**Teuffel, O., Ethier, M. C., Alibhai, S., Beyene, J., & Sung, L. (2011). Outpatient management of cancer patients with febrile neutropenia: a systematic review and meta-analysis. *Annals of Oncology, Advance Access*.**

**Country:**

Canada

**Design:**

Systematic review

**Population:**

Cancer patients (adult and pediatric) with low-risk febrile neutropenia

**Inclusion criteria:**

Randomized controlled trials (RCTs) comparing any outpatient antibiotic treatment to any inpatient antibiotic treatment, or any outpatient oral antibiotic treatment to any outpatient intravenous antibiotic treatment, for the management of febrile neutropenia in cancer patients.

**Interventions:**

- Outpatient antibiotic treatment versus inpatient antibiotic treatment

Or

- Outpatient oral antibiotic treatment versus outpatient intravenous antibiotics treatment

**Outcomes:**

- Treatment failure (defined as one or more of the following: death; persistence, recurrence or worsening of clinical signs or symptoms; any addition to, or modification of the assigned intervention, including readmission)
- Mortality (30 day)
- Toxicity
- Readmission

**Results:**

| Outcome | Trials (episodes) | Risk ratio (95% CI; *P* value) | Risk reduction (95% CI; *P* value) |
|---|---|---|---|
| **Inpatient versus Outpatient** | | | |
| Failure (PPA) | 6 (738) | 0.81 (0.55–1.19; 0.28) | −0.02 (−0.06 to 0.02; 0.29) |
| Adults | 4 (470) | 0.79 (0.52–1.20; 0.27) | −0.05 (−0.11 to 0.02; 0.15) |
| Children | 2 (268) | 0.93 (0.32–2.71; 0.89) | 0.00 (−0.06 to 0.05; 0.85) |
| Mortality | 6 (742) | 1.11 (0.41–3.05; 0.83) | 0.01 (−0.01 to 0.03; 0.54) |
| Adults | 4 (474) | 0.96 (0.27–3.43; 0.95) | 0.00 (−0.02 to 0.03; 0.81) |
| Children | 2 (268) | 1.43 (0.27–7.42; 0.67) | 0.01 (−0.02 to 0.04; 0.51) |
| Toxicity | Data only reported in one study | | |
| **Outpatient IV versus Outpatient oral** | | | |
| Failure (PPA) | 8 (857) | 0.93 (0.65–1.32; 0.67) | −0.02 (−0.08 to 0.04; 0.52) |
| Adults | 3 (218) | 0.95 (0.29–3.13; 0.94) | 0.00 (−0.18 to 0.19; 0.97) |
| Children | 5 (639) | 0.90 (0.64–1.26; 0.53) | −0.02 (−0.08 to 0.04; 0.50) |
| Mortality | No deaths in any of the included studies | | |
| Toxicity | 4 (404) | 0.59 (0.06–5.85; 0.65) | −0.03 (−0.07 to 0.02; 0.27) |
| Adults | 2 (177) | 0.72 (0.02–33.74; 0.87) | −0.03 (−0.28 to 0.21; 0.79) |
| Children | 2 (227) | 0.40 (0.02–9.55; 0.57) | −0.02 (−0.06 to 0.02; 0.40) |
| Readmission | 7 (816) | 0.62 (0.28–1.39; 0.25) | −0.03 (−0.08 to 0.01; 0.14) |
| Adults | 2 (177) | 0.47 (0.01–14.61; 0.66) | −0.03 (−0.28 to 0.21; 0.79) |
| Children | 5 (639) | 0.52 (0.24–1.09; 0.08) | −0.03 (−0.07 to 0.01; 0.19) |

**General comments:**

This was a well conducted, comprehensive and recent systematic review, carried out according to the recommendations of the PRISMA statement. Electronic searches of OVID Medline (from 1950 to February 2010), EMBASE (from 1980 to February 2010), and The Cochrane Central Register of Controlled Trials (CENTRAL; until the first quarter of 2010) were carried out. Relevant references and conference proceedings from 2007 to 2010 were also searched using the Web of Science and Scopus databases. Two review authors independently extracted data from included trials. The primary outcome measures were (1) all-cause mortality at 30 days, (2) adverse events requiring discontinuation/modification of therapy, and (3) readmission to the hospital. Subgroup analyses for all outcomes by age (children versus adults) were conducted. To assess methodological quality and risk of bias, included articles were examined for sequence generation, allocation concealment, blinding, incomplete outcome data, and intention-to-treat (ITT) analysis. The authors concluded that based on the current literature, outpatient treatment of FN is a safe and efficacious alternative to inpatient management, though variation between studies in terms of time to discharge, choice of antibiotic class, and age of study population may limit interpretation of the data.

**Country:**

USA

**Design:**

Randomised Controlled Trial

**Population:**

121 episodes of febrile neutropenia in adult patients (median age 47) with post-chemotherapy fever and neutropenia recruited between September 1994 and January 1999

**Inclusion criteria:**

- Fever (≥100.5°F at presentation or by patient measurement at home) that persisted after at least 24-hour of inpatient observation
- Neutropenia (ANC less than 500/µL) that persisted after at least 24-hour of inpatient observation
- Evaluated as low risk by the Talcott et al. criteria
- Residence within 2 hours by surface transportation of hospital experienced in emergency care of patients with cancer
- Informed consent
- Permission of treating physician

**Exclusion criteria**

- AIDS associated malignancy
- Neutropenia arising more than 21 days after chemotherapy
- Intensive chemotherapy requiring bone marrow or peripheral stem cell support
-

**Interventions:**

- Continued hospital care (n = 71 randomised; n = 66 analysed)

Versus

- Discharged to home care (n = 50 randomised; n = 47 analysed)

**Outcomes:**

- Duration of fever
- Duration of neutropenia
- Duration of fever and neutropenia
- Antibiotics changed after random assignment
- Hospital readmission
- Major medical complications (hypotension; other; any major complication)

**Results:**

| | **Hospital care** | **Early discharge** | **All patients** |
|---|---|---|---|
| **Duration of fever** | | | |
| Median | 3 | 3 | 3 |
| Mean | 3.2 | 3.4 | 3.3 |
| Range | 0-13 | 1-14 | 0-14 |
| **Duration of neutropenia** | | | |
| Median | 4 | 4 | 4 |
| Mean | 4.1 | 4.2 | 4.1 |
| Range | 1-10 | 1-15 | 1-15 |
| **Duration of fever and neutropenia** | | | |
| Median | 4 | 4 | 4 |
| Mean | 4.6 | 4.5 | 4.6 |
| Range | 2-13 | 1-15 | 1-15 |
| **Antibiotics changed after random assignment** | | | |
| No. (%) | 16 (24%) | 4 (9%) | 20 (18%) |
| **Hospital readmission** | | | |
| No. (%) | - | 4 (9%) | - |
| **Major medical complications (hypotension; other; any major complication)** | | | |
| Hypotension | 5 (8%) | 3 (6%) | 8 (8%) |
| Other (anal pain) | 1 (1%) | 1 (2%) | 2 (2%) |
| Any major complication | 5 (8%) | 4 (9%) | 9 (8%) |

**General comments:**

- Method of randomisation and allocation concealment were adequate
- Patients randomly assigned to home treatment were discharged when home antibiotics became available. All patients were required to continue the antibiotic regimen in use at time of enrolment
- Analyses were completer only
- Clinical characteristics of both groups were similar
- The study did not report a measure of treatment failure, and this could not be determined from the presented data. It was not therefore possible to add this study to Teuffel et al's meta analysis.