



Economic burden of chemotherapy-induced febrile neutropenia in patients with lymphoma: A systematic review

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Contents

1. Background	00
1.1. Direct, indirect and intangible cost	00
1.2. Perspective	00
1.3. Approaches for cost estimation	00
2. Methods	00
2.1. General characteristics of included studies	00
2.2. Data analysis of included studies	00
2.3. Parameters associated with higher FN cost	00
2.4. Quality assessment of included cost-of-illness studies	00
3. Results	00
3.1. Search results	00
3.2. General characteristics	00
3.3. Data analysis of included studies	00
3.3.1. Comparison of inpatient and outpatient cost	00
3.3.2. Comparison of direct and indirect cost within inpatient care	00
3.3.3. Incidence of cost component among direct cost within inpatient care	00
3.3.4. Incidence of cost component among direct cost within outpatient care	00
3.4. Parameters associated with higher FN cost	00
3.5. Quality assessment of included cost-of-illness studies	00
4. Discussion	00
5. Conclusions	00
Conflict of interest	00
Reviewers	00
Author contributions	00
References	00
Biographies	00

Abstract

The primary objective of this review was to identify the cost components that were most frequently associated with the economic burden of febrile neutropenia (FN) among patients with lymphoma. The secondary objective was to identify any parameter associated with higher FN cost. Ten cost of illness (COI) studies were identified. General characteristics on study design, country, perspective, and patient population were extracted and systematically reported. It was observed that majority (70%) of the studies employed the perspective of healthcare provider.

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20% of the studies considered long-term costs. Estimated costs were adjusted to 2013 US dollars and ranged from US\$5819 to US\$34,756. The cost components that were most frequently associated with economic burden were ward and medication costs. Inpatient management, male gender, discharged dead, and comorbidity were positively associated with higher FN costs. Future COI studies on FN should focus on the accurate estimation on ward and medication costs.

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1. Background

Febrile neutropenia (FN) is a common life-threatening complication that may arise after cancer patients undergo myelosuppressive chemotherapy [1,2]. Patients with lymphoma are highly associated with this complication of chemotherapy because these patients often receive highly myelosuppressive chemotherapy [1,3].

The complications of FN in patients with lymphoma were demonstrated by a recent study which reported that a mortality rate of 6.6% and a median length of hospital stay of 7 days [4]. Complications of FN may extend over the long term as potential chemotherapy dose reduction and dose delay may occur among lymphoma patients who experienced FN. These complications of FN can incur a considerable economic burden as patients may require additional supportive care treatments and additional hospitalization costs due to FN [5]. Therefore, the cost of FN could be substantial among patients with lymphoma.

Cost-of-illness (COI) studies estimate the resources consumed and lost as a result of a particular disease [6]. Results from the COI studies can improve understanding of the economic burden that a specific disease may have on society as a whole, healthcare providers, and the individual patient [7,8]. Furthermore, COI studies typically evaluate the cost of a particular disease. This can provide a fundamental basis for some economic evaluation studies, such as cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis studies [9].

1.1. Direct, indirect and intangible cost

There are three cost components estimated in a COI study. These include: (a) direct costs (medical and non-medical), (b) indirect costs, and (c) intangible costs. Direct costs estimate the opportunity costs of all kinds of resources used to treat FN. It can be further separated into direct medical costs and non-medical costs. Direct medical costs include ward charges, laboratory test charges, radiography charges, transfusion charges, medication charges, emergency room visit charges, physician visit charges, and home nursing visit charges [10]. Direct non-medical costs represent the costs incurred by patients or their family members which are directly associated with FN, but without medical nature, such as transportation charges.

Indirect costs refer to the productivity losses due to morbidity or mortality. Productivity loss is the forgone productivity caused by work absences [11]. In most COI studies, indirect costs can account for a large proportion of the total costs [11,12].

Intangible costs refer to patients' psychological pain, discomfort, anxiety and depression due to FN. These costs are often measured in the form of quality of life [13].

1.2. Perspective

The perspective taken is an important consideration in COI studies. Based on different perspective chosen, the cost estimation can vary. The most popular perspectives include those of the patient, the employers, the insurance company, the healthcare providers, and the government or the society. The societal perspective is the most comprehensive approach in the COI studies. This approach can avoid cost underestimation that may occur when a narrower perspective is taken [8].

1.3. Approaches for cost estimation

There are three common methods to estimate the direct costs: econometric, bottom-up and top-down approach [8,14]. Indirect costs may be estimated in three ways: the human capital approach, the friction cost approach and the willingness-to-pay approach [8]. The human capital approach is the most commonly used method, as it considers the forgone income of the patient and their caregivers and takes into account premature mortality and disability [8].

To date, the only available systematic review that evaluated the economic burden of FN was conducted in 2007 [15]. The review pooled costs from many different types of cancers, which resulted in a huge variation in the economic burden of FN [3]. In addition, the study methods used by the included COI studies including the perspectives, time horizon, and cost estimation method were not revealed. Hence, it is difficult to evaluate the validity of those cost studies. Furthermore, in that review, overall FN cost in patients with lymphoma was not breakdown into individual resource use. Therefore, the cost components that were most frequently associated with the economic burden of FN was not investigated.

In view of these limitations, we have conducted a systematic review to determine the cost components that were most frequently associated with the economic burden of FN related

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