

Cognitive Behavioral Therapy and Amitriptyline in Pediatric Chronic Migraine: *A Randomized Clinical Trial*

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Chronic Migraine in Youth

- **15 or more headache days/month**
- **Meet ICHD-II migraine criteria**
- **Typically severe level of disability**
- **No evidence-based treatments**

Chronic Migraine in Youth

- **In general population, ages 12-17, affects about 1%**
- **Yet, 60% of youth with CM have not seen a headache provider in past year**
- **But, up to 2 out of 3 patients that do seek headache specialty care**
- **Youth with migraine become adults with migraine**

Trial Rationale

- **Real world, treatment seeking sample**
- **Ethical and practical considerations/Choice of control arm**
- **Choice of prevention medication**
- **CBT based upon proven protocol & specific headache treatment evidence**

Trial Design

- Amitriptyline (Goal Dose: 1 mg/kg/day)
- Cognitive Behavioral Therapy
- Attention Control and Education Therapy

Two Arms:

1. CBT + A

2. ATT + A

Cognitive Behavioral Therapy

- **Headache Management Principles**
- **Biofeedback-Assisted Relaxation Training**
- **Activity Pacing**
- **Recognizing Negative Thoughts and Using Calming Statements**
- **Problem-Solving Skills**
- **Parent Coaching & Reinforcement of Coping**

Inclusion Criteria

- **Chronic Migraine by ICHD-II criteria**
- **15 or more headaches/month based upon prospective diary**
- **Male or Female between ages 10-17**
- **PedMIDAS Disability Score > 20, indicating at least moderate disruption in daily activities**

Exclusion Criteria

- **Abortive Medication Overuse**
- **Present or Lifetime psychiatric diagnosis meeting DSM-IV criteria for bipolar disorder, major depressive disorder, or psychosis (based upon K-SADS interview)**
- **PedMIDAS Score > 140, indicating need for multi-systemic therapies to address very significant level of disability**

Exclusion Criteria

- **No other current prophylactic antimigraine medication**
- **Other chronic pain condition such as fibromyalgia, complex regional pain syndrome-II**
- **Abnormal findings on ECG**
- **Disallowed Medications: opioids, antipsychotics, antimanics, barbituates, benzodiazepines, muscle relaxants, sedatives, tramadol, herbal products**

Trial Time Line

- **Medical Assessment and Screening**
- **Psychosocial Assessment and Screening**
- **Randomization**
- **Treatment Phase (Total of 20 weeks)**
 - **Weekly for 8 weeks**
 - **Monthly for 3 months**
- **Follow-Up Phase (Total of 12 months)**
 - **Every 3 months**

Aims

- **Evaluate Safety**
- **Evaluate Efficacy**
 - Reduction of Headache Days
 - Reduction of Disability
 - Clinical Impact: $\geq 50\%$ Headache Day Reduction & Disability Grade of Mild to None
- **Evaluate Durability**

Demographics

CBT + A (N=64)

ATT + A (N=71)

Age

14.4 ± 1.9

14.4 ± 2.1

Gender

79.7% female

79% female

Headache

21.4 ± 5.4

21.2 ± 5.1

Days

Disability

67.3 ± 29.8

69.2 ± 33.8

(PedMIDAS)

(Severe Grade)

(Severe Grade)

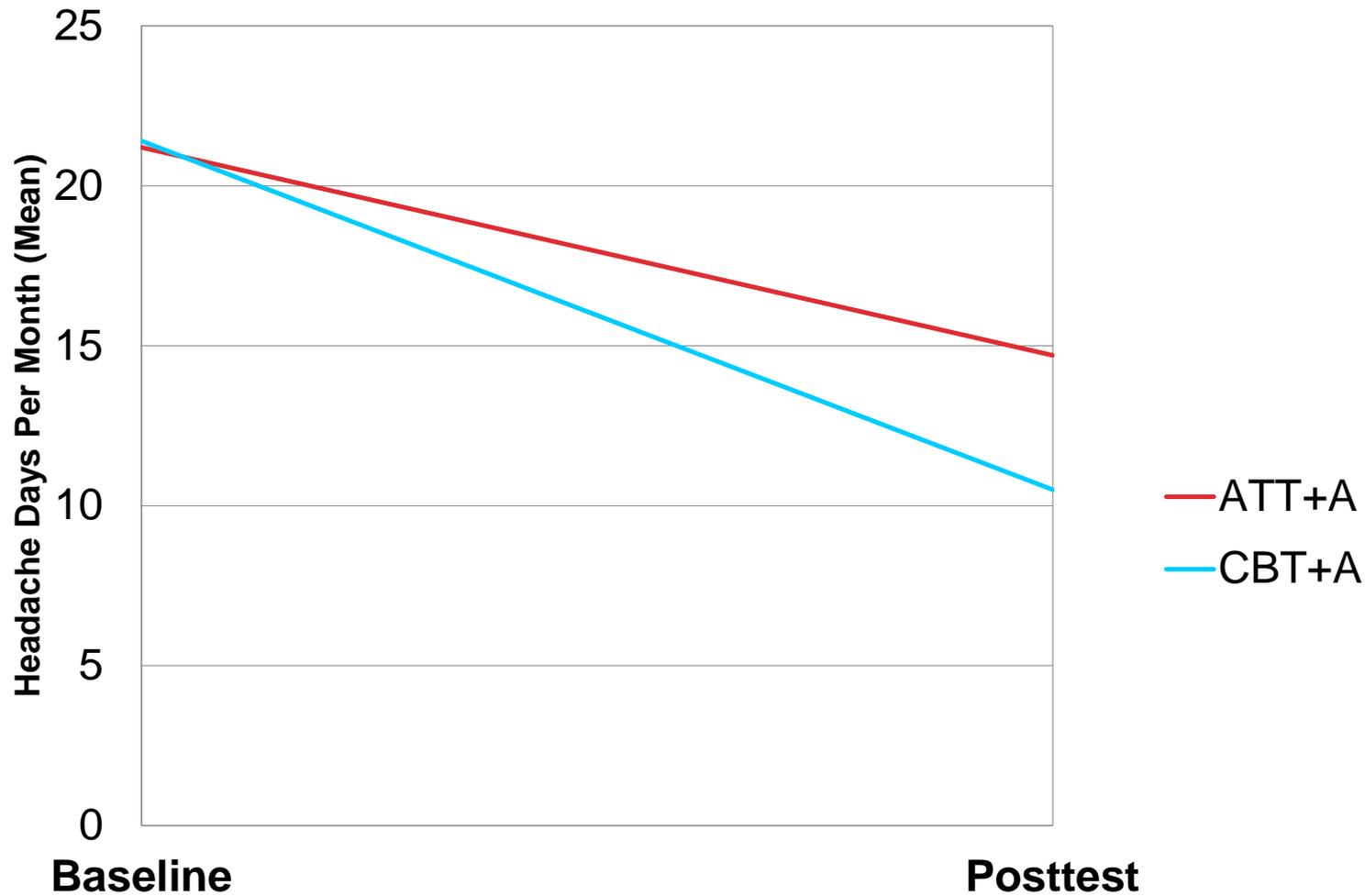
Outcomes

- **Average final dose of amitriptyline = 1.01 mg/kg/day**
- **No serious, related, and unexpected Adverse Events**
- **Total AEs = 199**

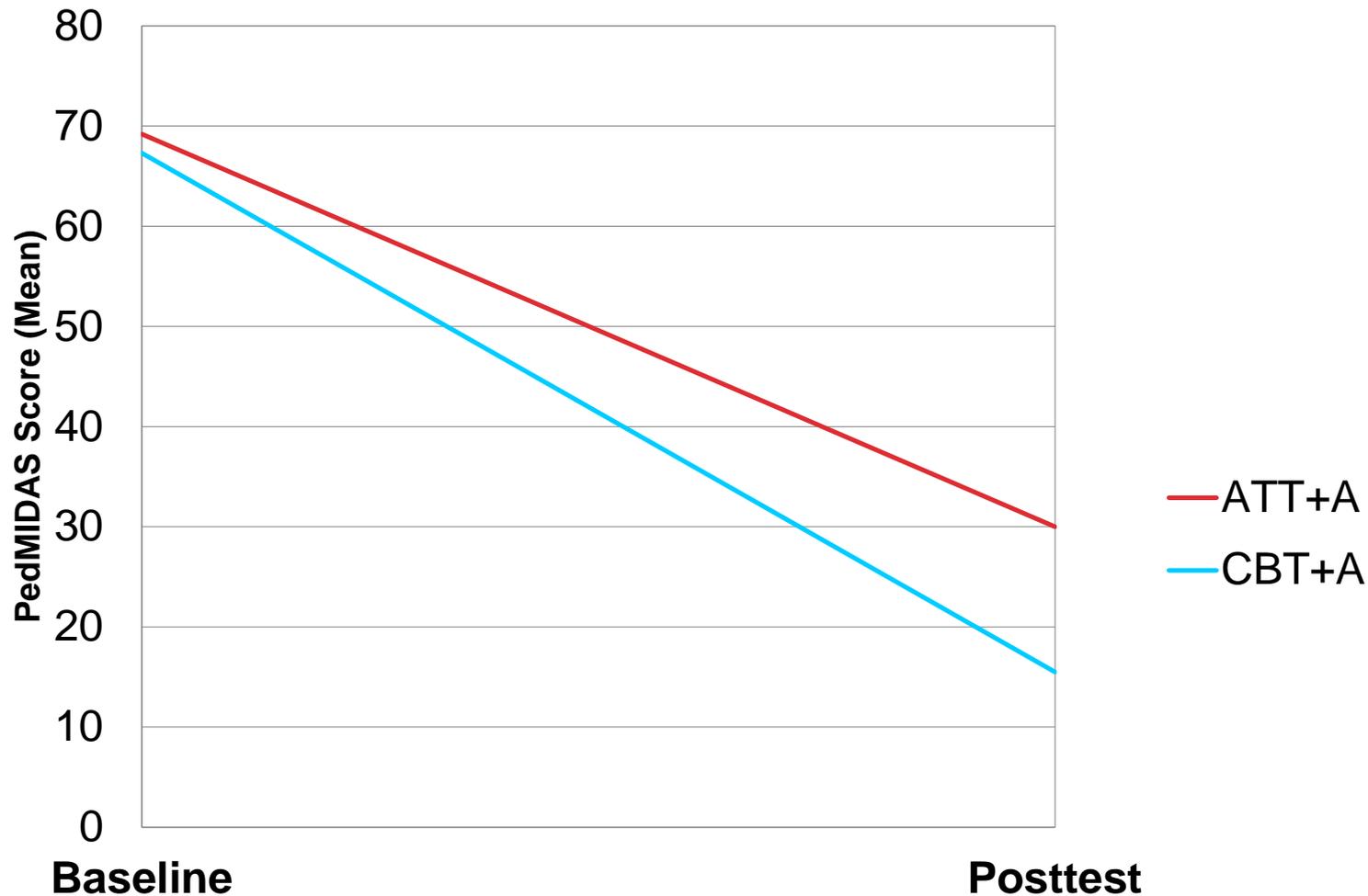
Outcomes

- Primary Endpoints:
Headache Days & Disability
- **Treatment Credibility and Integrity** (Both arms had high levels of credibility to participants and parents)

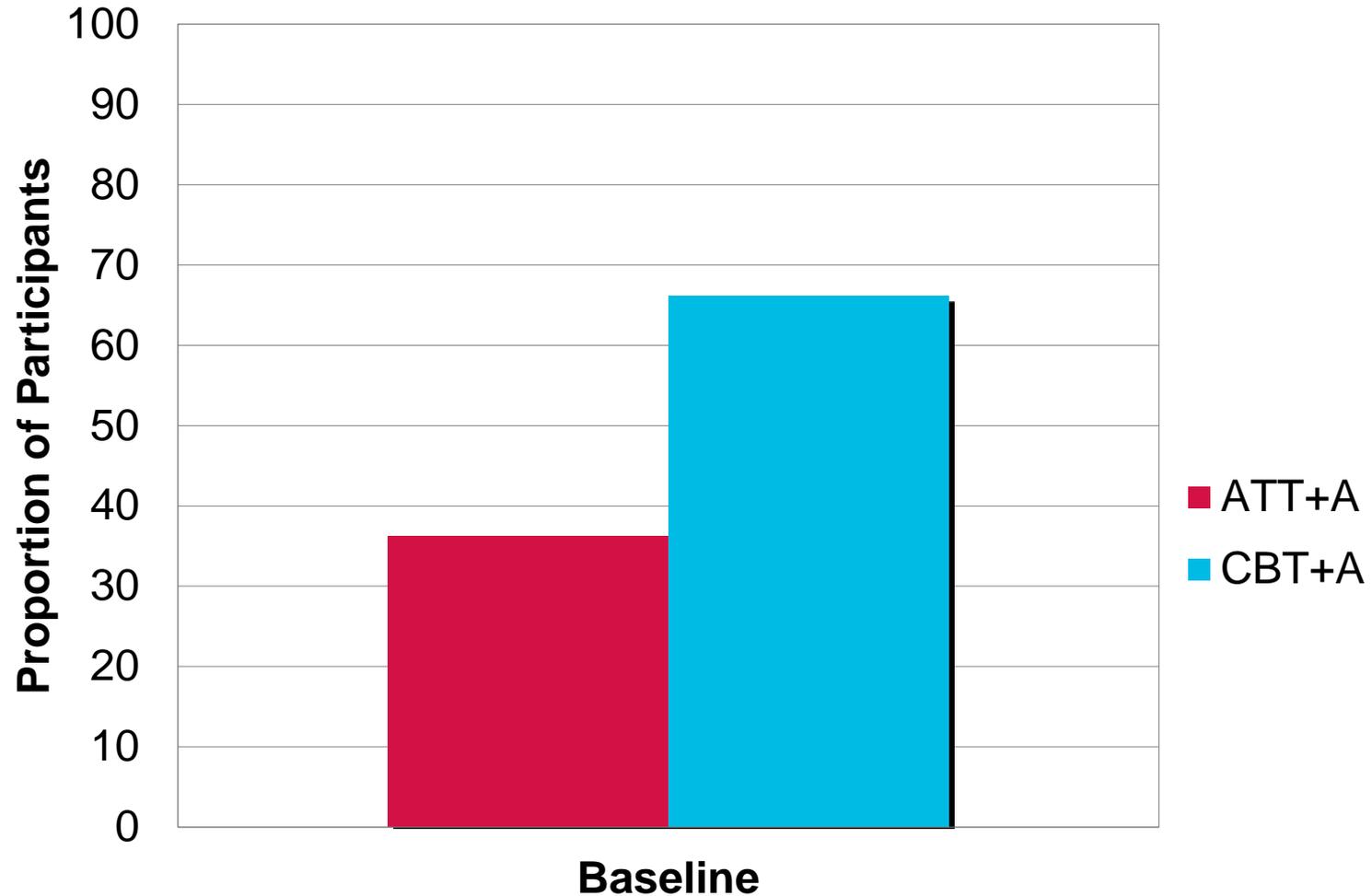
Headache Days



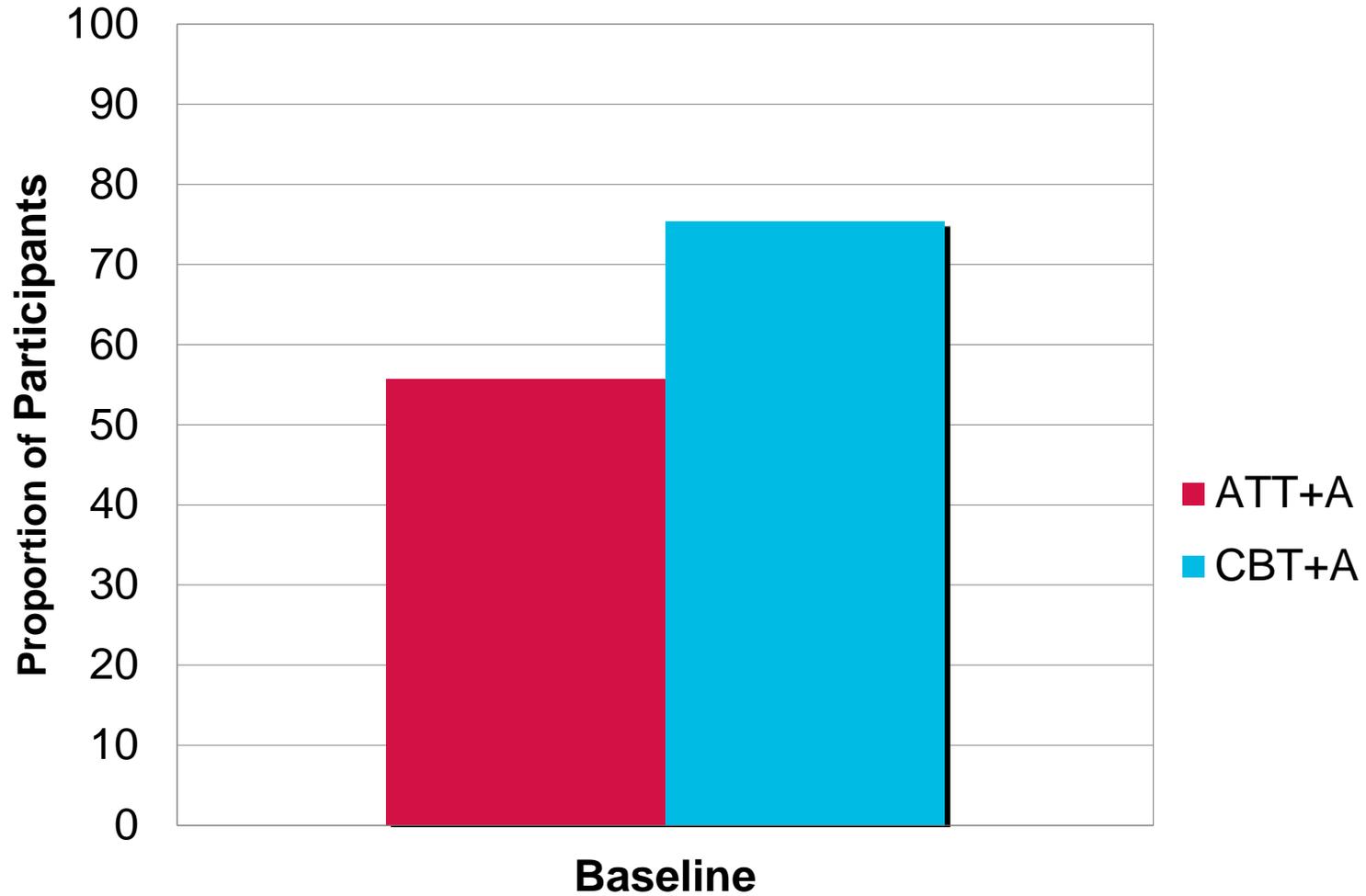
PedMIDAS



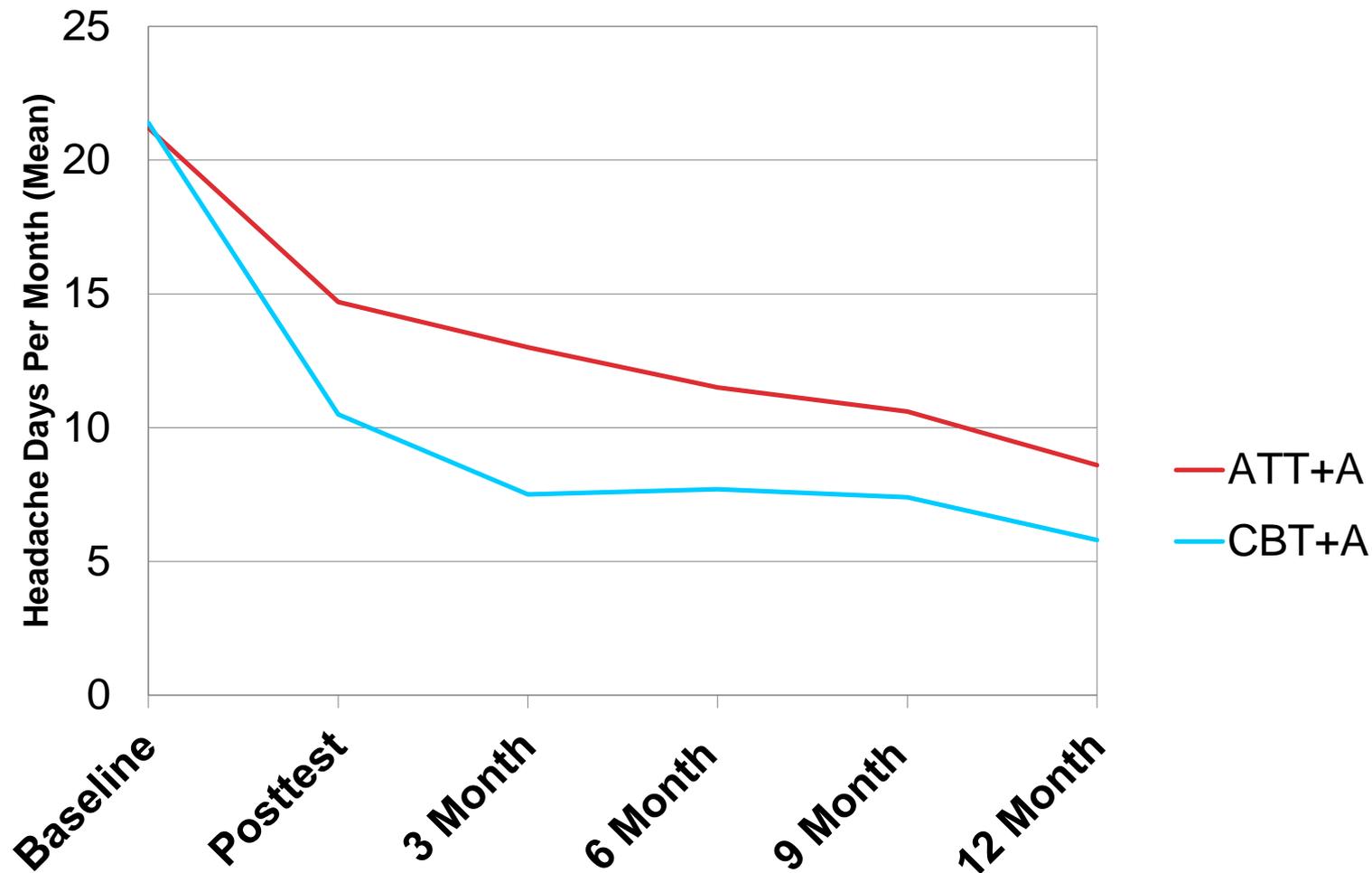
50% or More Headache Days Reduction



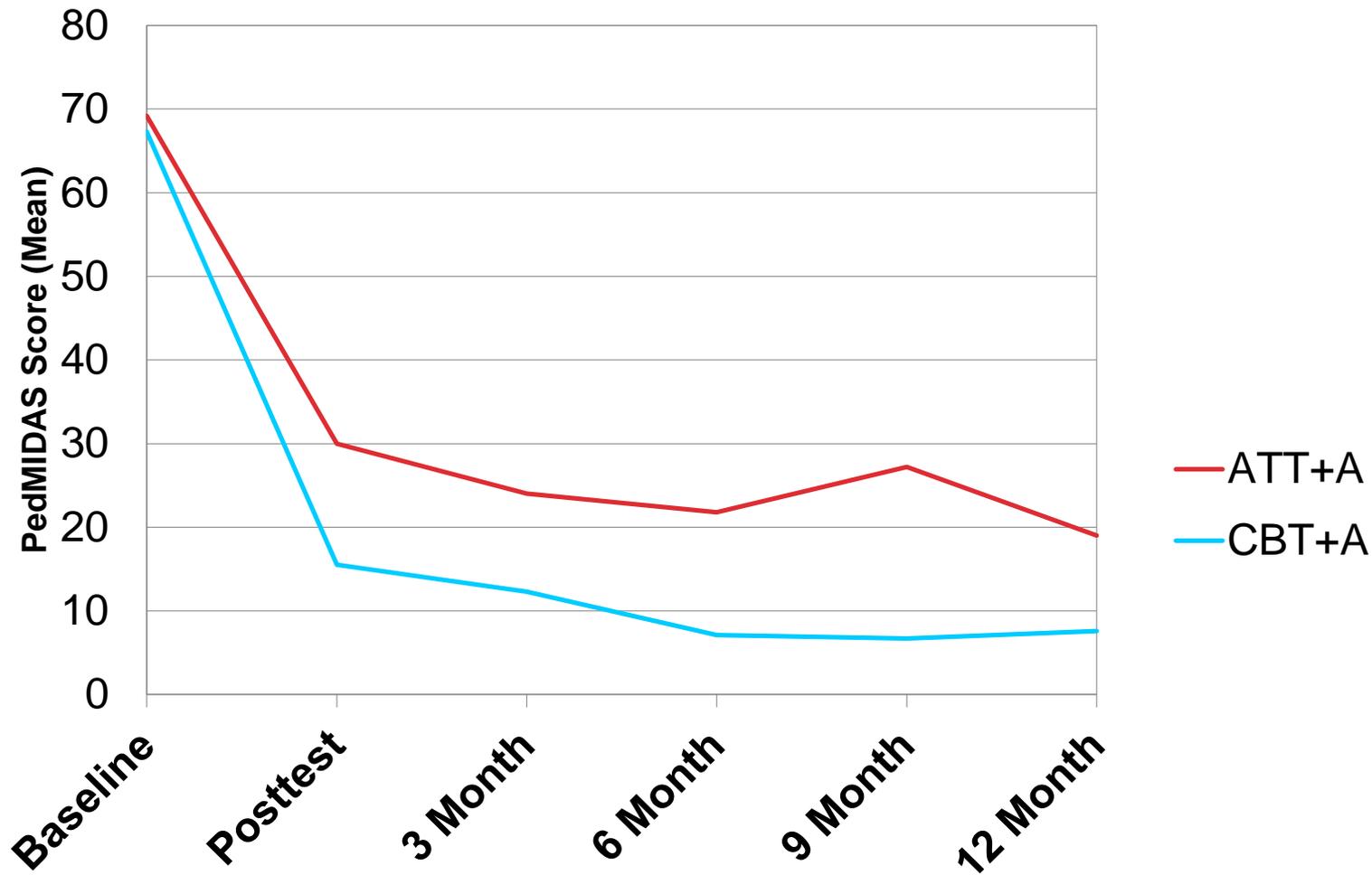
PedMIDAS < 20%



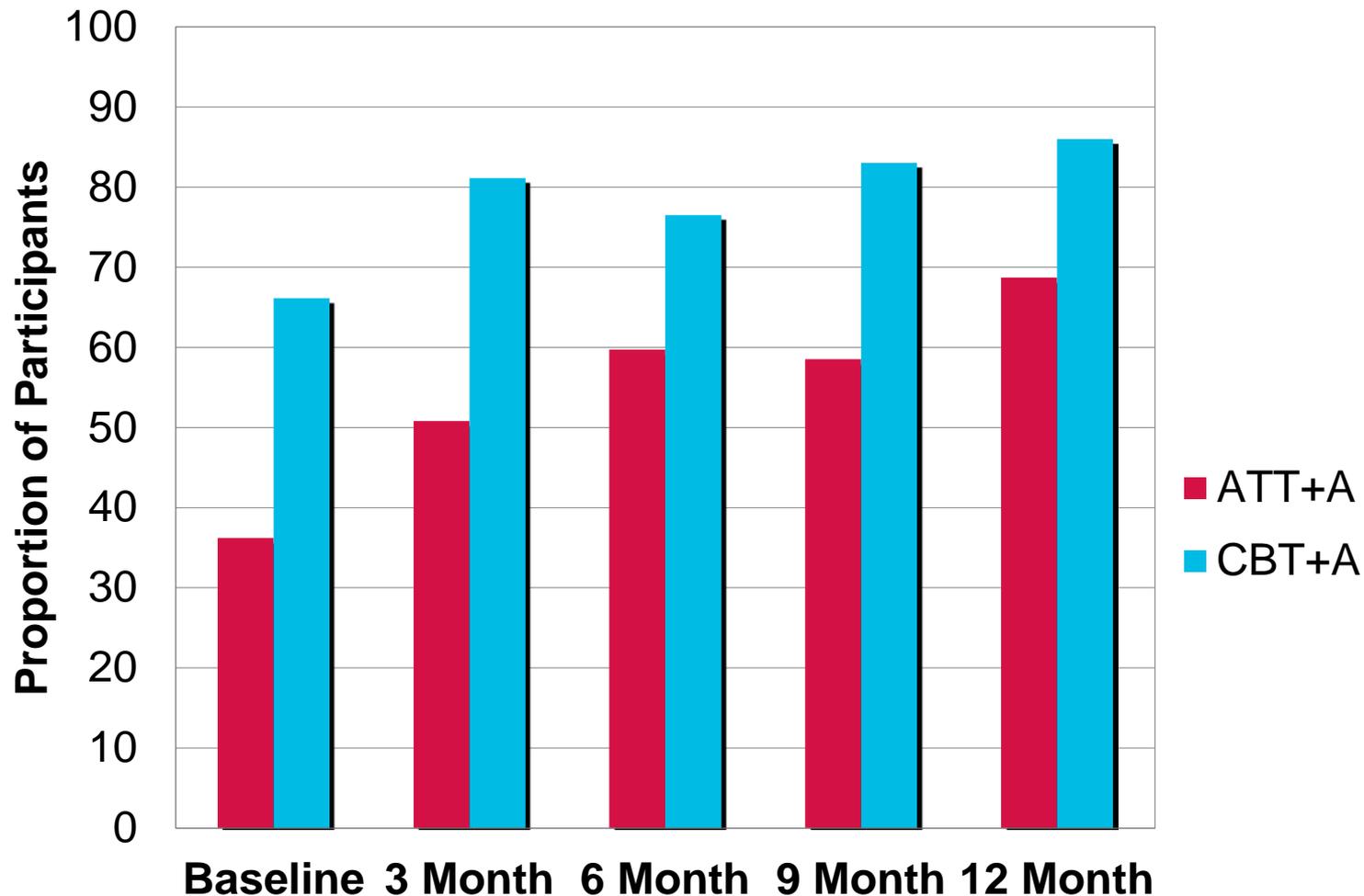
Headache Days



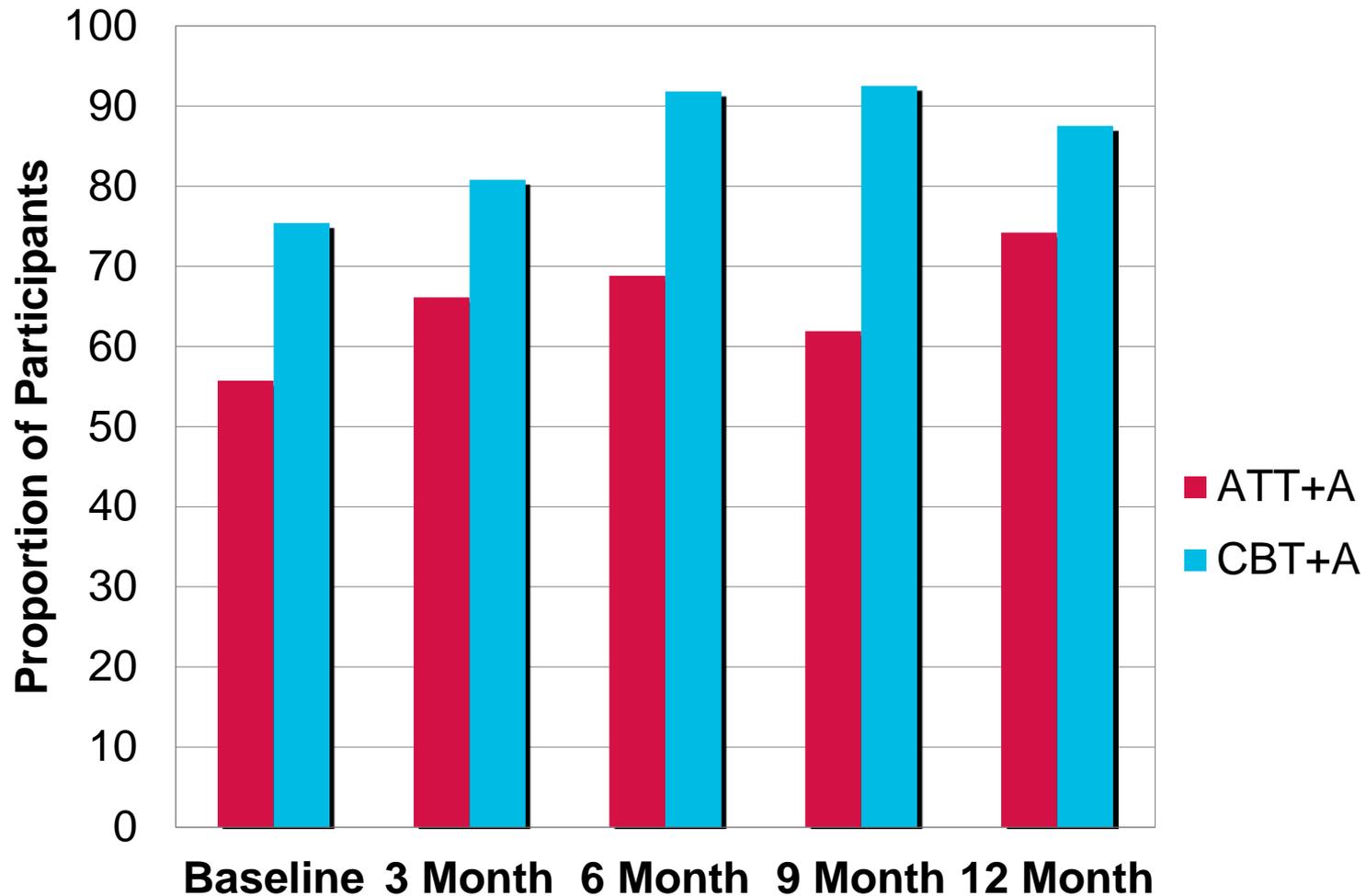
PedMIDAS



50% or More Headache Days Reduction



PedMIDAS < 20%



Conclusions

- **CBT + Amitriptyline is safe, well tolerated, credible, efficacious, & durable**
- **1st RCT to demonstrate clinically significant impact in pediatric chronic migraine**

Conclusions

- **Outcomes compare favorably to only FDA approved therapy for adults with chronic migraine (onabotulinumtoxin A)**
- **Need to test CBT + Placebo**

Implications

- **Given measured clinical impact, suggests a new standard of care**
- **Translation to practice in Cincinnati – A work in progress**

Application in Current Practice

- **Manualized treatment that can be basis of training**
- **Need for more trained providers and integration with neurology practice**
- **Evidence-based care needs to be reimbursed**

Questions

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- **Participants**
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- **Powers' Lab Team**