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Evaluating Use of Higher Dose Oxybutynin in Combination with Desmopressin for Refractory Nocturnal Enuresis

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Background

Nocturnal Enuresis (NE) is a common pediatric condition with an overall prevalence of 15-20% at 5 years of age, with a spontaneous resolution of about 15% per year. 2% Of children age 15 still suffer from the condition and limited treatment options exist. Behavioral therapy achieves success in nearly 3/4 of children, but many families prefer medical intervention, especially in older children. Pharmacologic therapies including Desmopressin (DDAVP) or Imipramine are effective in 40-50% of children. However Imipramine has serious safety concerns. DDAVP in combination with a fixed dose anticholinergic has been shown to be useful in individuals who fail DDAVP alone, but still fails to achieve success rates greater than 60%. **We hypothesize that by titrating up the dose of Oxybutynin in combination with DDAVP in patients who fail initial monotherapy, we will achieve higher rates of success with limited additional adverse events.** We will also record patient demographics, associated symptoms and co-morbidities to determine if we can predict treatment success in patient subgroups.

Treatment Options & Success Rates

- Bedwetting Alarm (Behavioral Therapy) ~75%
- DDAVP ~50%
- Imipramine ~40%
- DDAVP + Fixed Dose Anticholinergic 44-57%

Objectives

Primary Objective

- To investigate the efficacy of combination therapy (DDAVP + escalating dose Oxybutynin) in children with nocturnal enuresis refractory to maximal dose DDAVP

Secondary Objectives

- Identify risk factors for monotherapy refractory NE
- Identify factors that predict success with combination therapy

Methods

IRB approved retrospective analysis of NE patients, ages 7-18 seen at the UMMS Pediatric Urology Clinic from Nov, 2013 – Dec, 2014.

Inclusion Criteria

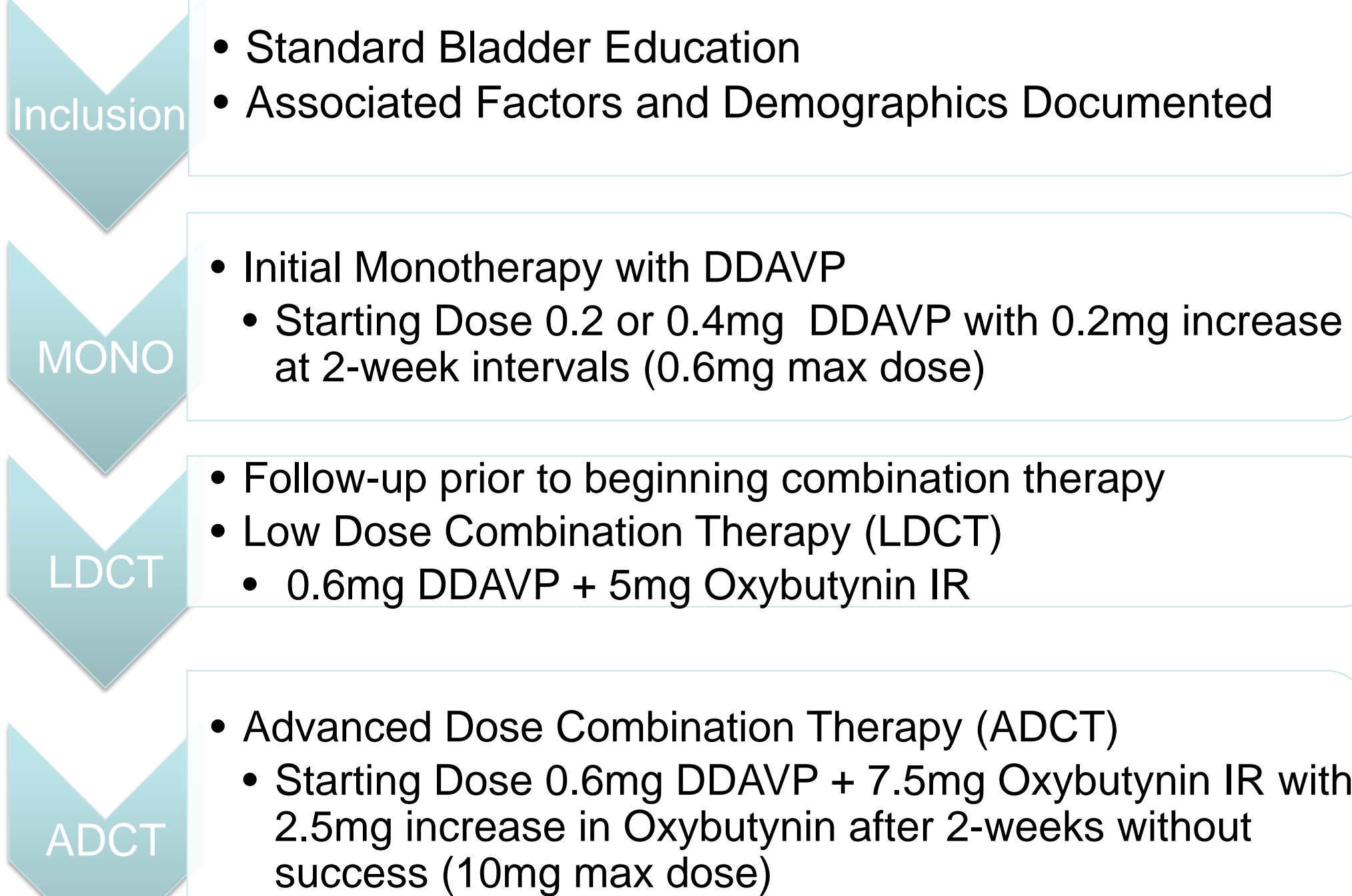
- ✓ Diagnosis of Primary Nocturnal Enuresis or Nocturnal Enuresis with Controlled* or resolved Daytime Voiding Symptoms (CDVS)
- ✓ Treatment with at least 1 dose DDAVP
- ✓ At least one follow-up visit in clinic

*controlled with daytime use anticholinergic

Exclusion Criteria

- Active daytime incontinence
- Dysfunctional voiding requiring PT
- Neurogenic bladder
- Noncompliance with therapy
- Failure to attend follow-up

Treatment Overview

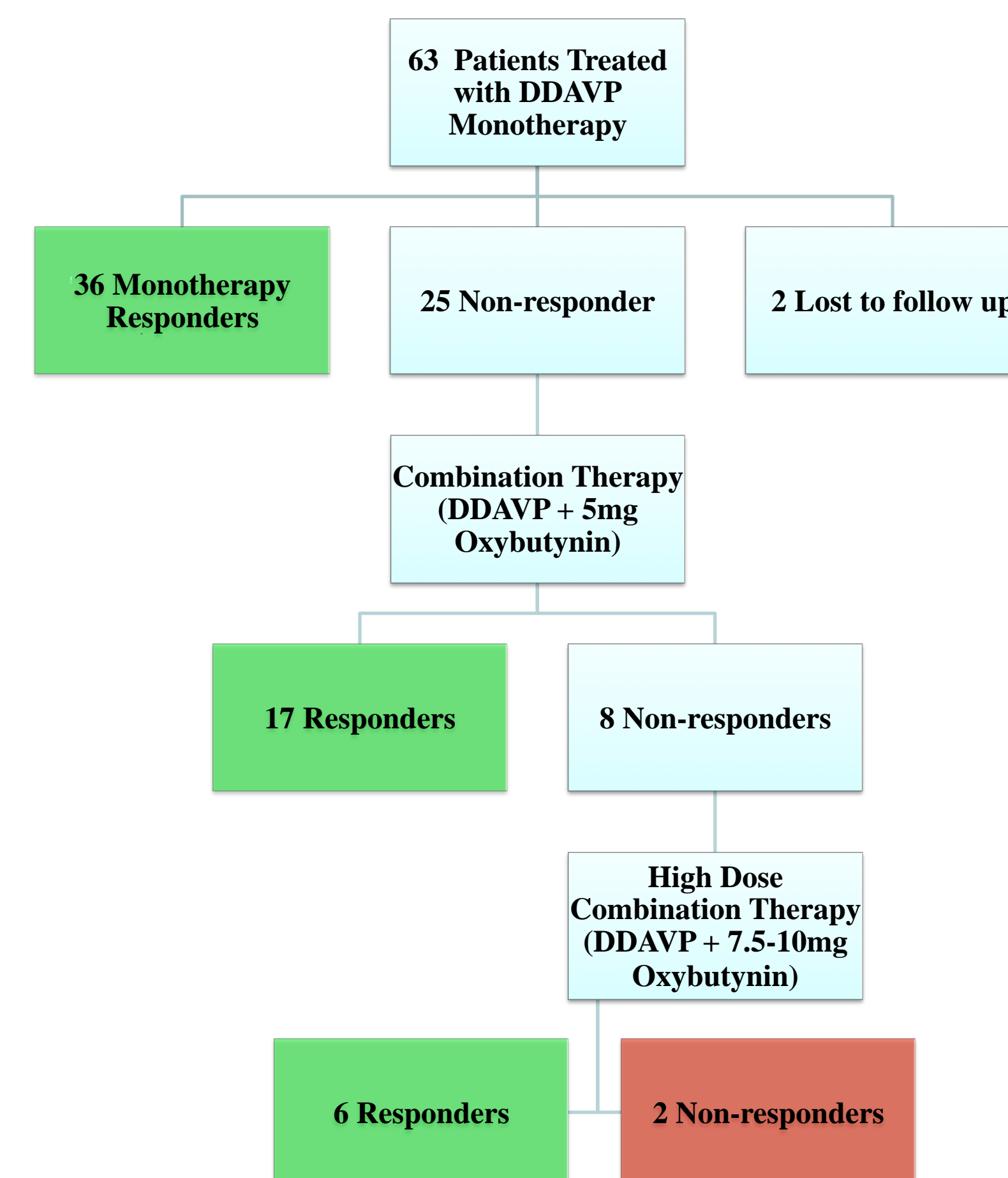


End Points

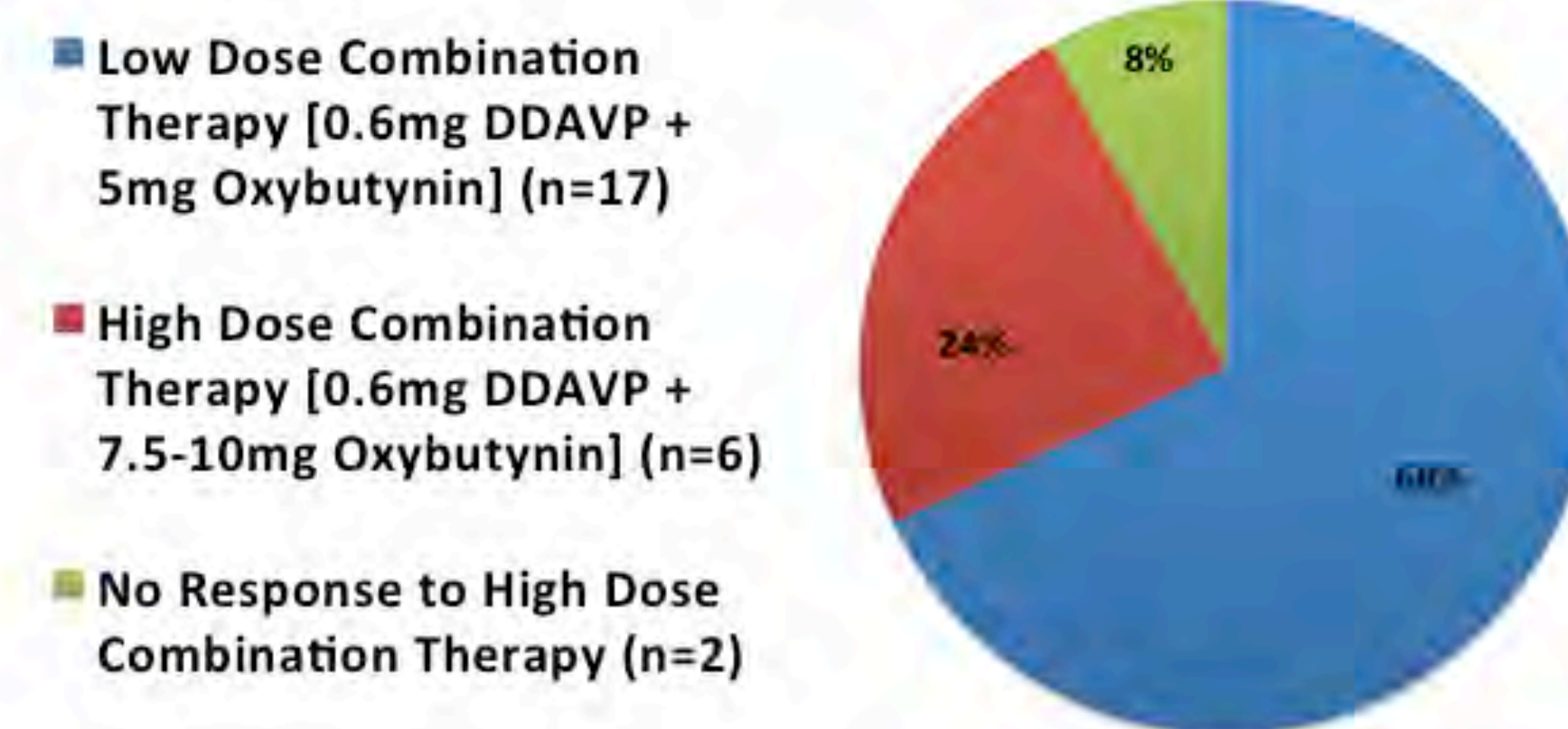
- Success on any medication was defined as 14 consecutive nights without bed-wetting event
- Telephone contact occurred during the dose titration interval until:
 1. Effective dose had been achieved
 2. Maximal doses of DDAVP and oxybutynin had been tried
- Adverse events were solicited verbally during the phone conversation or in the clinic

Results

Treatment Results



Response to Combination Therapy in Patients who Failed Monotherapy



Monotherapy Subgroup Analysis

Patient Subgroup	N	Response	No Response
Total	61	36 (59.0%)	25 (41.0%)
Constipation	21	13 (61.9%)	8 (38.1%)
Daytime Voiding Sx	18	7 (38.9%)	11 (61.1%)*
Low PVR	20	14 (70.0%)	6 (30.0%)
High PVR	4	2 (50.0%)	2 (50.0%)
ADHD/ADD	16	6 (37.5%)	10 (62.5%)*
Family History	16	11 (68.8%)	5 (31.3%)
Psych Med	8	6 (75.0%)	2 (25.0%)
BMI ≤ 24.9	48	27 (56.3%)	21 (43.8%)
Overweight	5	3 (60.0%)	2 (40.0%)
Obese	8	6 (75.0%)	2 (25.0%)
Male	37	22 (59.5%)	15 (40.5%)
Female	24	14 (58.3%)	10 (41.7%)

*Statistically Significant Association

Combination Therapy Subgroup Analysis

Patient Subgroup	N	LDCT	ADCT
All responders	23	17 (73.9%)	6 (26.1%)
Constipation	8	6 (75.0%)	2 (25.0%)
Daytime Voiding Sx	10	7 (70.0%)	3 (30.0%)
Low PVR	6	5 (83.3%)	1 (16.7%)
High PVR	1	1 (100.0%)	0 (0.0%)
ADHD/ADD	10	7 (70.0%)	3 (30.0%)
Family History	4	4 (100.0%)	0.0%
Psych Medication	2	1 (50.0%)	1 (50.0%)
BMI ≤ 24.9	20	14 (70.0%)	6 (30.0%)
Overweight	2	2 (100.0%)	0 (0.0%)
Obese	1	1 (100.0%)	0 (0.0%)
Male	13	8 (61.5%)	5 (38.5%)
Female	10	9 (90.0%)	1 (10.0%)

Acknowledgements

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Conclusions

- 97% Overall success rate using dose titration
- No reported adverse events
- ADD/ADHD and CDVS* subgroups had statistically significant decreased response to monotherapy
- High monotherapy response rate in low PVR, family History, Psych Medication and Obese subgroups
- Age was not a predictive factor
- High dose combination therapy is safe and effective

CDVS = Controlled Daytime Voiding Symptoms