Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
Bakshi et al (2009) USA,					
Retrospective Analysis **July 2003-July 2007**	To assess the outcomes of high dose cytosine arabinoside consolidation cycles versus inpatient in paediatric AML patients	N=30 patients received 90 HIDAC cycles • Median Age was 8 years (1.5-15) • 23 patients ha standard daunorubicin and cytosine arabinoside • 7 patients received daunorubcin, cytosine arabinoside and etopside as induction • 21/90 cycles were administered as inpatients and 69 as outpatient	Outpatient Chemotherapy	Inpatient Chemotherapy	• Mortality • Morbidity • Antifungal use • Median number of blood investigations (complete blood counts/liver function tests/renal function tests) was significantly lower in the outpatient group. • A median of 1 (0-4) unit of packed red blood cells was transfused per consolidation cycle in the outpatient setting and 2 (0-5) in the inpatient setting. • A median of 1 (0-13) platelet transfusions were administered at the outpatient clinic and 2 (0-12) in the inpatient setting • 25/69 consolidation cycles resulted in hospital admission and all were associated with febrile neutropenic episodes or documented infections • Hospital stay was significantly shorter in outpatient cycles compared with inpatient cycles ($p<0.001$) leading to a saving of 269 patient-days for the entire study group. • There was no significant difference between inpatient and outpatient mortality. • Febrile neutropenia was recorded in 66/90 cycles; 50 in the outpatient group and 16 in the inpatient group. • 16/50 outpatients and 10/16 inpatients required second line antibiotics ($p=0.03$) and mean duration of antibiotic administration was significantly lower in the outpatient group ($p=0.04$). • There was significantly more use of therapeutic antifungals in the inpatient group compared with the outpatient group. ***Comments*** ***Study Quality*** Not randomised Outpatient chemotherapy was administered to patients who could not get an inpatient bed in time to avoid treatment delays (possible selection bias)

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					Comments Only results from round 2 randomisation are relevant to this topic Patients were randomised to round 1 intensive chemotherapy and if they reached complete remission were eligible for round 2 randomisation between ambulatory and intensive postremission therapy with stratification by centres, AML type and round 1 treatment group.
					Study Quality Only patients with complete remission in after round 1 treatment were put forward for round 2 randomisation
Hutter et al (2009) Germany **Follow-up= 8 years**					
Retrospective cohort control **November 2000 (renovation happened in October 2006)**	To assess thecorrelation between improvement of room comfort conditions in patients with newly diagnosed AML on a haematological waard and the incidence of invasive pulmonary aspergillosis	N=63 N=28 patients after renovation works N=35 patients before renovation works	Post Room Renovation 2 patients per room Separate restroom in each room equipped with toilet, wash basin and shower No ventilation system, air filtration or room pressurisation No false ceilings	Pre Room Renovation 3 patients per room 6 patients sharing a toilet placed outside patients room Washing bowl inside patients room Showering involved crossing the hospital corridor	Incidence of invasive pulmonary aspergillosis Patients treated before renovation stayed 3 days longer compared with the treated on the newly renovated ward. There was no significant difference in median time of aplasia which was 1.0 longer (18.5 versus 19.5 days) in the pre-renovation cohort (p=0.69). 39% of pre-renovation patients and 34% of post-renovation patients developed an invasive pulmonary aspergillis (p=0.79) with diagnosis usually determined on CT scan. Patients in the post-renovation cohort received more CT scans (64% versus 54%) 2 patients in the pre-renovation group died during initial AML treatment versus 4 in the post-renovation group. Average *Aspergillus fumigates* was 7 (0-28) CFU/m^3 pre-renovation and was 19 (0-106) CFU/m^3 post-renovation. Aspergillus air concentration was measured 11 times from November 2002 until the ward closed and 9 times after the new ward opened and cumulative concentration of fungal spores was 75 (2-273) CFU/m^3 in the rooms pre-renovation compared with 209 (67-299) CFU/m^3 post renovation
					Comments

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td></td><td></td><td>No ventilation system, air filtration or room pressurisation
No false ceilings</td><td>Study Quality

Not biased
Small sample</td></tr>
<tr><td colspan="6">Lehrnbecher et al (2012), Multiple countries including UK</td></tr>
<tr><td>Retrospective Study</td><td>To assess institutional recommendations regarding restrictions of social contacts, pates and food and instructions on wearing face masks in public for children with standard risk ALL and any risk AML during intensive chemotherapy</td><td>N=336 centres in 27 countries</td><td>Recommendations on restrictions</td><td>Each other</td><td>• Variation in recommendations for social contact, exposure to pets, food and the use of face masks in public
• Restriction scores by location and centre size

N=336 centres in 27 countries (1-76 institutions per country) responded to the survey.
Overall response rate for the study was 61% (range per country was 34%-100%)
21 centres in the UK were approached of which 16 responded constituting 4.8% of the total centres responding to the survey.
The majority of centres had fewer than 20 newly diagnosed patients with ALL and fewer than 5 patients newly diagnosed with AML per year.
<table>
<tr><th></th><th>No. of newly diagnosed patients</th><th>No. of centres (%)</th></tr>
<tr><td>ALL</td><td><10</td><td>120 centres (36%)</td></tr>
<tr><td></td><td>10-19</td><td>112 centres (33%)</td></tr>
<tr><td></td><td>20-40</td><td>73 centres (22%)</td></tr>
<tr><td></td><td>>40</td><td>31 centres (5%)</td></tr>
<tr><td>AML</td><td><5</td><td>231 centres (68%)</td></tr>
<tr><td></td><td>5-10</td><td>26 centres (8%)</td></tr>
<tr><td></td><td>>10</td><td>79 centres (24%)</td></tr>
</table>
107 centres (32%) had written protocols for non-pharmacological anti-infective approaches and n=64 (64%) had a general agreement without a written policy.</td></tr>
</table>

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>
In 85 centres (25%) practitioners used an individualised approach
A physician was involved in the instruction of parents in 89% (n=299) of centres and a nurse in 71% of centres (n=238).
A handout was provided to parents in 52% (n=174) of centres and was the only information given in 4% (n=14) of cases.
42% of parents received a handout and were additionally provided with verbal information by a nurse or physician.

Social Contact
Most centres do not allow children with AML to visit indoor public place, attend daycare or kindergarten or attend school while recommendations for patients with ALL varied considerably.
Restrictions mostly related to neutropenia (58%) and to chemotherapy regimens.
The health of surrounding people was a pre-condition for reduced restrictions in 16% of centres.

Pets
There was wide variation in recommendations for both AML and ALL patients.
Restrictions under certain circumstances related to appropriate hand-washing after contact (27%), keeping animals already at home without introducing new pets (25%), restriction of pets in the bedroom or on the bed(22%), ensuring pets were assessed by a veterinary specialist (17%) and restrictions on cleaning of cages/litter trays (16%).

Food
Most centres had restrictions on raw meat, raw seafood and unpasteurised milk for both AML and ALL patients
There were wide variations in food restrictions around salad, nuts, takeaway food and unpeeled vegetables.
In 68% of cases, restrictions were generally related to neutropenia and specific chemotherapy regimens .
If uncooked vegetables or salad were allowed, appropriate cleaning was advised (12%).

Face Masks
9% (n=30) institutions recommended children with ALL wear face masks in public while 34% (n=114) recommend face masks for AML patients.
54% (n=181) never suggest facemasks for children with ALL and 41% (n=138) never suggest facemasks for children with AML.

Restriction scores in Europe were significantly higher than in USA, suggesting greater restrictions

<table>
<tr><th></th><th colspan="3">Social Restrictions (Max score, 12)</th><th colspan="3">Pet Restrictions (max score 10)</th><th colspan="3">Food Restrictions (Max score 10)</th></tr>
<tr><th></th><th>USA/Canada</th><th>Europe</th><th>P</th><th>USA/Canada</th><th>Europe</th><th>P</th><th>USA/Canada</th><th>Europe</th><th>P</th></tr>
<tr><td>ALL</td><td>5 (0-12)</td><td>7 (0-12)</td><td><0.001</td><td>3 (0-8)</td><td>5 (0-10)</td><td>0.06</td><td>6 (0-13)</td><td>10 (0-16)</td><td><0.001</td></tr>
<tr><td>AML</td><td>8 (0-12)</td><td>9 (0-12)</td><td>0.04</td><td>4 (0-10)</td><td>5 (0-10)</td><td>0.02</td><td>8 (0-16)</td><td>11 (0-16)</td><td><0.001</td></tr>
<tr><td>P</td><td><0.001</td><td>).007</td><td></td><td>0.007</td><td></td><td></td><td></td><td></td><td></td></tr>
</table>

Restriction scores did not differ by centre size

<table>
<tr><th></th><th colspan="3">Median Score (range)</th></tr>
<tr><th>New patients per year</th><th>Social Restrictions (max score 12)</th><th>Pet Restrictions (max score 10)</th><th>Food restrictions (max score 16)</th></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>ALL</td><td></td><td></td><td></td></tr>
<tr><td><10</td><td>7 (0-12)</td><td>5 (0-10)</td><td>9 (0-16)</td></tr>
<tr><td>10-19</td><td>6 (0-12)</td><td>4 (0-10)</td><td>10 (0-16)</td></tr>
<tr><td>20-40</td><td>6 (0-10)</td><td>6 (0-10)</td><td>8 (0-16)</td></tr>
<tr><td>>40</td><td>6 (0-10)</td><td>4 (0-10)</td><td>11 (0-16)</td></tr>
<tr><td>p</td><td>0.42</td><td>0.59</td><td>0.39</td></tr>
<tr><td>AML</td><td></td><td></td><td></td></tr>
<tr><td><5</td><td>9 (0-12)</td><td>5 (0-10)</td><td>10 (0-16)</td></tr>
<tr><td>5-10</td><td>9 (0-12)</td><td>5 (0-10)</td><td>12 (0-16)</td></tr>
<tr><td>>10</td><td>9(0-12)</td><td>4.5 (0-10)</td><td>10.5 (0-16)</td></tr>
</table>
Comments
Each question received a score of 2 for always restricted, 1 for sometimes restricted and 0 for no restrictions.

Study Quality
</td></tr>
<tr><td colspan="6">Luthi et al (2012), Switzerland</td></tr>
<tr><td>Retrospective study

November 1998-April 2001</td><td>N=17

Inclusion
16 years or older
Assigned to a relevant intensive chemotherapy treatment
Fitted with a central venous catheter
Live within 30km of the hospital
Relative consenting to be a care giver for the study duration</td><td>To evaluate the safety, feasibility and costs of home care for the administation of intensive chemotherapy</td><td>Chemotherapy in the home care setting</td><td>Inpatient chemotherapy

A subgroup of patients (n=7) received the same chemotherapy regimen at home and in the inpatient setting. These patients had already been treated in hospital and agreed to their next treatment being at home</td><td>

Feasibility
Safety
Quality of Life
Satisfaction of patients and relatives

Feasibility
1 physician visit and 2 nurse visits per day accounted for 621 visits during 46 treatment cycles (207 days of home treatment)
32 additional home visits were required as a result of technical problems with the pump (median, 1 visit per cycle; range 0-4 visits per cycle) and most visits were needed at the start of treatment.
Pump failure due to air bubbles was the main technical problem and was resolved by flushing the tube (n=21 cases)
Partial disconnection at the exit channel occurred in 9 cases and needle disconnection from the port of the catheter occurred in 2 cases
2 major pump failures were reported resulting in one overnight hospitalisation and a 4 day hospitalisation.

Safety
3 patients experienced medical complications; heart failure, angina attack and an allergic reaction to BCNU. All complications were treated at home and no hospitalisation was required
Grade 1-2 nausea and vomiting occurred during 36% of chemotherapy cycles are were dealt with at home
There were no requests for hospitalisation during home care from patients or carers
There were 8 unplanned hospital admissions following the home care period, 5 for febrile neutropenia, 2 for fever without documented infection and one for pneumonia.

Quality of Life</td></tr>
</table>

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					79% (73/92) questionnaires were returned completed. Mean FLIC score was 115.5±20.8 on day 1 of treatment (37 questionnaires) and remained stable until last day of treatment (114±21.1; 36 questionnaires). Questionnaires from 5 patients could be compared for home care and inpatient care (8 questionnaires; 37 chemotherapy cycles) and there was no difference in overall FLIC score or the seven individual FLIC categories. WHO performance status was 0 for 50% of patients on day 1 and remained stable at 0 in 28% of patients during chemotherapy and increased to one in 65% and 2 in 27% patients respectively. *Satisfaction of patients and relatives* 70% of patients returned questionnaires (32 questionnaires on 46 treatment cycles) 31 cases reported to be 'very satisfied' with home care and one case reported being 'satisfied' None of the patients showed a preference for inpatient care for next chemotherapy cycles 38% of patients stated a preference for home care and others had no declared preference Patient reported benefits of home care included a higher comfort level (100%), freedom and possibility to organise their own time (94%) and the reassurances and comfort of having a relative present (88%). 78% of patients were not concerned about the absence of a nurse 87% did not record any anxiety during home care treatment The main patient reported disadvantages were feelings of dependency on a relative (19%) and or being a burden (6%) Other concerns related to potential technical problems of the pump and side effects of chemotherapy Relative returned 29 questionnaires (63%) and all were in favour of home care and 97% were in favour of home care for next treatment (1 did not answer the question) 90% of relatives reported better tolerance to treatment (fewer side effects, less distress) as advantages of home care. Primary concerns about home care included the presence of strangers (nurse, physician) at home (16%), request for continuous presence as patients were not allowed to be alone for more than one hour (14%), anxiety and fatigue (14%) and lack of freedom for leisure and holidays (14%)
					Comments
					Study Quality Recall bias Small sample size

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td colspan="6">Schlesinger et al (2009)

Long enough to record the period covering engraftment after HSCT, neutropenia resolution and/or attainment of complete remission

Ranged from 100 days to 3 years</td></tr>
<tr><td>Systematic review and meta analysis</td><td>To quantify the evidence for infection control interventions among high risk cancer patients and haematopeitic stem cell recipients</td><td>Cancer patients in the hospital or ambulatory setting who were receiving chemotherapy for solid tumours, haematological malignancies and/or HSCT recipients.

N=40 studies

N=26 assessed protective isolation (14 randomised)
N=11 assessed outpatient versus inpatient care (non-randomised)
N=3 assessed unique interventions such as footwear exchange, Shinki bioclean rooms and a neutropenic diet

29 studies included patients with acute leukaemia
6 studies included other haematological cancers
2 studies included breast cancer patients undergoing HSCT
1 study included patients with aplastic anaemia
1 study included</td><td>Infection control interventions

Protective Isolation</td><td>No intervention

Placebo

Other interventions</td><td>• All cause mortality at 30 days, 100 days, and the longest follow-up in each study
• Rate of infection
• Type of infection
• Length of hospital stay
• Length of febrile period
• Infection related mortality
• Bacterial and fingal colonisation
• Antibiotic and actifungal treatment
• Adverse Events

All cause Mortality
Protective isolation with any combination of methods that included air quality control reduced the risk of death at 30 days (RR=0.6; 95% CI 0.5-0.72); 100 days (RR=0.79, 95% CI, 0.73-0.87) and at the longest available follow-up (RR=0.86, 95% CI 0.81-0.91).
No significant heterogeneity was observed when combining randomised and non-randomised studies (I^2=14.8%)

<table>
<tr><td>Protective environment/prophylactic antibiotics</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>30 day follow-up</td><td>9 studies
N=838 patients

RR=0.66 (0.49-0.87)</td><td>6 studies
N=5442

RR=0.57 (0.45-0.71)</td><td>15 studies
N=6280

RR=0.6 (0.5-0.72)</td></tr>
<tr><td>Any closest to 100 day follow-up</td><td>12 studies
N=1015 patients

RR=0.79 (0.73-0.87)</td><td>8 studies
N=5877 patients

RR=0.8 (0.72-0.88)</td><td>21 studies
N=6892 patients

RR=0.79 (0.73-0.87)</td></tr>
<tr><td>Longest follow-up</td><td>8 studies
N=691 patients

RR=0.84 (0.77-0.93)</td><td>5 studies
N=5382 patients

RR=0.87 (0.81-0.93)</td><td>13 studies
N=6073 patients

RR=0.86 (0.81-0.91)</td></tr>
<tr><td>PEPA versus no preventative measures</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any closest to 100 day follow-up</td><td>8 studies
N=538

RR=0.69 (0.56-0.84)</td><td>4 studies
N=512

RR=0.61 (0.43-0.85)</td><td>12 studies
N=1050

RR=0.66 (0.55-0.79)</td></tr>
<tr><td>Air Quality Control and Barrier Isolation</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td>patients high risk patients with sarcoma undergoing intensive chemotherapy</td><td></td><td></td><td>
<table>
<tr><td>Any closest to 100 day follow-up</td><td>8 studies
N=484

RR=0.86 (0.67-1.10)</td><td>2 studies
N=387

RR=1.20 (0.78-1.86)</td><td>10 studies
N=961

RR=0.93 (0.75-1.15)</td></tr>
<tr><td>Air Quality Control Alone</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any closest to 100 day follow-up</td><td>2 studies
N=66

RR=0.88 (0.58-1.33)</td><td>3 studies
N=5154

RR=0.81 (0.73-0.91)</td><td>5 studies
N=5220

RR=0.81-0.91)</td></tr>
<tr><td>Barrier Isolation Alone</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any closest to 100 day follow-up</td><td>2 studies
N=68

RR=1.25 (0.66-2.38)</td><td></td><td></td></tr>
<tr><td>Endogenous Flora Suppression</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any closest to 100 day follow-up</td><td>3 studies
N=155

RR=0.8 (0.56-1.16)</td><td>1 study
N=99

RR=1.11 (0.56-2.18)</td><td>3 studies
N=254

RR=0.88 (0.63-1.21)</td></tr>
</table>

Any clinically and/or microbiologically documented infection
Protective isolation significantly reduced the occurrence of any clinically and/or microbiologically documented infection when considering all studies together, studies assessing PEPA and studies assessing air quality control and barrier isolation. No significant difference was observed when assessing barrier isolation alone.

<table>
<tr><td>Protective environment/prophylactic antibiotics</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>11 studies
N=859

RR=0.61 (0.52-0.71)</td><td>9 studies
N=1045

RR=0.92 (0.79-1.06)</td><td>20 studied
N=1904

RR=0.75 (0.68-0.83)</td></tr>
<tr><td>PEPA versus no preventative measures</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>7 studies
N=439

RR=0.52 (0.42-.64)</td><td>6 studies
N=601

RR=0.75 (0.60-0.95)</td><td>13 studies
N=1040

RR=0.62 (0.53-0.76)</td></tr>
<tr><td>Air Quality Control and Barrier Isolation</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>7 studies
N=478

RR=0.71 (0.6-0.85)</td><td>2 studies
N=387

RR=0.35 (0.23-0.55)</td><td>9 studies
N=865

RR=0.61 (0.51-0.72)</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>Air Quality Control Alone</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>1 study
N=21

RR=0.91 (0.43-1.90)</td><td>3 studies
N=249

RR=1.54 (1.25-1.89)</td><td>4 studies
N=270

RR=1.48 (1.21-1.80)</td></tr>
<tr><td>Barrier Isolation Alone</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>2 studies
N=74

RR=1.64 90.93-2.89)</td><td></td><td></td></tr>
<tr><td>Endogenous Flora Suppression</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Any clinically and/or microbiologically documented infection</td><td>3 studies
N=136

RR=0.89 (0.72-1.10)</td><td>2 studies
N=228

RR=0.97 (0.65-1.46)</td><td>5 studies
N=364

RR=0.92 90.75-1.14)</td></tr>
</table>
Infection related mortality, bacteraemia, respiratory tract infections
Protective isolation resulted in significant reductions in infection related mortality, bacteraemia, and respiratory tract infections.
No significant benefit of protective isolation (all studies used air quality control) was observed in relation to mould infections nor was the need for systemic antifungal treatment reduced (RR=1.02, 95% CI 0.88-1.18).
Gram positive and gram negative infections were significantly reduced, though barrier isolation was needed to show a reduction in gram negative infections (RR= 0.49 (0.40-0.62) with barrier isolation (12 trials/n=1136) versus RR=0.87 (0.61-1.24) without barrier isolation (4 trials/n=328).
Need for systemic antibiotics did not differ when assessed on a per patient basis (RR=1.01, 0.94-1.09; 5 studies, 955 patients) but the number of antibiotic days was significantly lower with protective isolation (RR=0.81, 0.78-0.85; 3 studies, 6617 patient days).
Duration of hospital stay was shorter with protective isolation in 2 of 5 studies and was longer or similar length in the remaining 3 studies.
Discontinuation of the intervention was reported in 2-42% of patients as a result of psychological intolerance (usually occurring in older or sicker patients).
<table>
<tr><td>Protective environment/prophylactic antibiotics</td><td>Randomised</td><td>Non-randomised</td><td>All</td></tr>
<tr><td>Bacteraemia</td><td>9 studies
N=683

RR=0.48 (0.35-0.66)</td><td>6 studies
N=860

RR=0.79 (0.63-0.98)</td><td>15 studies
N=0.66 (0.55-0.79)

RR=0.66 (0.55-0.79)</td></tr>
<tr><td>Infections per 100 patient days</td><td>10 studies
N=36610

RR=0.59 (0.49-0.70)</td><td>4 studies
N=29821

RR=0.39 (0.27-0.55)</td><td>14 studies
N=66428

RR=0.53 (0.45-0.63)</td></tr>
</table>
</td></tr>
</table>

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results

Gram positive infections	10 studies N=966 RR=0.55 (0.4-0.76)	7 studies N=515 RR= 0.76 (0.62-0.91)	17 studies N=1481 RR=0.66 (0.56-0.79)
Gram negative infections	12 studies N=1136 RR=0.49 (0.40-0.62)	7 studies N=515 RR=0.70 (0.54-0.91)	19 studies N=1651 RR=0.55 (0.46-0.66)
Candida Infections	9 studies N=726 RR=0.31 (0.19-0.52)	6 studies N=5740 RR=0.84 (0.67-1.05)	15 studies N=6466 RR=0.69 (0.56-0.85)
Fungal Infections	6 studies N=388 RR=0.84 (0.33-2.14)	3 studies N=591 RR=0.42 (0.08-2.10)	9 studies N=979 RR=0.69 (0.31-1.53)
Infection related mortality	10 studies N=889 RR=0.54 (0.4-0.73)	6 studies N=860 RR=1.33 (0.89-1.99)	16 studies N=1749 RR=0.74 (0.59-0.93)
Respiratory Infection	10 studies N=776 RR=0.45 (0.32-0.63)	6 studies N=723 RR=0.77 (0.46-1.28)	16 studies N=1499 RR=0.53 (0.40-0.70)
Intervention discontinuation	5 studies N=394 RR=1.54 (0.93-2.56)	3 studies N=470 RR=57.0 (8.86-366)	8 studies N=864 RR=4.34 (2.78-6.76)

Neutropenic Care in the outpatient setting
11 non-randomised studies assessed neutropenic care in an outpatient setting (some degree of matching between inpatients and outpatients was used in 6 studies) and all included patients after HSCT.
A common requisite was for an adult caregiver to be available 24 hours and medical and nursing care was provided at home or in the outpatient clinic.
Febrile patients were discharged for further antibiotic treatment at home if stable.
All cause mortality was significantly lower in the outpatient setting (RR=0.72, 95% CI 0.53-0.97) at longest follow-up (median follow-up 12 months; range 1-36).
Febrile neutropenia or documented infections occurred less often in the outpatient group (RR=0.78, 95% CI 0.7-0.88; 8 studies, 757 patients), rates of bacteraemia were lower in the outpatient group but the difference was not significant (RR=0.68, 95% CI 0.43-1.05; 2 studies. 252 patients).

Comments

Study Inclusion Criteria
Prospective comparative studies including individual patient or cluster randomised trials, quasi-randomised trials,

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					controlled clinical trials, prospectively planned or prospective data collection for comparative cohort studies, before-after studies and interrupted time series studies. Studies comparing intervention with placebo, no treatment or another intervention All environmental measures, barrier precautions and other non-pharmacological measures used for prevention of acquisition of infectious agents or diseases. *Exclusions* Non-randomised studies comparing patients with different cancer types or had inherently different treatment protocols (HSCT versus chemotherapy). Studies done in outbreak settings Studies assessing pharmacological interventions such as antimicrobial prophylaxis and mouth rinse preparations unless these interventions were applied together or as a control for the infection control interventions. Children below the age of 15 years were included in 22 studies 3 studies did not specify the age of included patients Older studies used protective environment prophylactic antibiotic (PEPA) methods (use of a special room or plastic tent with built in air filtration device, total barrier isolation and use of non-absorbable antibiotics and other decontamination methods) 10 study groups assessed endogenous flora suppression alone; barrier isolation with endogenous suppression by non-absorbable antibiotics was assessed by six groups; barrier isolation alone in 5 groups, air quality control plus barrier isolation in 3 and air quality control alone was assessed in 1 study.
					Study Quality Not all haematology populations High risk patients
Sive et al (2012)					
Audit **) January 2005 – January 2011**	To present the experience in managing patients receiving intensive chemotherapy and HSCT protocols on daycare basis with full nursing and medical support while staying in a hotel within walking distance of the hospital	N=668 Inclusion • Patients aged 18 and over who consented to receive treatment within the ambulatory care unit and were independent of nursing care in the daily living (on their own or with a	Hotel Based Outpatient Care		• Admissions • Patients were reviewed daily by a dedicated ACU nursing team and clinician and a consultant review was carried out twice a week. • Predicted toxicities were assessed and vital signs (temperature, pulse and blood pressure were monitored) • Reviews were carried out in the ambulatory care unit, not in the hotel room and patients undergoing allogeneic transplant were treated exclusively in a side room to reduce the risk of infection. • Patients were provided with strict guidelines on when to contact the unit, instructed to call if they experienced rigors or a temperature of ≥38 degrees, persistent nausea, vomiting or diarrhoea or any other symptoms of concern • If a patient remained well throughout their ACU stay, they were discharged home while any patients with significant medical complications or who felt unable to cope in the hotel environment were admitted to the ward. *Admission Numbers* • There were 1443 admission to the Ambulatory Care Unit (9126 patient days) during the study period made up of 688 patients from 18-79 years of age. • Length of stay ranged from 1 to 42 days (median 5). • 82% of admissions were in haematology oncology patients with lymphoma being the largest single group of patients

<table>
<tr><th>Study Type/Setting</th><th>Aim</th><th>Population</th><th>Intervention</th><th>Comaprison</th><th>Outcomes and results</th></tr>
<tr><td></td><td></td><td>companion).
• Good command of written and spoken English (patient or companion)
• Able to follow advice in the event of becoming unwell
• A mobile phone
• Able to self administer oral medications and use a thermometer provided to them
• Mandatory companion for patients with limited mobility or receiving ifosfamide as part of their treatment (though all patients were recommended to have a companion).</td><td></td><td></td><td>by days of use.
• 1203 admissions were specifically for the administration of chemotherapy or HSCT and the for the monitoring period during the neutropenic phase immediately after treatment.
• Duration of stay varied based on treatment length and whether patients stayed in for monitoring during the neutropenic phase
• ESHAP (n=171), miniBEAM (n=57) and all acute myeloid leukaemia (n=80) were the most common regimens
• Autologous and allogeneic HSCT accounted for 368 treatment admissions with a median duration of stay of 9 days (2-25 days). There were 158 BEAM HSCT's , 136 melphalan autografts, 60 RI FMC and 10 BEAM-Campath allografts.
• For some chemotherapy regimens, patients discharged home after treatment stay were readmitted for monitoring during the neutropenic period
• Patients admitted to the ward and subsequently recovered but still requiring neutropenic monitoring were often readmitted to the ACU prior to going home.
• There were 158 monitoring admissions (1120 patient days; mean 7 days per admission) for the more myelosuppressive chemotherapy protocols such as the AML regimens and lymphoma protocols.

Outcomes of ACU stay
• Patients receiving less myelosuppressive regimens tended to be discharged home on treatment completion while patients receiving more intensive treatment almost always required readmission to the ward at some point.
• From 2008 onwards all allograft patients were admitted electively to the ward by the day of stem cell return regardless of their condition
• 813/1443 (56%) patients were discharged directly home
• 53/630 (9%) patients admitted to the ward were scheduled in advance
• 456/576 (79%) of unscheduled ward admissions were within ACU working hours, 66 (11%) were out of hours and 54 (9%) had no time recorded.
• The most common reason for unscheduled admission included infection or fever, nausea and vomiting and poor oral intake or dehydration.

ACU Episodes by treatment protocol
<table>
<tr><th>Treatment</th><th>Median Patients Age (range)</th><th>Number of ACU episodes</th><th>Total patients days in ACU (% of total)</th><th>Median length of ACU stay (days) (range)</th></tr>
<tr><td>AML intensive chemotherapy</td><td>41 (18-79)</td><td>80</td><td>818 (9%)</td><td>10 (1-30)</td></tr>
<tr><td>DA</td><td>48 (18-71)</td><td>21</td><td>251 (3%)</td><td>12 (3-30)</td></tr>
<tr><td>ADE</td><td>34 (27-39)</td><td>6</td><td>68 (1%)</td><td>14 (4-16)</td></tr>
<tr><td>MACE</td><td>38 (20-64)</td><td>15</td><td>139 (2%)</td><td>9 (4-15)</td></tr>
<tr><td>MiDAC</td><td>46 (20-71)</td><td>15</td><td>181 (2%)</td><td>12 (2-29)</td></tr>
<tr><td>HD AraC</td><td>36 (19-57)</td><td>17</td><td>137 (2%)</td><td>5 (1-16)</td></tr>
<tr><td>Other AML regimens</td><td>41 (20-79)</td><td>6</td><td>42 (<1%)</td><td>8 (2-5)</td></tr>
<tr><td>ALL intensive chemotherapy</td><td>26 (19-48)</td><td>36</td><td>253 (3%)</td><td>5 (2-42)</td></tr>
<tr><td>UKALL 2003 trial</td><td>19 (19-26)</td><td>17</td><td>70 (1%)</td><td>5 (2-19)</td></tr>
</table>
</td></tr>
</table>

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results

protocol				
UKALL12 trial protocol	27 (21-48)	19	183 (2%)	5 (2-42)
ATRA regimens	48 (40-53)	15	70 (1%)	8 (3-6)
Azacytidine	61 (32-62)	13	70 (1%)	5 (2-7)
ESHAP	44 (18-65)	171	961 (11%)	5 (2-15)
MiniBEAM	41 (18-63)	57	416 (5%)	6 (2-22)
CODOX-M/IVAC	35 (19-59)	21	185 (2%)	9 (3-15)
Other haematology chemotherapy	51 (19-74)	43	212 (2%)	4 (2-14)
Sarcoma Chemotherapy	24 (19-61)	379	1467 (16%)	4 (1-8)
Doxorubicin	45 (20-54)	10	35 (<1%)	4 (2-5)
Doxorubicin/Cisplatin	33 (26-54)	10	32 (<1%)	3 (2-5)
Doxorubicin/ifosfamide	34 (23-57)	42	153 (2%)	4 (2-5)
Etoposide/ifosfamide	29 (19-53)	63	293 (3%)	5 (2-7)
Ifosfamide	42 (21-61)	28	91 (1%)	3 (2-4)
MAP	24 (20-43)	116	535 (6%)	4 (2-8)
VAI	27 (20-46)	66	172 (2%)	3 (1-6)
VDC	24 (20-31)	17	54 (1%)	3 (1-5)
VIDE	22 (20-28)	18	63 (1%)	3 (2-6)
Other sarcoma chemotherapy	37 (24-61)	9	39 (<1%)	5 (2-6)
Other oncology chemotherapy	29 (23-46)	20	87 (1%)	4 (1-12)
RI FMC allograft	50 (25-63)	60	651 (7%)	9 (3-25)
RI BEAM-Campath allograft	36 (22-54)	10	72 91%)	8 (4-9)
Melphalan autograft	59 (32-70)	136	853(9%)	6 (2-12)
BEAM autograft	50 (18-69)	158	1444 (16%)	9 (3-18)
Other transplants	37 (21-45)	4	18 (<1%)	5 (3-6)
Monitoring	42 (18-71)	157	11071107 (12%)	6 (2-43)
Miscellaneous	38 (19-78)	83	442 (5%)	3 (1-25)

Comments
Chemotherapy regimens were the same as those given in the inpatient setting and all protocols and other medications were reviewed by a pharmacist.
Patients received medication counselling and a written reminder chart by the pharmacist
Supportive care and antimicrobial prophylaxis were given as required and according to the same protocols as ward based patients.

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					Study Quality
Sopko et al (2012)					
Retrospective Case series	To investigate the safety and feasibility of home care following consolidation chemotherapy	N=45	Home care after consolidation chemotherapy	Inpatient care after consolidation chemotherapy	• Discharge Rates • Mortality N=41 patients were discharged from hospital (73.2%) and the remaining 15 stayed in hospital. 17 patients required ambulatory management only while 24 patients required re-hospitalisation, primarily due to febrile neutropenia. In 36 febrile episodes the microbiologically documented infection was the most common cause of fever (61%) with the remaining episodes being of unknown origin. Patients re-hospitalised were admitted for a mean 10.9 days (6-35 days) versus a mean hospitalisation time of 30 days for inpatients (17-38). Mean duration of hospitalisation for inpatients from the time they became febrile to discharge was 14.3 days (7-22 days). 10 outpatients (43.5%) responded to initial therapy for febrile episodes compared with 2(16.7%) patients in the inpatient group. *Mortality* There were 2 (4.8%) deaths in the outpatients group compared with 1 (6.6%) death in the inpatient group
					Comments Patients who went home had to check their vital parameters daily, avoid obviously sick people, avoid places with large numbers of people, eat only fresh and well cooked meals, visit the clinic weekly and contact the clinic if there were any changes in clinical status. Change in clinical status resulted in patients being immediately admitted to clinic and a complete laboratory and clinical check performed Patients re-admitted to hospital and patients who remained in hospital were treated and managed in the same way Patients were usually discharged after several days of non-febrile period and when clinical and laboratory signs of infection were gone.

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					Study Quality This was a patient choice study. All patients offered the choice to go home after consolidation treatment or to stay in hospital were considered fit to go home therefore there is a high risk of selection bias with patients who choosing to go home likely to be different in some way to those who choose to remain in hospital.
Stevens et al (2005), Canada					
Randomised cross over trial	To compare two models of health care delivery for children with ALL	N=50 eligible N=29 agreed to take part Reasons for refusal included parents who preferred to bring their child to hospital for treatment, preferred to keep them at home or provided no reason. *Inclusions* Children attending the oncology outpatient clinic of the study setting for cancer treatment Aged 2-16 years Diagnosed with ALL in the year prior to enrolment Treated on a standard high risk ALL protocol by a paediatric oncologist Cared for at home by parents Spoke and read English or had an interpreter available	Home Chemotherapy	Hospital Chemotherapy	• Quality of life (child) • Effect on parental care givers • Adverse effects • Cost Phase 1 data were collected at Time 1 (baseline prior to randomisation); time 2 (3 months after start of phase 1); and time 3 (6 months after start/end of phase 1) Phase 2 data were collected at time 4 (3 months after start of phase 2) and time 5 (6 months after start/end of phase 2) N=23 children completed both home and hospital phases of the study There was no significant difference in baseline characteristics between the groups at the time of randomisation 24/29 patients who began the study were at the maintenance phase of their chemotherapy protocol *Quality of Life* • Children in the home group experienced a decrease in factor 1 (sensitivity to restrictions in physical functioning and ability of maintain a normal physical routine) of the POQOLS measure when they switched from home based treatment to hospital based treatment with an average change of 5.2. • Standard care patients experienced an improvement in QoL when they switched to home based treatment with an average score of -10.5 • The difference between the groups was significant (p=0.023) • There was no significant difference between the groups in relation to factor 2 (emotional distress) of factor 3 (reaction to current medical treatment) measures (p=0.95 and p=0.39 respectively). • Patients in the home based group had significantly higher scores for factor 2 (emotional distress) measures compared with the hospital treatment group (pairwise comparison at the end of each 6 months phase p=0.043). • There was no significant difference in factor 3 measures (p=0.061) • In a long term comparison (end of each 6 month phase), values of factor 1 measures did not differ with sites of chemotherapy administration. • There was no significant difference between the groups in CBCL (child behaviour checklist) scores at any of the follow-up periods *Burden Of Care* No evidence of an effect of the location of chemotherapy administration was observed on the parental burden of care (assessed using the caregiving burden scale).

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
		Resided in the greater metropolitan area *Exclusions* Children with other major congenital illnesses Children who did not have a patent central venous catheter for the administration of medications			***Comments*** • Baseline data was collected prior to randomisation • The two phase cross-over design allow the children serve as their own controls • Children were randomly assigned by the study site manager to either hospital (standard care) or home (treatment) chemotherapy for phase 1 (6 months) and children transferred to the other treatment group at 6 months for phase 2. ***Study Quality***
Stevens et al (2004), Canada					
Prospective descriptive study, nested in a randomised cross over trial	To evaluate quality of life, nature and incidence of adverse effects, parental caregiver burden and direct and indirect costs of a home chemotherapy program for children with cancer	N=33 health practitioners which included nurses, paediatric oncologists, administrators/unit managers, laboratory and pharmacy personnel *Inclusion* Aged 2-16 years Diagnosed with Acute Lymphoblastic Leukaemia for <1 year Treated on a hospital-based leukaemia protocol for newly diagnosed patients with high risk ALL Cared for by a paediatric oncologist and by parents at home in the greater metropolitan area of Toronto	Home Chemotherapy	Hospital Chemotherapy	• Perceived family benefits • Human Resources and service delivery implications • Hospital health practitioners perspective • Community Health practitoners perspective *Perceived Family Benefits* All practitioners claimed that the programme had a positive impact on daily life and psychological well-being of children and families particularly in relation to disruption and psychological stress. Health practitioners reported a reduction in disruption due to reduced travelling, reduced hospital clinic waiting time and reduced time missed from school and work. *"I think the big advantage is certainly it helps the children and their families to maintain a more normal routine on that day – to be able to avoid having to miss work and school – and have a big disruption and cost added to their day to come all the way down here for treatment that could be provided in a much shorter period and at a time that's more convenient for them."* Health practitioners reported noting fewer signs of psychological distress in children and parents during the home chemotherapy phase; children appeared happier and more comfortable while parents appeared to have more of a sense of control over the illness and treatment. *"Most kids seem to like it [chemotherapy] at home; they are happier. But I find that with community nursing in general. Some of the kids are so withdrawn when they come into the hospital, and are so different at home. So are the parents. Parents are usually more at ease at home, feel they have more control at home."* *Human Resources and Service Delivery Implications* Home chemotherapy was supported by both groups (home/hospital treatment) and by all types of health practitioners and they suggested ways in which the service could be improved to ensure a successful and safe healthcare delivery service. The advantages conferred by consistency in personnel and practice were emphasised by hospital based practitioners.

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					Children in the hospital setting were seen by the same practitioner which helped parents and children become comfortable and trusting while in the community setting, care providers were less consistent. *"I'm the consistent person that gives the chemotherapy and the children; they adapt to you and the way you do things, and you get to know them. That's consistent, that helps them."* [Clinic Nurse] *"Whoever was working that day would go to see the patients. It was mostly the three of us...whoever was working was going. It took longer, but generally not in the first time but within a few times, they would get comfortable with the procedure"* [Community Nurse] Both groups considered it to be important that community health practitioners should have specific education in relation to home care, administration of chemotherapy to children and meeting psychological needs of children with cancer and their families. 4 home care nurses took part in a 3 day educational session on chemotherapy administration and reported that they found the course extremely valuable. All health practitioners were of the opinion that practice standards should be similar for nurses administrating chemotherapy regardless of setting. Health practitioners agreed that the major benefit of hospital treatment was that the resources and treatments were all centralised and orchestrated. *"Their [children and parents] only experience has been with [hospital name] and you whip your child in and they get a little finger poke and then sometimes an hour or two later the results are back and then it's very smooth."* While having home chemotherapy, children had to go to community laboratories to have their blood work completed, many technicians lacked paediatric experience and were insensitive to their needs. *"The biggest one [problem] we have run into has been the whole lab issue and the fact that we've discovered that laboratories in the community are not very child friendly* [hospital programme director] There was also an issue with laboratory results not being communicated to the community nurses for subsequent drug prescription and home delivery resulting in increased workload while nurses retrieving results from hospital physicians. Some suggestions were put forward to streamline and refine the communication process with many responders suggesting one central person to liaise between the hospital and community. Some hospital physicians reported feeling less confident about prescribing chemotherapy agents for children due to the inability to assess the child directly and be in charge of the healthcare process in the community. They also reported feeling unclear about issues relating to liability and responsibility. Health practitioners felt that it was important that identifying eligibility criteria was important and thought that this should include families having a flexible schedule to accommodate treatment times, be familiar with the process of receiving chemotherapy and the types of chemotherapy, have the ability to handle change, to be housed in safe and clean living conditions, have high levels of compliance and be comfortable with healthcare delivered in the home. *"Not every family wants to have their home environment invaded with hospital equipment; they want to keep*

Study Type/Setting	Aim	Population	Intervention	Comaprison	Outcomes and results
					that a safe place." [community nurse] *Hospital Health Practitioners* 2 clinic nurses and 3 paediatric oncologists reported no change in their workload ; 5 clinic nurses and 1 physician reported an increase due to the increased volume of paperwork and 3 clinic nurses reported a decrease. The home chemotherapy programme was associated with less interaction with children and families which was considered to be both a positive (fewer patients in outpatient clinics, health practitioners less busy, more time for children in attendance) and negative (distressing because they were not sure how the children were coping with treatment) thing. *"You look forward to their visits, I do anyways. Because the communication of how they're really doing and how things are going is fort of broken down, there's a gap because you don't see them every two weeks."* [hospital clinic nurse] 13/14 community health practitioners reported an increase in workload primarily due to increased paperwork and increased time communicating with other health practitioners to expedite the process. *"It has added to my responsibilities, the day before having to give chemo, I am doing a lot of phone calling. Labs, clinic, chemo.. it can be very time consuming and very frustrating but the actual visit time is not the issue."* [community nurse] Community practitioners reported they had increased their repertoire of skills and 'felt good' about helping families which increased their personal satisfaction. It was also reported that partnership between community and hospital was enhanced by effective communication with opportunities to collaborate and share ideas and optimise treatments. Responses suggested an increased level of frustration as the home chemotherapy programme was challenging to accommodate in terms of scheduling between health practitioners and families. *"I found that we were juggling a lot. Trying to work around the teenagers schedules because you would end up calling them to say that you were going to come and do the chemo and they would say 'Oh no I'm off to something or other tonight' So I had to go the home early at 7:30 the next morning. So of course we tried to do that but when you have a lot of patients you just cannot do it. We can't always work around their schedule and I think that really needs to be made clear."* [community nurse]
					Comments Individual, moderately structures interviews with open-ended questions about the strengths and limitations of providing home chemotherapy to children, resource, training and education implications, extending the program and impact on the health practitioners' role. Interviews were between 20-90 minutes long depending on time available and information provided and was conducted by experienced interviewers.
					Study Quality