Infection-control interventions for cancer patients after chemotherapy: a systematic review and meta-analysis

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CRD summary
This review concluded that protective isolation interventions including administration of prophylactic antibiotics reduced mortality in cancer patients or stem cell transplant recipients at high risk of infection. Outpatient management of stem cell transplant recipients reduced mortality in observational studies and should be evaluated in randomised trials. The authors' conclusions reflected the evidence presented and appeared likely to be reliable.

Authors' objectives
To quantify the evidence for infection control interventions for high-risk cancer patients and haematopoietic stem cell transplant (HSCT) recipients.

Searching
The authors searched Cochrane Central Register of Controlled Trials (to 2006), PubMed (to 2008) and LILACS (to 2006). Proceedings of named conferences were searched to 2006 for unpublished trials. Bibliographies of all included studies and relevant reviews were screened. No language restrictions were imposed. Search terms were not reported, but were available on request from the authors.

Study selection
Prospective comparative studies assessing environmental measures, barrier precautions and other non-pharmacological interventions for infection control were eligible for the review. Eligible participants were patients receiving chemotherapy for cancer in hospital or ambulatory settings and HSCT recipients. The primary outcome was all-cause mortality at 30 days, 100 days and longest follow-up. Predefined secondary outcomes were reported. Most included studies assessed protective isolation (air quality control, barrier isolation and prophylactic antibiotics alone or in combination) or outpatient (versus inpatient) care for patients with haematological malignancies or HSCT recipients. Eligible comparators for protective isolation interventions were placebo, no treatment or another intervention, but actual comparators in included studies were not reported.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
For randomised controlled trials (RCTs), methods of allocation sequence generation, allocation concealment, blinding, intention-to-treat analysis and number of patients excluded from outcome assessment were evaluated by two reviewers independently. Differences were resolved by discussion with a third reviewer. The authors did not report that they assessed validity of other study designs.

Data extraction
For dichotomous outcomes, relative risks (RRs) and 95% confidence intervals (CIs) were calculated from the numbers of patients and events in each group. Mean differences were calculated for continuous outcomes. Data were extracted preferentially by intention-to-treat. Two reviewers independently extracted data. Differences were resolved by discussion with a third reviewer.

Methods of synthesis
Studies were pooled by meta-analysis using fixed-effect models. A random-effects model was used if significant heterogeneity was present. Heterogeneity was assessed using a $\chi^2$ test (pc0.1 being taken as significant) and the $I^2$ statistic. Subgroup analyses by patient risk category and type of prevention measure were performed to explore heterogeneity. All analyses were stratified by study design (randomised or non-randomised).

Results of the review
Forty studies were included in the review: 26 (n = 7,405; 14 RCTs) assessed protective isolation; 11 non-randomised studies (n = 1,158) compared outpatient and inpatient care; and three studies (n = 165) assessed other interventions.

Protective isolation interventions significantly reduced mortality at 30 days (RR 0.60, 95% CI: 0.50, 0.72), 100 days (RR 0.78, 95% CI: 0.71, 0.86) and longest follow-up (RR 0.86, 95% CI: 0.81, 0.91). Similar significant reductions were seen when RCTs were analysed separately. Air quality control and barrier isolation without prophylactic antibiotics did not significantly reduce mortality. In HSCT recipients, mortality at longest follow-up was significantly lower in outpatients compared with inpatients (RR 0.72, 95% CI: 0.53, 0.97). Results for other outcomes and analyses were reported.

**Authors' conclusions**
Antibiotic prophylaxis was the main component responsible for the beneficial effect of complex protective isolation interventions. Outpatient management of patients with haematological cancer should be evaluated in randomised trials.

**CRD commentary**
This review had clear inclusion criteria. The search covered a number of relevant databases without language restrictions and included an attempt to locate unpublished studies. Study selection and data extraction were done by two independent reviewers, reducing the risk of errors and bias in the review process. Validity of included RCTs was assessed, but it did not appear that the results were used in the analysis. However, randomised and non-randomised studies were assessed separately. Relevant details of included studies were presented in the paper and tables were available online, although more details of experimental and control interventions would have been helpful.

Studies of similar interventions were pooled by meta-analysis; the absence of significant statistical heterogeneity suggested that this was appropriate. Clinical differences between studies were investigated by subgroup analyses that appeared to have been specified in advance. As noted by the authors, a possible limitation of the review was the inclusion of some older studies of protective isolation that may not have reflected current conditions.

The authors' conclusions reflected the evidence presented, were supported by evidence from other sources and appeared likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that for HSCT recipients and patients with acute leukaemia, efforts should be directed towards administering effective prophylaxis. Barrier precautions might improve the efficacy of prophylaxis and reduce cross-transmission of resistant pathogens. Air quality control should probably be reserved for patients at highest risk of invasive mould infections and for endemic or outbreak settings.

Research: The authors stated that an RCT to assess the additional value of air quality control to strict barrier precautions and prophylaxis is ethical and justified where air filtration was not available or not used for all patients. They also recommended trials to assess sterile or low-bacterial diets and to assess specific components of barrier precautions in hospital for patients with solid tumours. Future studies should assess the interventions’ effects on quality of life.

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