed using the scoring system by Evans and Pollock (Evans 1984).

The odds ratio (OR) and the rate difference (RD) will be computed for each report, along with their 95% confidence intervals (CI), using the RevMan software (v. 5.0) to be compared against the previous results (Amato 2006). The common OR and the pooled RD with 95% CI for all studies will be computed according to both the "fixed effect" model and the "random effects" model; the latter is more conservative when there is heterogeneity among the studies. A chi

square test for heterogeneity will be routinely performed using the built-in feature in the RevMan software (v. 5.0).

Stratified meta-analyses will be conducted to control for factors which could influence recurrence. These will include both known risk factors (site and stage of the tumors), and possible risk factors, either transfusion-related (type, amount, and timing of PBT), or surgery-related (amount of blood loss, type and duration of operation, experience of surgeons).

Confounders such as age, sex, complicating disease, etc. will be considered for possible stratified analyses of the pooled transfusion effects. If individual studies analyse such confounders by multivariate techniques, these will be presented and discussed qualitatively. Finally, sensitivity analyses will also be planned to check the consistency of the pooled estimates in response to changes of the included studies.

Power calculations for each identified paper will be performed according to Fleiss (Fleiss 1973).

RESULTS

Description of studies

The additional search identified 278 reports on the possible influence of PBT on colorectal cancer recurrence, published up to December 2009. An assessment of these revealed 29 repetitive publications, 71 review articles or letters, and 115 papers with different objectives, or no data. Twenty-seven further studies, on a total of 9,803 patients, were excluded because they analyzed either survival or mortality: 15 (6,531 patients) showed a detrimental transfusion effect, 11 were inconclusive, and one even stressed a protective transfusion effect on recurrence.

This led to 36 original studies being considered for this meta-analysis, for a total of 12,127 patients. Twenty-three papers showed a statistically significant adverse effect of PBT on the outcome of 8,029 patients; 15 studies showed no difference in 4,098 patients, and one of them reported a protective effect of PBT on recurrence of stage C2 patients. Seven were Randomized Controlled Trials

(Frankish 1985, Cheslyn-Curtis 1990, Harder 1990, Tartter 1992, Heiss 1994, Houbiers 1994, Busch 1995), three of which were performed with different objectives, and derived their results on PBT effect retrospectively. Three were prospective cohorts (Sene 1993, Sibbering 1994, Mynster 2001).

In 23 studies recurrence was further checked by multivariable analyses, in order to control for possible confounders: PBT were found to have an independent effect on recurrence in 14 studies (4,472 patients), to have no influence in eight (2,938 patients), and even to show a protective effect for colon cancer patients in one (Weiden 1987). Notably, in one study the failure to show an independent effect was marginal ($p=0.057$, Modin 1992); another was significant for more than three units (Houbiers 1994), and two further studies, claiming no independent effect on recurrence, did show evidence of such an effect on survival (van Lawick 1988, Liewald 1990). The average relative risk for PBT was 2.23.

Risk of bias in included studies

The 36 included studies had a mean quality score of 66 ± 12 , according to Evans and Pollock.

Most of the included studies had small sample sizes. The mean sample size was of 337 ± 231 patients; the power to detect the difference actually observed in each report was less than 80% in 30 of them, and none of the studies showing no PBT effect was able to achieve it.

Effects of interventions

Overall meta-analysis

The individual estimates from the included papers (up to December 2009) led to exclude a publication bias (Figure 1). The results of the overall meta-analysis showed a recurrence rate of 37% in the transfused group, and of 26% in the non-transfused group, with a transfused to non-transfused ratio of 1.90. The common OR was 1.68 (95% CI, 1.54 to 1.83, Figure 2), and the pooled RD 0.11 (95% CI, 0.09 to 0.13), almost superimposable to previous estimates (Amato 1998). Significant heterogeneity was detected ($\chi^2=103.5$, $df=35$, $p<0.01$).

Figure 1. Funnel plot of comparison: 1 Studies on Recurrence, outcome: 1.1 All Studies.

Figure 2. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.1 All Studies.

Sensitivity analyses were conducted to test the robustness of these estimates. Similar results were obtained when the analysis included only either the retrospective studies (OR=1.91; 95%CI, 1.71 to 2.13, [Figure 3](#)), or the studies with multivariable procedures (OR=1.71; 95%CI, 1.53 to 1.90, [Figure 4](#)). Interestingly, the inclusion

of the studies with higher quality (OR=1.71; 95%CI, 1.46 to 2.01, [Figure 5](#)), or of the prospective studies (OR=1.36; 95%CI, 1.18 to 1.56), or of the randomised trials specifically designed to test the PBT effect (OR=1.65; 95%CI, 1.31 to 2.08, [Figure 6](#)), yielded similar and significant ORs, but with no significant heterogeneity.

Figure 3. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.3 Retrospective Studies.

Figure 4. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.4 Multivariate Analysis.

Figure 5. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.7 Top 25% Quality.

Figure 6. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.2 Prospective Studies and Randomized Controlled Studies.

Site and Stage of Disease

Colonic tumors recurred in 31% of the cases, and in 11 studies showed pooled estimates similar to those computed in all studies ($OR = 1.64$; 95%CI, 1.36 to 1.98). Information on rectal cancers was

available in 12 studies, leading to a common OR larger than that obtained for colon cancers, and with no significant heterogeneity ($OR = 2.03$; 95%CI, 1.61 to 2.57, Figure 7).

Figure 7. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.8 Colon Cancer.

Sixty-one percent of patients with Astler-Coller stage A-B1-2 were transfused, with an overall recurrence rate of 30% (OR=1.93; 95%CI, 1.58 to 2.37, [Figure 8](#)). Sixty-eight percent of those with a more advanced stage received a transfusion, and showed an overall

recurrence rate of 53% (OR=1.51; 95%CI, 1.18 to 1.92, [Figure 9](#)). Both these pooled ORs showed a significant heterogeneity across studies.

Figure 8. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.10 Dukes A-B.

Figure 9. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.11 Dukes C.

Transfusion-related risk factors

The timing of PBT seemed not to affect the risk of recurrences. Pre-operative data, obtained from five studies, showed an overall recurrence rate of 30% ([Figure 10](#)), similar to those computed for intra- and post-operative transfusions (32% and 30%, respectively), derived from nine studies ([Figure 11](#) and [Figure 12](#)). Their ORs were close to those obtained in all studies, and with no significant heterogeneity.

Both red blood cells and whole blood were associated with an increased risk of recurrence. Seven (OR=1.65; 95%CI, 1.35 to 2.01, [Figure 13](#)) and five studies (OR=2.07; 95%CI, 1.55 to 2.76, [Figure 14](#)), respectively, contributed to this analysis, while data on plasma were present in one study only.

Figure 10. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.12 Pre-operative Transfusions.

Figure 11. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.13 Intra-operative Transfusions.

Figure 12. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.14 Post-operative Transfusions.

Figure 13. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.15 Red Blood Cells.

Figure 14. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.16 Whole Blood.

Finally, increased risks were observed with an increased number of transfused units: one to two units showed an OR of 1.40 (95% CI, 1.18 to 1.67, [Figure 15](#)), which became 1.69 for three to four units

(95% CI, 1.40 to 2.03, [Figure 16](#)), and 2.02 for five or more units (95% CI, 1.65 to 2.48, [Figure 17](#)). Significant heterogeneity was detected in these analyses.

Figure 15. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.17 1-2 Transfused Units.

Figure 16. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.18 3-4 Transfused Units.

Figure 17. Forest plot of comparison: 1 Studies on Recurrence, outcome: 1.19 $\geq$ 5 Transfused Units.

Surgery-related risk factors

The incompleteness of numerical data did not allow to stratify patients for factors such as seniority of surgeons, type of operation, duration of surgery, operative blood loss, or technical details, which could have helped to clarify the causal role of PBT in colorectal cancer recurrence.

DISCUSSION

In the first study on the possible effect of PBT over recurrent colorectal cancer, the hypothesis made by the authors was that the immunosuppressive effect of blood transfusions, well established through its use in renal transplantation, could be extended to cancer patients (Burrows 1982). Blood transfusion effects in dialysis patients are now generally accepted and, although their exact mechanisms are still obscure (Nielsen 1995), a generalized suppression of cell-mediated immunity has been suspected (Francis 1989, Waymack 1989, Blumberg 1989, Tartter 1988). However, the transient reduction in helper and suppressor cells that follows normal surgery is unlikely to be affected by blood transfusions, and, in cancer surgery, the postoperative depression of in vitro lymphocyte responses attributable to transfusions is not documented by all authors (Blumberg 1989).

Studies with animal models might have contributed to a better understanding of the role of PBT on cancer growth but, unfortunately, they created more questions than answers, due to great differences in timing, route, tumors, species, and strains used (Marquet 1993; Jeekel 1995). Moreover, the specifically responsible blood component has not been identified: both red blood cells, white blood cells, and plasma have been involved (Francis 1981; Francis 1985,). Finally, another debated issue refers to the questioned immunogenicity of tumors as opposed to allografts. In fact, they differ in terms of type and duration of antigen expression, and their comparability is therefore cast into doubt (Blumberg 1989).

With this background, many authors have investigated the relationship between the recurrence of some tumors and PBT (Tartter 1985; Vamvakas 1995), as well as factors affecting morbidity, mortality and survival for colorectal cancer patients (Lobaziewicz 2008; Macadam 2005). The greatest amount of

research has been conducted on colorectal cancer, with respect to which this meta-analysis has identified 36 original papers, widely differing in their designs, analysis, and results. Nearly two thirds of them, however, reported a significant detrimental effect of PBT on recurrent tumors. Furthermore, in almost all negative studies the inspection of both the observed difference and the power of the study itself should have led the authors to state that results were inconclusive, or that a type-II error was possible: this was considered in only a few such papers (Francis 1987; Weiden 1987; Jakobsen 1990). In fact, in order to identify a difference of 15% with 80% certainty, and accepting a 5% significance level, one would need 226 to 275 patients, taking into account non-cancer deaths and patients lost to follow-up. In this respect, many studies had insufficient sample sizes. Therefore, their pooling substantially reduced the possibility of a beta-error, and increased the likelihood of detecting small differences.

All these considerations, as well as the non conclusive evidence from the literature, have represented the rationale for the present meta-analysis. Our results show a harmful transfusion effect, with overall odds of recurring 68% higher and rate difference 11% larger in transfused patents operated for colorectal cancer. These results are significant, and are consistent when examining only retrospective studies, or studies with multivariable analyses. However, significant heterogeneity was detected in these cases, thus confirming the wide differences in design and populations of the included studies. A further analysis was conducted including only the studies of higher quality, the prospective studies, or the specific RCTs: significant findings of the same magnitude in effects size were obtained in these cases, but without heterogeneity. Furthermore, all these results confirm our early reports (Amato 1998), and are also supported by the more recent findings by Chung et al. (Chung 1993) and by Vamvakas et al. (Vamvakas 1993), derived from a smaller number of trials ($n=8$ and 9 , respectively). In particular, the pooled estimate obtained by Vamvakas et al. in their first "qualitative" meta-analysis ($OR=1.37$, 35b) is similar to our estimate when only prospective studies are taken into account, and their subsequent meta-analysis for explanation showed an overall unadjusted relative risk for colorectal cancer recurrence of 1.50 (95%CI, 1.18 to 1.90) in 15 studies, being 1.18 (95%CI, 0.93 to 1.51) in seven prospective studies, and 1.68 (95%CI, 1.35 to 2.08)

in 16 studies with regression analyses. The authors concluded that a possible effect of confounding could not completely explain the unadjusted transfusion effect (Vamvakas 1995).

Particularly interesting are the results of the four specific randomised controlled trials, which have been performed recently with the specific aim of verifying the detrimental association between allogenic PBT and colorectal cancer recurrence (Tartter 1992; Busch 1995; Heiss 1994; Houbiers 1994). The first study, designed to use allogenic packed red cells in the transfusion arm as opposed to no transfusions, showed a detrimental effect of PBT, with a two and half risk of recurring for transfused patients (Tartter 1992). The other three studies compared autologous to allogenic blood. Among them, that by Heiss et al. showed a two times bigger risk of recurrence with transfusions, although their 95%CI were not significant (Heiss 1994). Busch et al. highlighted a detrimental effect of allogenic transfusions (OR=1.85, 95%CI 1.22 to 2.82), although they attributed the increased transfusion risk to the conditions necessitating the transfusions, more than to PBT per se (Busch 1995). Finally, Houbiers et al. showed a non significant effect of PBT on recurrence (OR=1.23, 95%CI 0.87 to 1.73) but, surprisingly, they found a difference in survival in favour of non-transfused patients (Houbiers 1994). The conclusions of both the latter studies, however, have raised some questions, related not only to a relatively large proportion of patients receiving allogenic blood even in the autologous arm, but also to other methodological issues. The pooled PBT effect computed in these studies was in accordance with that observed overall, but without significant heterogeneity. It has to be underlined that none of the RCTs could randomise between transfusion and no-transfusion.

A meaningful interpretation of our results was also achieved by considering PBT effect over recurrence in patients stratified by known prognostic factors. With regard to tumor site, both rectal and colon cancers confirmed a detrimental effect of PBT, in contrast with one conclusion of Vamvakas et al. (Vamvakas 1993). Rectal cancers, which were transfused more often than colon cancers, showed a higher risk of recurring, with an approximately twofold increase in their odds. Colonic cancers showed a lower recurrence risk when given PBT, and this might be further impacted by the increasing adoption of adjuvant chemotherapy regimens. As far as the different tumor stages were concerned, a significant PBT effect was confirmed consistently throughout, although with significant heterogeneity across studies. This effect was less evident in the advanced C stage, where it was probably masked by the concomitant negative effect of advanced disease, known as the major cause of recurrent colorectal cancer, and weighting more than transfusion as an independent prognostic factor in all multivariable analyses examined.

Our results were also stratified according to other prognostic factors that could have been independently associated with blood transfusions and cancer recurrence. These included variables such as preoperative anaemia, duration of operations, volume of blood loss, as well as amount, type and timing of PBT, which have been linked to depressed immune response and early cancer recurrence. These analyses could have helped to clarify whether transfusion

was simply a "proxy variable", that is a variable reaching statistical significance despite any lack of causality with recurrence. In fact, transfusions could simply be an index of "nasty" tumors, which cause severe anaemia and are at increased risk of recurring, more than a direct cause of recurrence per se.

The analyses involving transfusion-related factors showed that recurrences were more likely with transfusions independent of their timing, and the type of blood product used. They also showed a dose-dependent relationship, with three or more units of transfused blood almost doubling the risk observed with one or two units. It has to be stressed that some heterogeneity was detected in these studies, and that these areas could be explored only in part, due to absent or unclear definitions for the type of blood used, and to the absence of specific data for the timing of PBT. No data were available to fully elucidate the effect of leukocyte depletion on recurrence.

Finally, none of the analyses considering surgical trauma or operative techniques could be carried out. A definition of these factors, which could have better clarified a possible cause-effect mechanism, was seldom given and only a few papers presented data to allow meaningful comparisons. In particular, it was impossible to address the complete removal of the mesorectum in the case of rectal cancer (a common practice these days, which might require more blood transfusions but achieve better local tumor control), as well as the possible differences related to number and seniority of the involved surgeons, issues that could have explained many differences in the reported recurrence rates.

AUTHORS' CONCLUSIONS

Implications for practice

The additional evidence published up to December 2009, when integrated with the previous data, confirms the previous conclusion of a moderate association between PBT and an increased risk of recurrence in colorectal cancer patients operated for cure. This still proves valid in both colon and rectal cancers, for early and advanced tumor stages, and most likely occurs in a dose-dependent way, regardless of the timing and type of the transfused blood. Because of the important implications of these implications, carefully restricted indications for PBT should be considered in colorectal cancer patients undergoing curative surgery.

Implications for research

The above conclusion should represent the working hypothesis for future clinical trials, whose great challenge will be to control also for surgical procedures, quality and type of the blood to administer, target hematocrit, and concomitant use of immunomodulators or adjuvant chemotherapy.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Beynon 1989

Methods	Retrospective Study
Participants	519 Dukes A-C, colorectal cancer patients
Interventions	74.2% perioperative transfusions
Outcomes	recurrence rate
Notes	Log-linear model used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Blumberg 1990

Methods	Retrospective Study
Participants	197 Dukes A-C2, colorectal cancer patients
Interventions	65.5% perioperative transfusions (whole blood, packed red cells)
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Burrows 1987

Methods	Retrospective Study
Participants	295 Dukes B2-C2, colorectal cancer patients
Interventions	60.0% perioperative transfusions
Outcomes	disease-free survival
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Busch 1995

Methods	Randomized Controlled Trial
Participants	423 Dukes A-C, colorectal cancer patients
Interventions	66.0% intra- and postoperative transfusions (allogenic and autologous)
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Cheslyn-Curtis 1990

Methods	Randomized Controlled Trial
Participants	961 Dukes A-C, colorectal cancer patients
Interventions	61.5% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Creasy 1987

Methods	Retrospective Study
Participants	68 Dukes A-C, sigmoid cancer patients
Interventions	48.5% perioperative transfusions
Outcomes	disease-free survival
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Deleplanque 1992

Methods	Retrospective Study
Participants	753 Dukes B-C, colorectal cancer patients
Interventions	82.2% perioperative transfusions
Outcomes	disease-free survival
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Edna 1998

Methods	Retrospective Study
Participants	336 Dukes A-C, colorectal cancer patients
Interventions	70% perioperative transfusions
Outcomes	recurrence-free survival overall survival cancer survival
Notes	

Risk of bias

Edna 1998 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Francis 1987

Methods	Retrospective Study
Participants	87 Dukes A-C, colorectal cancer patients
Interventions	60.9% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Frankish 1985

Methods	Randomized Controlled Trial
Participants	174 Dukes A-C, colorectal cancer patients
Interventions	59.2% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Fuhrman 1992

Methods	Retrospective Study
Participants	33 Dukes B-C, rectal cancer patients
Interventions	24.2% intra- and post-operative transfusions
Outcomes	recurrence rate

Fuhrman 1992 (Continued)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Harder 1990

Methods	Randomized Controlled Trial
Participants	266 Dukes A-C, colorectal cancer patients
Interventions	74.8% perioperative transfusions
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Heiss 1994

Methods	Randomized Controlled Trial
Participants	100 Dukes A-C, colorectal cancer patients
Interventions	52.0% intra- and post-operative transfusions (allogenic and autologous)
Outcomes	recurrence rate disease-free survival
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Houbiers 1994

Methods	Randomized Controlled Trial
Participants	697 Dukes A-C2, colorectal cancer patients

Houbiers 1994 (Continued)

Interventions	64.0% intra- and post-operative transfusions (leukocyte-depleted packed cells)
Outcomes	recurrence rate disease-free survival
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Jahnson 1992

Methods	Retrospective Study
Participants	217 Dukes B-C, colorectal cancer patients
Interventions	63.6% perioperative transfusions (whole blood, packed red cells)
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Jakobsen 1990

Methods	Retrospective Study
Participants	265 Dukes A-C, colorectal cancer patients
Interventions	82.3% perioperative transfusions
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Kjems 1991

Methods	Retrospective Study
Participants	141 Dukes B-C, colorectal cancer patients
Interventions	74.9% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Leite 1993

Methods	Retrospective Study
Participants	128 Dukes A-C, colorectal cancer patients
Interventions	57.0% perioperative transfusions (whole blood, packed red cells, plasma)
Outcomes	disease-free survival
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Liewald 1990

Methods	Retrospective Study
Participants	439 Dukes A-C, colorectal cancer patients
Interventions	69.2% perioperative transfusions (whole blood, packed red cells)
Outcomes	recurrence rate
Notes	Logistic regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Marsh 1990

Methods	Retrospective Study
Participants	132 Dukes B-C, colorectal cancer patients
Interventions	17.4% perioperative transfusions (whole blood, packed red cells, plasma)
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Mecklin 1989a

Methods	Retrospective Study
Participants	520 Dukes A-C, colorectal cancer patients
Interventions	68.3% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Modin 1992

Methods	Retrospective Study
Participants	712 Dukes B-C, colorectal cancer patients
Interventions	73.3% perioperative transfusions (whole blood, packed red cells, plasma)
Outcomes	recurrence rate
Notes	Poisson regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
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Modin 1992 (Continued)

Allocation concealment?	Unclear risk	D - Not used
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Mynster 2001

Methods	Prospective Cohort (within a Randomized Trial)
Participants	524 Dukes A-C, colorectal cancer patients
Interventions	60% perioperative RBC (SAM-G) transfusions
Outcomes	recurrence rate survival
Notes	Cox regression and Logistic regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Parrott 1986

Methods	Retrospective Study
Participants	335 Dukes A-C, colorectal cancer patients
Interventions	66.6% perioperative transfusions
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Pellicer 1990

Methods	Retrospective Study
Participants	403 Dukes B-C, colorectal cancer patients
Interventions	68.0% perioperative transfusions
Outcomes	recurrence rate
Notes	

Perioperative blood transfusions and recurrence of colorectal cancer (Review)

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Pellicer 1990 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Pinto 1989

Methods	Retrospective Study
Participants	248 Dukes A-C1, colorectal cancer patients
Interventions	74.6% perioperative transfusions (whole blood, packed red cells)
Outcomes	recurrence rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Rasmussen 1997

Methods	Retrospective Study
Participants	70 Dukes A-C rectal cancer patients
Interventions	36% perioperative transfusions (whole blood in SAMG)
Outcomes	recurrence rate
Notes	Logistic regression on recurrence rate

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Sene 1993

Methods	Prospective Cohort
Participants	379 Dukes A-C, colorectal cancer patients
Interventions	58.3% perioperative transfusions

Sene 1993 (Continued)

Outcomes	recurrence rate	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Sibbering 1994

Methods	Prospective Cohort	
Participants	266 Dukes A-C, colorectal cancer patients	
Interventions	45.5% perioperative transfusions	
Outcomes	disease-free survival	
Notes	Cox regression used	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Steup 1994

Methods	Retrospective Study	
Participants	644 Dukes A-C, colorectal cancer patients	
Interventions	65.4% perioperative transfusions (whole blood, packed red cells)	
Outcomes	recurrence rate	
Notes	Cox regression used	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Tang 1993

Methods	Retrospective Study	
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Tang 1993 (Continued)

Participants	725 Dukes B-C, colorectal cancer patients	
Interventions	65.1% perioperative transfusions (whole blood, packed red cells, plasma)	
Outcomes	recurrence rate	
Notes	Cox regression used	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Tartter 1992

Methods	Randomized Controlled Trial	
Participants	339 Dukes A-C2, colorectal cancer patients	
Interventions	34.2% perioperative transfusions (packed red cells)	
Outcomes	recurrence rate	
Notes	Cox regression used	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

van Lawick 1988

Methods	Retrospective Study	
Participants	164 Dukes A-C, colorectal cancer patients	
Interventions	71.3% perioperative transfusions (whole blood, packed red cells)	
Outcomes	disease-free survival	
Notes	Cox regression used	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Weiden 1987

Methods	Retrospective Study
Participants	171 Dukes A-C2, colorectal cancer patients
Interventions	60.2% perioperative transfusions (whole blood, packed red cells)
Outcomes	recurrence rate
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Werner 1988

Methods	Retrospective Study
Participants	129 Dukes A-D, colorectal cancer patients
Interventions	74.4% perioperative transfusions (type?)
Outcomes	recurrence-free survival
Notes	Cox regression used. Dukes D present in 3 pts (2 rectal ca.)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Wobbes 1989

Methods	Retrospective Study
Participants	270 Dukes A-C, colorectal cancer patients
Interventions	68.1% perioperative transfusions (whole blood, packed red cells)
Outcomes	disease-free survival
Notes	Cox regression used

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Akyol 1992	No data
Altomare 1995	No data
Amato 1994	No data (letter)
Amato 2006	Review
Ambiru 1999	No data (liver mets)
Andreu 1996	Review
Apolone 1990	Review
Araujo SE	No data
Arnoux 1988	Repetitive
Auer 2000	No data (carcinoid)
Aufevre 1994	Review
Bachoo 2000	No data
Barbatzas 1996	No data
Basili 2008	No data
Benevento 2000	No data (mets)
Benoist 2001	No data on recurrence rates
Bentzen 1990	Survival
Bjerrum 2006	Review
Blair 1985	Survival
Blajchman 1998	Review
Blumberg 1985	Repetitive
Blumberg 1986	Repetitive
Blumberg 1987	Review
Blumberg 1988	Repetitive
Blumberg 1989	Review
Blumberg 1990a	Review

Study	Reason for exclusion
Blumberg 1993	No data (letter)
Blumberg 1994	No data (letter)
Blumberg 1994a	Review
Blumberg 1995	No data (letter)
Blumberg Agarwal 83	Repetitive
Bock 1990	No data (laryngeal ca.)
Bordin 1995	Review
Braga 1995	No data
Bristow 2003	No data
Brivio 1993	No data
Browning 2009	No data
Buell 2001	No data (liver mets)
Bulow 2001	No data
Burdy 2001	No data
Burrows 1982	Repetitive
Burrows 1983	Repetitive
Busch 1992	Repetitive
Busch 1993	Repetitive
Busch 1993a	No data (letter)
Busch 1993b	Repetitive
Busch 1994	Repetitive
Busch 1994a	Review
Busch 1995a	Repetitive, letter
Cady 1992	No data (liver mets)
Ceelen 1996	No data (mets)
Cheslyn-Curtiss 1988	Repetitive
Chiarugi 1996	Repetitive
Chiarugi 2000	No data (adjuvant)

Study	Reason for exclusion
Christodoulakis 2005	No data
Chu 2006	No data
Chung 1993	Review
Coop Study Gr 1989	Review
Corman 1986	Survival
Corman 1988	Repetitive
Cowen 1981	No data (polyps)
Crowson 1989	Survival
Cunliffe 1988	No data (letter)
Curley 2004	Review
de Canniere 1993	No data
Devon 2009	Review
Ding 2009	No data
Dionigi 2007	Review
Dolezal 1997	No data (letter)
Donohue 1995	No data (adjuvant treatment in >50% patients). Survival?
Douillard 1986	No data
Dunne 2002	No data
Edwards 2009	No data
Eisenkop 2004	No data (ovarian cancer)
Elias 1996	Review
Elorza 1992	No data
Faenza 1992	Survival
Fernandez-Fernandez	Survival
Fielding 1985	Review
Ford 1994	No data
Foster 1985	Survival
Foster 1988	Repetitive

Study	Reason for exclusion
Foster 1988a	No data (letter)
Francis 1985	Repetitive
Francis 1988	No data (letter)
Francis 1988 Comment	No data (letter)
Francis 1988a	Review
Francis 1989	No data (letter)
Gangi 2000	No data (liver mets)
Garau 1994	Survival
Gauthier-Benoit 1990	No data (survival?)
Genetet 1991	Review
Gibbons 1988	No data (prostate ca.)
Gigot 2002	No data (liver mets)
Gonzales 2008	No data
Gorog 1996	No data
Gouvas 2009	No data
Guma 1998	Review
Hamblin 1986	Review
Hansler 2003	No data
Harder 1989	Repetitive (Laffer)
Harford 1988	Review
Heiss 1992	Repetitive (survival)
Heiss 1993	Repetitive (survival)
Heiss 1994a	No data (letter)
Heiss 1996	No data
Hemming 2003	No data
Hermaneck 1996	Review
Hill 2003	Review
Hodgson 1982	No data (letter)

Study	Reason for exclusion
Hoh 1990	No data
Isbister 2000	No data
Jadallah 1999	Survival (positive effect at univariate and multivariate analyses). No data on recurrence at univariate analysis; negative on recurrence at multivariate analysis.
Jagoditsch 2006	No data
Jeekel 1995	Review
Jeekel 1996	No data
Jensen 1994	No data (letter)
Jensen 2005	Repetitive
Jensen 2006	Survival
Johnson 1998	No data (liver mets)
Kama 2003	No data
Kapiteijn 2002	No data
Kapoor 2008	No data
Katoh 2008	No data
Kiff 1987	Repetitive
Klingler 1989	Survival
Kooby 2003	No data (liver mets)
Kreimeier 1996	Review
Laffer 1989	Repetitive (Harder '90)
Lambert 1990	No data (mets)
Lange 2009	Repetitive
Lasser 1999	No data
Laurent 2003	No data (liver mets)
Lawrance 1990	No data
Lee 2009	No data
Leite 1991	Repetitive
Leung 1999	Survival

Study	Reason for exclusion
Li 2006	Survival
Lichtiger 1990	No data
Lidder 2004	Repetitive
Lidder 2007	No data
Lobaziewicz 2008	No data
Luna-Perez 2001	No data (survival)
Lykke 2003	Review
Macadam 2005	No data
Mador 1985	No data (prostate cancer)
Mala 2002	No data (liver mets)
Mannaerts 2002	No data
Maroun 2003	No data
Marquet 1993	Review
Mathiesen 1998	No data
Matviichuk 1998	No data
McDonough 2001	No data (prostate cancer)
Mecklin 1989	Review
Mikamo 1995	No data (mets)
Miki 2006	Survival
Mincheff 1995	Review
Molland 1995	Survival
Morschel 1996	No data
Munoz 2009	No data
Mynster 2000	Repetitive
Nathanson 1985	Survival
Ness 1992	No data (prostate ca.)
Ng 2006	No data
Nielsen 1988	Review

Study	Reason for exclusion
Nielsen 1995	Review
Nogueras 1993	No data
Norfolk 1995	No data
Nursal 2006	No data
O'Byrne 1989	No data (letter)
O'Rourke 2004	No data (hepatectomy)
Okuyama 2005	No data
Onodera 1989	Survival
Ostgaard 1996	Review
Ota 1985	Survival
Parrott 1987	Repetitive (survival?)
Parrott 1988 Comment	No data (letter)
Pasic 2008	No data
Quigley 1996	No data
Quintiliani 1991	Survival
Remzi 2006	No data
Rhoads 1966	No data
Rickard 2004	No data
Rivoire 1992	Review
Rodriguez-Ramirez 2006	No data
Ross 1987	Survival
Ross 1993	No data (letter)
Ross 1994	No data (letter)
Sabalic 2006	No data
Sato 2003	No data
Scheele 1999	No data (liver mets)
Schricker 1990	No data (survival?)
Schriemer 1988	Review

Study	Reason for exclusion
Schwandner 1999	No data
Seifert 2004	No data (liver mets)
Shander 2004	Review
Sjo 2008	Survival
Skankberg 2007	Survival
Soloway 1995	No data (prostate ca.)
Staudacher 2006	No data
Stephenson 1988	No data (liver mets)
Stephenson 1993	No data (letter)
Tartter 1984	No data (lung ca.)
Tartter 1985	No data
Tartter 1987	No data (limphocytes)
Tartter 1988	Review
Tartter 1988a	Review
Tartter 1988b	No data
Tartter 1989	Review
Tartter 1989a	None
Tartter 1995	Review
Tartter 1996	No data
Taylor 1988	Review
Taylor 1990	Review
Teshima 1997	No data (prostate cancer)
Ulrich 2009	No data
Valbonesi 1999	Review
Vamvakas 1993	Review (Meta-analysis)
Vamvakas 1995	Review (Meta-analysis)
van De Watering 2001	Repetitive (Houbiers 1994)
van Rossen 1999	No data (RBC)

Study	Reason for exclusion
Vente 1989	Survival
Vignali 1996	No data
Vignot 2005	Review
Voogt 1987	Survival
Vuong 2007	No data
Walsh 1992	No data (polyps)
Waymack 1989	Survival
Weber 2003	No data (liver mets)
Weiden 1990	Review
Wiig 1990	Review
Wirsching 1988	Repetitive (Liewald '90)
Wolters 1996	Survival
Wu 1988	Review
Wu 1997	No data
Wu 2008	No data
Yamamoto 1999	No data
Yo 2001	No data
Younes 1991	No data (liver mets)
Zimmerman 1991	Survival
Zimmermann-Nielsen	No data on curative cases only (palliative cases included)
Zincke 1994	No data (prostate ca.)
Ziv 1991	No data (LFC)

DATA AND ANALYSES

Comparison 1. Studies on Recurrence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All Studies	36	12127	Odds Ratio (M-H, Fixed, 95% CI)	1.68 [1.54, 1.83]
2 Prospective Studies	10	4126	Odds Ratio (M-H, Fixed, 95% CI)	1.36 [1.18, 1.56]
2.1 RCTs	7	2957	Odds Ratio (M-H, Fixed, 95% CI)	1.42 [1.20, 1.67]
2.2 PCs	3	1169	Odds Ratio (M-H, Fixed, 95% CI)	1.22 [0.95, 1.58]
3 Retrospective Studies	26	8001	Odds Ratio (M-H, Fixed, 95% CI)	1.91 [1.71, 2.13]
4 Multivariate Analysis	23	7581	Odds Ratio (M-H, Fixed, 95% CI)	1.71 [1.53, 1.90]
5 RCTs/PCs	10	4126	Odds Ratio (M-H, Fixed, 95% CI)	1.36 [1.18, 1.56]
6 Specific RCTs	4	1556	Odds Ratio (M-H, Fixed, 95% CI)	1.65 [1.31, 2.08]
7 Top 25% Quality	12	4717	Odds Ratio (M-H, Fixed, 95% CI)	1.61 [1.41, 1.84]
8 Colon Cancer	11	2405	Odds Ratio (M-H, Fixed, 95% CI)	1.64 [1.36, 1.98]
9 Rectal Cancer	12	1963	Odds Ratio (M-H, Fixed, 95% CI)	2.03 [1.61, 2.57]
10 Dukes A-B	12	2551	Odds Ratio (M-H, Fixed, 95% CI)	1.93 [1.58, 2.37]
11 Dukes C	12	1307	Odds Ratio (M-H, Fixed, 95% CI)	1.51 [1.18, 1.92]
12 Pre-operative Transfusions	5	1123	Odds Ratio (M-H, Fixed, 95% CI)	1.50 [1.10, 2.06]
13 Intra-operative Transfusions	9	2611	Odds Ratio (M-H, Fixed, 95% CI)	1.74 [1.45, 2.08]
14 Post-operative Transfusions	9	2183	Odds Ratio (M-H, Fixed, 95% CI)	1.67 [1.36, 2.05]
15 Red Blood Cells	7	2110	Odds Ratio (M-H, Fixed, 95% CI)	1.65 [1.35, 2.01]
16 Whole Blood	5	1014	Odds Ratio (M-H, Fixed, 95% CI)	2.07 [1.55, 2.76]
17 1-2 Transfused Units	12	2884	Odds Ratio (M-H, Fixed, 95% CI)	1.40 [1.18, 1.67]
18 3-4 Transfused Units	10	2311	Odds Ratio (M-H, Fixed, 95% CI)	1.69 [1.40, 2.03]
19 >=5 Transfused Units	9	2019	Odds Ratio (M-H, Fixed, 95% CI)	2.02 [1.65, 2.48]

Analysis 1.1. Comparison 1 Studies on Recurrence, Outcome 1 All Studies.

Analysis 1.2. Comparison 1 Studies on Recurrence, Outcome 2 Prospective Studies.

Analysis 1.3. Comparison 1 Studies on Recurrence, Outcome 3 Retrospective Studies.

Analysis 1.4. Comparison 1 Studies on Recurrence, Outcome 4 Multivariate Analysis.

Analysis 1.5. Comparison 1 Studies on Recurrence, Outcome 5 RCTs/PCs.

Analysis 1.6. Comparison 1 Studies on Recurrence, Outcome 6 Specific RCTs.

Analysis 1.7. Comparison 1 Studies on Recurrence, Outcome 7 Top 25% Quality.

Analysis 1.8. Comparison 1 Studies on Recurrence, Outcome 8 Colon Cancer.

Analysis 1.9. Comparison 1 Studies on Recurrence, Outcome 9 Rectal Cancer.

Analysis 1.10. Comparison 1 Studies on Recurrence, Outcome 10 Dukes A-B.

Analysis 1.11. Comparison 1 Studies on Recurrence, Outcome 11 Dukes C.

Analysis 1.12. Comparison 1 Studies on Recurrence, Outcome 12 Pre-operative Transfusions.

Analysis 1.13. Comparison 1 Studies on Recurrence, Outcome 13 Intra-operative Transfusions.

Analysis 1.14. Comparison 1 Studies on Recurrence, Outcome 14 Post-operative Transfusions.

Analysis 1.15. Comparison 1 Studies on Recurrence, Outcome 15 Red Blood Cells.

Analysis 1.16. Comparison 1 Studies on Recurrence, Outcome 16 Whole Blood.

Analysis 1.17. Comparison 1 Studies on Recurrence, Outcome 17 1-2 Transfused Units.

Analysis 1.18. Comparison 1 Studies on Recurrence, Outcome 18 3-4 Transfused Units.

Analysis 1.19. Comparison 1 Studies on Recurrence, Outcome 19 ≥ 5 Transfused Units.

WHAT'S NEW

Date	Event	Description
1 November 2010	New search has been performed	Results updated to reflect the updated search to December 2009

HISTORY

Protocol first published: Issue 4, 2004

Review first published: Issue 1, 2006

Date	Event	Description
5 August 2008	Amended	Converted to new review format.
13 November 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

A. Amato: review of papers from beginning to end (1982-2009)

M. Pescatori: review of papers between 1982 to 1996.

DECLARATIONS OF INTEREST

I certify that I have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of the review (e.g. employment, consultancy, stock ownership, honoraria, expert testimony).

INDEX TERMS

Medical Subject Headings (MeSH)

*Transfusion Reaction; Colorectal Neoplasms [*etiology] [immunology]; Neoplasm Recurrence, Local [*etiology] [immunology]

MeSH check words

Humans