

# Adherence and Recurrence Rates of *C. difficile* After A 6-week Tapering Regimen of Oral Vancomycin Solution

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## ABSTRACT

**Background** – *Clostridium difficile* infection (CDI) is the leading cause of antibiotic-associated diarrhea with high recurrence rates. Vancomycin, administered orally, is effective for treatment of CDI. Based on results from a single-center study in 2009<sup>1</sup>, a standardized 6-week tapering regimen of oral vancomycin solution (four times daily for 2 weeks, then twice daily for two weeks, then once daily for two weeks) was adopted in 2011 as the standard of care for both initial & recurrent cases of CDI in an effort to decrease CDI relapse rates. The oral solution is more cost-effective than the oral capsules and is assigned an expiration date of 14 days after compounding. Since this regimen involves known barriers to medication adherence, this study was conducted to assess the rates of complete adherence and CDI relapse.

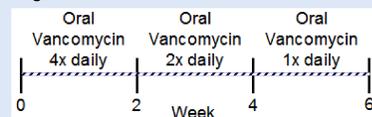
**Methods** – Retrospective analysis of pharmacy fill records & patient charts was performed. **Date range:** January 1<sup>st</sup>, 2011 through September 30<sup>th</sup>, 2012. **Inclusion:** Positive *C. difficile* toxin test, ≥18 years old, and prescribed the 6-week regimen. **Exclusion:** early discontinuation of the taper by physician, use of vancomycin capsules, non-Kaiser Permanente (KP) member, and prescription filled at a non-KP pharmacy.

**Results** – **Primary Outcome:** Of 105 patients, 49 (47%) patients were adherent. 86 of 105 patients (82%) received at least 4 weeks of oral vancomycin. **Secondary Outcomes:** Rates of 90-day CDI recurrence, hospital admission due to CDI, ED visits due to CDI, and all-cause mortality were not significantly different between patients who were adherent & patients who were non-adherent. However, the 90-day CDI recurrence rate among all groups was ~12%, less than reported in the literature of 20%.

**Conclusions** – There is a high rate of non-adherence to the 6-week regimen, but the majority of patients completed at least 4 weeks of treatment. The effective duration for the taper may be shorter than 6 weeks, considering >80% of patients received at least 4 weeks of oral vancomycin and the overall CDI recurrence rate in this study was ~12% vs. 20%, as reported in literature. Further studies will be needed to assess the optimal duration of effective therapy.

## BACKGROUND

- CDI is a leading cause of antibiotic-associated diarrhea and has a high recurrence rate.
- In 2011, a 6-week tapering regimen was adopted as the standard of care at our institution for the treatment of CDI<sup>1</sup>
- The 6-week regimen was as follows:



- The compounded oral vancomycin solution was the preferred, cost-effective formulation.

## OBJECTIVES

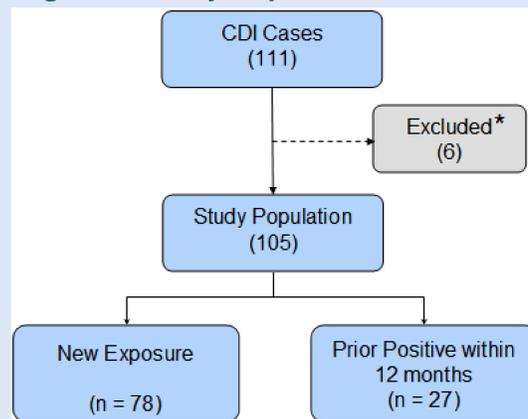
- Determine adherence rate to the 6-week regimen of oral vancomycin in patients with CDI in the GSAA.
- Compare CDI relapse rates between patients who were adherent to the regimen vs. patients who were non-adherent.

## METHODS

- **Design:** Retrospective cohort study
- **Study Period:** January 1, 2011 – September 30, 2012
- **Statistics:** Chi-square test, Fisher's Exact test
- **Inclusion Criteria:** Positive *C. difficile* toxin test; Age ≥18 years; Compounded oral vancomycin solution per the 6-week regimen
- **Exclusion Criteria:** Early discontinuation of 6-week regimen by physician; Use of oral vancomycin capsules; compounded oral vancomycin solution is filled at a non-KP pharmacy; non-member

## RESULTS

Figure 1. Study Population



\*See Methods for Inclusion/Exclusion criteria

Table 1. Demographics

Age	n (%)	Ethnicity	n (%)
≥65	63 (60)	White	70 (67)
		Hispanic	13 (12)
		Black	11 (10)
		Asian	7 (7)
		Native American	2 (2)
		Pacific Islander	1 (1)
		Declined to State	1 (1)
Gender	n (%)		
Female	68 (65)		
Language	n (%)		
English	101 (96)		

Figure 2. Adherence to the 6-week tapering regimen based on prescription fills

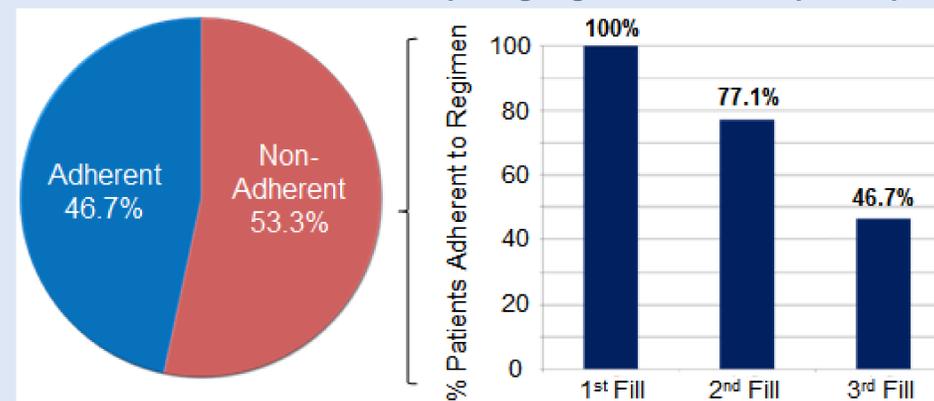


Table 3. Overall 90-Day Recurrence Rates

	New Exposure n = 78	Prior Positive n = 27	Total n = 105
Overall 90-day CDI Recurrence Rate, n (%)	9 (11.5)	2 (7.4)	11 (10.5)

Table 4. Recurrence Rates – New Exposure

New Exposure n = 78	Adherent n = 37	Non-Adherent n = 41	OR (95% CI)
Recurrence, n (%)	5 (13.5)	4 (9.8)	1.45 (0.30-7.15)
Hospital Admission, n (%)	5 (13.5)	1 (2.4)	6.25 (0.67-149)
ED Visit, n (%)	1 (2.7)	3 (7.3)	0.352 (0.013-4.1)
All-Cause Mortality, n (%)	0 (0)	2 (4.9)	n/a

### Definitions:

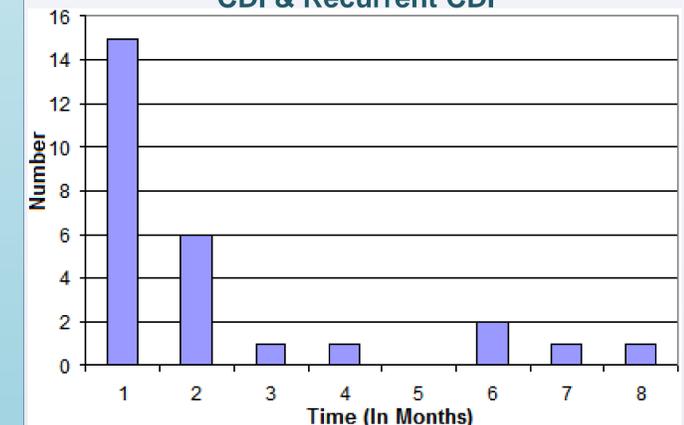
OR = Odds Ratio; Adherent = Patients picked up all 3 fills at expected times; Non-Adherent = Missed ≥1 fill OR late to fill by ≥7 days; Recurrence = Positive *C. difficile* toxin test after completion of 6-week regimen; New Exposure = No positive *C. difficile* toxin test within 1 year of index date; Prior Positive = Presence of positive *C. difficile* toxin test within 1 year prior to index date

Table 5. Recurrence Rates – Prior Positive

Prior Positive n = 27	Adherent n = 12	Non-Adherent n = 15	OR (95% CI)
Recurrence, n (%)	1 (8.3)	1 (6.7)	1.27 (0.30-53.8)
Hospital Admission, n (%)	0 (0)	1 (6.7)	n/a
ED Visit, n (%)	2 (16.7)	1 (6.7)	2.80 (0.16-91.2)
All-Cause Mortality, n (%)	1 (8.3)	0 (0)	n/a

## Results (continued)

Figure 3. Time Between Prior Positive CDI & Recurrent CDI



## STUDY ENDPOINTS

- **Primary:** Adherence to 6-week tapering regimen
- **Secondary:** (Within 90 days after completion of regimen)
  - Recurrence due to CDI
  - Hospital admission
  - ED visit
  - Death

## CONCLUSIONS

- 53.3% of patients were non-adherent to the 6-week regimen. Non-adherence was not associated with a significant increase in CDI recurrence.
- However 77% of the non-adherent patients had 4 weeks of oral vancomycin. This may suggest that 4 week regimen maybe as efficacious in treating CDI as a 6-week regimen.
- The effective duration of oral vancomycin tapers may be less than 6 weeks since overall CDI recurrence rate was ~12%, less than previously published rates of 20-25%.<sup>2,3</sup>
- The tapering regimen of liquid oral vancomycin solution remains a cost-effective and well-tolerated treatment for both new exposure and prior positive CDI cases.

## STRENGTHS & LIMITATIONS

### Strengths

- Integrated health system
- Strong data on prescription fill

### Limitations

- Retrospective design
- Prescription pick-up used as surrogate for adherence
- Variables not measured:
  - Health literacy
  - Patient education
- Compounding of vancomycin solution may limit applicability of regimen outside of Kaiser

## ACKNOWLEDGEMENTS

- Jim Chan, PharmD; Daniel B Klein, MD; Erin Sugiyama, PharmD; Bach-Nga Shenoy, PharmD

## REFERENCES

1. Lieu D, et al. Oral vancomycin 6-week taper regimen, as treatment for both initial and recurrent disease, reduces relapse of *Clostridium difficile* infection (CDI). Abstract presented at 47<sup>th</sup> Annual Meeting of the Infectious Disease Society of America, 2009 Oct 29-Nov 1.
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