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The Ongoing Challenge of Clostridioides difficile Infection in Austria: Economic Evaluation of Two Recommended Treatment Pathways

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Background

Clostridioides difficile is a significant nosocomial pathogen associated with severe, potentially life-threatening Clostridioides difficile infections (CDI), particularly following disruption of the gut microbiota during antibiotic treatment. Transmission occurs via the fecal-oral route through resilient spores. While most infections are acquired in hospitals or long-term care settings, 20%–30% occur in outpatient environments. In Austria, the estimated number of adult CDI cases is between 900 and 1,000 in 2025.

Objectives

The aim of this analysis is to evaluate the cost-effectiveness of current clinical practice which is based on reimbursement limitations regarding the Austrian reimbursement codex (reference pathway [Table 2]) versus the new Austrian guideline from the Austrian Society of Gastroenterology and Hepatology (ÖGGH), which recommends use of fidaxomicin (Dificlir®) as first-line therapy (ÖGGH pathway [Table 1]).

Table 1: ÖGGH pathway

Therapy line	Index CDI	1st CDI recurrence	2nd CDI recurrence
1st	Fidaxomicin 200mg (Standard regimen)	Fidaxomicin 200mg (Extended regimen)	FMT*
2nd	Vancomycin 125mg	Vancomycin 125mg "pulse & taper"	FMT
3rd	Metronidazole 500mg (only in mild cases/outpatients)	Fidaxomicin 200mg (Standard regimen) plus Bezlotoxumab	FMT

*Faecal microbiota transplantation (FMT)

Table 2: Reference pathway

Therapy line	Index CDI	1st CDI recurrence	2nd CDI recurrence
1st	Vancomycin 125mg	Vancomycin 125mg plus Bezlotoxumab	FMT
2nd	Fidaxomicin 200mg (Standard regimen)	Vancomycin 125mg "pulse & taper"	Vancomycin 125mg plus Bezlotoxumab
3rd	Metronidazole 500mg	Fidaxomicin 200mg (Standard regimen) plus Bezlotoxumab	Vancomycin 125mg "pulse & taper"

Methods

A published and validated model (Swart et al. 2023) was adapted for Austria and a decision tree model was developed to reflect the CDI treatment pathway. Each patient could undergo up to three successive treatments per infection episode to achieve a response and may experience up to two recurrences. Model inputs—including patient characteristics, treatment response rates, recurrence probabilities, utilities, CDI-related mortality, and healthcare costs (2025€)—were sourced from published literature. Uncertainty is addressed by an univariate deterministic sensitivity analysis (DSA) and a probabilistic sensitivity analysis (PSA) (Table 3). The present economic analysis was performed in accordance with the "ISPOR Good Research Practices Task Force Report" guidelines (Caro et al. 2012). Regarding the local use of CDI-related treatments, and specific efficacy data, a model validation with an Austrian clinical expert was done.

Table 3: Overview of methods applied

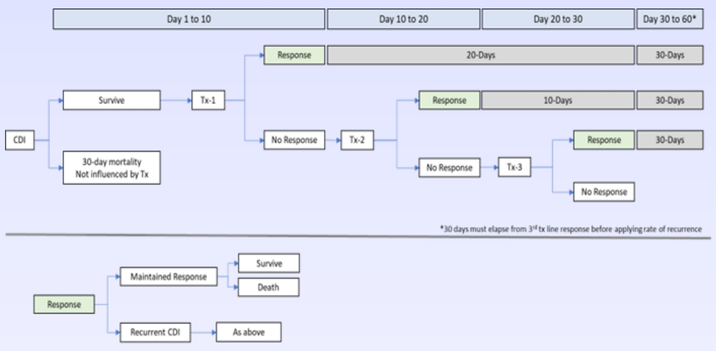
Methods	
Type of study	Cost-effectiveness analysis (CEA) and cost-utility analysis (CUA)
Type of the model	A CUA based on a decision tree model using 2 different treatment pathways
Perspective	Austrian healthcare payer perspective
Time horizon	Lifetime
Treatment duration	Fixed at 10 days according to clinical guidelines
Discount rate	3% per anno for costs and outcomes
Population	Patients with new diagnosed or recurrent CDI (mean age: 73 years)
Intervention	ÖGGH pathway
Comparator	Reference pathway
Outcomes	Life years (LYs) saved; quality-adjusted life years (QALYs) saved; total cost; incremental cost-utility ratio (ICUR) & incremental cost-effectiveness ratio (ICER)
Utilities	Age-dependent utilities are based on Ara & Brazier (2010) CDI-dependent disutilities were derived from Wilcox et al. (2017)
Timing	2025

Model structure

Treatment response rates, risk of recurrence rates, and mortality rates for the population included were used to model the following (Figure 1):

- The model consists of 3 CDI episodes (identical for both pathways): Index CDI, first and second CDI-related recurrence.
- Newly diagnosed or recurrent CDI patients enter the decision tree and survive or die within 30 days after diagnosis (mortality risk is constant over time).
- Surviving patients receive 1st line therapy and have a response or no response. Responders can show a maintained response, or they suffer due to a recurrence.
- Non-responders continue with 2nd line therapy and go through the same process as in the previous therapy line.
- Those with maintained response will survive or die in the remaining lifetime.
- Recurrent patients enter the decision tree from the beginning. The number of recurrences per treatment pathway is limited to max. 2 relapses.
- For all modelled treatments, it is assumed that the determination of therapy-specific efficacy occurs after the 10-day treatment period.
- Outcomes and treatment costs associated with CDI episodes are calculated for each line of therapy.

Figure 1: Model design



Clinical Data

- The efficacy data of various CDI-related treatments are based on a systematic literature review and a network-meta-analysis (NMA) by Beinortas et al. (2018). This NMA was performed as "random effects NMA" which allows direct and indirect treatment comparisons.
- The different treatment response rates and risk of recurrence rates were based on odds ratios (OR) which were taken from Beinortas et al. (2018). These OR were used to derive the specific treatment response rate and risk of recurrence rate associated with each CDI-related therapy included.
- For all modelled therapies, time on treatment is 10 days.
- The CDI-associated mortality rates were calculated for each CDI episode based on data derived from Crobach et al. (2019), Lübbert et al. (2016), and an Austrian clinical expert. The background mortality is based on life tables of the Austrian general population.

Resource Use and Costs

- All direct cost components are based on values for 2025.
- All drug costs (including fidaxomicin) are based on reimbursement list prices.
- All drugs are administered per oral route except for bezlotoxumab (intravenous [IV]).
- IV drug administration cost are applied, and no vial sharing is considered.
- Direct cost components: Treatment cost, drug administration cost, monitoring costs in the outpatient setting, and hospitalization costs

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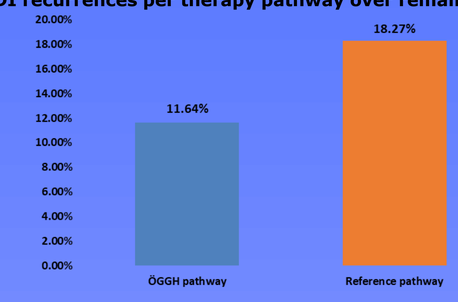
Results

Base case results

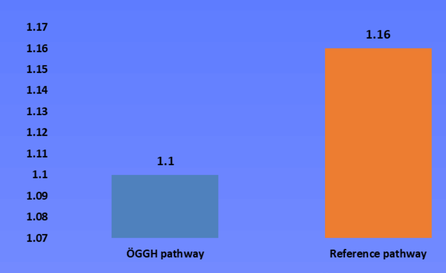
Regarding the percentage of CDI-related recurrences, the ÖGGH pathway presents 11.64% whereas the current reference pathway leads to 18.27% (Figure 2). Also, the ÖGGH pathway is associated with less hospital admissions (1.10 versus 1.16) (Figure 3).

Figure 2: Total percentage of CDI recurrences per therapy pathway over remaining lifetime



Source: own calculations (Figure 2 & Figure 3)

Figure 3: Total number of hospital admissions per therapy pathway over remaining lifetime



Furthermore, the average lifetime cost per patient is €4,081.46 for the ÖGGH pathway and €4,085.77 for the reference pathway, resulting in incremental savings of €4.31 (€252.56 additional treatment costs offset by €256.87 savings) (Table 4).

Table 4: Overview of cost components as well as total cost per therapy pathway and CDI episode

CDI episode	Therapy pathway	Treatment cost + Drug administration cost	Outpatient monitoring cost	Hospitalization cost	Sum
Index CDI	ÖGGH	€491.97	€14.12	€3,097.11	€3,603.20
	Reference	€198.47	€14.12	€3,097.11	€3,309.70
1st CDI recurrence	ÖGGH	€22.54	€0.83	€413.13	€436,50
	Reference	€58.87	€1.20	€595.09	€655.16
2nd CDI recurrence	ÖGGH	€1.72	€0.08	€39.96	€41.76
	Reference	€6.32	€0.23	€114.35	€120.90
Total cost	**ÖGGH**	€516.23	€15.03	€3,550.20	**€4,081.46**
	Reference	€263.67	€15.55	€3,806.55	**€4,085.77**

Source: own calculations

Cost-effectiveness results

The ÖGGH strategy also yields improved health outcomes, with 0.10 additional QALYs (7.01 versus 6.91) and a survival benefit of 0.17 LYs (10.75 versus 10.58). This results in a dominant ICUR (-€43.11 per QALY gained) (Table 5).

Table 5: Cost-effectiveness results

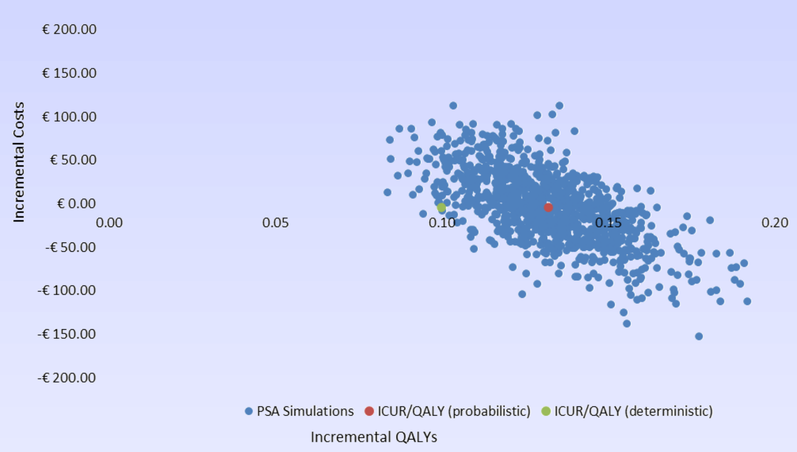
Cost components	ÖGGH pathway	Reference pathway	Difference
Treatment cost + Drug administration cost	**€516.23**	**€263.67**	**€252.56**
Fidaxomicin	*€490.81*	*€99.13*	*€391.68*
Vancomycin	*€23.26*	*€160.30*	*-€137.04*
Metronidazole	*€0.43*	*€0.43*	*€0.00*
FMT*	*€1.72*	*€3.81*	*-€2.09*
Outpatient monitoring cost	**€15.03**	**€15.51**	**-€0.52**
Hospitalization cost	**€3,550.21**	**€3,806.55**	**-€256.35**
Total cost	**€4,081.46**	**€4,085.77**	**-€4.31**
Total LYs	10.75	10.58	0.17
ICER per LY gained		**DOMINANT** (-€25.32)	
Total QALYs	7.01	6.91	0.10
ICUR per QALY gained		**DOMINANT** (-€43.11)	

*In Austrian hospital outpatient clinics, FMT will be delivered during colonoscopy. Source: own calculations

Sensitivity Analysis

DSA and PSA are performed to examine the robustness of the model.

Figure 4: Scatterplot, ÖGGH pathway versus reference pathway

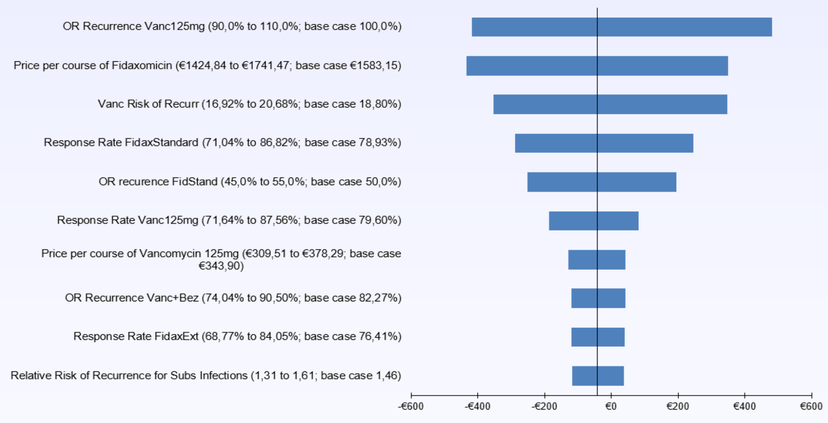


The Monte-Carlo PSA results of 1,000 second-order simulations plotting incremental cost versus incremental effects (Figure 4). The acceptability curve reveals that in case of a willingness-to-pay of about €23,000-€34,000 the ÖGGH pathway is a cost-effective option versus the reference pathway in 100.0% of the simulations.

Source: own calculations

The DSA uses a tornado diagram to depict the effect of variations on base case results, with the highest impact for "OR Recurrence Vancomycin 125mg" (90%; 110%) and the lowest impact for "Relative Risk of Recurrence for Subsequent Infections " (1.31; 1.61) (Figure 5).

Figure 5: Tornado diagram, ÖGGH pathway versus reference pathway



Source: own calculations

Conclusion

From the Austrian healthcare system perspective, the ÖGGH guideline is the dominant strategy, providing improved health outcomes at lower costs, and represents a cost-effective option for CDI management in Austria.

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Additional literature with the author

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