CRD summary
This review compared consolidation therapy with autologous bone marrow transplantation (ABMT) and non-myeloablative chemotherapy for adults with acute myeloid leukaemia in first remission. The authors concluded that there is no evidence to support the use of ABMT in these people. This conclusion seems reliable.

Authors' objectives
To compare the efficacy of consolidation therapy with autologous bone marrow transplantation (ABMT) versus non-myeloablative chemotherapy alone or no further treatment following induction therapy, for adults with acute myeloid leukaemia (AML) in first remission who did not have a histocompatible sibling donor.

Searching
MEDLINE and PREMEDLINE (1966 to September 2002), EMBASE (1980 to September 2002), the Cochrane Controlled Trials Register (Issue 3, 2002), Cancerlit (1975 to August 2002) and reference lists were searched; there were no language restrictions. Primary authors were contacted if important data were not available in the published studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that compared ABMT versus chemotherapy or no further treatment were eligible for inclusion. Also eligible were cohort studies that offered allogeneic bone marrow transplant to all eligible participants with an available sibling donor at first remission and randomised all remaining participants to ABMT versus chemotherapy or no further treatment.

Specific interventions included in the review
Studies were eligible for inclusion if they compared ABMT versus chemotherapy or no further treatment. The exact transplantation and chemotherapy regimens used differed between the individual studies and were reported in the review.

Participants included in the review
Studies were eligible if they included adults aged 15 to 55 years with primary or de novo AML in first remission, who did not have a matched sibling donor (or if data about patients in the specified age range could be extracted). Trials that included people with secondary AML were also eligible as long as these patients were not the sole focus. The authors reported eligibility criteria for each individual study included in the review.

Outcomes assessed in the review
The authors did not explicitly state the outcomes that studies had to include in order to be eligible for the review. The primary outcomes in the review were overall and disease-free survival at 48 months. The secondary outcomes were treatment-related mortality and the proportion of participants who achieved and remained in second remission if they relapsed during consolidation therapy (salvage rate).

How were decisions on the relevance of primary studies made?
Two authors independently assessed potential studies for relevance by examining titles and abstracts. Articles considered relevant by either author were retrieved for a more in-depth assessment by both authors. The authors were not blinded to the study outcomes or authorship when assessing relevance. Only articles deemed relevant by both authors were included. Any disagreements were resolved by consensus or referral to a third author. Kappa scores were calculated for inter-rater agreement on relevance.
Assessment of study quality
The authors used an 8-item checklist to assess whether: whether all eligible participants were assessed for a sibling donor; all patients with a sibling donor were assigned allogeneic bone marrow transplant and all remaining participants were randomly assigned to comparison groups; randomisation was centralised; allocation was concealed; randomisation was stratified; the outcome assessors were blinded; and the outcomes were assessed on an intention-to-treat basis. The completeness of follow-up was assessed using a 4-point ordinal scale (less than 1%, 1 to 5%, greater than 5% to 20%, greater than 20%). Two authors independently assessed the studies for validity using a checklist. A kappa score for inter-rater agreement was calculated.

Data extraction
Two authors independently extracted the data using a standardised data extraction form. Any disagreements were resolved by consensus. Data were extracted on the study accrual period, eligibility criteria, interventions, median follow-up and outcomes.

Methods of synthesis
How were the studies combined?
The authors summarised trends in study findings narratively and pooled the data quantitatively using a fixed-effect model, weighting by inverse variance, to calculate differences in disease-free and overall survival at 48 months or the nearest recorded assessment point. Publication bias was assessed by visual inspection of funnel plots, and was corrected for using trim-and-fill techniques.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Cochran Q test.

Results of the review
Six RCTs (or randomised trials following cohort accrual) with 1,044 participants were included in the review.

The authors reported substantial inter-rater agreement in the validity assessment (weighted kappa 0.70).

People who received ABMT had better disease-free survival at 48 months than those who received chemotherapy or no further treatment (ratio of disease-free survival probabilities in 6 trials 1.24, 95% confidence interval, CI: 1.06, 1.44, P=0.006; heterogeneity P=0.38). The ratio of overall survival probabilities (from 5 trials) was 1.01 (95% CI: 0.89, 1.15, P=0.86; heterogeneity P=0.33). There was no statistically significant difference in disease-free survival (P=0.38) or overall survival (P=0.33) between the studies.

ABMT was associated with a statistically significantly greater risk of death during first remission (odds ratio from 6 studies 2.63, 95% CI: 1.6, 4.32, P<0.001).

Funnel plots suggested some degree of publication bias, in that the results of small negative trials might not have been published. The authors performed a modelled analysis to correct for this and found that publication bias was unlikely to have made a statistically significant difference to the findings.

Authors’ conclusions
There was no evidence to support the routine use of ABMT in adults with AML in first remission.

CRD commentary
This review included a defined research question and pre-specified inclusion criteria. The search strategy appeared appropriate and, although the review was restricted to published studies, the authors’ attempt to assess the impact of publication bias suggested that small unpublished studies would have made little difference to the findings. The authors
described the methods used to select, quality assess, and analyse the included studies in some detail. This gives confidence in the quality of the review and the studies on which it was based.

There was no statistical heterogeneity in the included studies so it appears appropriate to have pooled the data quantitatively. Not all data were available to conduct pooled analyses, but the methods used to account for these omissions seemed suitable. Where necessary, the authors included estimates of outcomes at 48 months, but also conducted analyses with and without studies where relevant data were not available. The similarity of the findings when using both techniques gives more confidence in their generalisability.

Overall, the authors’ conclusions appear to be supported by the data presented.

Implications of the review for practice and research
Practice: The authors stated that the results did not support the use of ABMT in all eligible patients. They suggested that non-myeloablative chemotherapy should be used during first remission for people with AML who do not have a matched sibling donor, with the option of salvage therapy with ABMT or transplant from an unrelated donor for those who relapse.

Research: The authors stated that further research is necessary to identify subgroups who might benefit from routine ABMT, such as people with cytogenetic features associated with poor risk.

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