<table>
<tr><th>Reference and country</th><th>Study type and period</th><th>Study quality</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcomes</th><th>Source of funding</th><th>Additional comments</th></tr>
<tr><td>Cooper et al (2011)</td><td>Systematic review of RCTs</td><td>See GRADE tables for quality summary according to outcomes</td><td>23 trials. See GRADE tables for number of patients according to outcomes</td><td>Adult cancer patients with solid tumours or lymphoma</td><td>Primary G-CSF prophylaxis. Antibiotic prophylaxis permitted if identical in both trial arms.</td><td>No G-CSF prophylaxis (placebo or nothing)</td><td>All cycles of chemotherapy in the study. Number of cycles varied between studies from 4 to 11. The length of each cycle varied from 1 to 3 weeks.</td><td>Febrile neutropenia.

Subgroup anaylsis according to type of G-CSF.

Comparison between pegfilgrastim and filgrastim also reported (see GRADE table).</td><td>Amgen Ltd</td><td>Unclear whether FN risk was calculated using febrile patients or febrile episodes (possibly multiple per patient).</td></tr>
<tr><td>Rahman and Khan (2009)

Bangladesh</td><td>RCT

2006-2007</td><td>Unclear allocation concealment, no blinding</td><td>80</td><td>Adult patients with acute leukaemia, hospitalized and at risk of neutropenia (ANC <0.5 X10^{9}/l)</td><td>Levofloxacin prophylaxis, 500mg, orally once daily from start of chemotherapy until resolution of neutropenia or documentation of fever</td><td>Placebo</td><td>Patients were examined daily for clinical signs of infection. The duration of follow-up was not reported</td><td>Febrile neutropenia:
<table><tr><th>Group</th><th>n</th><th>N</th></tr><tr><td>levofloxacin</td><td>17</td><td>40</td></tr><tr><td>placebo</td><td>18</td><td>40</td></tr></table>
Microbiologically documented infection
<table><tr><th>Group</th><th>n</th><th>N</th></tr><tr><td>levofloxacin</td><td>4</td><td>40</td></tr></table></td><td>Bangladesh Medical Research Council and Square Pharmaceutical Ltd.</td><td></td></tr>
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Reference and country	Study type and period	Study quality	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcomes	Source of funding	Additional comments
								placebo 7 40		
Hecht et al (2010) USA	RCT 2003-2008	Unclear allocation concealment, no blinding mentioned	252	Adult patients with colorectal cancer receiving FOLFOX, FOLFIRI or FOIL chemotherapy	Pegfilgrastim (6mg – administered per cycle on day 4)	Placebo	ANC and temperature were assessed at the start of each cycle. Between cycles patients were advised to consult their doctor in the case of fever. There was long term follow-up for overall survival up to 2 years following study period.	Neutropenic fever **Group** / **n** / **N** pegfilgrastim 2 123 placebo 9 118 Mortality during the treatment period **Group** / **n** / **N** pegfilgrastim 7 123 placebo 7 118	Amgen Inc.	

Reference and country	Study type and period	Study quality	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcomes	Source of funding	Additional comments
Gafter-Gvili et al (2005) Israel	Systematic review of RCTs. Search date 2005	See GRADE tables for quality summary according to outcomes	101 trials with 12599 patients. See GRADE tables for number of patients according to outcomes	Patients with cancer and neutropenia induced by chemotherapy or bone marrow transplantation.	Prophylactic antibiotics (quinolones, co-trimoxazole, and others)	Other antibiotic, placebo or no intervention	Not reported – but outcomes typically measured over one course of treatment.	See GRADE tables for results of outcomes relevant to the review question **Primary outcomes:** Mortality, measured at 30 day follow-up or at the end of the follow-up in each study. The number of patients that developed febrile episodes **Secondary outcomes:** Clinically documented infection, microbiologically documented infection, bacteraemia, superinfection rates, hospital admission rates, length of hospital stay	Not reported	
Gafter-Gvili et al (2007) Israel	Systematic review of RCTs. Search date 2006	See GRADE tables for quality summary according to outcomes	58 trials with 7878 patients. See GRADE tables for number of patients according to	Patients with cancer and neutropenia induced by chemotherapy or bone marrow transplantation.	Prophylactic antibiotics (quinolones)	Placebo, no intervention or cotrimoxazole	Not reported – but outcomes typically measured over one course of treatment.	See GRADE tables for results of outcomes relevant to the review question **Primary outcomes** Microbiologically documented infection with bacteria resistant to the antibiotic used for prophylaxis. Colonisation with bacteria resistant to the	Not reported – no conflict of interest reported.	

Reference and country	Study type and period	Study quality	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcomes	Source of funding	Additional comments
			outcomes					antibiotic used for prophylaxis. **Secondary outcomes** Colonisation by resistant bacteria in relation to the presence of resistant bacteria prior to antibiotic prophylaxis. Infections resistant to antibiotics other than quinolones following prophylaxis.		
Herbst et al (2008)	Systematic review of RCTs. Search date 200?	See GRADE tables for quality summary according to outcomes	2 trials including 195 patients. See GRADE tables for number of patients according to outcomes	Patients with cancer undergoing myeloppressive chemotherapy, bone marrow transplantation or stem cell transplantation.	G(M)-CSF prophylaxis	Antibiotic prophylaxis	Maximum follow up was 2 years (for overall survival)	See GRADE tables for results of outcomes relevant to the review question **Primary outcomes** Overall survival, microbiologically or clinically documented infection. **Secondary outcomes** Severe infections, infectious episodes, frequency of febrile neutropenia (using study definitions), all cause mortality and quality of life.	German Federal Ministry of Education and Research	

Reference and country	Study type and period	Study quality	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcomes	Source of funding	Additional comments
Sung et al (2007) USA	Systematic review of RCTs. Search date 2007	See GRADE tables for quality summary according to outcomes	148 trials with 16839 patients or cycles. See GRADE tables for number of patients according to outcomes	Patients receiving cancer chemotherapy or stem cell transplant	Prophylactic colony stimulating factors (G-CSF, GM-CSF or PEG). Prophylactic antibiotics could be used	Placebo or no prophylactic colony stimulating factor. Prophylactic antibiotics could be used	Not reported – but outcomes typically measured over one course of treatment.	See GRADE tables for results of outcomes relevant to the review question All-cause mortality, infection related mortality. Any documented infection, microbiologically documented infection, sterile site bacterial infection, documented fungal infection and clinically documented infection. Febrile neutropenia, duration of febrile neutropenia, duration of fever, time to ANC recovery. Duration of IV antibiotics, administration of systemic antifungals, duration of antifungals and duration of hospitalization.	Part funded by the Canadian Institutes of Health Research.	

Reference and country	Study type and period	Study quality	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcomes	Source of funding	Additional comments
Pinto et al 2007. USA	Systematic review of RCTs. Search date 2006.	See GRADE tables for quality summary according to outcomes. The review does not report allocation concealment was adequate in the included trials.	5 trials including 617 patients.	Adults with non-myeloid cancer including solid tumours and lymphoma.	Single sub-cutaneous injection (6 mg or 100□g/kg) of pegfilgrastim used as prophylaxis after the start of chemotherapy	Daily injection (up to 14 days) of 5□g/kg of filgrastim used as prophylaxis after the start of chemotherapy	Outcomes reported over one course of chemotherapy	See GRADE tables for results of outcomes relevant to the review question **Primary outcomes** Grade IV neutropenia, febrile neutropenia, time to ANC recovery and bone pain	Amgen Inc.	
Spunt et al 2010. USA, Australia	Multicentre phase II RCT. 2000-2007	No blinding, allocation concealment unclear.	44	Children and young adults (2 to 22 years) with sarcoma, median age 11 years.	Single sub-cutaneous injection (6 mg or 100□g/kg) of pegfilgrastim used as prophylaxis after the start of chemotherapy	Daily injection (up to 14 days) of 5□g/kg of filgrastim used as prophylaxis after the start of chemotherapy	Outcomes measured over cycle 1 and cycle 3	Febrile neutropenia (ANC <0.5 X 10^9/L and oral temperature > 38.2°C) **Group** / **n** / **N** PEG / 31 / 37 filgrastim / 5 / 6 Other outcomes: duration of grade 4 neutropenia, time to ANC recovery,	Amgen Inc., National Cancer Institute, Cancer Centre support grants	

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								pharmacokinetics of pegfilgrastim and filgrastim.		
Massey et al (2009) UK	Systematic review of RCTs. Search date 2008	See GRADE tables for quality summary according to outcomes.	Ten RCTs including 705 patients.	Patients with neutropenia (due to treatment or disease)	Granulocyte transfusions given as prophylaxis, prior to the development of documented infection.	No granulocyte transfusion.	Time points for assessment of mortality were not clearly stated in all trials, and varied from 21 days to 100 days.	**Primary outcome** Death from any cause **Secondary outcomes** Death due to infection, number of infections, number of days of antimicrobial treatment, change in neutrophil count, duration of neutropenia		