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# Pharmacoeconomic Evaluations of Oral Anticancer Agents. Thematic Systematic

# **Review**

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## Background

Around 14.1 million new cancer cases and 8.2 million deaths caused by cancer were reported in 2012, expected to rise up to 22 million within the next 2 decades. The parenteral route (intravenous dosage form) has been the most common administration route for chemotherapeutic agents, which is associated with the need for hospitalization and a range of significant adverse drug reaction. A new generation of chemotherapies that is orally administered has been introduced to practices as a superior and more efficient therapeutic alternative. Oral anticancer drugs (OACDs) have shown to be eliminating the need for hospitalization, decreasing the rate of adverse drug reactions and, ultimately, improving patients' quality of life. Economically, this translates into reduction in inpatient hospitalization costs, including several of the associated costs, such as the cost of treating side effects. A disadvantage of OACDs however, is the increased acquisition costs as compared to those for the intravenously administered alternatives. This resulted into resistance to include OACDs by several international insurance schemes and drug formulary practices, including in Qatar.

### Objectives

The current project sought to analyze the medical literature in relation to published economic evaluations (pharmacoeconomics) of OACDs, especially as compared to the parenteral alternatives. This will identify the decision analytic modeling conducted as well as the variety of methods used. Strengths and weaknesses of study designs will be determined, including gaps in knowledge.

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#### Methodology

A thematic systematic review was conducted using the search engines: PubMed, Medline, EconLit, Embase and Economic Evaluation Database. The following 3 categories were considered: (i) therapy (chemotherapy [Mesh]); (ii) dosage form (oral [Mesh]); and (iii) research design (economics [Mesh] OR cost-benefit analysis [Mesh]). These included full-text, English articles incorporating comparative economic evaluations of oral chemotherapies. Excluded studies were: non-comparative, non-economic based models, of secondary indications (not cancer), and/or reviews. This process was followed by two stages of manual exclusion; based on title/abstract content and, then, the full-text article content. A data extraction form was developed and pilot tested for the purpose of data collection. Article inclusion and data collection was conducted twice, each by a different investigator. Included articles were finally summarized according to methodological themes of interest.

#### Results

A total of 235 records were identified. After screening and removing duplicates, only 18 studies were deemed eligible study inclusion. It was found that the pharmacoeconomics evaluations were mostly of cost-utility analyses (13 out of 18), measuring cost per quality adjusted life years (QALY) gained, and from the payer perspective (15 out of 18). Primary sources of clinical and economic data were randomized clinical trials, expert panels and medical charts. Other sources included medicine databases, reimbursement schedules, drug policies and price lists, treatment guidelines, case reports and patient interviews. In 13 out of 18 cases, dominance status was reported in favor of OACDs, in relation to cost and/or clinical effect. Decision analytic modeling was used in the majority of studies, mostly constituting Markov modeling for the simulation of life long use of drugs. Sensitivity analyses were conducted in most studies, mostly constituting one-way sensitivity analysis to ensure robustness of study results. The types of cancers, where the effect of OACDs was studied, were the metastatic renal carcinoma, gastrointestinal tumors, colon cancer, chronic myeloid leukemia and non-small cell lung cancer. Most included articles were published during the last seven years. Most studies were conducted in the UK, US and Europe, while none were conducted in Australia or the Middle East.

#### Conclusion

This is first systematic review of the economic methods used in the evaluation of OACDs. There seems to be a recent increasing interest of this type of research, whereby the QALYs measurement is of priority for the decision making in relation to the comparative value of OACDs in practices. Most important, is that despite the higher acquisition cost, OACDs were demonstrated to be mostly superior over the parenteral alternatives. Furthermore, the decision analytic modeling, mostly constituting Markov modeling, is valued and enables a structured decision analyses of therapies. The pharmacoeconomics research is difficult to generalize, whereby published economic evaluations are locally specific, especially for the purpose of practical interpretation. The current review of literature proposes valuable methods for the local Qatari implementation and guidance of decision makers. This is most relevant to National Center for Cancer Care & Research (NCCCR), which is the only tertiary service provider of cancer therapy in Qatar, where confusion in relation to the use of oral chemotherapies exists, particularly the therapies vinorelbine and capacitabine.