Development of a Measure for the Impacts of Pediatric Achondroplasia on Children's Daily Functioning and Well-being

Kathryn M. Pfeiffer[1], Meryl Brod[1], Dorthe Viuff[2], Sho Ota[3], Jill Gianettoni[3], Jonathan A. Leff[3]

[1]The Brod Group, [2]Ascendis Pharma A/S, [3]Ascendis Pharma, Inc.

BACKGROUND

- The clinical complications and medical impacts of achondroplasia (ACH) in children and adults are well studied[1,2]
- Frequent complications of ACH in childhood include recurrent ear infections (otitis media), sleep apnea, hearing loss, teeth crowding/misalignment, and speech delay or articulation problems, while frequent complications in adulthood include chronic back and leg pain, spinal stenosis, sleep apnea, and obesity[2,3]
- Research has also shown that infants and young children with ACH experience delays in some developmental milestones, including gross motor, fine motor, communication, and feeding milestones[4,5]
- Less is known about the broader impacts of ACH on children's lives, including impacts on functioning and daily life, emotional well-being, and social well-being

OBJECTIVE

The purpose of the study was to investigate the impacts of ACH on children's daily lives to support the development of the Achondroplasia Child Experience Measure – Impact (ACEM – Impact), which assesses the impacts of ACH on the functioning and well-being of children aged 2 to <12 years.

METHODS

The qualitative research study design was based on an adapted grounded theory approach and followed FDA guidelines for the development of patient-reported outcome measures (PROs).

Based on a literature review and clinical expert interviews, a semi-structured interview guide was developed to elicit parents' experiences related to ACH.

Concept elicitation sample inclusion criteria:

- an adult aged 18 years or older
- able to read, write, and speak English (in the United States [US]) or Spanish (in Spain)
- parent of a child (<18 years of age) diagnosed with ACH; and
- actively involved in the child's care

Concept elicitation sample exclusion criteria:

- A cognitive impairment or other medical condition, including psychiatric conditions, that would affect a participant's ability to take part in a telephone interview or focus group

It should be noted that this study was part of a larger study of parents of children with ACH <18 years of age, and this study focused only on parent participants with children aged 2 to <12 years.

Individual telephone interviews and 1 parent focus group were conducted in the US and Spain with 36 parents of children aged 2 to <12 years with ACH.

Interview and focus group transcripts were analyzed for content and coded by themes using a qualitative analysis software program.

The qualitative analysis report was used to develop a preliminary theoretical model of pediatric ACH, including signs/symptoms, impacts, and modifiers, and to inform the content and structure of the ACEM – Impact measure.

Only impacts identified as major would be included in the measure.

Criteria for Identifying Major Impacts

- Endorsement of at least 30% of parent participants in at least 2 of the 3 child age groups analyzed; or an endorsement of 25% to 29% of parent participants in at least 2 of the 3 age groups if conceptually important
  - Endorsement percentages were considered across differing age groups to ensure relevance to children of different ages
- Would be responsive to treatment
- Considered bothersome, limiting, or difficult
- Impacts must be proximal (rather than distal)

Once the ACEM – Impact measure was developed, cognitive debriefing interviews were conducted with an additional 16 parents in the US to ensure that measure items were relevant and appropriate, and that instructions and items were easy to understand and complete.

RESULTS

Parent Participant Sample Description

Participant sample characteristics are shown in Table 1.

- Average age of parents was 41.5 years (SD, 6.6; range, 32-68)
- Thirty-one parents were mothers (86.1%), and 5 parents were fathers (13.9%)
- Most participants were married (80.6%, n=29), 8.3% were partnered (n=3), 5.6% were divorced (n=2), and 5.6% were single (n=2)
- Seven parents (19.4%), all residing in the US, also had a diagnosis of ACH

Table 1. Parent participant demographic characteristics

	Spain (n=11)	US (n=25)	Total (N=36)
Age, mean(SD)	40.4(3.1)	42.0(7.6)	41.5(6.6)
(range)	(35-43)	(32-68)	(32-68)
Relationship to child, n(%)			
mother	8(72.7)	23(92.0)	31(86.1)
father	3(27.3)	2(8.0)	5(13.9)
Marital status, n(%)			
single	2(18.2)	0	2(5.6)
married	6(54.5)	23(92.0)	29(80.6)
partnered	3(27.3)	0	3(8.3)
divorced	0	2(8.0)	2(5.6)
Education, n(%)			
less than high school	2(18.2)	1(4.0)	3(8.3)
high school or equivalent	4(36.4)	2(8.0)	6(16.7)
college degree	5(45.5)	12(48.0)	17(47.2)
post-graduate school	0	10(40.0)	10(27.8)
Work status, n(%)			
full-time	6(54.5)	10(40.0)	16(44.4)
part-time	3(27.3)	3(12.0)	6(16.7)
student	0	2(8.0)	2(5.6)
retired	0	1(4.0)	1(2.8)
not working (other)	2(18.2)	9(36.0)	11(30.6)
Parent has ACH			
n(%) yes	0	7(28.0)	7(19.4)

Percentages may not add to 100 due to rounding. ACH = achondroplasia; SD = standard deviation.

RESULTS

Demographic/Health Characteristics for Children of Parent Participants

Demographic/health characteristics for the children of parent participants are shown in Table 2.

- 30.6% of parent participants (n=11) had children aged 2 to <5 years with achondroplasia, 36.1% of parents (n=13) had children aged 5 to <9 years, and 33.3% of parents (n=12) had children aged 9 to <12 years
- Nineteen children (52.8%) were female and 17 (47.2%) were male
- Twelve parents (33.3%) reported child's health status as "excellent," 14 (38.9%) reported as "very good," 7 (19.4%) parents reported as "good," and 3 parents (8.3%) reported as "fair"

Table 2. Demographic/health characteristics of children of parent participants

	Spain (n=11)	US (n=25)	Total (N=36)
Child age, n(%)			
2 to <5 years	5(45.5)	6(24.0)	11(30.6)
5 to <9 years	4(36.4)	9(36.0)	13(36.1)
9 to <12 years	2(18.2)	10(40.0)	12(33.3)
Child gender, n(%)			
female	7(63.6)	12(48.0)	19(52.8)
male	4(36.4)	13(52.0)	17(47.2)
Health status (parent-reported), n(%)			
excellent	3(27.3)	9(36.0)	12(33.3)
very good	3(27.3)	11(44.0)	14(38.9)
good	3(27.3)	4(16.0)	7(19.4)
fair	2(18.2)	1(4.0)	3(8.3)
Age/time diagnosed with ACH, n(%)			
in utero	9(81.8)	12(48.0)	21(58.3)
at birth	1(9.1)	4(16.0)	5(13.9)
<2 months of age	1(9.1)	2(8.0)	3(8.3)
2-6 months of age	0	5(20.0)	5(13.9)
unknown (adopted)	0	2(8.0)	2(5.6)

Percentages may not add to 100 due to rounding. ACH = achondroplasia; SD = standard deviation.

The qualitative analysis and the development of a preliminary theoretical model identified four conceptual domains for the impacts of ACH, as well as major impacts in each domain:

- **Functioning and daily life,** including school participation:
  – 13 major impacts (Figures 1 & 2)
- **Emotional well-being:**
  – 6 major impacts (Figure 3)
- **Social well-being:**
  – 7 major impacts (Figure 4)
- **Need for assistance/adaptive devices:**
  – 5 major impacts (Figure 5)

Preliminary theoretical model for Symptoms, Signs, and Impacts of achondroplasia (children ages 2 <12 years)

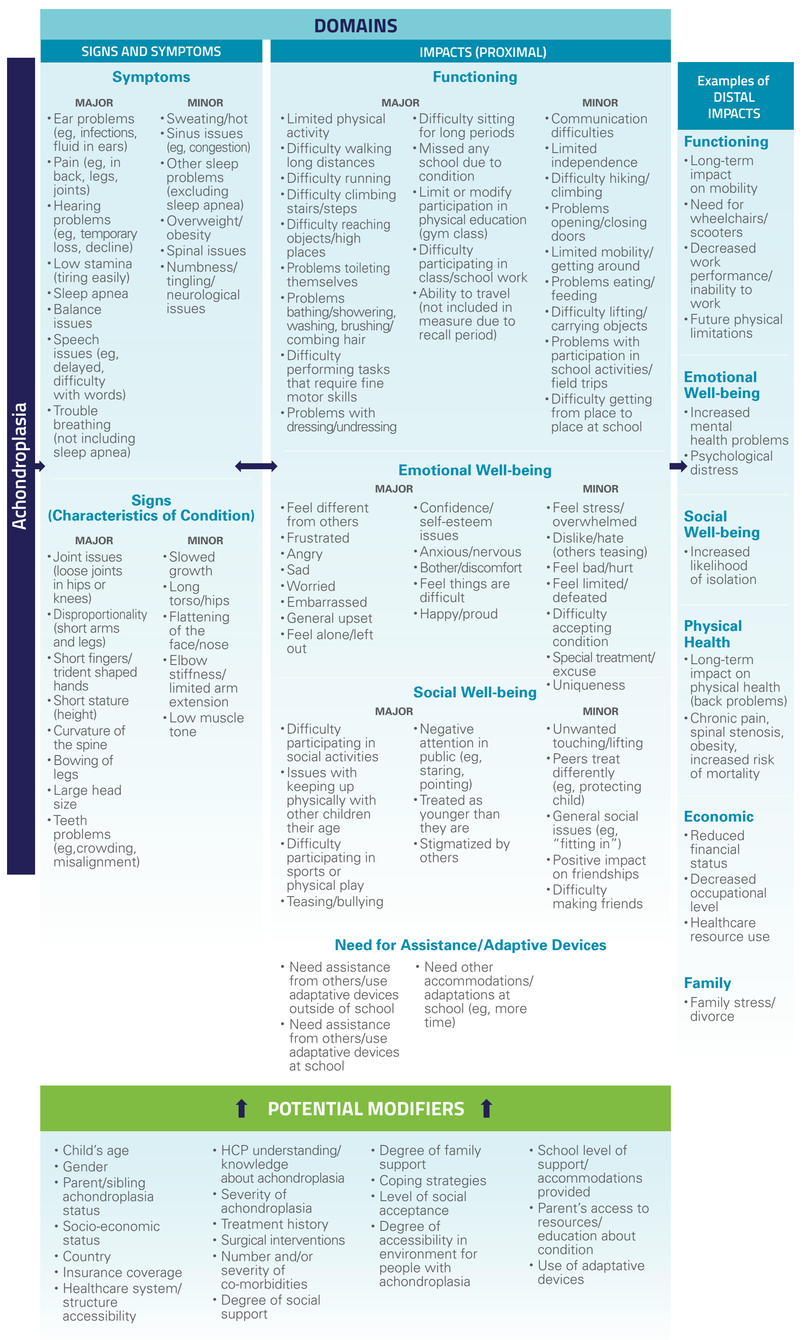
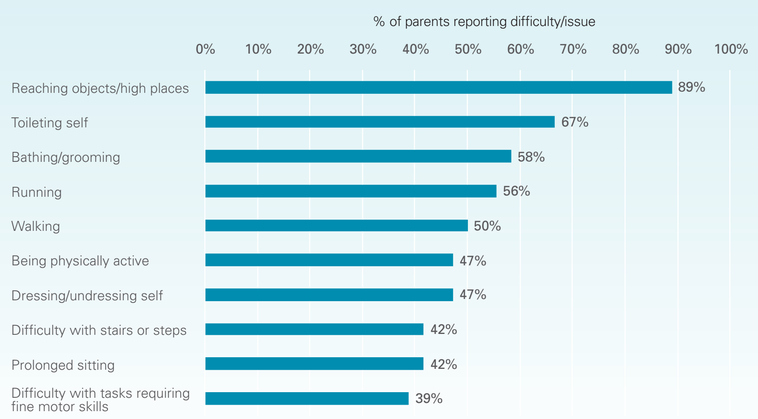


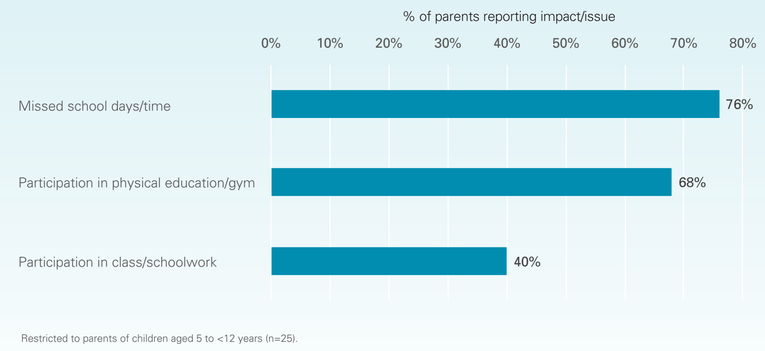
Figure 1. Major impacts on children's functioning and daily life



N=36.

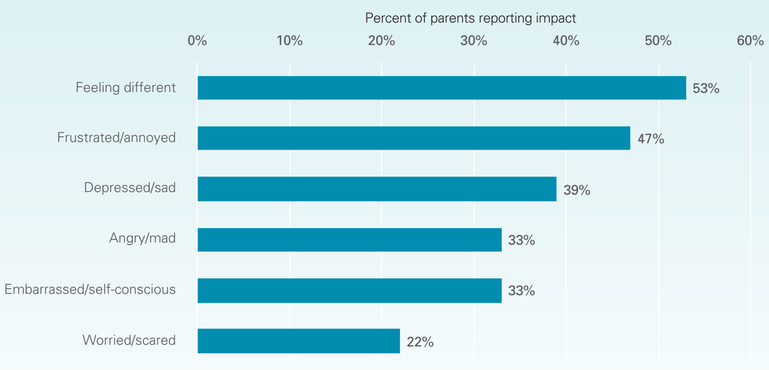
RESULTS

Figure 2. Major impacts on children's school participation among school-aged children



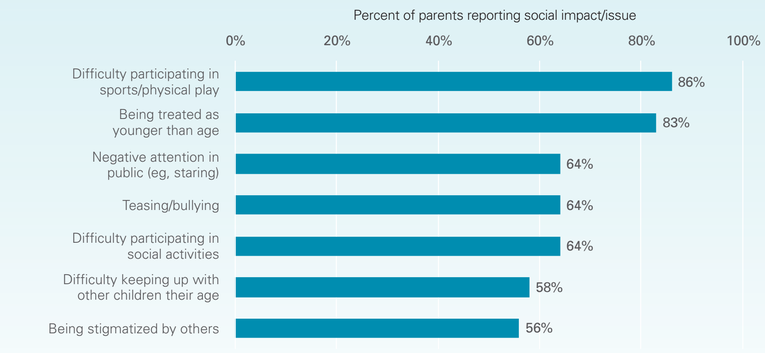
Restricted to parents of children aged 5 to <12 years (n=25).

Figure 3. Major impacts on children's emotional well-being



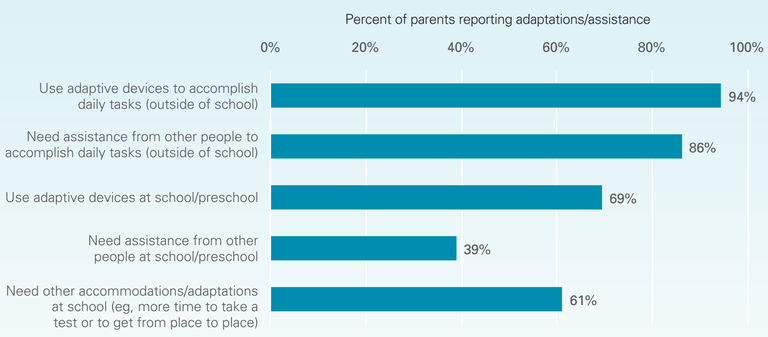
N=36.

Figure 4. Major impacts on children's social well-being



N=36.

Figure 5. Major impacts: need for assistance/adaptive devices



N=36.

The newly developed ACEM – Impact measure included 31 items in 4 conceptual domains.

- The ACEM – Impact was designed as an observer-reported outcome (ObsRO) measure to be completed by parents of children aged 2 to <12 years with ACH
- Based on the cognitive debriefing interviews, minor edits to the measure were made to improve understanding and readability

The ACEM – Impact is a validation-ready parent ObsRO designed to assess the impacts of ACH on the functioning and well-being of children aged 2 to <12 years with ACH.

CONCLUSIONS

- The study provides evidence to support the content validity for the validation-ready ACEM – Impact parent ObsRO measure to assess the impacts of ACH on daily functioning and emotional and social well-being in children aged 2 to <12 years
- A future psychometric validation study of the ACEM – Impact is needed to further assess measure validity and reliability
- As new treatments for pediatric ACH are being developed, it is critical for clinicians to understand and assess the impacts of ACH on children's general functioning and well-being that may be improved with treatment

1. Pauli RM. Achondroplasia: a comprehensive clinical review. *Orphanet J Rare Dis.* 2019;14(1):1.
2. Hunter AG, Bankier A, Rogers JG, Sillence D, Scott CI, Jr. Medical complications of achondroplasia: a multicentre patient review. *J Med Genet.* 1998;35(9):705-712.
3. Wright MJ, Irving MD. Clinical management of achondroplasia. *Arch Dis Child.* 2012;97(2):129-134.
4. Ireland PJ, Donaghey S, McGill J, et al. Development in children with achondroplasia: a prospective clinical cohort study. *Dev Med Child Neurol.* 2012;54(6):532-537.
5. Ireland PJ, Johnson S, Donaghey S, et al. Developmental milestones in infants and young Australasian children with achondroplasia. *J Dev Behav Pediatr.* 2010;31(1):41-47.