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Cost-Effectiveness Analysis Evaluating Fidaxomicin versus Oral Vancomycin for the Treatment of *Clostridium difficile* Infection in the United States

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ABSTRACT

Objectives: Fidaxomicin is a novel treatment for *Clostridium difficile* infections (CDIs). This new treatment, however, is associated with a higher acquisition cost compared with alternatives. The objective of this study was to evaluate the cost-effectiveness of fidaxomicin or oral vancomycin for the treatment of CDIs. **Methods:** We performed a cost-utility analysis comparing fidaxomicin with oral vancomycin for the treatment of CDIs in the United States by creating a decision analytic model from the third-party payer perspective. **Results:** The incremental cost-effectiveness ratio with fidaxomicin compared with oral vancomycin was $67,576/quality-adjusted life-year. A probabilistic Monte Carlo sensitivity analysis showed that fidaxomicin had an 80.2% chance of being cost-effective at a willingness-to-pay threshold of $100,000/quality-adjusted life-year. Fidaxomicin remained cost-effective under all fluctuations of both fidaxomicin and oral vancomycin costs. The decision analytic model was sensitive to variations in clinical cure and recurrence rates. Secondary analyses revealed that fidaxomicin was cost-effective in patients receiving concominant antimicrobials, in patients with mild to moderate CDIs, and when compared with oral metronidazole in patients with mild to moderate disease. Fidaxomicin was dominated by oral vancomycin if CDI was caused by the NAP1/BI/027 *Clostridium difficile* strain and was dominant in institutions that did not compound oral vancomycin.
Conclusion: Results of our model showed that fidaxomicin may be a more cost-effective option for the treatment of CDIs when compared with oral vancomycin under most scenarios tested.

Keywords: *Clostridium difficile*, *Clostridium difficile*–associated diarrhea, cost-effectiveness, fidaxomicin, oral vancomycin, vancomycin.

Background

Clostridium difficile is the leading pathogen responsible for nosocomial diarrhea in the United States [1]. It is estimated that *Clostridium difficile* is responsible for causing more than 330,000 cases of infectious diarrhea in hospitalized patients annually [2,3]. Furthermore, the incidence, severity, and mortality of *Clostridium difficile* infections (CDIs) is rising [1,2,4]. For decades, metronidazole and oral vancomycin have been cornerstones of treatment for CDIs. Effectiveness of metronidazole, however, has waned in recent years, and recurrent CDI is experienced in 20% to 30% of the patients successfully treated with metronidazole or vancomycin [5,6]. In addition to its impact on the patient, CDIs increase health care costs because of extended lengths of stay and rehospitalizations from recurrent disease [7]. The annual economic impact of CDIs in the United States has been estimated to range between $750 million and $3.2 billion [7–9].

Fidaxomicin is a macrocyclic antibiotic and the first treatment approved for CDIs in over 20 years. Studies have shown that fidaxomicin provides similar clinical cure rates compared with oral vancomycin for mild to severe CDIs, while being superior at sustaining clinical response for up to 28 days [10]. Fidaxomicin has been found to have higher in vitro activity against *Clostridium difficile* than does vancomycin, while having minimal effect on normal gut flora [11,12]. These differences between fidaxomicin and current standards make it a favorable treatment option for CDIs. However, disparities between costs of treatment are significant. The wholesale acquisition cost for a 10-day treatment course of fidaxomicin is $2800 [13]. The cost of a 10-day treatment course with vancomycin pulvules (Vancocin) is $1161 [13]; however, many institutions decrease this cost substantially by compounding oral solution from the intravenous (IV) powder. Given the high cost of therapy, fidaxomicin's use in clinical practice has been met with resistance and cost-benefit analyses to compare the cost-effectiveness of fidaxomicin with other standards of care have been called for [14,15]. To date, the cost-effectiveness of treating CDIs with fidaxomicin compared with other available agents has not been determined. The objective of this study was to estimate the cost-effectiveness of fidaxomicin or oral vancomycin for the treatment of CDIs in the United States.

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Methods

We compared fidaxomicin with oral vancomycin for the treatment of CDIs by creating a decision analytic model (DATA, TreeAge Software, Inc., Williamstown, MA). Our analysis was submitted to our institutional Investigational Review Board and determined to be exempt according to policy. Our model was based, in part, on previously published decision analytic models that investigated the potential value of a *C. difficile* vaccine and the overall attributable cost of CDIs [16,17]. These models incorporated the use of oral vancomycin and metronidazole in their treatment algorithms. To investigate the clinical and economic impact of fidaxomicin, we incorporated data published in a randomized, open-label, multicenter trial conducted in the United States and Canada by Louie et al. [10]. The primary base-case outcome measure was incremental cost/quality-adjusted life-years (QALYs) from the payer perspective.

Model Design

Our model structure is displayed in Figure 1. Patients in each treatment arm matched the intention-to-treat population from the randomized multicenter trial and were excluded if they presented with life-threatening or fulminant CDI, and toxic megacolon [10]. Patients received a 10-day course of either fidaxomicin or oral vancomycin for initial episodes of CDI or first recurrence and were either treated as an outpatient or hospitalized, regardless of disease severity. We assumed that all patients who failed initial therapy received 3-day courses of therapy and then changed to oral vancomycin 500 mg every 6 hours for an additional 10 days followed by a 4-week oral vancomycin taper. Patients who failed therapy as an outpatient required hospitalization. Recurrence was defined as reappearance of CDIs within 4 weeks after successful treatment [10,18].

Patients in all study arms with more than one recurrence received therapy recommended by international guidelines, oral vancomycin for 10 days followed by an oral vancomycin taper [19]. Patients failing to respond to a therapy change or treatment of a recurrence progressed to surgery or ongoing pharmacologic therapy with 10 days of oral vancomycin 500 mg every 6 hours and IV metronidazole followed by 4-week vancomycin taper. Patients then either survived or died after surgery or ongoing pharmacologic therapy. We modeled up to three episodes of CDI, and patients were continued in the model until cure with no recurrence or the decision for surgery was required.

Model Variables

All model variables are reported in Table 1. In the aforementioned clinical trial, clinical cure in the modified intention-to-treat

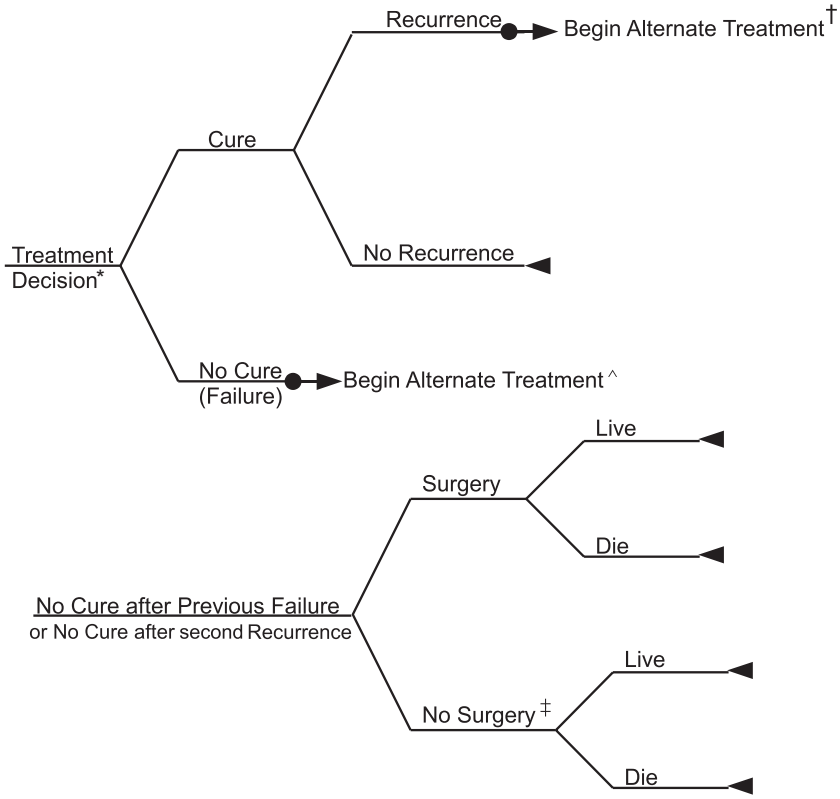

Fig. 1 – Decision tree comparing fidaxomicin versus vancomycin treatment in patients with CDIs. CDIs, *Clostridium difficile* infections. *Treatment of initial CDI (fidaxomicin, metronidazole, or oral vancomycin), first or second recurrence, or first treatment failure (regardless of inpatient or outpatient setting). ^Patient received 3 days of initial therapy before declared failure. Hospitalization following treatment failure was assumed. After first failure, therapy changed to oral vancomycin 500 mg every 6 hours for 10 days followed by a 4-week vancomycin taper. †Recurrence defined as reappearance of CDI within 4 weeks after successful treatment. First recurrences were treated with the original selected agent. Second recurrences were treated with oral vancomycin 125 mg every 6 hours for 10 days followed by a 4-week vancomycin taper. ‡Ten days of oral vancomycin 500 mg every 6 hours plus intravenous metronidazole 500 mg every 8 hours followed by a 4-week vancomycin taper.