RESEARCH LETTER

Underdosing of Benzodiazepines in Patients With Status Epilepticus Enrolled in Established Status Epilepticus Treatment Trial

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Study Objective

Characterize patterns of benzodiazepine (BZD) use in status epilepticus (SE) in a geographically diverse population

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Methods

- Administered BZD doses were compared with guideline-recommended doses from Neurocritical Care Society and American Epilepsy Society
- Pre-enrollment data was used to describe patterns of benzodiazepine (BZD) use:
  - 1) drug choice, dose, and route of administration;
  - 2) timing and setting in which the drugs were administered; and
  - 3) patient weight (< 40 or ≥ 40 kg for LZP, ≤ 40 or > 40 kg for MDZ, and < 66. 7 or ≥ 66. 7 kg for DZP)
- Sample size: 207 subjects (88 children and 119 adults) enrolled at 41 sites

- Brophy GM et al., Neurocrit Care 2012;17(1): 3–23
- Glauser T et al., Epilepsy Currents, Vol. 16, No. 1 (Jan/Feb) 2016 pp. 48–61

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Results

- All BZD doses
- First dose of the first BZD
- Patterns of use by route, setting and age group

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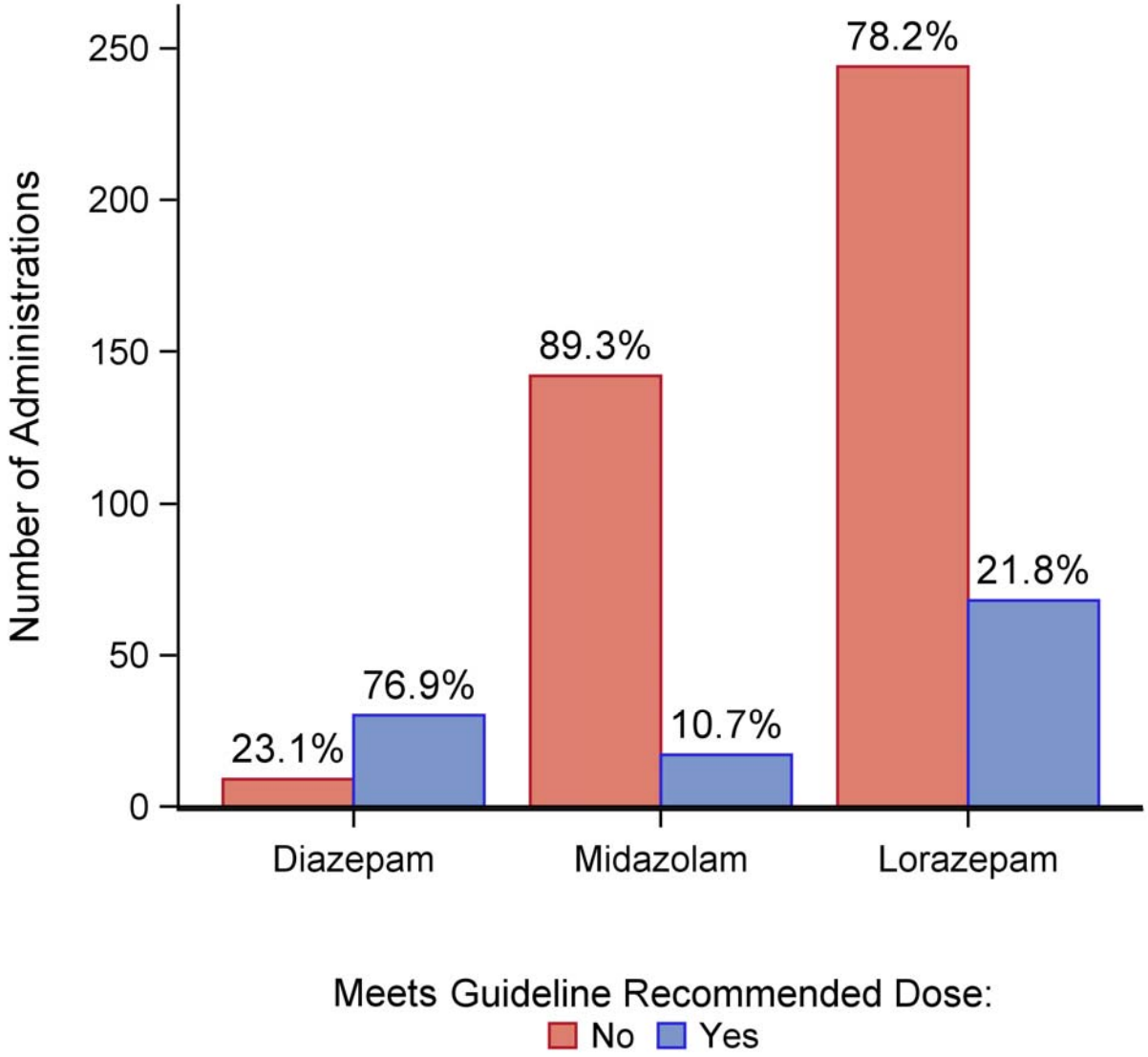
All Benzodiazepine Doses (n=511)



Underdosing for all doses mainly for MDZ and LZP

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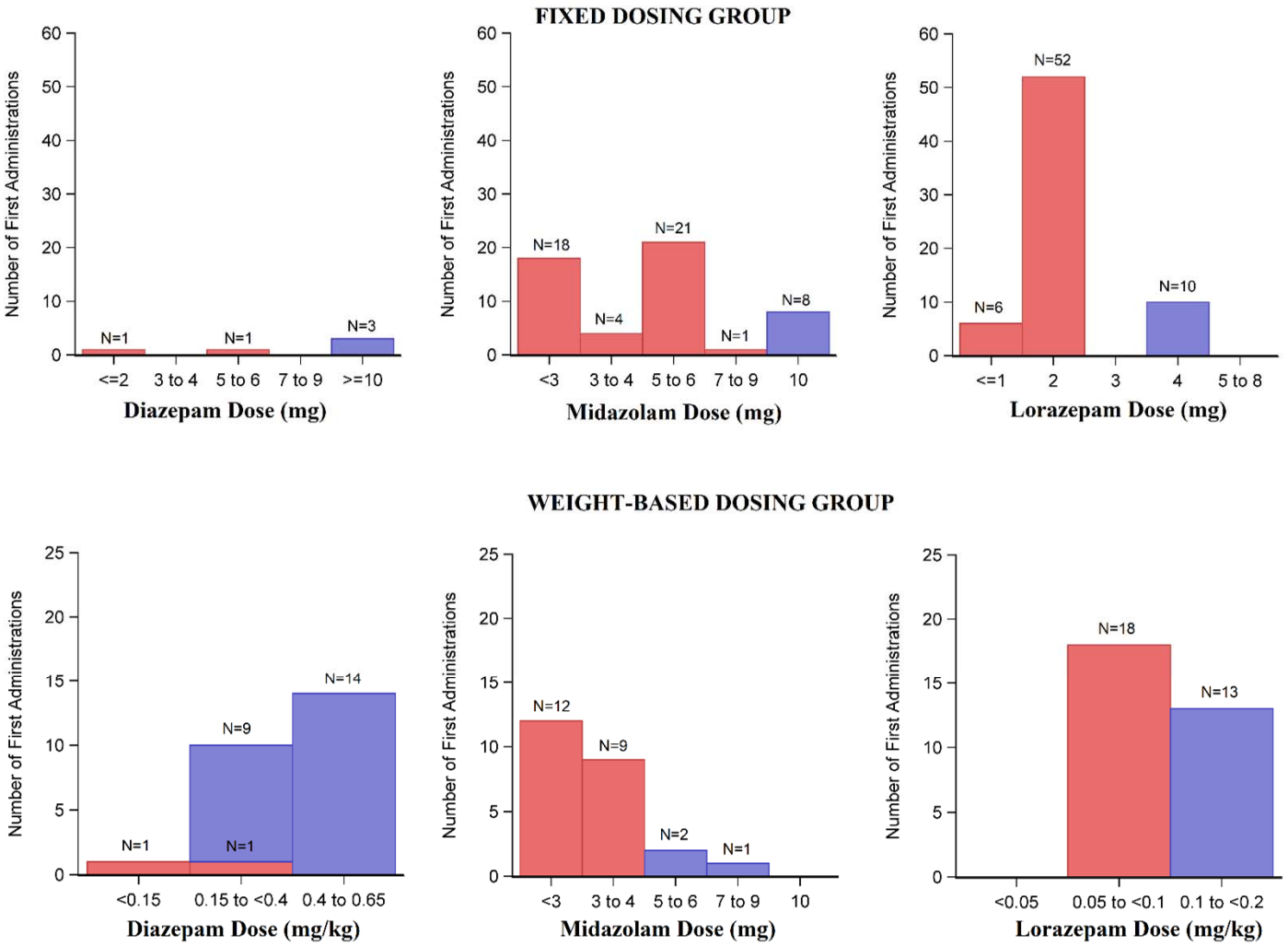
First Dose of First Benzodiazepine (n=207)



~ 80% of patients received lower than guideline recommended doses for LZP and MDZ

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Patterns of BZD Use by Route, Setting and Age Group

	Lorazepam		Midazolam		Diazepam		Total	
	N= 312		N= 159		N= 40		N=511	
	n	%	n	%	n	%	n	%
Route of administration								
Intravenous	295	95%	72	45%	12	31%	379	74%
Intramuscular	15	5%	65	41%	0	0%	80	16%
Transmucosal*	2	1%	22	14%	27	69%	51	10%
Setting								
Prior to EMS	4	1%	9	6%	26	65%	39	8%
EMS	14	5%	108	68%	9	23%	131	26%
ED	294	94%	42	26%	5	13%	341	67%
Age group								
Pediatric**	97	31%	66	42%	27	68%	190	37%
Adult	215	69%	93	58%	12	30%	320	63%

EMS- Emergency Medical Services; ED- Emergency Department

*Transmucosal administration for diazepam was per rectum, while intranasal or buccal routes were used for lorazepam and midazolam. **The pediatric group includes ages less than or equal to 17, the adult group includes those greater than 17. Administration information for one case was missing due to unknown dose and route.

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Summary of Findings

- The most commonly administered doses by drug, route, and setting were: rectal DZP in pre-hospital settings, IM/IV MDZ in EMS, and IV LZP in the ED.
- Approximately 70% of patients received a lower than guideline recommended first dose of the first drug.
  - The underdosing percentage was higher for LZP and MDZ (~80%)
- Observed practice was not consistent with evidence-based guidelines

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Thank you!

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Guideline Recommended Doses vs. ESETT Protocol Eligibility Criteria

		Guideline Recommended Doses per Administration*	ESETT Eligibility Criteria for Minimally Adequate Cumulative Dose**	
Drug	Route		Dose for ≥ 32 kg Patients (mg)	Dose for < 32 kg Patients (mg/kg)
Diazepam	IV Rectal	0.15-0.2 mg/kg/dose, max: 10 mg/dose, may repeat dose once If IV route not available, then 0.2-0.5 mg/kg/dose, max: 20 mg/dose	10	0.3
Lorazepam	IV	0.1 mg/kg/dose, max: 4 mg/dose, may repeat dose once	4	0.1
Midazolam	IV IM IN/Buccal	IM Dosing: 10 mg for > 40 kg, 5 mg for 13-40 kg Dosing not specified	10 10	0.2 0.3

*Brophy GM et al., Neurocrit Care 2012;17(1):3–23 and Glauser T et al., Epilepsy Currents, Vol. 16, No. 1 (Jan/Feb) 2016 pp. 48–61

**Cut-off criteria for the transmucosal routes were the same as those for the intravenous route

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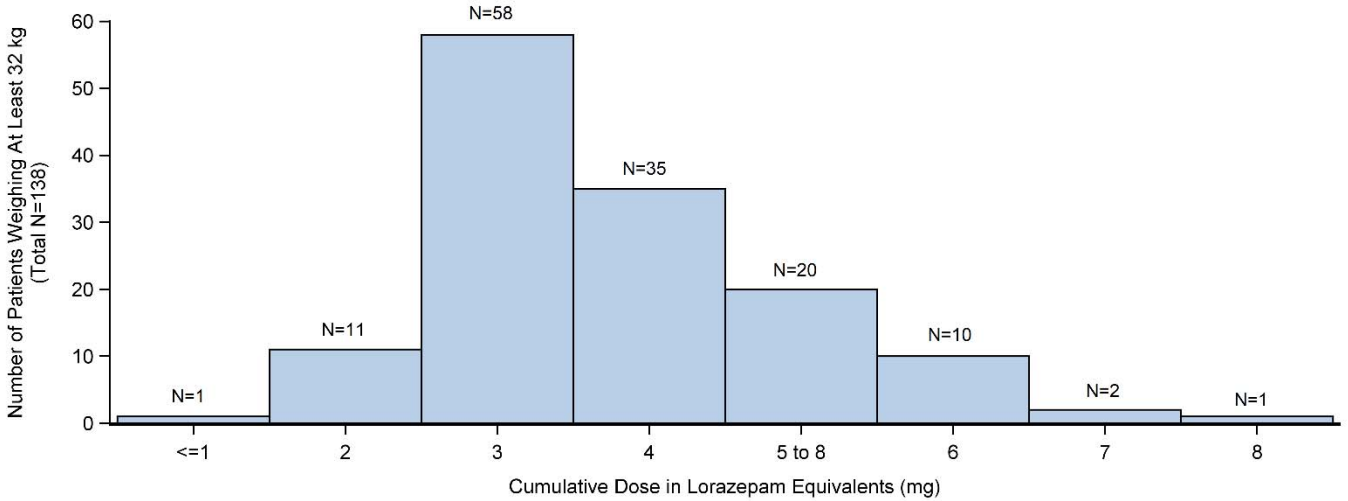
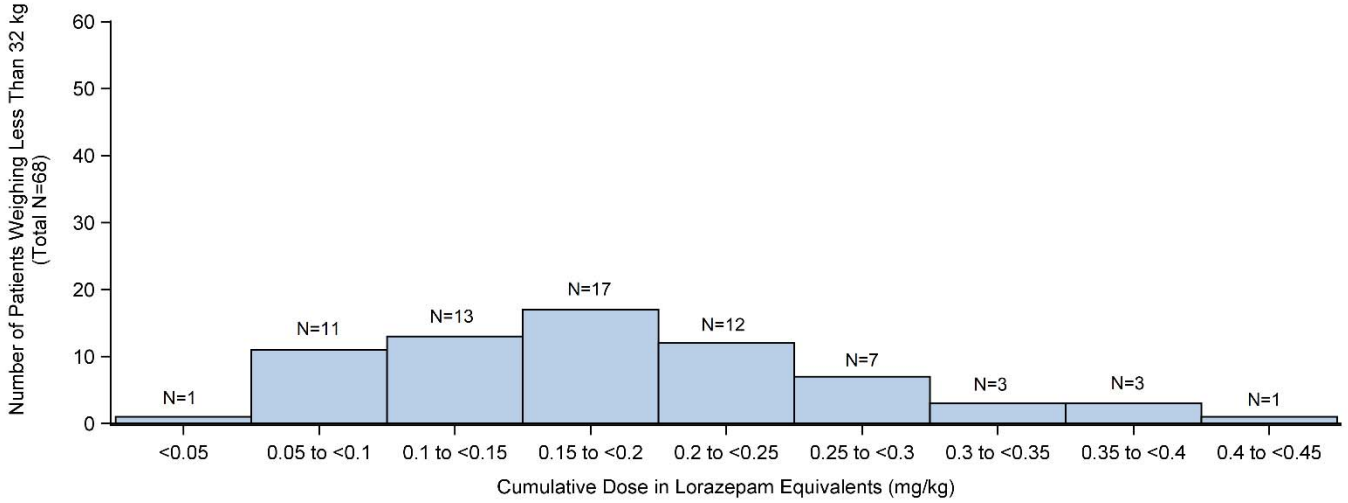
Cumulative Dose in LZP Equivalents





Cumulative adequate LZP equivalent dose required for ESETT eligibility is ≥ 4 mg for those > 32 kg and ≥ 0.1 mg/kg for ≤ 32 kg

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