

# Early Results from the CAHtalog™ Registry

A registry collecting longitudinal real-world data from US patients living with Congenital Adrenal Hyperplasia (CAH)

**Note: We refer to classic CAH as CAH; deviations from classic CAH are denoted by using specific terminology (e.g., non-classic CAH).**





# CAHtalog™ Registry Overview

# CAHtalog is a US-based digital registry of Classic CAH patients with large-scale medical record-based RWD



*PicnicHealth is our trusted technology partner to generate large-scale registry data from patients' medical records.*



*As the sponsor, Neurocrine leads the CAHtalog study design & analysis and provides funding for the registry.*

## CAH Researchers



*CAH researchers will analyze CAHtalog data to advance clinical research and develop new treatments.*



*CARES drives recruitment and ensures that CAHtalog's research serves the needs of CAH patient community.*



## Patients with Classic CAH

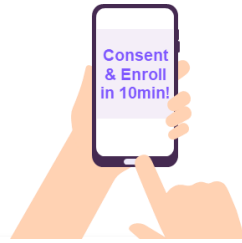
*Patients have the opportunity to contribute to research by signing up and sharing their experiences of living with CAH.*

RWD, real-word data.

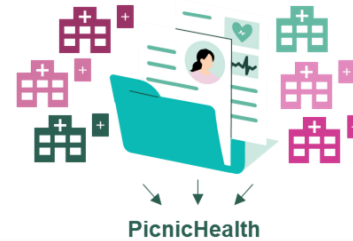
PicnicHealth. Congenital adrenal hyperplasia (CAH) registry. Accessed June 22, 2023. <https://picnichealth.com/cah>.

# Patients can consent, enroll, and participate in CAHtalog from the comfort of home in less than 10 minutes; no site visits are needed

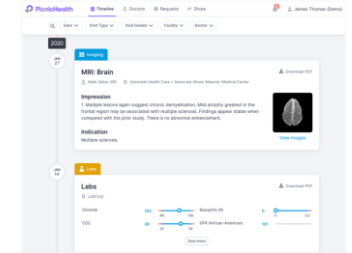
Patients and caregivers can enroll by scanning the QR or visiting [www.CAHtalog.com](http://www.CAHtalog.com)



After enrolling, we'll ask for the **contact of the patient's most recent primary care provider and endocrinologist**. Nothing else is required.



**PicnicHealth collects medical records from all available healthcare providers.** Patients don't fill out forms or call hospitals; PicnicHealth takes care of all the hard work.



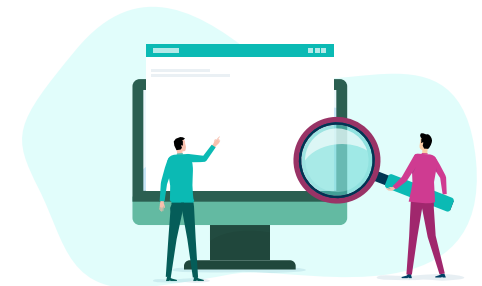
Patients receive a copy of your digitized medical records in a **well-organized, patient-friendly "PicnicHealth Timeline."**



Patients can earn up to \$150/year by participating in short, **optional bi-annual surveys** to further share their experiences with CAH



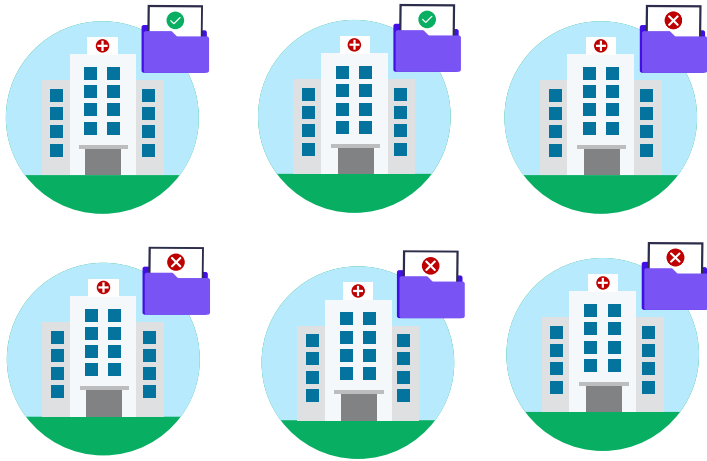
**Tens of thousands of "structured data" points per patient** are abstracted from medical records. PicnicHealth **de-identifies the data** before sharing with researchers.



Key concepts from **"unstructured data"** (e.g., physician notes) can undergo a **custom chart review by PicnicHealth.**

Note: CAHtalog is not a clinical trial, but rather a patient registry for people living with classic CAH. Results presented today are from a cohort of 69 pediatric and adult CAHtalog participants.

# Challenges in Accessing Complete Medical Records



MyChart and other local portals typically will not have records from every hospital/clinic the patient has visited



Images from CTs and MRIs are often unavailable in MyChart and instead must be shared via CDs and DVDs

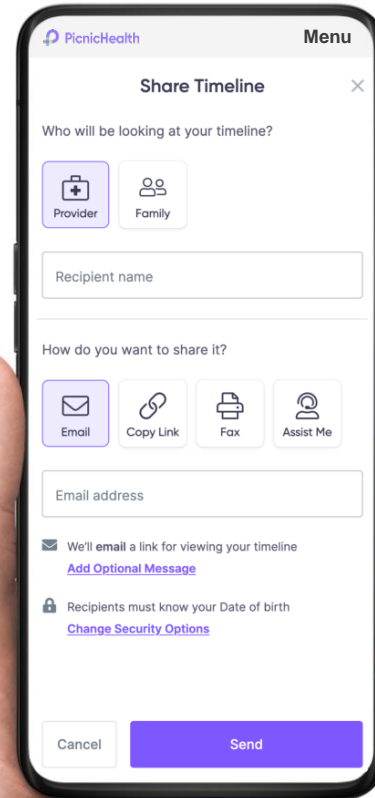
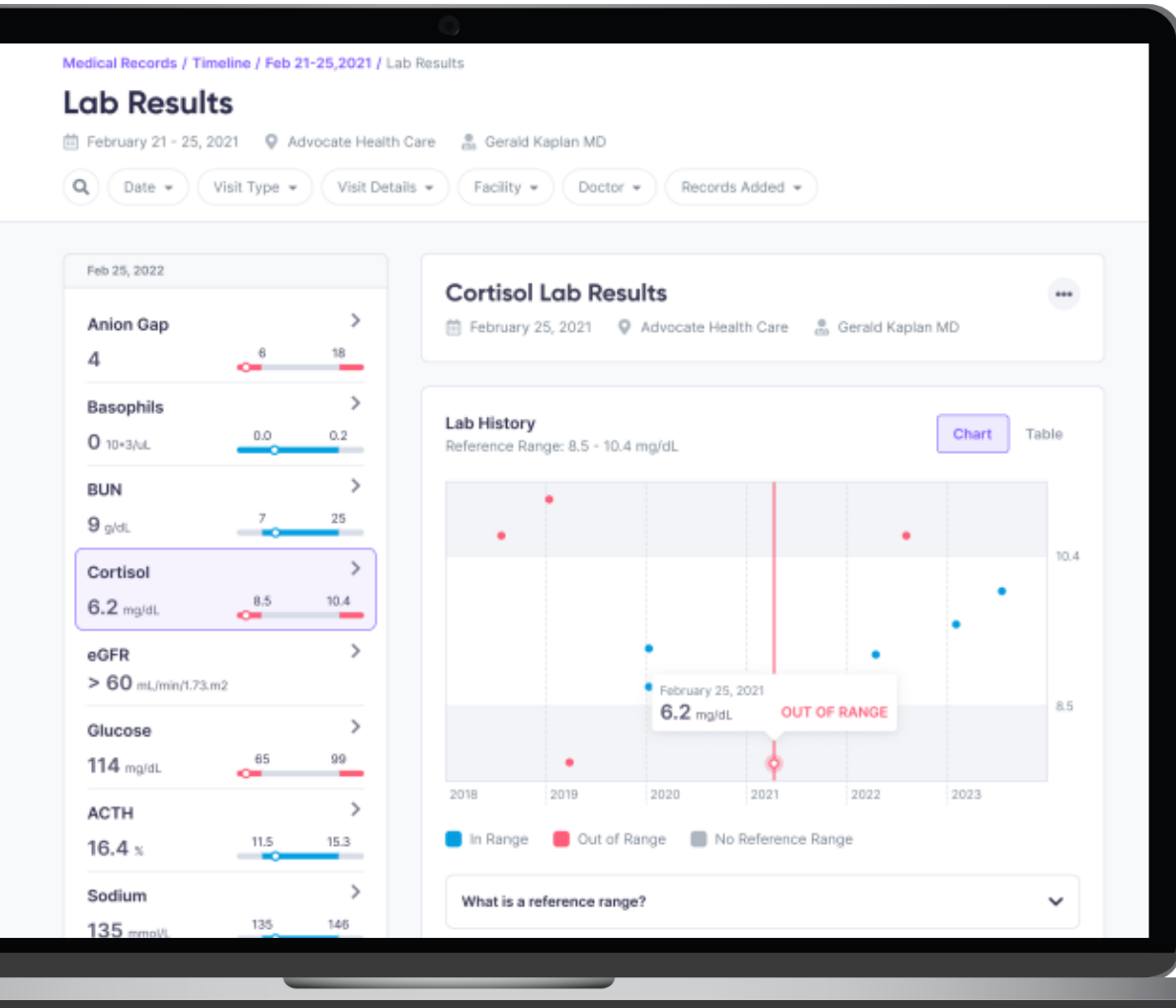


When patients seek emergency care while traveling out of town, the ER clinician may be unable to quickly access important medical records

CT, computed tomography; ER, emergency room; MRI, magnetic resonance imaging.

PicnicHealth. Congenital adrenal hyperplasia (CAH) registry. Accessed May 20, 2024. <https://picnichealth.com/cah>.

# The PicnicHealth timeline provides a comprehensive solution to the challenges of accessing complete medical records



Click here for demo:

<https://demo.picnichealth.com/records>



This example PicnicHealth Timeline is for demonstration purposes only

# Why is CAHtalog important?



## Advancements in CAH research with CAHtalog and other registries may lead to:

- Closing gaps in our understanding of CAH
- New approaches for treating CAH
- More clinicians and policymakers recognizing the importance of CAH



## Key CAHtalog research objectives include characterizing:

- Natural history and real-world burden of illness<sup>1</sup>
- Longitudinal patterns of GC treatment and A4 control<sup>2</sup>
- Relationship between GC dose vs. clinical outcomes<sup>2</sup>

A4, androstenedione; GC, glucocorticoid.

1. White P et al. Poster presentation at ENDO; May 2-5, 2024; Boston, MA. 2. Lekarev O et al. Late-breaker poster presentation at ENDO; May 2-5, 2024; Boston, MA.



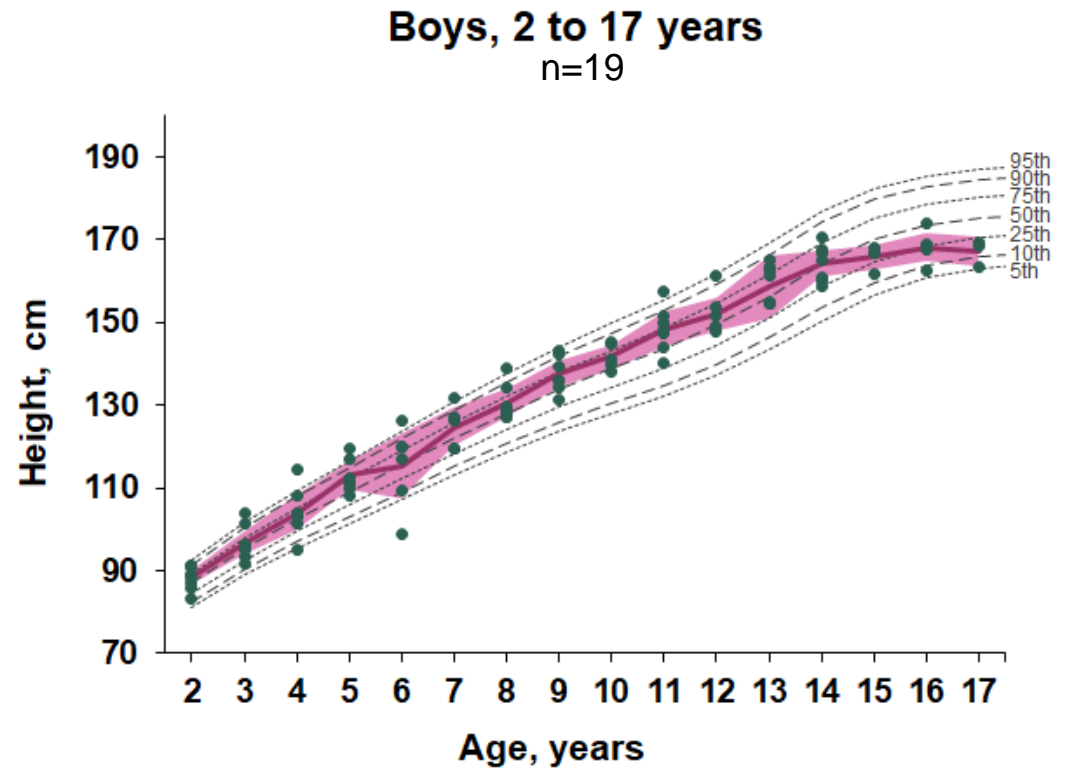
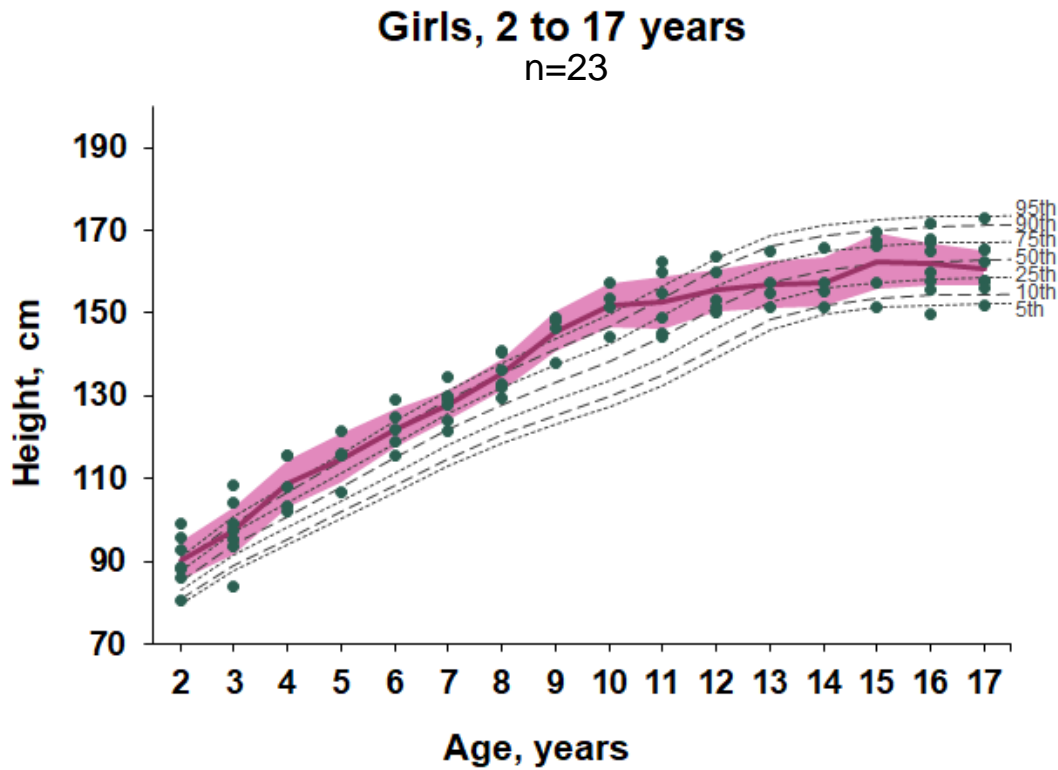
# CAHtalog™ Registry Data

White P et al. Poster presentation at ENDO; June 1-4, 2024; Boston, MA.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.



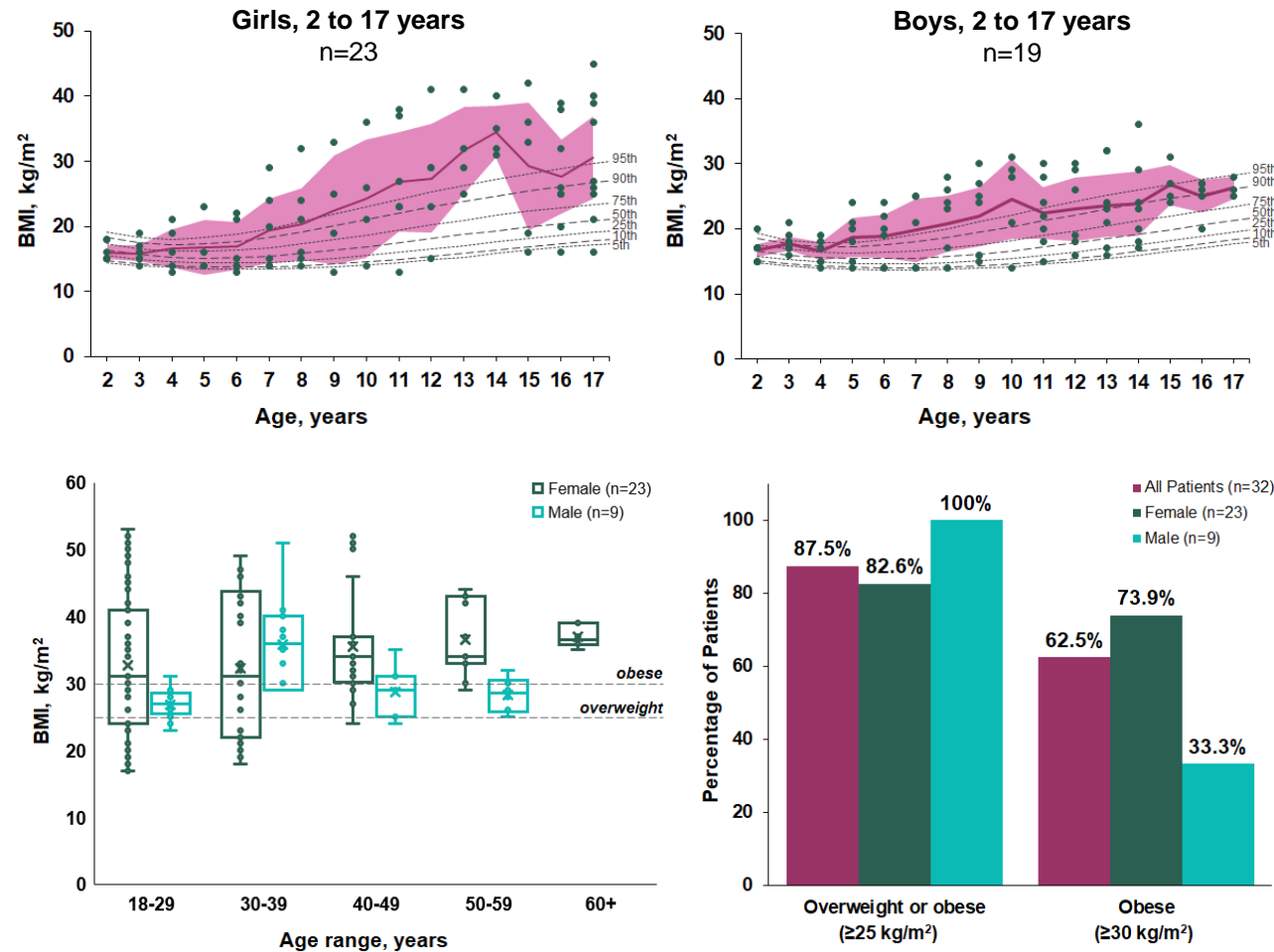
# Pediatric patients had early growth acceleration followed by blunted pubertal growth



## Key Results

**Pediatric patients had early growth acceleration followed by blunted pubertal growth.** This trend was more pronounced in females, with mean height-for-age generally exceeding the 90<sup>th</sup> percentile in ages 4-10 but dropping below the 50<sup>th</sup> percentile at ages 13-17

# Obesity was observed from childhood through adulthood



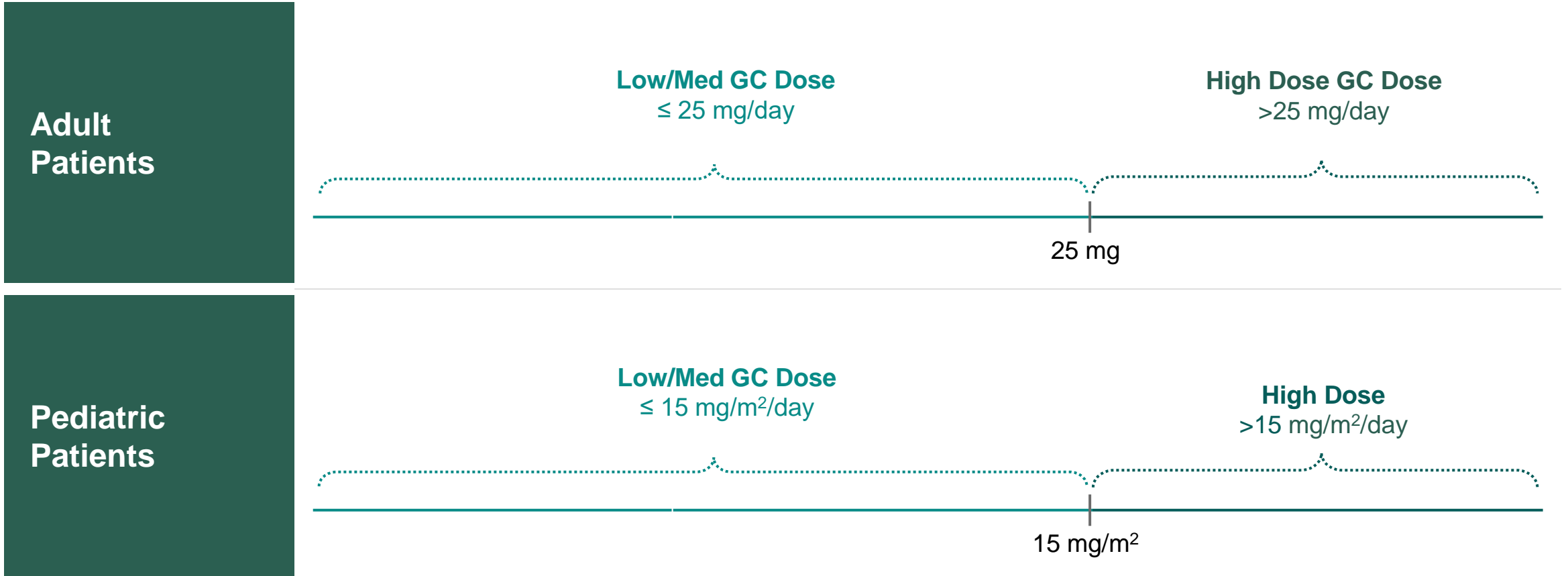
## Key Results

Obesity was observed from childhood through adulthood. In adults, obesity (BMI  $\geq 30$ ) was highly prevalent (64%), exceeding NHANES 2017-2018 general population prevalence (42%)

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey.

White P et al. Poster presentation at ENDO; Jun 1-4, 2024; Chicago IL.

# GC Dose Cutoffs for GC vs. Clinical Outcomes Analysis



## Key Point

Cutoffs were chosen to match with upper range of Endocrine Society Treatment Guidelines (15 to 25 mg/day for adults or 10 to 15 mg/m<sup>2</sup>/day for pediatrics)<sup>1</sup>

GC, glucocorticoid.

1. Speiser PW, et al. *J Clin Endocrinol Metab.* 2018;103(11):4043-4088.

# Coding Definition for Comorbidities in GC vs. Clinical Outcomes Analysis

Disease/GC Related	Comorbidities	ICD codes	Chart Review	Labs & Vital Signs
Both CAH and GC Related	Anxiety disorders <sup>a</sup>	✓		
	Depression <sup>b</sup>	✓		
	Metabolic complications <sup>c</sup>	✓		✓ HbA1c >5.7% or Total cholesterol >240 mg/dL or LDL >130 mg/dL or HDL <50 mg/dL or triglycerides >200 mg/dL
	Type II Diabetes	✓		✓ HbA1c >6.4%
	Short Stature (peds only)	✓		✓ Height ≤ the bottom 3 percentile for the same age/sex population
GC Related	Fracture	✓		
	Hypertensive Disease	✓		✓ SBP ≥ 130 mmHg or DBP ≥ 80 mmHg
	Infectious Disease	✓		
	Sleep Disorders <sup>d</sup>	✓	✓	
	Obesity	✓		✓ Adults aged ≥ 18: BMI ≥30.0 kg/m <sup>2</sup> ; Children/teens aged 2-<18: BMI ≥95th percentile



For this analysis, all comorbidities were grounded on ICD codes, and supplemented by labs, vital signs, and/or chart review when available

<sup>a</sup>Including phobia and other anxiety disorders.

<sup>b</sup>Including depressive episode and major depressive disorders.

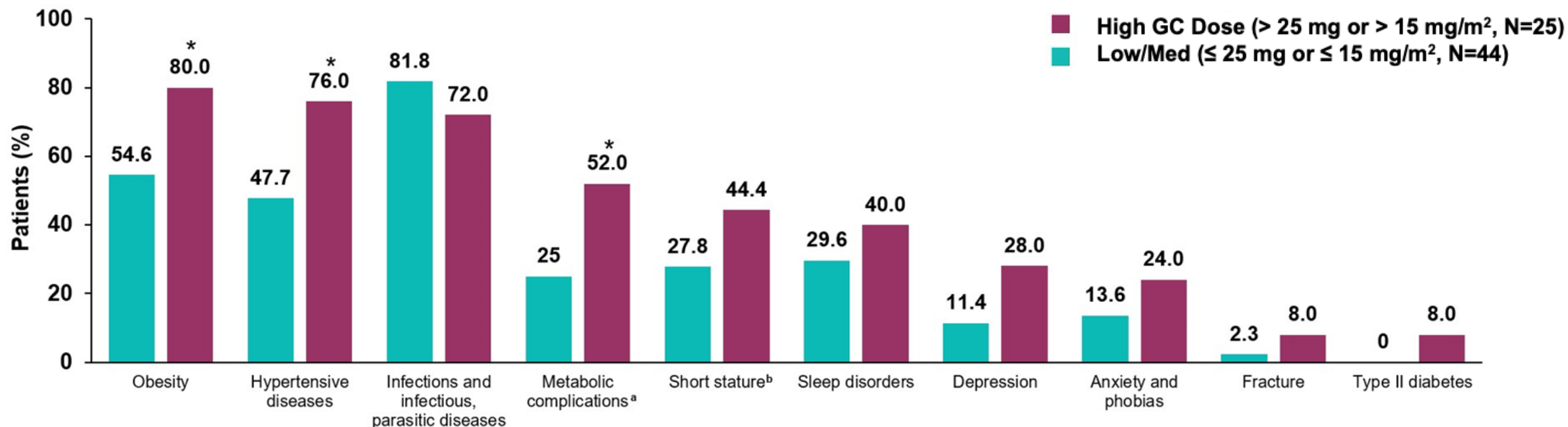
<sup>c</sup>Including hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, pre-diabetes/ hyperglycemia, and insulin resistance.

<sup>d</sup>Including insomnia and other sleep disorders.

BMI, body mass index; DBP, diastolic blood pressure; GC, glucocorticoid; HbA1c, hemoglobin A1C; HDL, high-density lipoprotein; ICD, International Classification of Diseases; LDL, low-density lipoprotein; SBP, systolic blood pressure.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

# Disease and GC Related Comorbidities in Adult and Pediatric Patients



## Key Results

**Higher rates of comorbidities related to GCs were observed among patients with high GC doses, with statistical significance for obesity, hypertensive diseases, and metabolic complications.**

This analysis likely underestimated the prevalence of complications due to the reliance on healthcare providers to consistently document patients' comorbidities

\*P<0.05 vs low/med GC dose.

<sup>a</sup>Including hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, pre-diabetes/hyperglycemia, and insulin resistance.

<sup>b</sup>Assessed only in pediatric patients with high (n=36) or low/med GC dose (n=9).

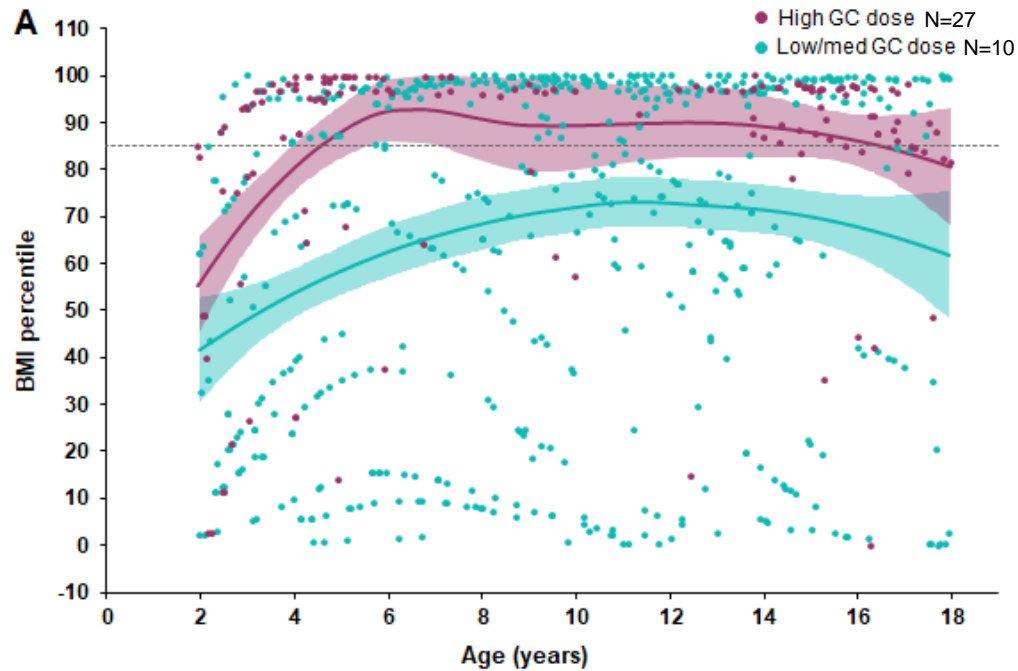
GC, glucocorticoid.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

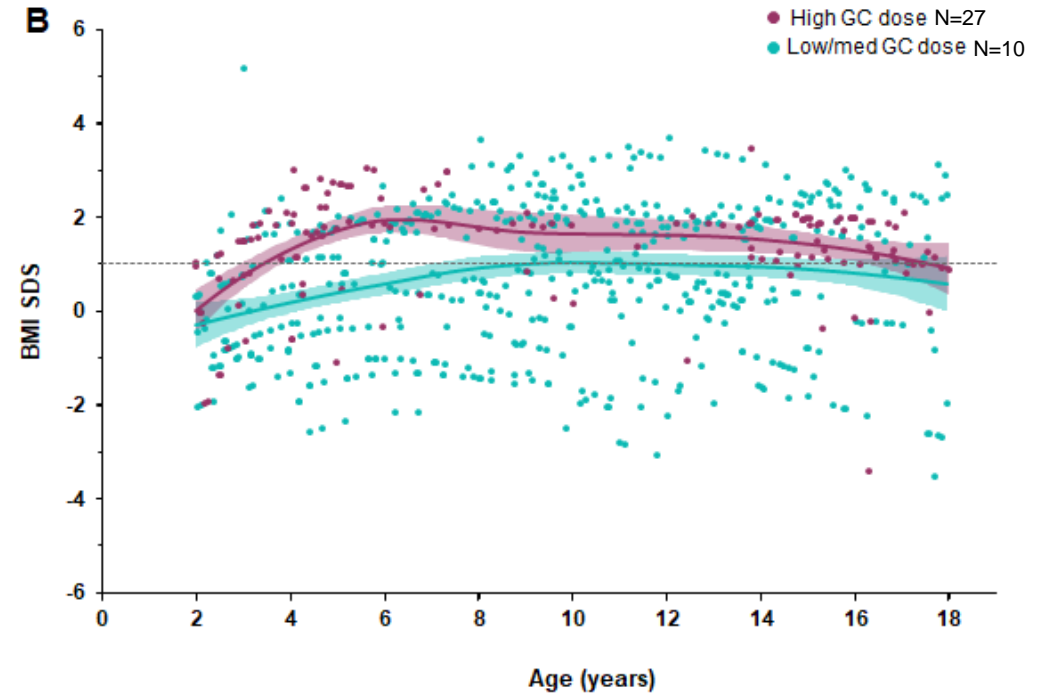
# GC Dose vs. Clinical Outcomes: BMI & Adiposity Rebound

High GC Dose (> 25 mg or > 15 mg/m<sup>2</sup>) vs. Low/Med (≤ 25 mg or ≤ 15 mg/m<sup>2</sup>)

Scatter Plot of BMI percentile per CDC chart



Scatter Plot of BMI SDS



## Key Results

Adiposity rebound starts prematurely in patients taking high GC doses, with BMI elevation initiating at age 2 rather than after age 6

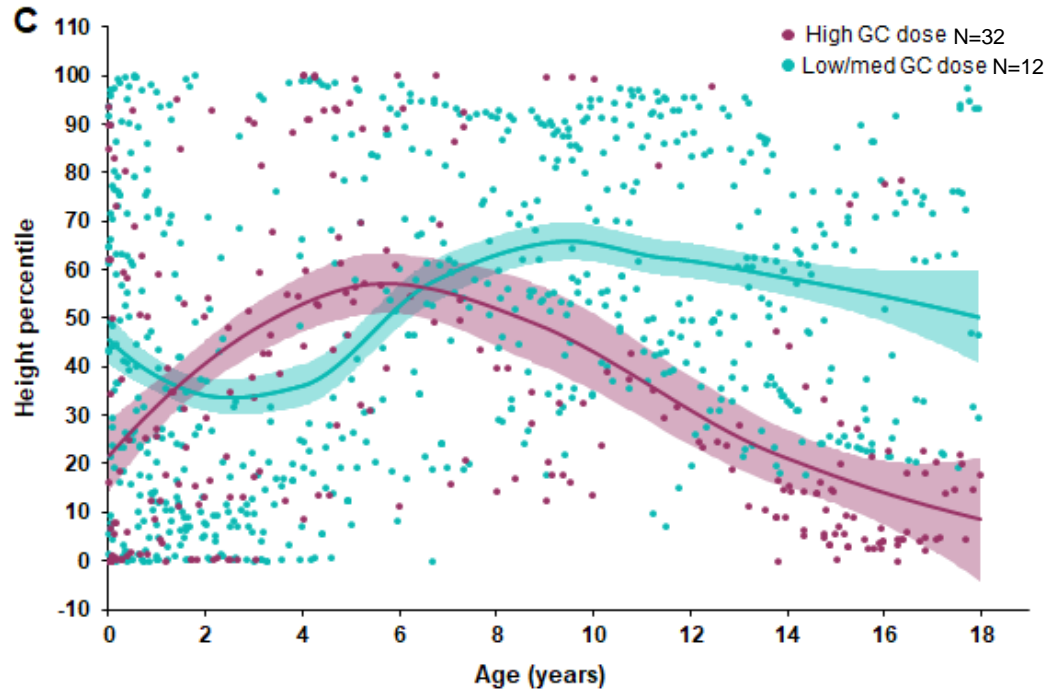
BMI, body mass index; CDC, Centers for Disease Control and Prevention; GC, glucocorticoid; SDS, standard deviation scores.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

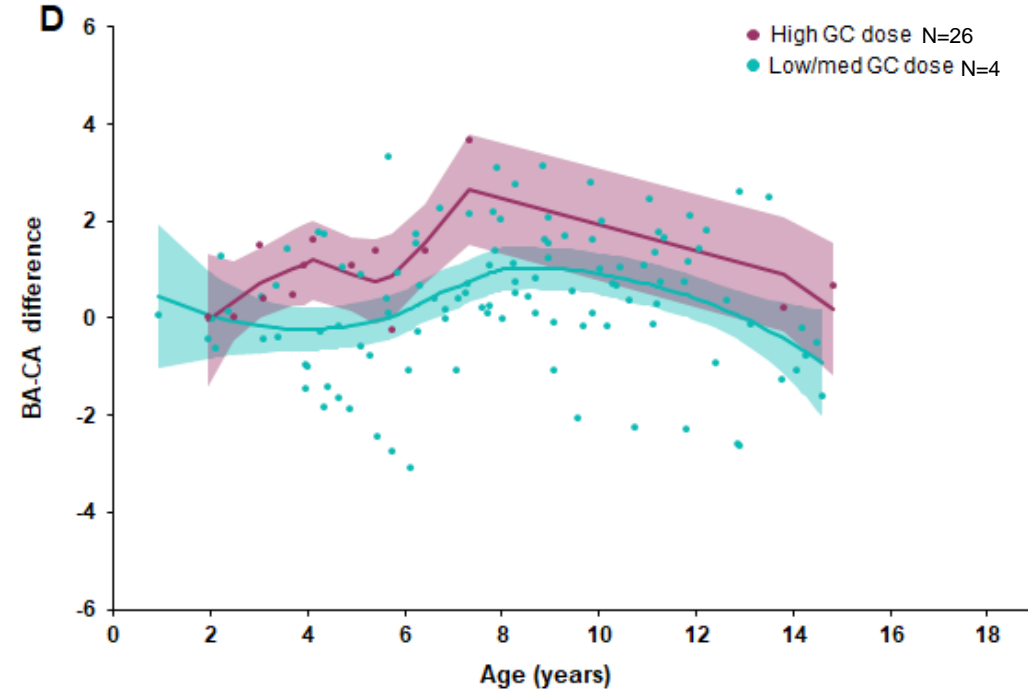
# GC Dose vs. Clinical Outcomes: Height and Bone Age

High GC Dose (> 25 mg or > 15 mg/m<sup>2</sup>) vs. Low/Med (≤ 25 mg or ≤ 15 mg/m<sup>2</sup>)

Scatter Plot of height percentile



Scatter Plot of Bone age to age difference



## Key Results

**Accelerated growth attributed to advance bone age** manifest during the **early years**. However, beyond **6 years** of age, the pediatric populations receiving **high GC doses** exhibit **significant growth impairments**, evidenced by declining height percentiles over time.

BA-CA, bone age to chronological age; GC, glucocorticoid.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

# Important Considerations for Interpreting GC vs. Clinical Outcomes Data

1

- Due to **small sample size**, we currently cannot robustly:
  - Stratify by both GC dose *and* androgen levels (Many complications are related to both GC dose and CAH itself.)
  - Perform additional subgroup analyses (e.g., by gender and age)
  - Analyze GC dose as a continuous variable or in more than two categorical groups
  - Adjust for confounders

2

- **Limited Scope and Simplified Comparisons:** The analyses rely on unadjusted comparisons which limit control over potential confounders, and are thus descriptive in nature, including the use of p-values.

3

- **Statistical Correlation, Not Causation:** While our results demonstrate statistical correlations, they do not establish direct causation.

## Future Work

These are early findings from a small cohort:

We are actively working towards **increasing the sample size** to enhance the robustness and generalizability of future analyses.

GC, glucocorticoid.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA



# We aimed to visualize the transition of patients through health states based on lower vs. higher GC doses and A4 levels

	Lower GC dose	Higher GC dose
Higher A4	<b>PED:</b> $\leq 11$ mg/m <sup>2</sup> /d HCe, A4 $\geq$ ULN <b>ADULT:</b> $\leq 20$ mg/d HCe, A4 $\geq$ ULN	<b>PED:</b> $> 11$ mg/m <sup>2</sup> /d HCe, A4 $\geq$ ULN <b>ADULT:</b> $> 20$ mg/d HCe, A4 $\geq$ ULN
Lower A4	<b>PED:</b> $\leq 11$ mg/m <sup>2</sup> /d HCe, A4 $<$ ULN <b>ADULT:</b> $\leq 20$ mg/d HCe, A4 $<$ ULN	<b>PED:</b> $> 11$ mg/m <sup>2</sup> /d HCe, A4 $<$ ULN <b>ADULT:</b> $> 20$ mg/d HCe, A4 $<$ ULN

## Key Point

Clinician feedback underscored that **patients typically do not stay in one single health state, but transition frequently between states throughout their patient journeys**

A4, androstenedione; GC, glucocorticoid; HCe, hydrocortisone equivalent; ULN, upper limit of normal.

Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

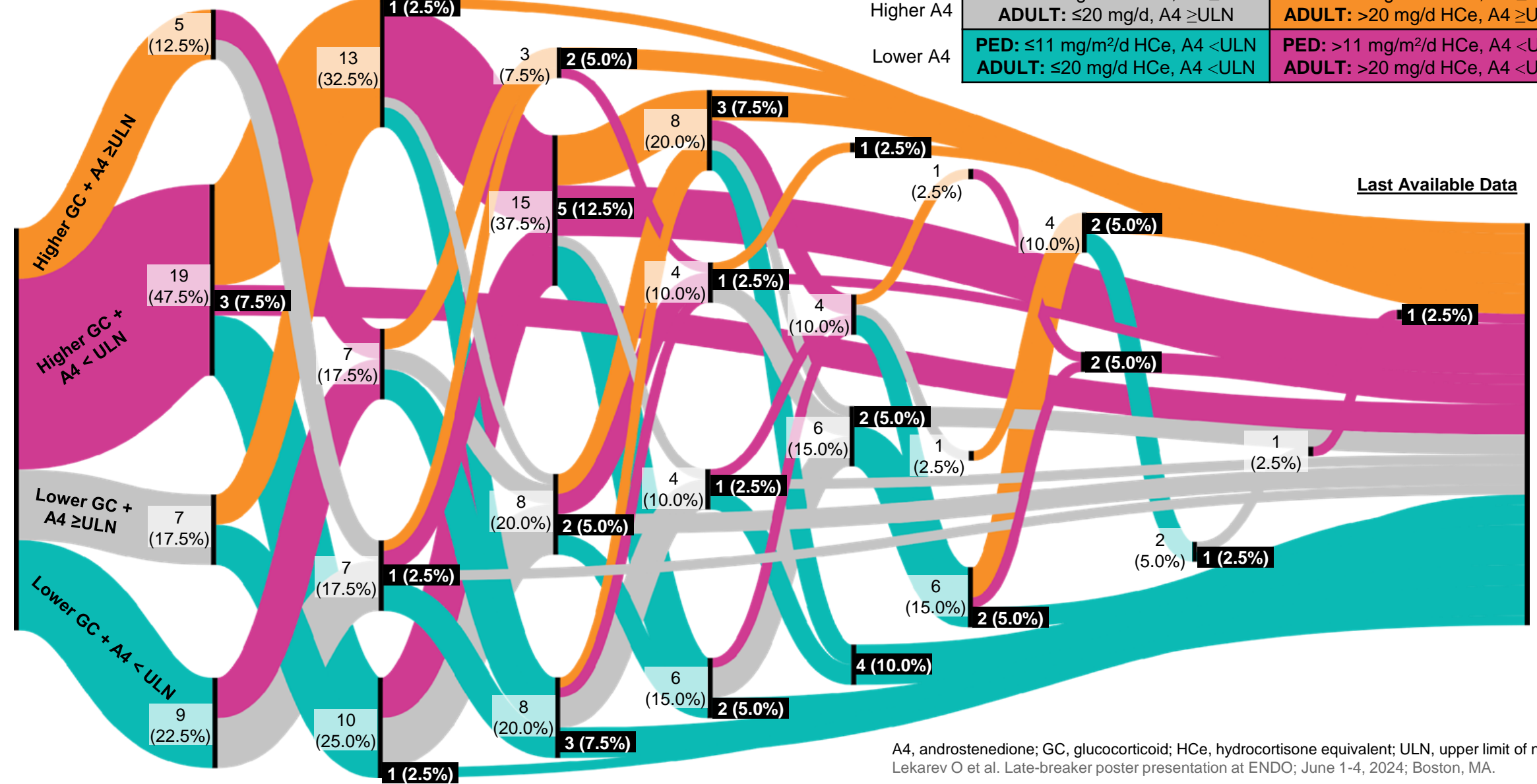
# All patients (100%) had higher GCs and/or loss of androstenedione control at some point, or multiple points, of their journeys

1st Recorded Data

Lower GC dose

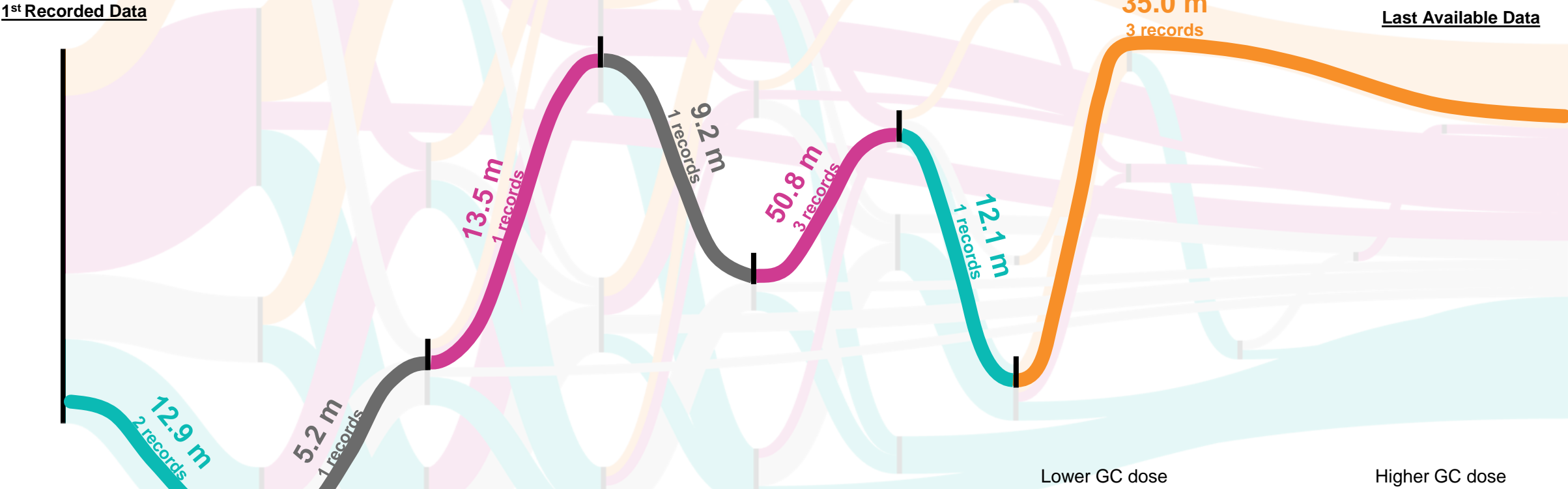
Higher GC dose

Higher A4	PED: $\leq 11$ mg/m <sup>2</sup> /d HCe, A4 $\geq$ ULN ADULT: $\leq 20$ mg/d HCe, A4 $\geq$ ULN	PED: $> 11$ mg/m <sup>2</sup> /d HCe, A4 $\geq$ ULN ADULT: $> 20$ mg/d HCe, A4 $\geq$ ULN
Lower A4	PED: $\leq 11$ mg/m <sup>2</sup> /d HCe, A4 $<$ ULN ADULT: $\leq 20$ mg/d HCe, A4 $<$ ULN	PED: $> 11$ mg/m <sup>2</sup> /d HCe, A4 $<$ ULN ADULT: $> 20$ mg/d HCe, A4 $<$ ULN



A4, androstenedione; GC, glucocorticoid; HCe, hydrocortisone equivalent; ULN, upper limit of normal. Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

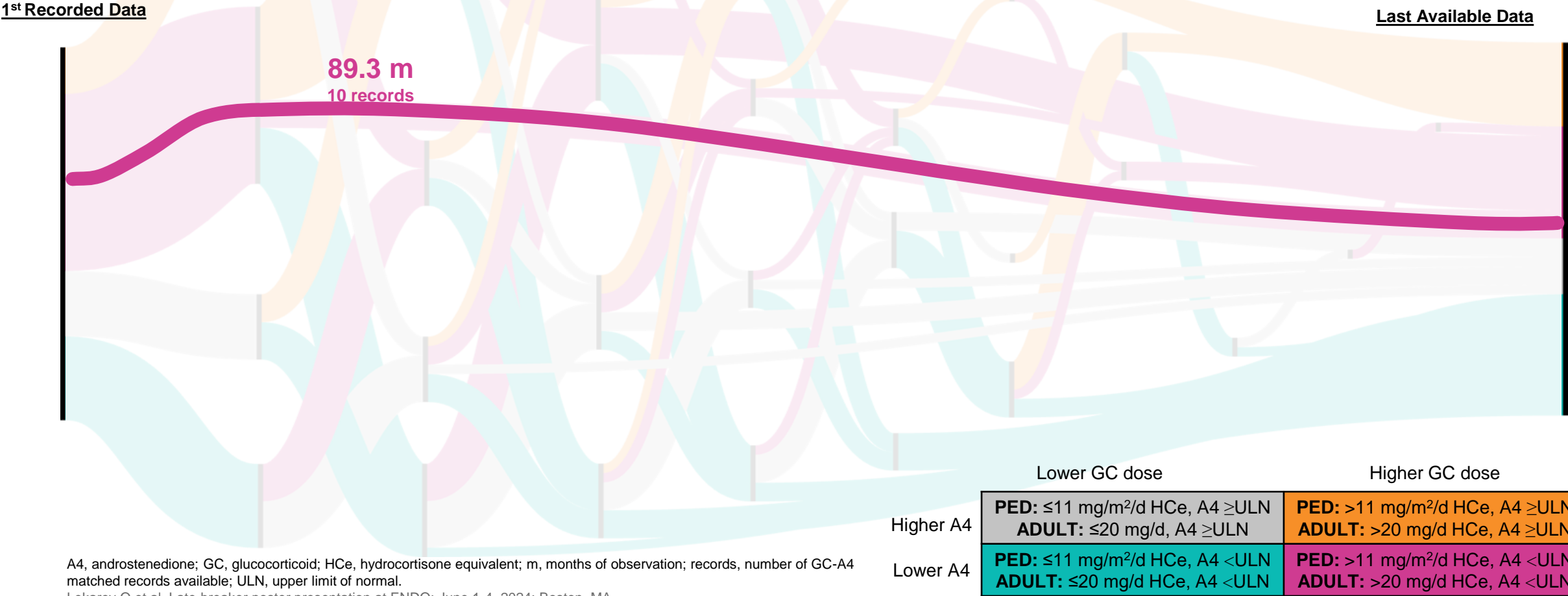
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	Lower GC dose	Higher GC dose
Higher A4	<b>PED:</b> ≤11 mg/m <sup>2</sup> /d HCe, A4 ≥ULN <b>ADULT:</b> ≤20 mg/d, A4 ≥ULN	<b>PED:</b> >11 mg/m <sup>2</sup> /d HCe, A4 ≥ULN <b>ADULT:</b> >20 mg/d HCe, A4 ≥ULN
Lower A4	<b>PED:</b> ≤11 mg/m <sup>2</sup> /d HCe, A4 <ULN <b>ADULT:</b> ≤20 mg/d HCe, A4 <ULN	<b>PED:</b> >11 mg/m <sup>2</sup> /d HCe, A4 <ULN <b>ADULT:</b> >20 mg/d HCe, A4 <ULN

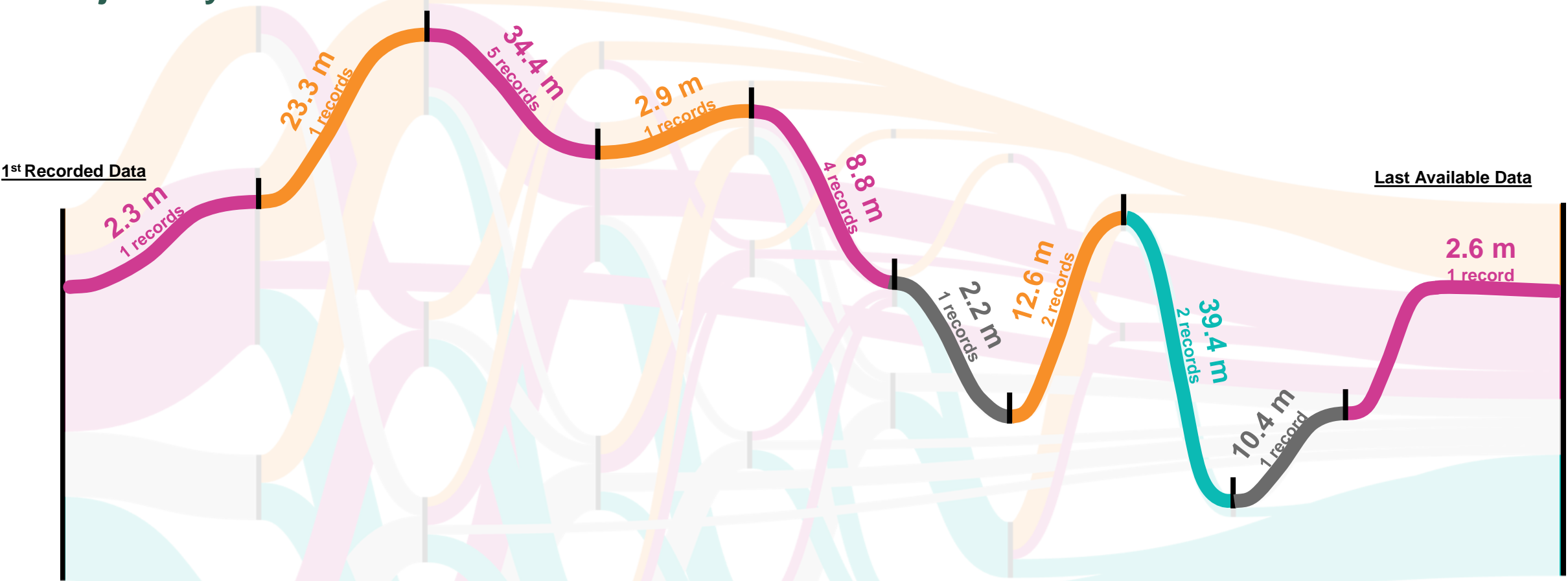
A4, androstenedione; GC, glucocorticoid; HCe, hydrocortisone equivalent; m, months of observation; records, number of GC-A4 matched records available; ULN, upper limit of normal.  
Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

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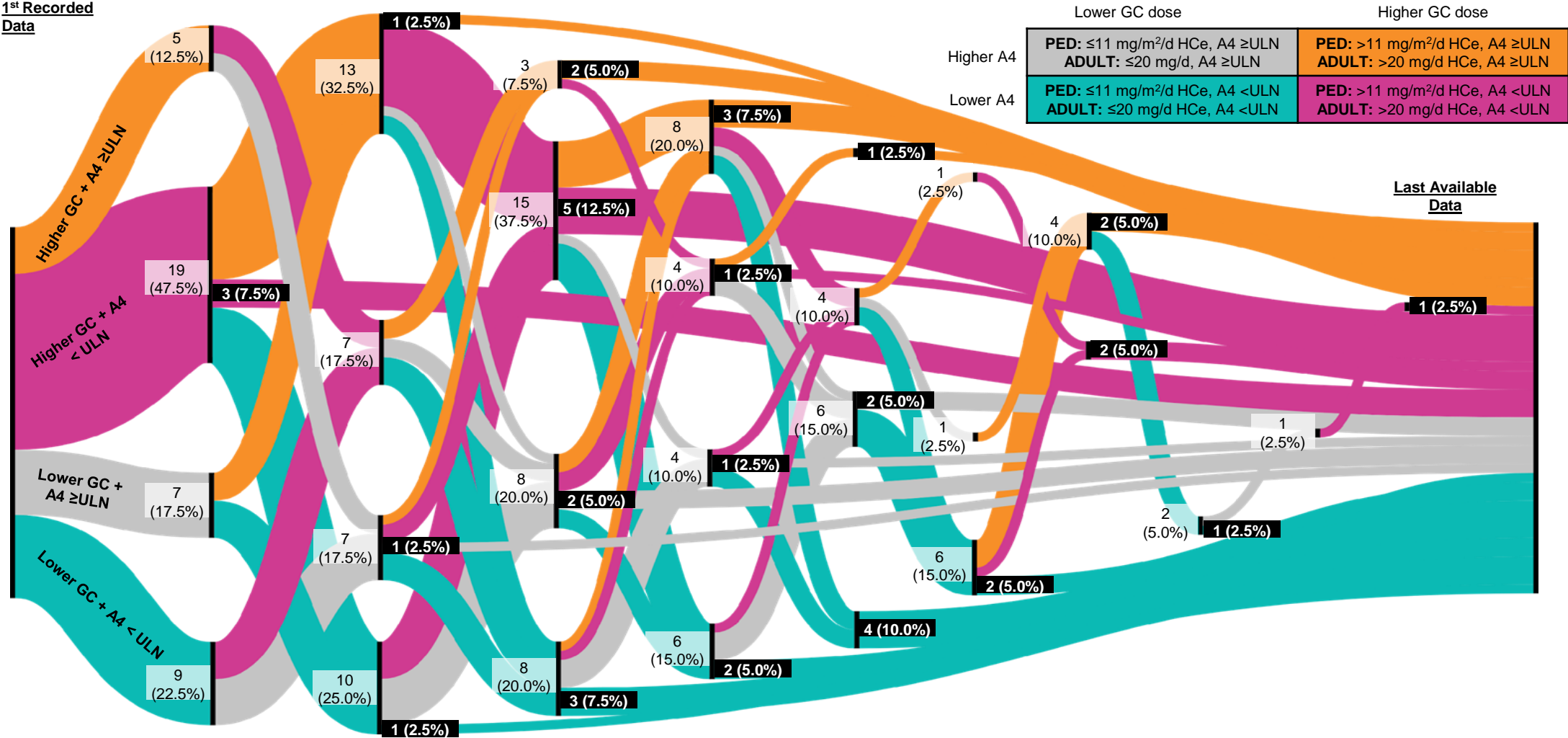
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 Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

	Lower GC dose	Higher GC dose
Higher A4	<b>PED:</b> ≤11 mg/m <sup>2</sup> /d HCe, A4 ≥ULN <b>ADULT:</b> ≤20 mg/d HCe, A4 ≥ULN	<b>PED:</b> >11 mg/m <sup>2</sup> /d HCe, A4 ≥ULN <b>ADULT:</b> >20 mg/d HCe, A4 ≥ULN
Lower A4	<b>PED:</b> ≤11 mg/m <sup>2</sup> /d HCe, A4 <ULN <b>ADULT:</b> ≤20 mg/d HCe, A4 <ULN	<b>PED:</b> >11 mg/m <sup>2</sup> /d HCe, A4 <ULN <b>ADULT:</b> >20 mg/d HCe, A4 <ULN

# All patients (100%) had higher GCs and/or loss of androstenedione control at some point, or multiple points, of their journeys



A4, androstenedione; GC, glucocorticoid; HCe, hydrocortisone equivalent; ULN, upper limit of normal. Lekarev O et al. Late-breaker poster presentation at ENDO; June 1-4, 2024; Boston, MA.

## Key Takeaway

Taken together, these analyses suggest that **with existing treatment approaches, disease control today does not equate to disease control tomorrow**

# Important considerations for interpreting Sankey diagrams of changes in health states

## Absence of Temporal Context

Diagram depicts order of transitions between health states for each patient, but doesn't show length of time patients spend in each health state

## Observation Period

Each patient journey represented equally regardless of each patient's observation period (median [range]: 6.5 [1.2, 20.8] years)

## Number of Records per Patient

The number of available matched A4-GC dose records varied for each patient (median [range]: 9 [3, 19] records)



**Sample Bias:** As is typical of many registry studies, patients who voluntarily enrolled into CAHtalog may have been more likely to be engaged in their care

- **70% received care at a CARES Comprehensive Care Center/Center of Excellence or large academic hospital**



**Timing of Androstenedione Measurements:** captured levels might not fully characterize disease control due to lack of information about the timing of the measurement relative to GC dose



# How to Help Recruit for CAHtalog™



# For HCPs, sharing the opportunity to participate in the CAHtalog registry with patients is easy

## 1. Identify

Clinicians have identified eligible participants through a variety of ways:



- General recollection
- Database query
- Review of notes



## 2. Share

Educate eligible patients about the registry however you prefer, leveraging Central IRB-approved materials:

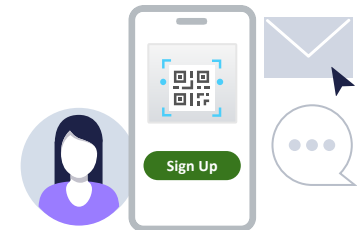


- Physical brochure
- Digital message (portal, email, etc.)



## 3. Sign Up

Patients sign up on their own within 10 minutes via virtual landing page

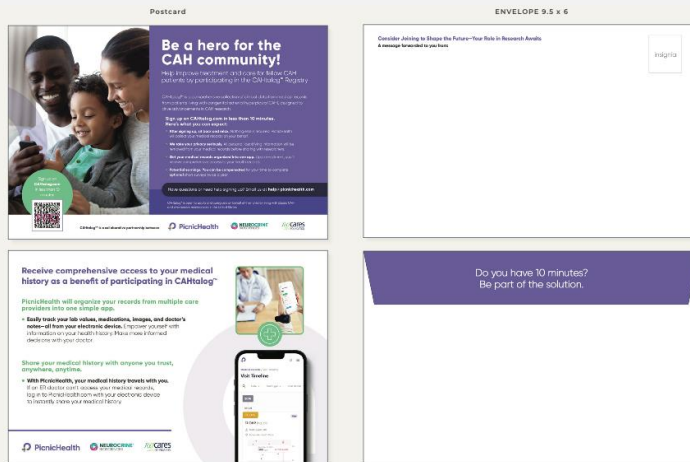


# Support is available in distributing materials and requesting local research and/or privacy approvals

[Upon request to help@picnichealth.com](mailto:help@picnichealth.com), PicnicHealth is available to provide:

## Central IRB Approved Patient Brochures & Postage-Paid Envelopes

- Providers can provide brochures to patients in person or via mail



## Central IRB Approved Digital Message Templates

- Message template can be emailed or messaged directly to patients by HCPs

Dear [Patient Name],

I wanted to inform you about an opportunity to participate in the CAHtalog™ Registry, which is sponsored by Neurocrine Biosciences in partnership with the CARES Foundation and PicnicHealth.

You can learn more and sign up here: [www.CAHtalog.com](http://www.CAHtalog.com).

Please see below for more information.

Sincerely,  
[Insert HCP Name. If desired, insert HCP email signature and/or contact info.]

**Help improve treatment and care for CAH patients by participating in the CAHtalog™ Registry.**

CAHtalog™ is a comprehensive collection of medical records from patients living with classic congenital adrenal hyperplasia (CAH), specifically curated to drive advancements in CAH research.

**Sign up on CAHtalog.com in less than 10 minutes.** Here's what you can expect:

- **After signing up, sit back and relax.** Nothing else is required. PicnicHealth will collect your medical records on your behalf.
- **We take your privacy seriously.** All personal identifying information will be removed from your medical records before sharing with researchers.
- **Get your medical records organized into one simple app.** Upon enrollment, you'll receive comprehensive access to your health records as a benefit of participating.
- **Potential Earnings. You can be compensated for your time to complete optional short surveys twice a year.**

Have questions or need help signing up? Email PicnicHealth at [help@picnichealth.com](mailto:help@picnichealth.com)

CAHtalog™ is open to adults and caregivers on behalf of their children living with classic CAH and who receive medical care in the United States.

Visit [CAHtalog.com](http://CAHtalog.com) today to learn more and sign up!

## Assistance with local research and/or privacy approval

- All patient-facing materials have been approved by a central IRB
- However, some institutions may need additional local research and/or privacy approvals. *PicnicHealth can assist with the preparation of submissions and/or questions upon request.*
- Email templates you can send to local institution IRB for guidance are available:

Subject: Request for Guidance on Sharing Patient Materials for Observational Research Study

Dear [IRB Contact],

I am writing to seek guidance regarding referring patients for a virtual, observational research study currently underway. To support this research, I would like to share with some of my patients certain patient materials, including a patient postcard and/or a digital message through our provider portal or email. These materials have already been approved by a central IRB, and would refer patients to a virtual landing page, from which they will separately and individually sign up and consent to be considered for the study.

I wanted to inquire whether any specific approvals or waivers from IRB are required before proceeding to share these materials. I would appreciate any guidance on if there are any forms or processes I should follow.

Thank you for your attention to this request. I look forward to your guidance.

Best regards,  
<Your Name>

# Central IRB-Approved CAHtalog Brochures and Postage-Paid Envelopes



## Be a hero for the CAH community!

Help improve treatment and care for fellow CAH patients by participating in the CAHtalog™ Registry

CAHtalog is a comprehensive collection of clinical data from medical records from patients living with classic congenital adrenal hyperplasia (CAH), designed to drive advancements in CAH research.

**Sign up on CAHtalog.com in less than 10 minutes. Here's what you can expect:**

- **After signing up, sit back and relax.** Nothing else is required. PicnicHealth will collect your medical records on your behalf.
- **We take your privacy seriously.** All personal identifying information will be removed from your medical records before sharing with researchers.
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CAHtalog is a collaborative partnership between





Sign up on [CAHtalog.com](https://CAHtalog.com) in less than 10 minutes




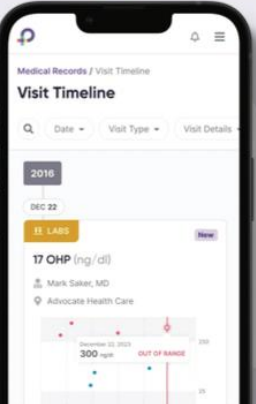
## Receive comprehensive access to your medical history as a benefit of participating in CAHtalog™


**PicnicHealth will organize your records from multiple care providers into one simple app.**

- **Easily track your lab values, medications, images, and doctor's notes—all from your electronic device.** Empower yourself with information on your health history. Make more informed decisions with your doctor.

**Share your medical history with anyone you trust, anywhere, anytime.**

- **With PicnicHealth, your medical history travels with you.** If an ER doctor can't access your medical records, log in to PicnicHealth.com with your electronic device to instantly share your medical history.






Neurocrine Medical Affairs

[www.neurocrinemedical.com](http://www.neurocrinemedical.com)



1-877-641-3461

