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Decision-Analytic Modeling in the Economic Evaluations of Systemic Antifungals for the Prophylaxis against Invasive Fungal Infections – A Thematic Systematic Review

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Background

The interest in the economic evaluations of “prophylactic” systemic antifungals is on the rise, especially with the emergence of newer expensive agents for prophylaxis of invasive fungal infections (IFI). Decision analytic modeling is a systematic approach that has become integral in the economic evaluation process for the purpose of simplifying the decision making. This systematic review aims to identify the prevalence of decision-analytic modeling in the pharmaco-economic literature regarding prophylactic therapies for systemic fungal infections, and to identify variations in model designs used along with defining specific areas of strengths and weaknesses.

Method

A systematic literature search was conducted using the e-databases Pubmed, Medline, Embase, Economic Evaluation, Econlit, and Cochrane to obtain all model-based economic evaluations of antifungal agents. Search terms were under three categories: (i) therapy (antifungal agent [Mesh] OR Prophylaxis); (ii) disease (mycosis [Mesh] OR fungal disease [Mesh] OR invasive OR systemic); and (iii) research design (economics [Mesh] OR decision analysis [Mesh] OR costs and cost analysis [Mesh]). Publications were included if they were journal articles, full text publications, human studies, English language. Study articles were excluded if they were reviews, studying topical antifungal, non-invasive infections, or non-economic models. Journal article inclusion and data extraction, via a data collection form, were conducted twice, each by different researcher.

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Results

Out of 841 citations, only 19 articles were eligible for inclusion. Most of studies were relatively recent, conducted in 2008–2013. Seventeen of them used sources of clinical data from pooled randomized control trials. Evaluations were mostly in USA (7), the remaining in Australia, Canada, Spain, The Netherland, Korea, Greece, France, Germany, and Switzerland (1–2 articles each). All articles utilized the cost-effectiveness method using decision tree models; including 10 using Markov modeling for simulating future use of medications. This was, as appropriate, associated with discounting type of cost adjustment. Drug comparisons in included studies (27/29) were mostly between an old cheaper antifungals and more expensive newer ones. The 19 articles incorporated 15 studies with cost per life year gained measure, six with cost per IFI avoided, one with cost per Quality Adjusted Life Year, and four included cost saving per patient measure. Most important, is that same clinical measures were defined differently in different studies. Most studies reported dominance state, the majority were in favor of posaconazole (9 out of 12), and five studies required incremental cost effectiveness ratio analysis. Only direct medical costs were considered in studies despite that six articles had social perspectives instead of the hospital perspective. All articles had adjusted costs either for inflation (9/19 articles) or discounting. Fourteen articles used only one way sensitivity analysis while few used a combination with multivariate (2) or scenario (3) analyses.

Conclusion

Decision making in relation to prophylactic antifungals is not complex, including the economic considerations; whereby straightforward therapy dominance status was demonstrated in the majority of studies. Most important, is that the literature evidence in relation the cost-effectiveness of systematic antifungals is not cumulative in nature, which is due to that same outcomes are defined differently in studies. This also meant that literature economic models are incomparable and not generalizable since different decision makers appear to be interested in different outcomes, including for the same antifungal agent. Studies are limited by not considering cost of side effects and alternative therapy options. Further studies are needed to compare among the newer more expensive agents, where evidence is lacking. Also, studies should be enhanced by better adhering to guidelines in relation to standardized definitions of health states, enabling a cumulative evidence generation and generalizability of findings.