

Tracy N. Zembles¹, PharmD, BCPS-AQ ID; Anna Kissell², PharmD, BCPPS;
Peter L. Havens³, MD, MS; Nathan E. Thompson⁴, MD, PharmD; Anna R. Huppler³, MD

¹Department of Enterprise Safety, Children's Hospital and Health System, Milwaukee, WI

²Department of Pharmacy, Children's Hospital and Health System, Milwaukee, WI

³Department of Pediatrics, Medical College of Wisconsin, Children's Research Institute, Milwaukee, WI

⁴Department of Pediatrics, Critical Care Medicine, Medical College of Wisconsin, Children's Research Institute, Milwaukee, WI

tzembles@chw.org

Introduction

- Voriconazole widely and increasingly used in children
- Pediatric pharmacokinetics: wide inter-patient and intra-patient variability
- American Academy of Pediatrics (AAP): age-based dosing
 - 2-12 years: 9 mg/kg q12 hr x 2 followed by 8 mg/kg q12 hr IV
 - >12 years: 6 mg/kg q12 hr x 2 followed by 4 mg/kg q12 hr IV
- Therapeutic drug monitoring (TDM) recommended
- Target trough concentrations of 1-2 mcg/ml to 6 mcg/ml

Methods

- Quality Improvement initiative for voriconazole use and monitoring
 - Baseline data collected 2010-2013
 - Clinical Practice Guideline (CPG) instituted to standardize initial dosing, dose adjustments, and TDM
 - Pharmacists specializing in pharmacokinetics granted authority to manage voriconazole use per the CPG
 - PDSA cycles to refine the CPG; data collection through 12/31/17
- Inclusion: courses of voriconazole in hospitalized patients for empiric or pathogen-directed treatment of a fungal infection
- Exclusion: courses of voriconazole for prophylaxis or initiated for outpatients

Results

Table 1. Characteristics of patients managed by CPG

	CPG #1	CPG #2
Implementation date	4/1/15	3/1/16
Number of unique patients	17	8
Total number of courses	20	10
Median age, years (range)	12.5 (1.7-26.9)	5.9 (1.6-28)
Median weight, kg (range)	39.2 (8-89.5)	20.5 (9-77)
Median duration of therapy, days (range)	17 (1-56)	44 (28-119)

Figure 1. Percent of patients on voriconazole with TDM

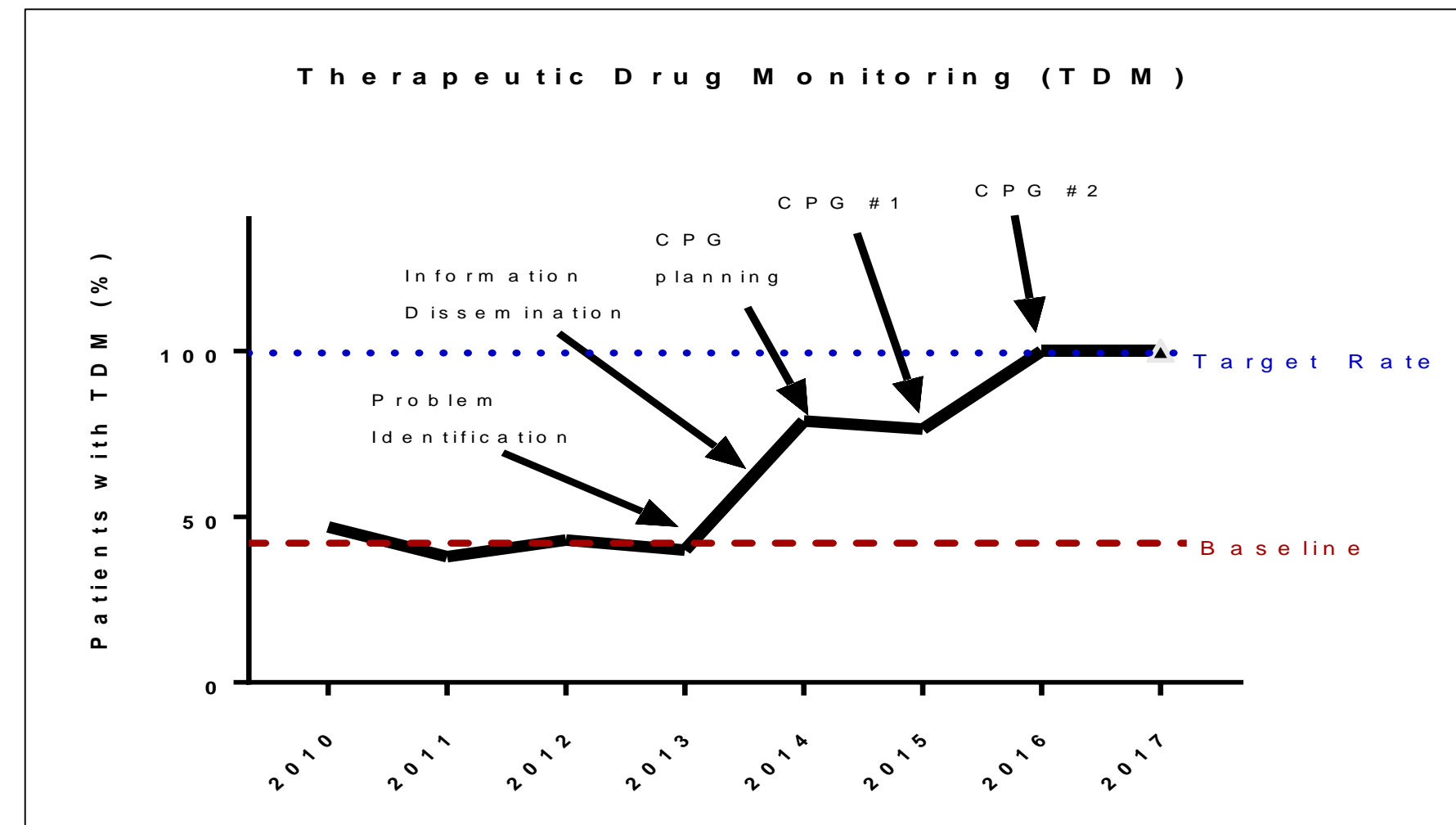


Table 2. First steady-state voriconazole trough concentration after initial dose in patients managed by CPG

	< 1 mcg/ml	1-6 mcg/ml	> 6 mcg/ml
Initial dose per the AAP recommendation (n = 17), n (%)	4 (23.5)	9 (53)	4 (23.5)
Initial dose greater than the AAP recommendation (n = 3), n (%)	1 (33.3)	2 (66.6)	0
Initial dose less than the AAP recommendation (n = 7), n (%)	1 (14.3)	4 (57.1)	2 (28.5)
Overall courses (n = 27), n (%)	6 (22.2)	15 (55.6)	6 (22.2)

Figure 2. TDM measurements before and after achieving therapeutic voriconazole concentration for patients managed by CPG

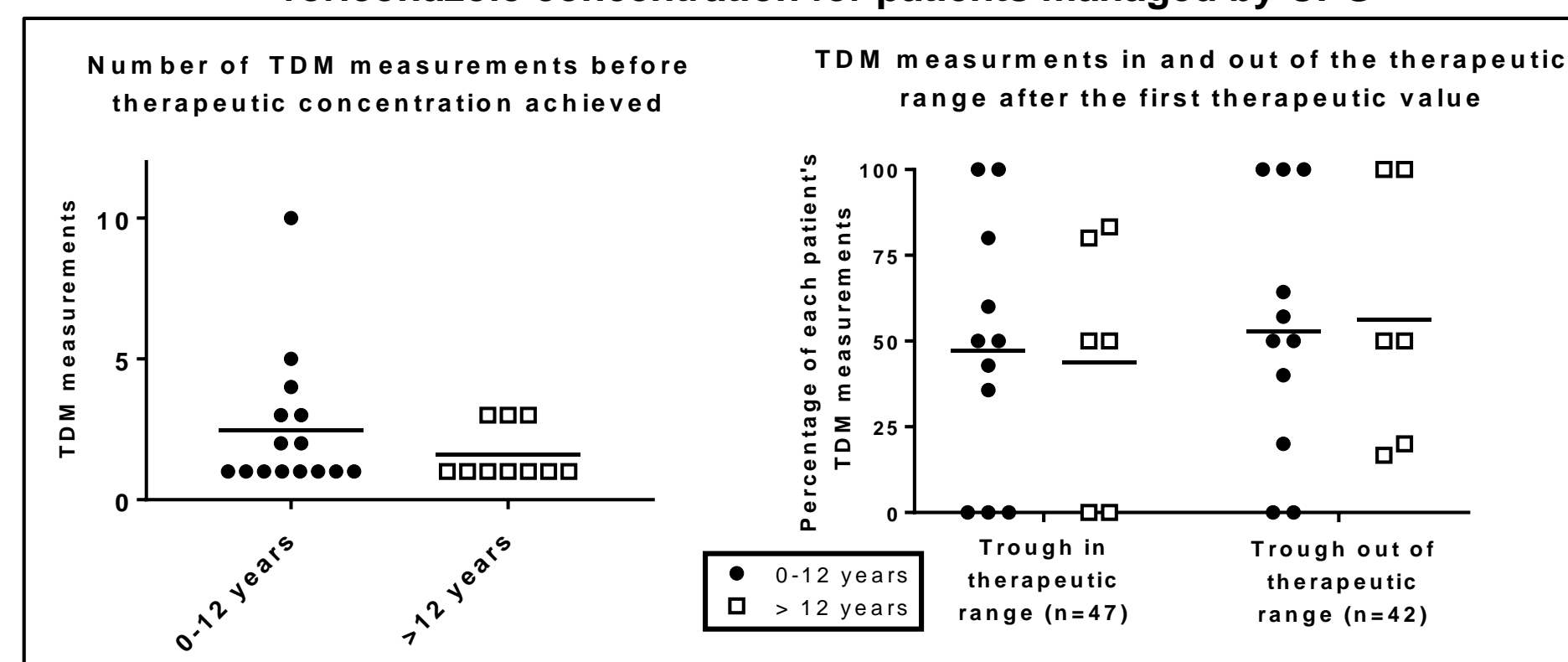
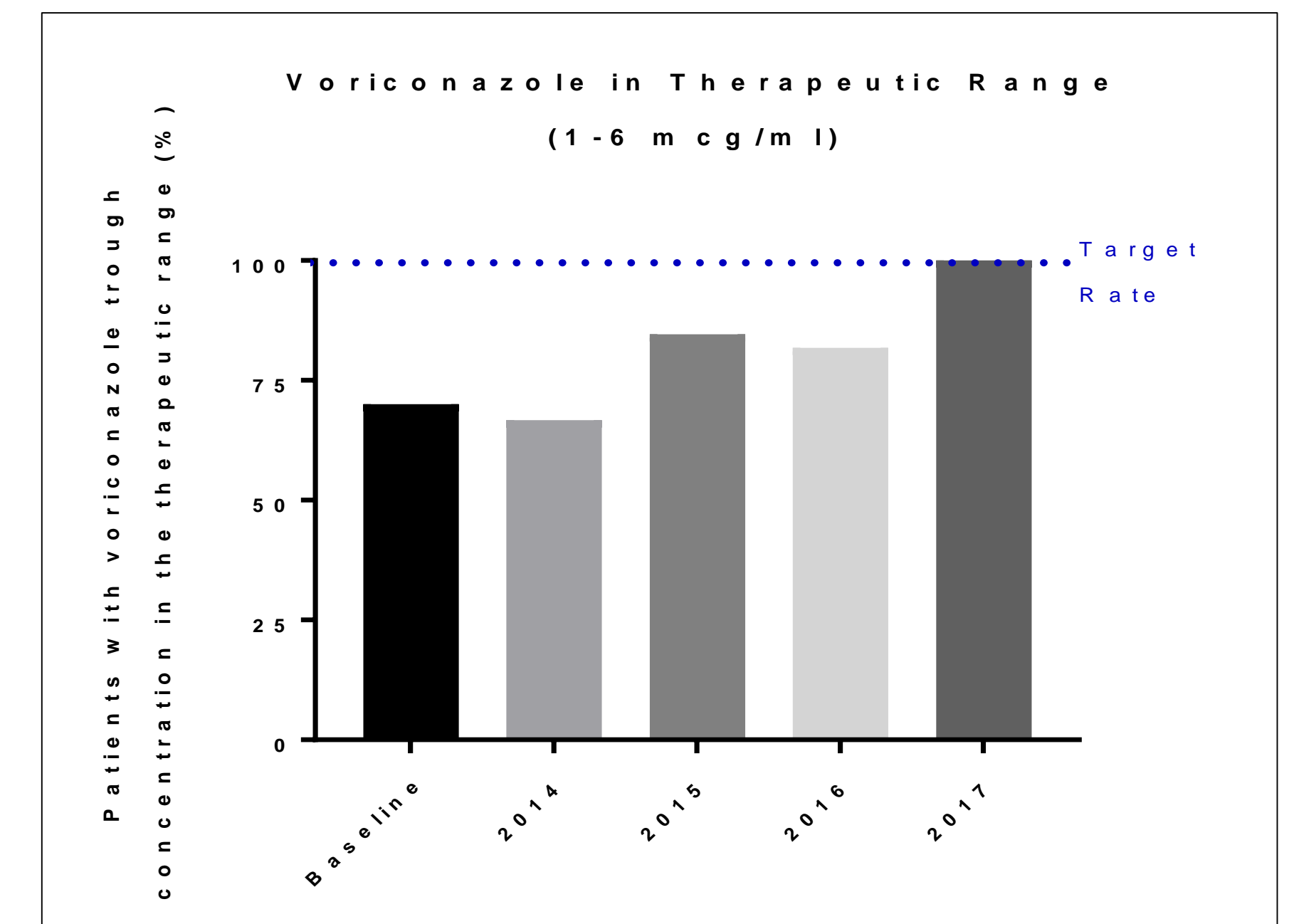


Figure 3. Percent of patients achieving at least one voriconazole trough concentration within the therapeutic range during treatment



Summary

- A voriconazole CPG managed by pharmacists can improve monitoring and therapeutic target achievement
 - 100% of patients received TDM and 100% of patients reached the therapeutic range
- Inter- and intra-patient variability necessitates the use of TDM to inform dosage adjustments
 - Pediatric patients, especially under age 12 years, require dosing changes to reach and maintain therapeutic troughs
 - Variability can be managed with ongoing TDM after achieving first therapeutic serum trough concentration

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