ARDEA OUTCOMES

Beyond Patient Journals - Using GAS to Capture the Patient Voice

Ardea Insights Webinar Series

Februrary 26th, 2021

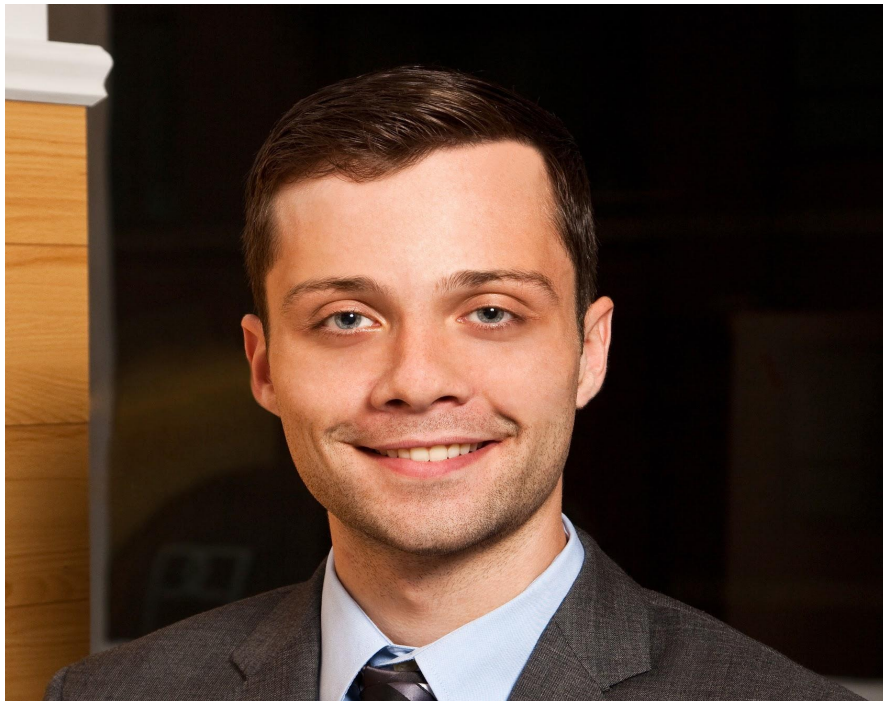
ARDEA

OUTCOMES

Ardea Insights Webinar Presenters

CEO

Chere Chapman



Biostatistician

Taylor Dunn

ARDEA OUTCOMES

ARDEA OUTCOMES

Poll #1

Webinar Objectives

1) **General understanding of Goal Attainment Scaling (GAS)**
   a) Overview of GAS
   b) Value as an GAS endpoint
   c) Basics of the GAS method

2) **Insights into the interpretation of GAS data in Clinical Development**
   a) A GAS Success Story: Using GAS to evaluate therapeutic interventions in Cerebral Palsy
   b) Common pitfalls with standardized measures and how GAS can help

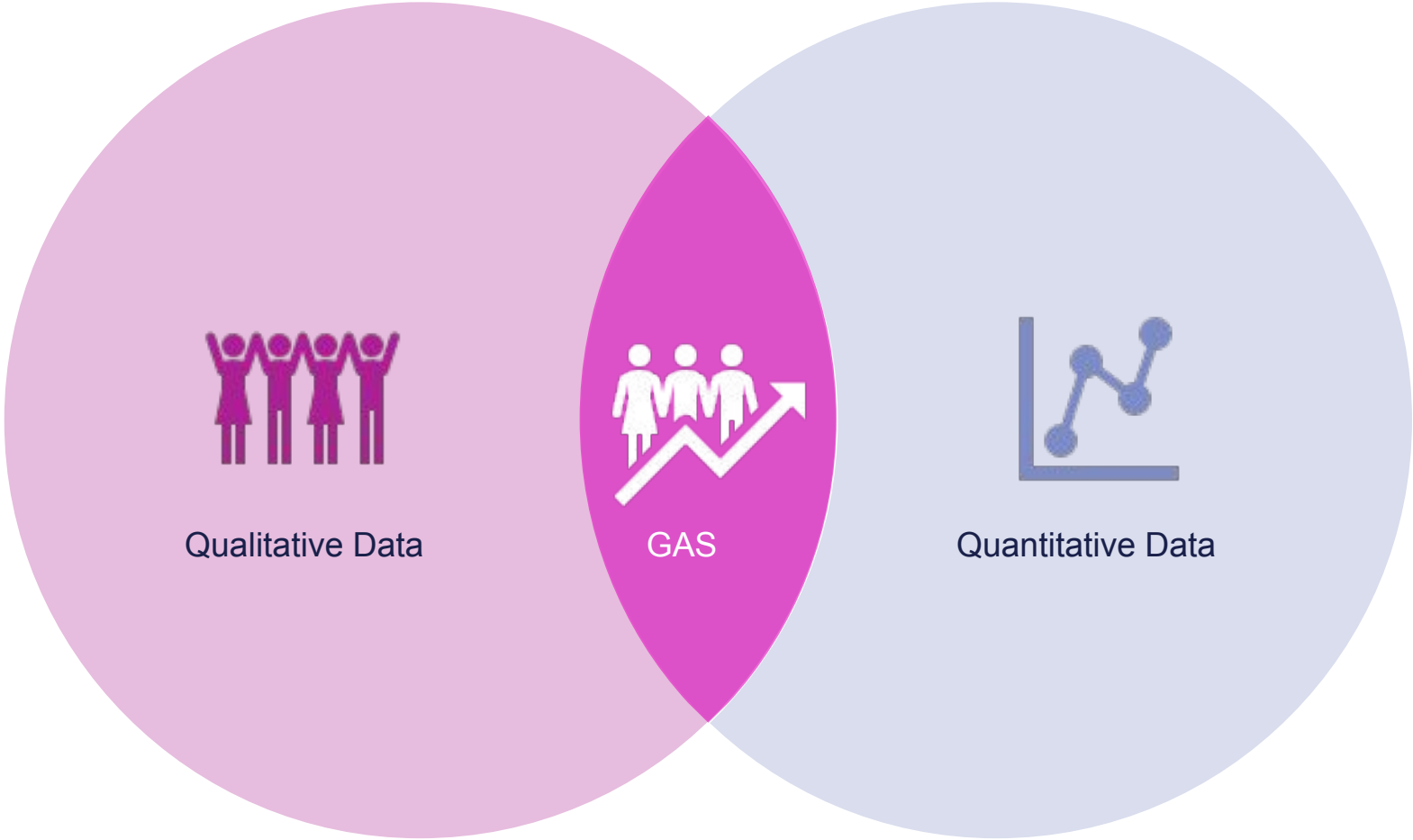
ARDEA OUTCOMES

GOAL ATTAINMENT SCALING

MEASURES THE EXTENT TO WHICH A PATIENT'S INDIVIDUAL GOALS ARE ACHIEVED WITH INTERVENTION.

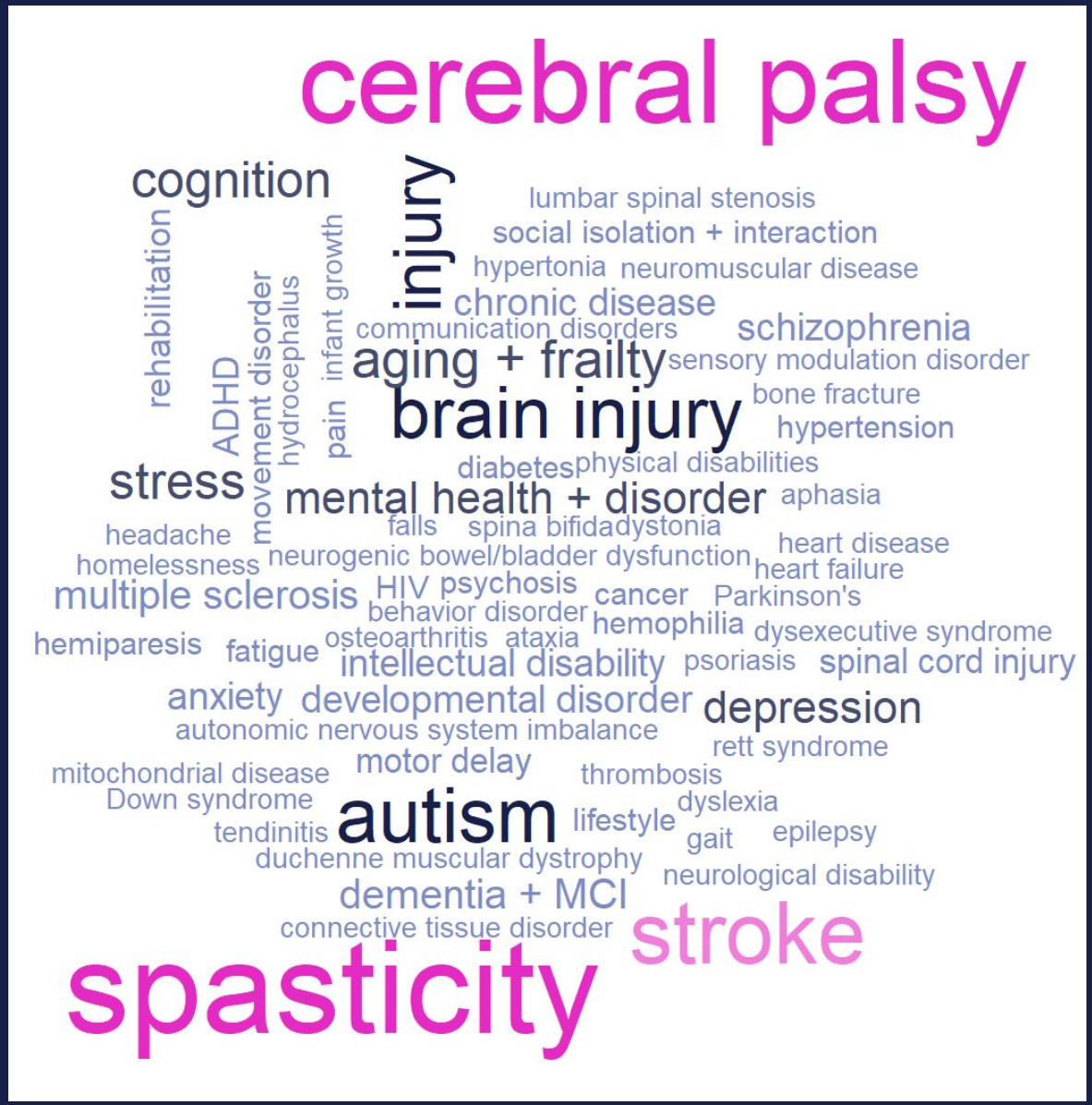
ARDEA OUTCOMES

GAS data can generate both quantitative and qualitative insights.



ARDEA OUTCOMES

GOAL ATTAINMENT SCALING IS GAINING PROMINENCE IN IN RESEARCH.



ARDEA OUTCOMES

GAS provides value throughout the clinical development lifecycle.

PHASE 01 → PHASE 02 → PHASE 03 → PHASE 04

- GAS is a **Patient-Centric Outcome Measure**
- GAS may be used Phase 1B onward

Phase 4 → Reported by patients as a PRO/RWE

Phase 1→4:GAS is facilitated by a Clinician: some similarities to a Clin-RO but coming from the patient

Best **introduced early** in clinical development

- ✔ Changes the nature of the dialogue between patient and clinician

Data shows **efficacy** and **effectiveness**

- ✔ GAS data is meaningful to patients, caregivers, sponsors and regulators

Data is **inherently clinically meaningful** and relevant

- ✔ Promotes shared decision-making
- ✔ Incorporates wishes and concerns of patients or caregivers

Modified GAS data **captured direct from patients** or caregivers

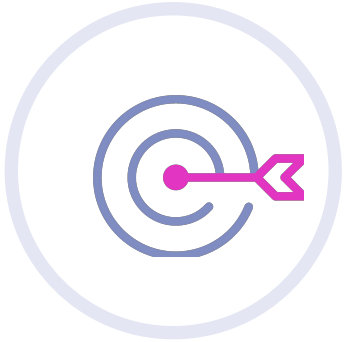
- ✔ GAS is motivating
- ✔ GAS can promote adherence

ARDEA OUTCOMES

Goal Attainment Scaling is a three step process.

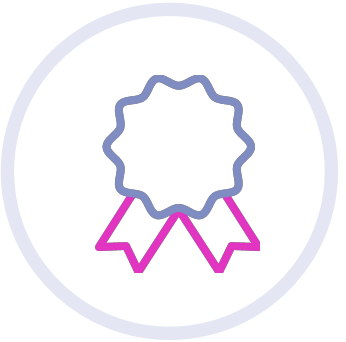
IDENTIFY GOALS

Clinician to facilitate interview for subject or caregiver to identify goals



BUILD GAS SCALES

Set the 5-point goal attainment scale for each identified goal



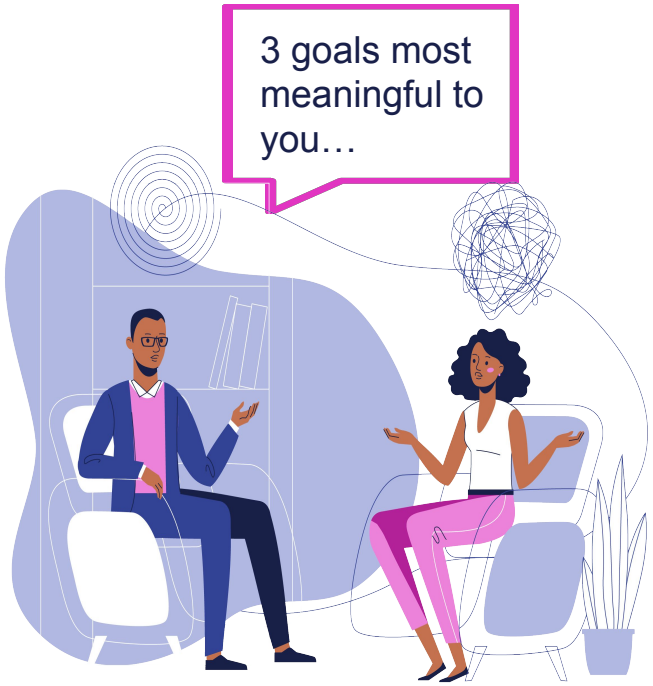
MEASURE ATTAINMENT

Rate during follow-up whether the goals have been attained

ARDEA OUTCOMES

The **Goal-Setting Visit** focuses on what is important to the participant.

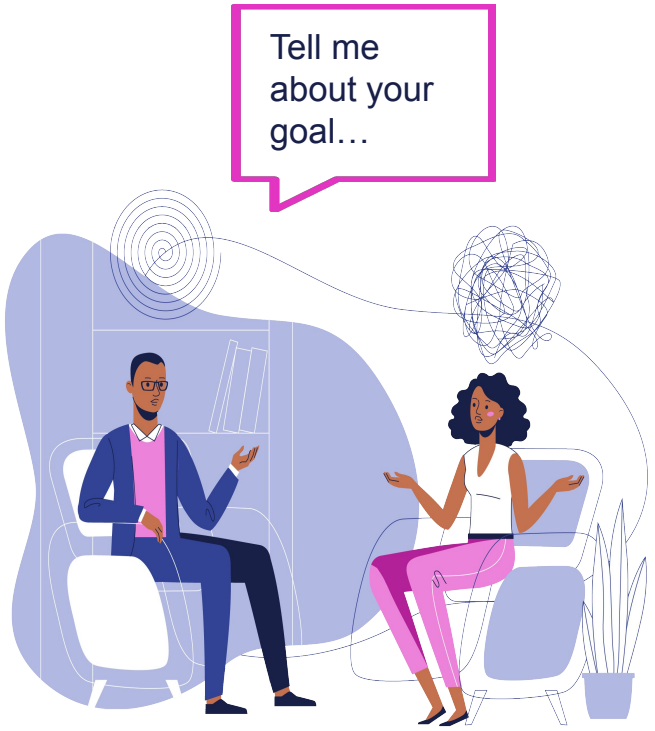
ARDEA OUTCOMES



Goal Title	
Much Better than the Goal	+2
Somewhat Better than the Goal	+1
The Goal	0
Baseline Status	-1
Much Worse than the Goal	-2

During **Follow-Up Visits** clinicians and participants rate goal attainment.

	Subject Rating	GAS Interviewer Rating
Much Better than the Goal Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliqui.	○ +2	○ +2
Somewhat Better than the Goal Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat.	○ +1	○ +1
The Goal Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis.	○ 0	○ 0
Baseline Status Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor.	○ -1	○ -1
Much Worse than the Goal Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor.	○ -2	○ -2



ARDEA OUTCOMES

ARDEA OUTCOMES

Poll #2

ARDEA OUTCOMES

A GAS Success Story:

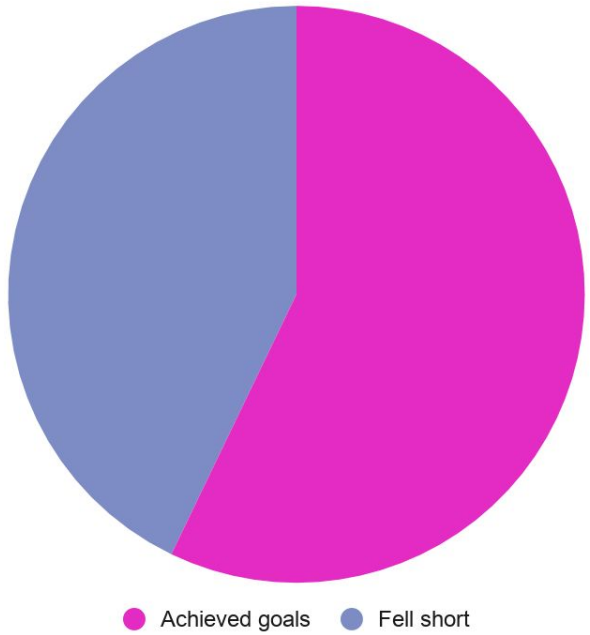
Using GAS to evaluate therapeutic interventions in children with cerebral palsy

Cerebral palsy was one of the first complex disease areas to embrace GAS.

First used with children in a phase II trial,

GAS showed promise in measuring functional outcomes.

- All children made progress on their goals
- At 6 months: **8/14 children had GAS T-scores ≥ 50**
- Standardized outcomes showed no change



Wallen et al. Functional outcomes of intramuscular botulinum toxin type a in the upper limbs of children with cerebral palsy: a phase II trial. *Arch Phys Med Rehabil*. 2004;85(2):192-200. doi:10.1016/j.apmr.2003.05.008

ARDEA OUTCOMES

Cerebral palsy was one of the first complex disease areas to embrace GAS.

Following positive results from phase II, **GAS was chosen as a primary outcome** in phase III.

"**Families had no difficulty** in identifying several functional goals and indicated that **the process was very positive**."

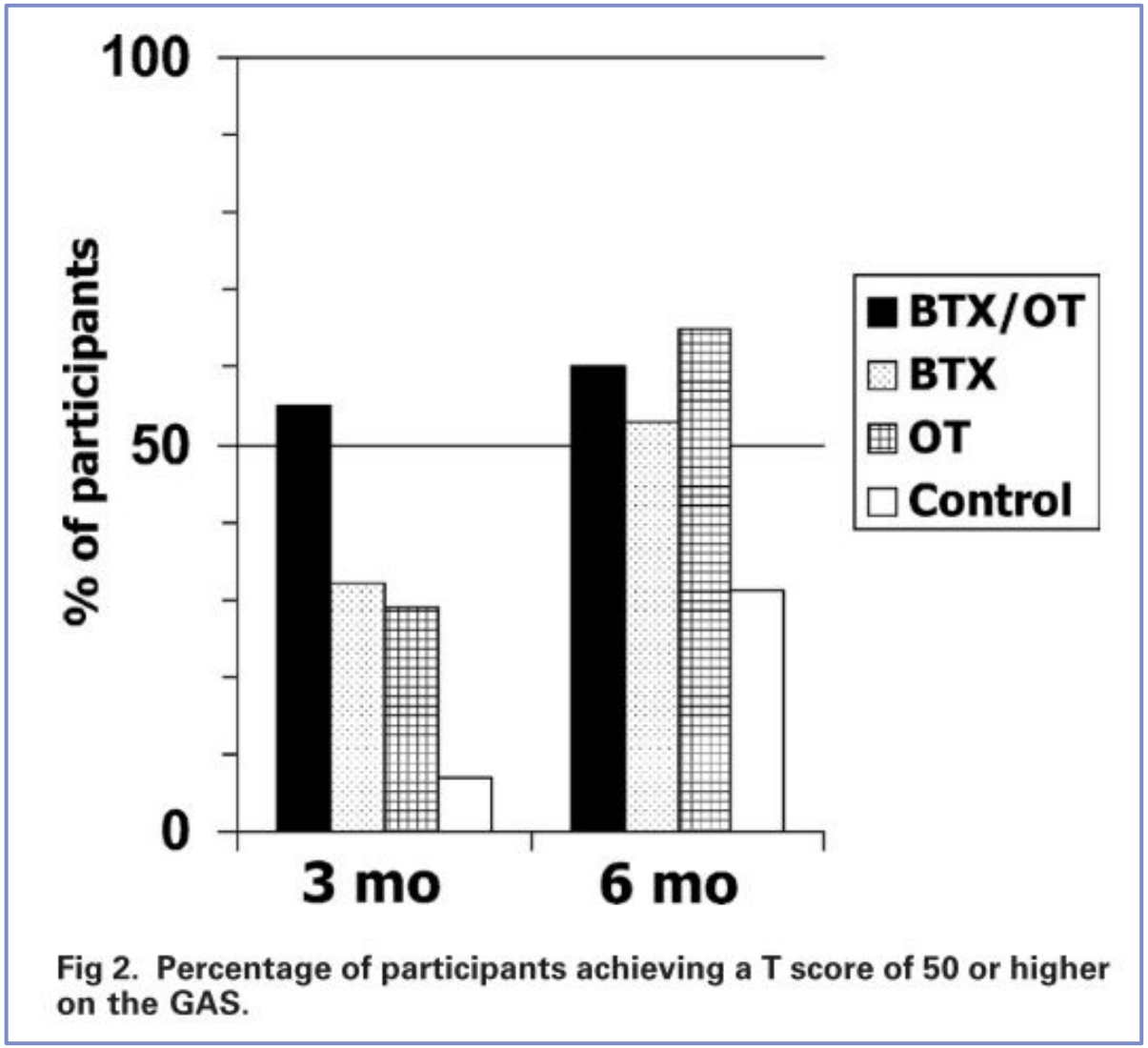


Fig 2. Percentage of participants achieving a T score of 50 or higher on the GAS.

Wallen et al. Functional Outcomes of Intramuscular Botulinum Toxin Type A and Occupational Therapy in the Upper Limbs of Children With Cerebral Palsy: A Randomized Controlled Trial. *Arch Phys Med Rehabil*. 2007;88(1):1-10.

ARDEA OUTCOMES

GAS is focused and comprehensive by design.

ARDEA OUTCOMES

Standardized outcomes can be cumbersome and may miss important change.

By allowing patients to identify their most important outcomes, **GAS is both focused and comprehensive by design.**

"**The failure to detect change** on this measure reinforces the need to select outcome measures of specific goals of importance to families … Change on those areas targeted by families may have been subsumed into **the large number of items of the PEDI**, many of which were not targeted as goals for intervention."

- Wallen et al. 2007

Example: the Pediatric Evaluation of Disability Inventory (**PEDI**)

Table 1. CONTENT OF THE PEDIATRIC EVALUATION OF DISABILITY INVENTORY

	Self-Care Domain	Mobility Domain	Social Function Domain
Functional skills scales	Types of food textures Use of utensils Use of drinking containers Toothbrushing Hairbrushing Nose care Handwashing Washing body and face Pullover/front-opening garments Fasteners Pants Shoes/socks Toileting tasks Management of bladder Management of bowel	Toilet transfers Chair/wheelchair transfers Car transfers Bed mobility/transfers Tub transfers Method of indoor locomotion Distance/speed indoors Pulls/carries objects Method of outdoor locomotion Distance/speed outdoors Outdoor surfaces Upstairs Downstairs	Comprehension of word meanings Comprehension of sentence complexity Functional use of expressive communication Complexity of expressive communication Problem resolution Social interactive play Peer interactions Self-information Time orientation Household chores Self-protection Community function
Complex activities assessed with caregiver assistance and modifications scales	Eating Grooming Bathing Dressing upper body Dressing lower body Toileting Bladder management Bowel management	Chair/toilet transfers Car transfers Bed mobility/transfers Tub transfers Indoor locomotion Outdoor locomotion Stairs	Functional comprehension Functional expression Joint problem solving Peer play Safety

Haley et al. Pediatric Evaluation of Disability Inventory: Clinical Interpretation of Summary Scores Using Rasch Rating Scale Methodology. Phys Med Rehabil Clin N Am. 1993;4(3):529-540.

ARDEA OUTCOMES

Standardized outcomes can be cumbersome and may miss important change.

By allowing patients to identify their most important outcomes, **GAS is both focused and comprehensive by design.**

Example: the Pediatric Evaluation of Disability Inventory (**PEDI**) and the Gross Motor Function Measure (**GMFM**)

Description of the activity	ICF-CY Classification	Frequency of its use in the GAS scales
Acquiring skills to use writing implements	d1450	1
Using general skills and strategies of the writing process	d1700	1
Discussion with one person	d3550	1
Using writing machines	d3601	1
Grasping	d4401	1
Manipulating	d4402	5
Fine hand use	d440	2
Sports	d9201	1
Total		13

13/64 (20%) of **goals were not covered** by either the PEDI or the GMFM-66.

Steenbeek et al. Responsiveness of Goal Attainment Scaling in comparison to two standardized measures in outcome evaluation of children with cerebral palsy. *Clin Rehabil*. 2011;25(12):1128-1139.

ARDEA OUTCOMES

GAS embraces heterogeneity of disease expression and severity.

ARDEA OUTCOMES

Standardized outcomes may fail to capture heterogeneity of disease expression.

By allowing for personalized outcomes, **GAS embraces heterogeneity of disease expression.**

"Further, using these individualized outcomes resolved some of the difficulties of finding consistent measurement tools across our **clinically representative but heterogenous group of children with CP**."

Wallen et al. Functional Outcomes of Intramuscular Botulinum Toxin Type A and Occupational Therapy in the Upper Limbs of Children With Cerebral Palsy: A Randomized Controlled Trial. *Arch Phys Med Rehabil*. 2007;88(1):1-10.

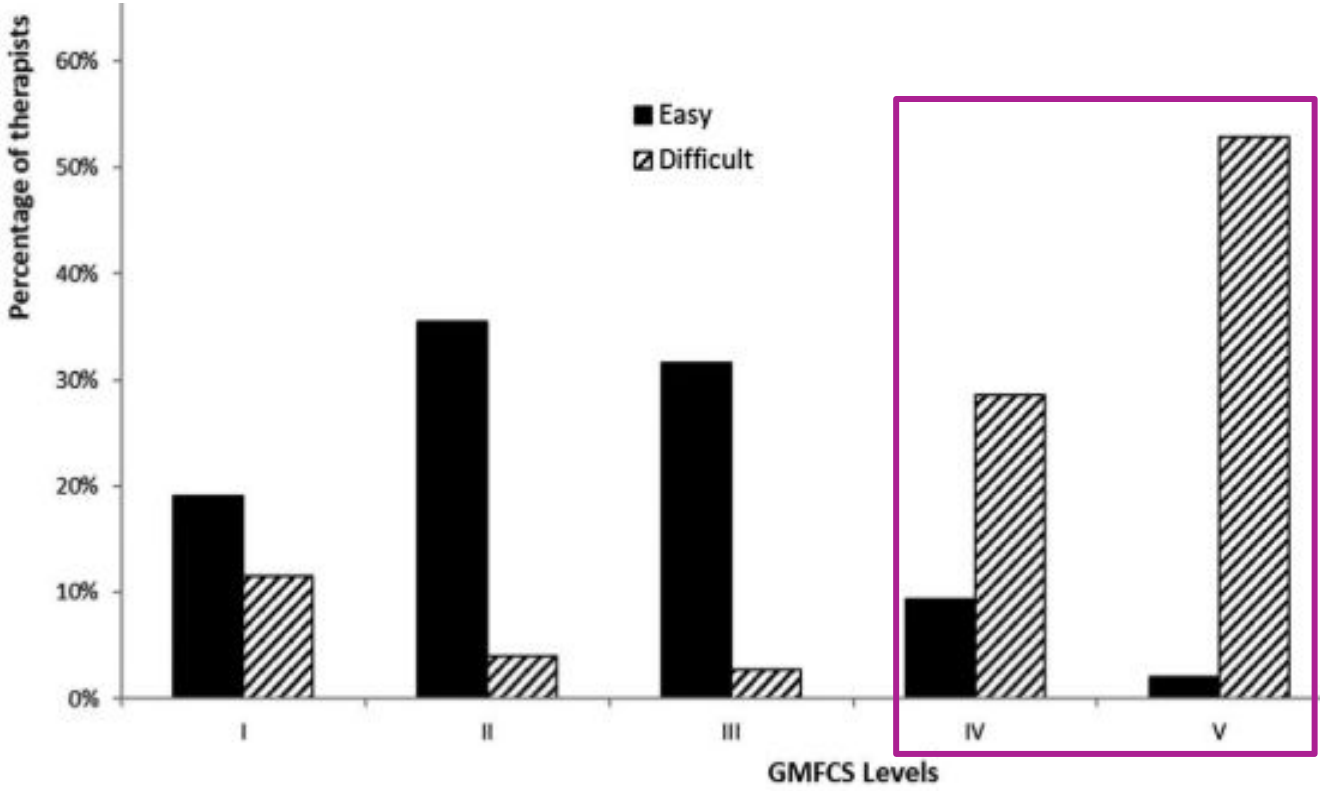
"Failure to detect improvement with a general quantitative measurement instrument could be caused by lack of sensitivity to a change at individual level... **functional treatment goals need to be well-defined and tailored to the individuals needs of the patients and the parents.**"

Steenbeek et al. The effect of botulinum toxin type A treatment of the lower extremity on the level of functional abilities in children with cerebral palsy: Evaluation with goal attainment scaling. *Clin Rehabil*. 2005;19(3):274-282.

ARDEA OUTCOMES

Standardized outcomes may fail to capture the range of disease severity.

By allowing for personalized outcomes, **GAS embraces heterogeneity of disease severity across the study population.**



81% of therapists reported difficulty in selecting responsive outcome measures for **children with more severe impairment**.

Knox et al. Use of outcome measures in children with severe cerebral palsy: A survey of U.K. physiotherapists. *Physiother Res Int*. 2019;24(4):1-9.

ARDEA OUTCOMES

GAS offers additional insights into the patient experience and how the intervention is working.

ARDEA OUTCOMES

Patient-centered outcomes are increasingly expected in clinical development.

GAS meets this need by generating **qualitative insights about the patient experience**.

Table 5: Categories of Goals Selected by Participants and Families, and Most Frequently Identified Goals Within Each Category

Goal Category	%* (n)	Most Frequently Identified Goals Within Each Category
Leisure	27 (89)	Catching a ball (n=22)
		Maintain grasp on bike/scooter handle (n=8)
Dressing	23 (77)	Pushing arm through a sleeve (n=29)
		Pulling up pants/underpants (n=11)
Eating	21 (70)	Holding a bowl/plate (n=20)
		Maintaining a knife, fork or spoon in hand (n=20)
		Holding a cup/bottle to drink (n=18)
Postural/weight bearing	13 (44)	More aesthetic posture of arm while walking/running (n=7)
		Holding a walker (n=7)
		Weight bearing while sitting (n=5)
School/preschool	10 (32)	Stabilizing paper to write or draw (n=19)
		Use a communication or toy switch (n=6)
Other self-care	7 (23)	Dressing in relation to toileting (n=4)
		Washing self (n=4)
Other	1 (5)	Using arm for signing to communicate (n=2)

*Total number of goals is 334; values are percentage of total goals set.

"**It has been enlightening to note that the largest category of goals was related to leisure activities**. This reinforced the need to consider leisure as an important focus for intervention."

Wallen et al. Functional Outcomes of Intramuscular Botulinum Toxin Type A and Occupational Therapy in the Upper Limbs of Children With Cerebral Palsy: A Randomized Controlled Trial. *Arch Phys Med Rehabil*. 2007;88(1):1-10.

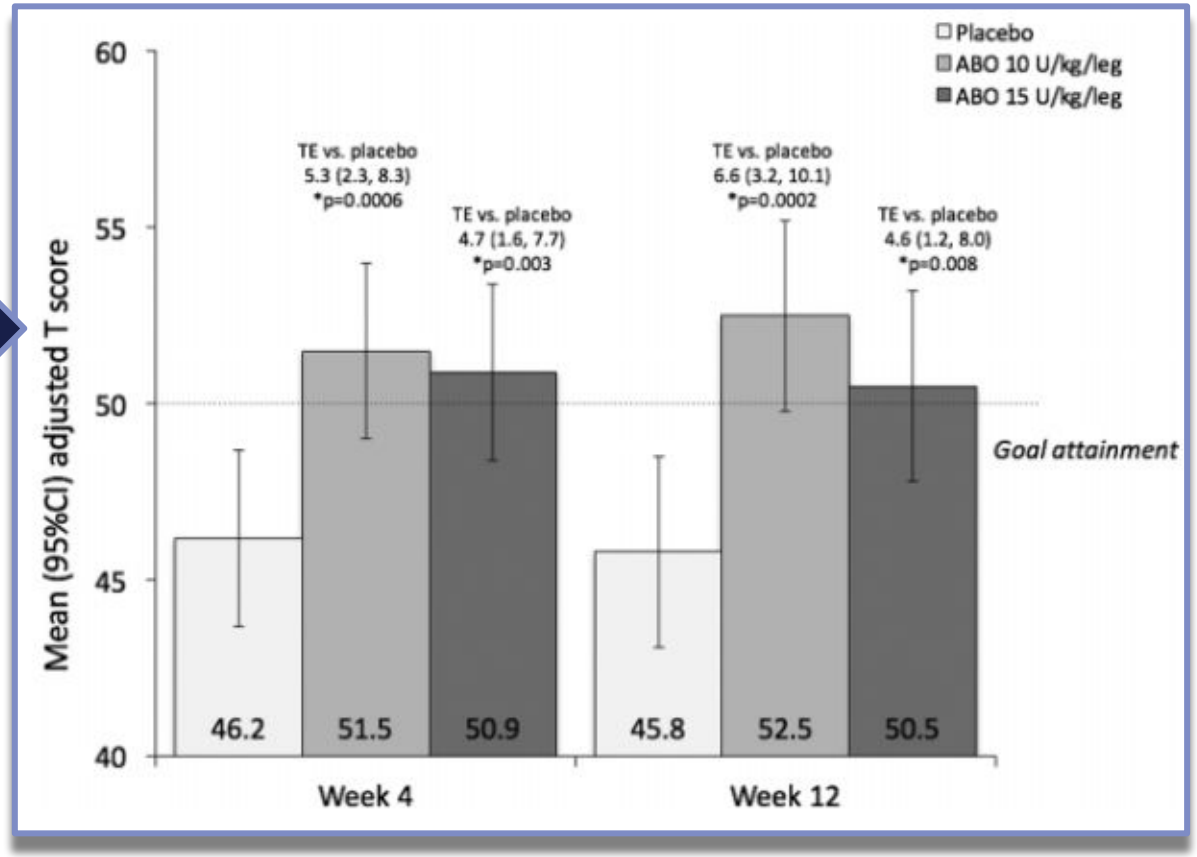
ARDEA OUTCOMES

GAS offers valuable qualitative insights beyond overall treatment efficacy.

Which goals were attained or not attained tells us **how the treatment is working.**

First-order of inference

Higher overall goal attainment in active treatment vs placebo at 4 weeks, and maintained at 12 weeks.



Tilton et al. AbobotulinumtoxinA (Dysport ®) Improves Function According to Goal Attainment in Children With Dynamic Equinus Due to Cerebral Palsy. *J Child Neurol*. 2017;32(5):482-487.

ARDEA OUTCOMES

GAS offers valuable qualitative insights beyond overall treatment efficacy.

Which goals were attained or not attained tells us **how the treatment is working.**

Second-order of inference

5 most commonly selected goals: attainment higher in active treatment groups vs placebo

With one exception: **improved balance.**

Table 2. Responder Analyses for Achievement of Primary Goal and for the Five Most Commonly Chosen Individual Goals.[a]

	Placebo group (n = 77)	AbobotulinumtoxinA 10 U/kg group (n = 79)	AbobotulinumtoxinA 15 U/kg group (n = 79)
Primary goal achievement (at any time during study), n (%)	47/76 (62)	62/79 (79)	60/79 (76)
Individual goal analysis			
Improved walking pattern			
Best goal attainment T score, mean (SD)	45.4 (8.8)	54.2 (9.6)	52.7 (10.0)
Responder rate at week 4, n (%)	21/53 (40)	38/48 (79)	38/63 (60)
Responder rate at week 12, n (%)	19/49 (39)	31/43 (72)	38/60 (63)
Improved balance			
Best goal attainment T score, mean (SD)	47.9 (7.9)	51.3 (9.2)	48.5 (10.8)
Responder rate at week 4, n (%)	10/19 (53)	18/29 (62)	10/26 (39)
Responder rate at week 12, n (%)	9/16 (56)	16/26 (62)	14/25 (56)
Decreased frequency of falling			
Best goal attainment T score, mean (SD)	50.4 (10.6)	59.1 (11.5)	56.5 (10.6)
Responder rate at week 4, n (%)	14/25 (56)	18/22 (82)	18/26 (69)
Responder rate at week 12, n (%)	8/19 (42)	18/20 (90)	17/24 (71)
Decreased frequency of tripping			
Best goal attainment T score, mean (SD)	51.5 (12.8)	52.5 (10.6)	57.1 (9.9)
Responder rate at week 4, n (%)	6/13 (46)	9/16 (56)	13/17 (77)
Responder rate at week 12, n (%)	8/13 (62)	9/14 (64)	14/16 (88)
Improved endurance			
Best goal attainment T score, mean (SD)	50.0 (8.9)	56.1 (7.8)	58.2 (10.8)
Responder rate at week 4, n (%)	6/11 (55)	13/18 (72)	7/11 (64)
Responder rate at week 12, n (%)	5/11 (46)	14/16 (88)	10/11 (91)

Tilton et al. AbobotulinumtoxinA (Dysport ®) Improves Function According to Goal Attainment in Children With Dynamic Equinus Due to Cerebral Palsy. *J Child Neurol*. 2017;32(5):482-487.

ARDEA OUTCOMES

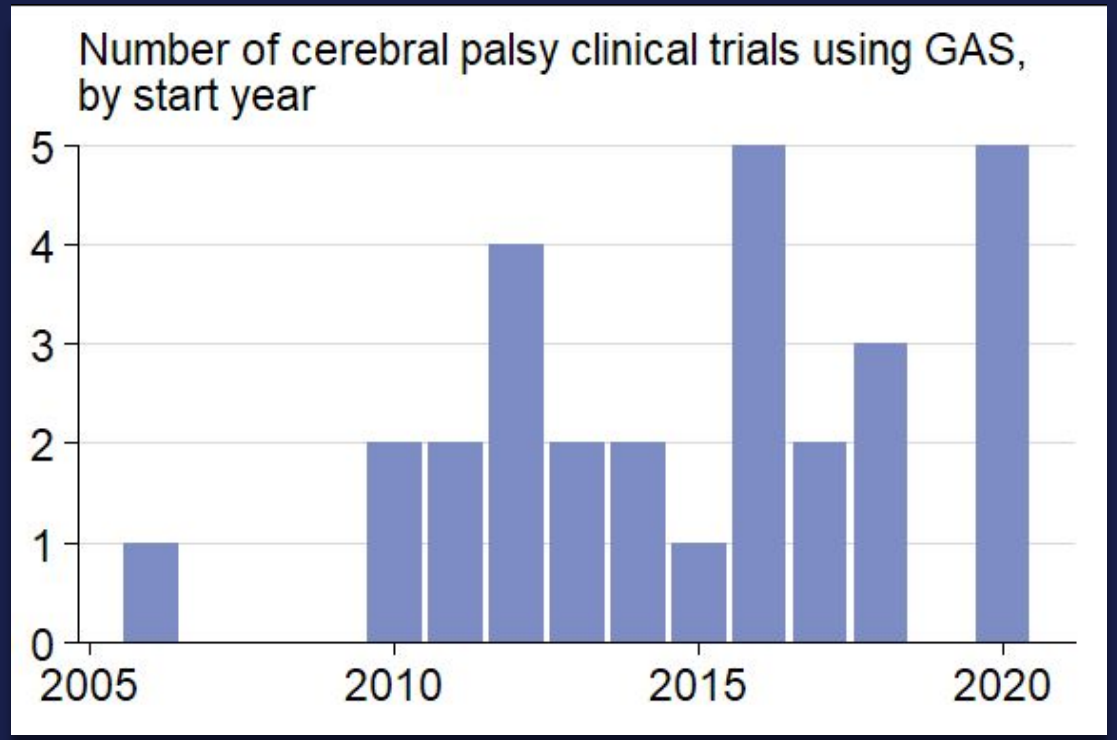
GAS is focused and comprehensive by design.

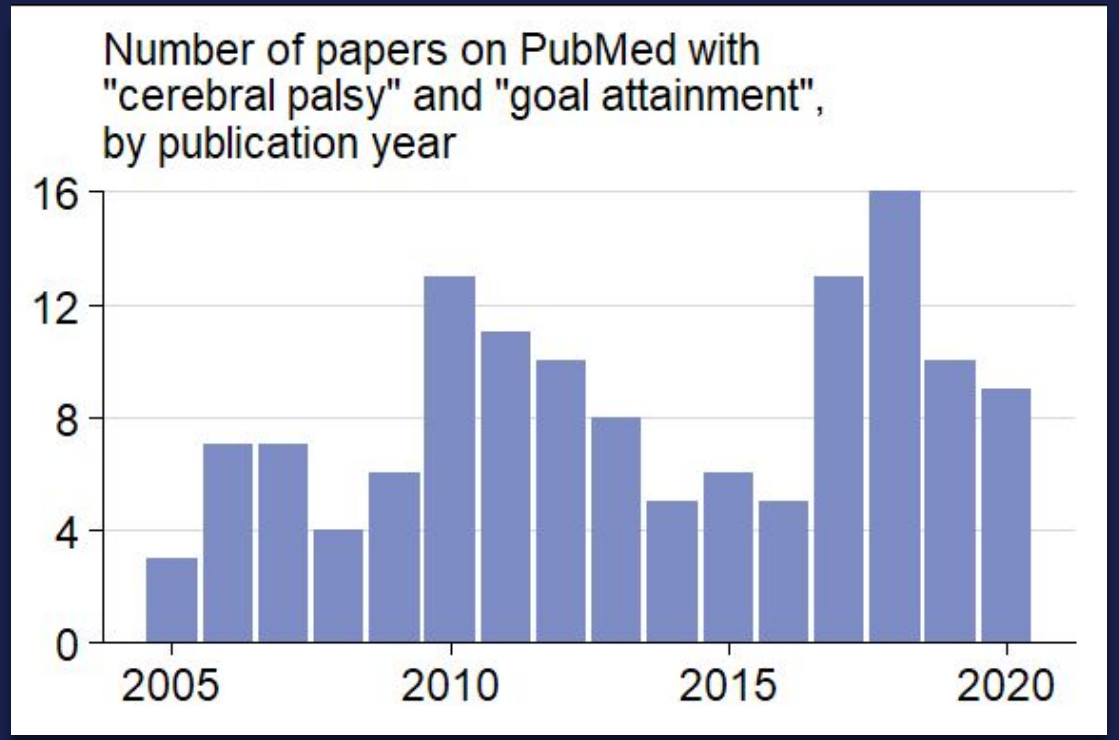
GAS embraces heterogeneity.

GAS generates patient experience data and qualitative insights.

ARDEA OUTCOMES

GAS has proven a valuable tool in trials and research of cerebral palsy.





ARDEA OUTCOMES

ARDEA OUTCOMES

Poll #3

Discussion

ARDEA
OUTCOMES

Thank you.
Ardea Outcomes.

Chere Chapman, CEO

chere.chapman@ardeaoutcomes.com

+1(902)410-3888

SH300-1701 Hollis Street,
Halifax, Nova Scotia Canada B3J 3M8

LinkedIn
ca.linkedin.com/company/ardeaoutcomes

Twitter
@ardeaoutcomes

Email
chere.chapman@ardeaoutcomes.com

Phone
+1(902)410-3888

ARDEA OUTCOMES

References

1. Wallen MA, O'Flaherty SJ, Waugh M-CA. Functional outcomes of intramuscular botulinum toxin type a in the upper limbs of children with cerebral palsy: a phase II trial. Arch Phys Med Rehabil. 2004;85(2):192-200. doi:10.1016/j.apmr.2003.05.008

2. Wallen M, O'Flaherty SJ, Waugh M-CA. Functional Outcomes of Intramuscular Botulinum Toxin Type A and Occupational Therapy in the Upper Limbs of Children With Cerebral Palsy: A Randomized Controlled Trial. Arch Phys Med Rehabil. 2007;88(1):1-10. doi:10.1016/j.apmr.2006.10.017

3. Steenbeek D, Gorter JW, Ketelaar M, Galama K, Lindeman E. Responsiveness of Goal Attainment Scaling in comparison to two standardized measures in outcome evaluation of children with cerebral palsy. Clin Rehabil. 2011;25(12):1128-1139. doi:10.1177/0269215511407220

4. Steenbeek D, Meester-Delver A, Becher JG, Lankhorst GJ. The effect of botulinum toxin type A treatment of the lower extremity on the level of functional abilities in children with cerebral palsy: Evaluation with goal attainment scaling. Clin Rehabil. 2005;19(3):274-282. doi:10.1191/0269215505cr859oa

5. Knox V, Vuoskoski P, Mandy A. Use of outcome measures in children with severe cerebral palsy: A survey of U.K. physiotherapists. Physiother Res Int. 2019;24(4):1-9. doi:10.1002/pri.1786

6. Tilton A, Russman B, Aydin R, et al. AbobotulinumtoxinA (Dysport ®) Improves Function According to Goal Attainment in Children With Dynamic Equinus Due to Cerebral Palsy. J Child Neurol. 2017;32(5):482-487. doi:10.1177/0883073816686910

7. Haley SM, Ludlow LH, Coster WJ. Pediatric Evaluation of Disability Inventory: Clinical Interpretation of Summary Scores Using Rasch Rating Scale Methodology. Phys Med Rehabil Clin N Am. 1993;4(3):529-540. doi:10.1016/S1047-9651(18)30568-0

ARDEA OUTCOMES