Assessing the Impact of Linezolid Clinical Decision Support on Linezolid Use at a Pediatric Academic Medical Center

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Introduction

Linezolid Use In Pediatrics

- Linezolid is part of a novel class of oxazolidinone antibiotics and is one of the *last antimicrobial options* for resistant gram positive organisms in children.
- Despite its clinical utility it is also associated with many side effects including bone marrow suppression, lactic acidosis and dangerous drug interactions.
- *Linezolid use increased 279%* across pediatric hospitals between 2002-2007[1].

Pediatric Antimicrobial Stewardship Programs (ASP) and Clinical Decision Support

- Approximately 60% of pediatric inpatients receive antimicrobials, however there is wide variability among pediatric hospitals[2].
- As of 2009 only 24% of free standing children's hospitals had an ASP and 27% were planning one[3].
- The most commonly cited barriers to developing ASPs are time and funding[4].
- Comprehensive computerized clinical decision support (CDS) has been shown to decrease treatment duration, increase appropriateness of therapy and decrease cost. However they are costly and labor intensive to implement[5].
- Antimicrobial specific CDS is less costly to implement, however, efficacy data are mixed. There are no studies of CDS specifically targeting linezolid.

References

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2. Gerber, J. S. *et al.* Variability in antibiotic use at children's hospitals. *Pediatrics* **126,** 1067–1073 (2010).
3. Hersh, A. L., Beekmann, S. E., Polgreen, P. M., Zaoutis, T. E. & Newland, J. G. Antimicrobial stewardship programs in pediatrics. *Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America* **30,** 1211–1217 (2009).
4. Johannsson, B. *et al.* Improving Antimicrobial Stewardship: The Evolution of Programmatic Strategies and Barriers. *Infection Control and Hospital Epidemiology* **32,** 367–374 (2011).
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Methods & Materials

Study Design

Single center, prospective pre- and post-intervention cohort study evaluating linezolid computer-assisted CDS (Figure 1) on the rate of linezolid use, patient demographics and appropriateness of use. (See Flow Chart 1) Study included all courses of linezolid administered during the study period. Exclusion: Single Dose and Cystic Fibrosis.

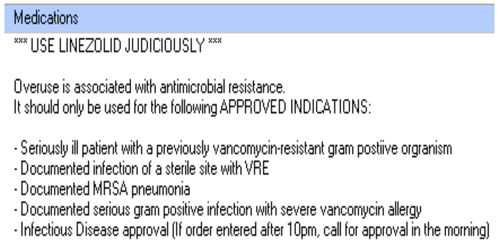
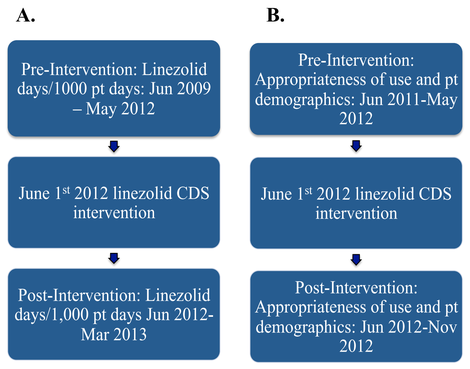


Figure 1. Clinical Decision support with approved indications for linezolid use and reminders about antimicrobial resistance. Dosing standards are included and free text for the indication is required to place the order.



Flow Chart 1. A. Extracted data for total linezolid days and total patient days and compared linezolid days/1000 patient days to post intervention averages (Jun 2009-Mar 2013). **B.** Reviewed a subset (n=85) of charts in duplicate (AWK and JL) for appropriateness of use and patient characteristics and compared to post intervention (Jun 2011-Nov 2012) .

Results

PATIENT DEMOGRAPHICS			
Gender	Male	38	44.7%
	Female	47	55.3%
	Total N	85	
Age	Age < 1 years	13	14.3%
	Age 1 – 12 years	46	54.7%
	Age >12 years	26	31.0%
	Total N	85	
Immunosuppression	History of Stem Cell	8	9.4%
	Transplant	27	31.8%
	History of SOT	50	58.9%
	Non-transplant patients	85	
	Total N		
Renal function	Chronic Kidney Disease	8	9.4%
	Acute Kidney Injury	17	20.0%
	Total N	85	
ICU Level of Care	Admitted to the ICU	46	54.1%
	Not admitted to the ICU	39	45.9%
	Total N	85	

Table 1. Demographic information on the subset of patients receiving linezolid between June 2011 and November 2012. (N=85)

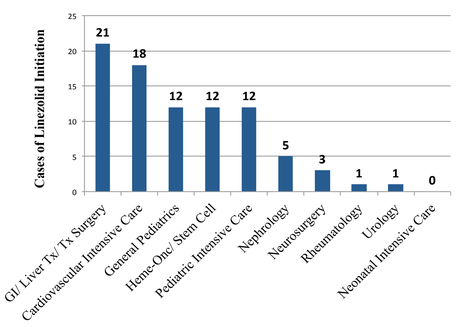


Figure 2. Linezolid courses initiated by clinical services from June 2011 – November 2012. (N=85)

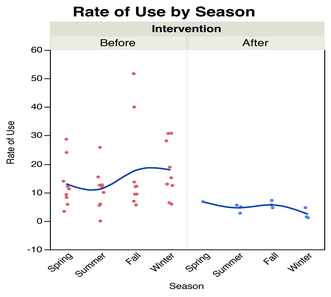


Figure 3: Linezolid Days/1000 patient days: variability and rate of use by season pre- and post-intervention.

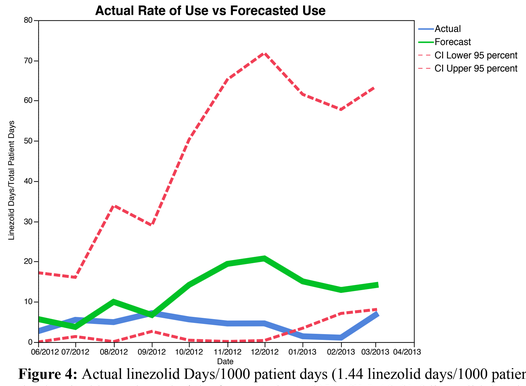


Figure 4: Actual linezolid Days/1000 patient days (1.44 linezolid days/1000 patients days) exited lower bound of the forecasted rate (95% CI 3.46-61.6 linezolid days/ 1000 patient days) in January 2013, Winters' exponential smoothing model. Actual rate remained outside of the forecasted 95% CI for the remainder of the study. Forecasted rates were calculated based on 3 years of linezolid rate of use data.

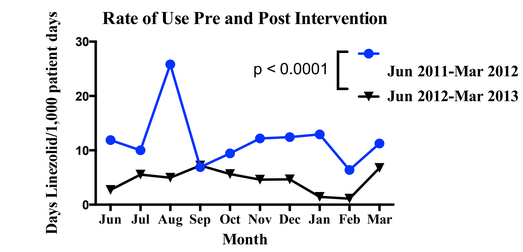


Figure 5: Mann-Whitney test comparing linezolid days/1000 patient days in the same interval (Jun-Mar) pre and post intervention.

Appropriate Indications	Total # (%)	Inappropriate Indications	Total # (%)
Total	N=39 (46)	Total	N=46 (54)
Seriously ill patient with prior vancomycin resistant gram positive organism (infection or colonization)	N=5 (13)	Empiric therapy in a seriously ill patient (No Hx of VRE)	N=13 (28)
MRSA Pneumonia or MRSA infection with desire for PO conversion	N=9 (23)	Empiric therapy in a well appearing patient (Hx of VRE Colonization)	N=9 (20)
True Vancomycin Allergy	N=4 (10)	Redman's Syndrome	N=6 (13)
Sterile Site VRE Infection	N=7 (18)	Enterococcus (Not VRE)	N=3 (7)
Evidence of acute kidney injury while on vancomycin	N=5 (13)	Pre-existing concern for vancomycin nephrotoxicity	N=4 (9)
Gram positive organism with an elevated but susceptible MIC to vancomycin	N=5 (13)	Gram Positive organism with no indication for linezolid	N=4 (9)
Enterococcus Sepsis (Empiric)	N=1 (3)	No IV Access	N=1 (2)
Other	N=3 (8)	Other/Undefined	N=6 (13)

Table 2. Appropriate indications were extracted from the CDS and developed by the ASP. Additional indications were considered on chart review as above. All charts were reviewed in duplicate (k stat 89%, 3rd party review for differences).

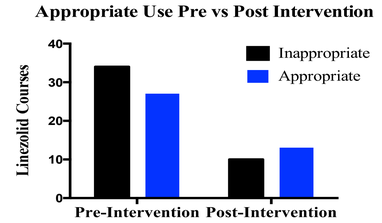


Figure 6. Appropriate vs Inappropriate courses of linezolid pre- and post-intervention. Linezolid use appropriate in 56% of post-intervention cases vs 44% pre intervention. Non-significant (p=0.141), Fisher's exact test.

Pre-CDS: 2011						
	Jun	Jul	Aug	Sep	Oct	Nov
Inappropriate Courses	5	2	3	2	2	5
Average Monthly Costs	$2688.84					
Post-CDS: 2012						
	Jun	Jul	Aug	Sep	Oct	Nov
Inappropriate Courses	2	1	2	0	4	2
Average Monthly Costs	$1204.46					

Table 3. Average cost associated with inappropriate linezolid use per month; potential annualized cost saving associated with implementation of CDS was determined using the average costs per month associated with inappropriate linezolid. The difference between $2,688.84 in the pre-intervention period and $1,204.46 was $1,484.48. Multiplying the cost saving of $1,484.48 by 12 months in 1 year gives annualized cost saving of $17,812.56 associated with the implementation of CDS.

Conclusions

- **Targeted Clinical Decision Support (CDS) may be an effective Antimicrobial Stewardship Program (ASP) tool to reduce overall use and inappropriate use of the targeted antimicrobial**
- Targeted CDS can be implemented when time and/or funding are limiting implementation of a comprehensive ASP.
- This targeted CDS was associated with a net-cost savings on linezolid drug cost. Further interventions to limit inappropriate use could lead to additional savings.