# Children and adolescents in the United States with Congenital Adrenal Hyperplasia are not at increased risk for Attention-Deficit/Hyperactivity Disorder

Lauren A Harasymiw<sup>1</sup>, Scott D Grosse<sup>2</sup>, Kyriakie Sarafoglou<sup>3</sup>

<sup>1</sup> University of Minnesota Medical School, Department of Pediatrics, Minneapolis, MN, USA; <sup>2</sup> National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>3</sup> University of Minnesota Masonic Children's Hospital, Divisions of Pediatric Endocrinology and Genetics & Metabolism, Minneapolis, MN, USA

#### Introduction

- Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is characterized by impaired cortisol synthesis and disruption in the hypothalamic pituitary adrenal (HPA) axis regulation leading to excessive adrenal androgen production (Figure 1) [1].
- HPA axis function has been shown to be closely tied to mental health symptoms. In particular, hypocortisolemia and hyperandrogenism have been linked to Attention-Deficit Hyperactivity Disorder (ADHD) [2-3].
- The only previous study to directly assess the risk for ADHD among pediatric patients with CAH was based on a small sample of children and adolescents (n=54), and reported an increased rate of ADHD in males as compared to the reported prevalence in the general population [3-4].

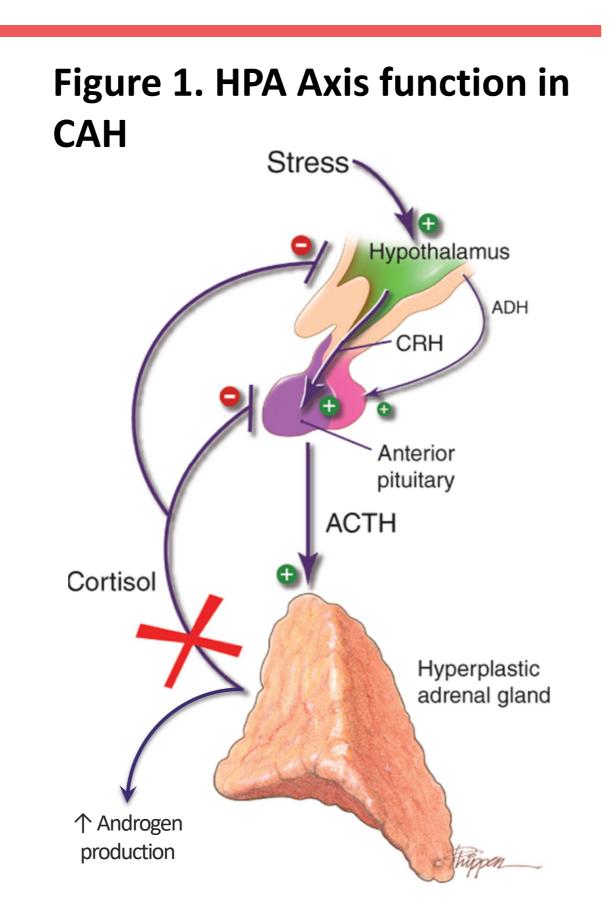


Image adapted from Sarafoglou K, Hoffmann GF, Roth KS. *Pediatric* Endocrinology and Inborn Errors of Metabolism, 2e; 2017

The objective of the current study was to investigate the prevalence of ADHD in large administrative samples of insured children and adolescents with CAH compared to the general pediatric population in the United States.

#### Methods

- We used the Treatment Pathways® interface to analyze health insurance claims data in the IBM® MarketScan® Commercial and Medicaid Claims Databases.
- Data from all individuals who met the inclusion criteria during the study period were included (Figure 2).
- CAH prevalence was measured as the percentage of children and adolescents with ≥2 claims with E25.0 ICD-10 codes for CAH *and* ≥2 glucocorticoid prescriptions filled during the study period.
- A comparison group for the general population was created by including all individuals who meet the study inclusion criteria but did not meet the criteria for CAH.
- ADHD prevalence was measured using a published claims-based algorithm [5].
- During analysis, subjects were stratified by enrollment in either an employersponsored private (Commercial) or public (Medicaid) insurance plan, and by age (5-11 years vs 12-18 years).
- Odds Ratios (OR) and confidence intervals (CI) were calculated to compared the risk for ADHD in the CAH population with the general population.

### Figure 2. Study Inclusion Criteria

Enrolled in a participating private employer-sponsored or public health insurance program



At least 12 months continuous enrollment between October 2015 -December 2017



At least one outpatient claim made during the study period



Between 5-18 years old at the start of the study period

### Acknowledgments

- This research was supported by National Institutes of Health (NIH) grants F30 CA223591 to Dr. Harasymiw, and NIH T32 GM008244 to the University of Minnesota MSTP
- This research was also supported by the National Institutes of Health's National Center for Advancing Translational Sciences, grant UL1TR002494. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health's National Center for Advancing Translational Sciences.
- Dr. Sarafoglou receives support from the DHHS FDA, NIH NCI, NSF, Spruce Biosciences, Alexion and Neurocrine.
- MarketScan® data are licensed by IBM® to the Centers for Disease Control and Prevention (CDC) for public health use by CDC researchers. The views and findings in this report do not necessarily reflect the official position of the CDC.

#### Results

 The study period prevalence of CAH in the Commercial and Medicaid samples was 1/9,500 (Table 1) and 1/14,000 (Table 2), respectively.

Table 1. Commercial sample

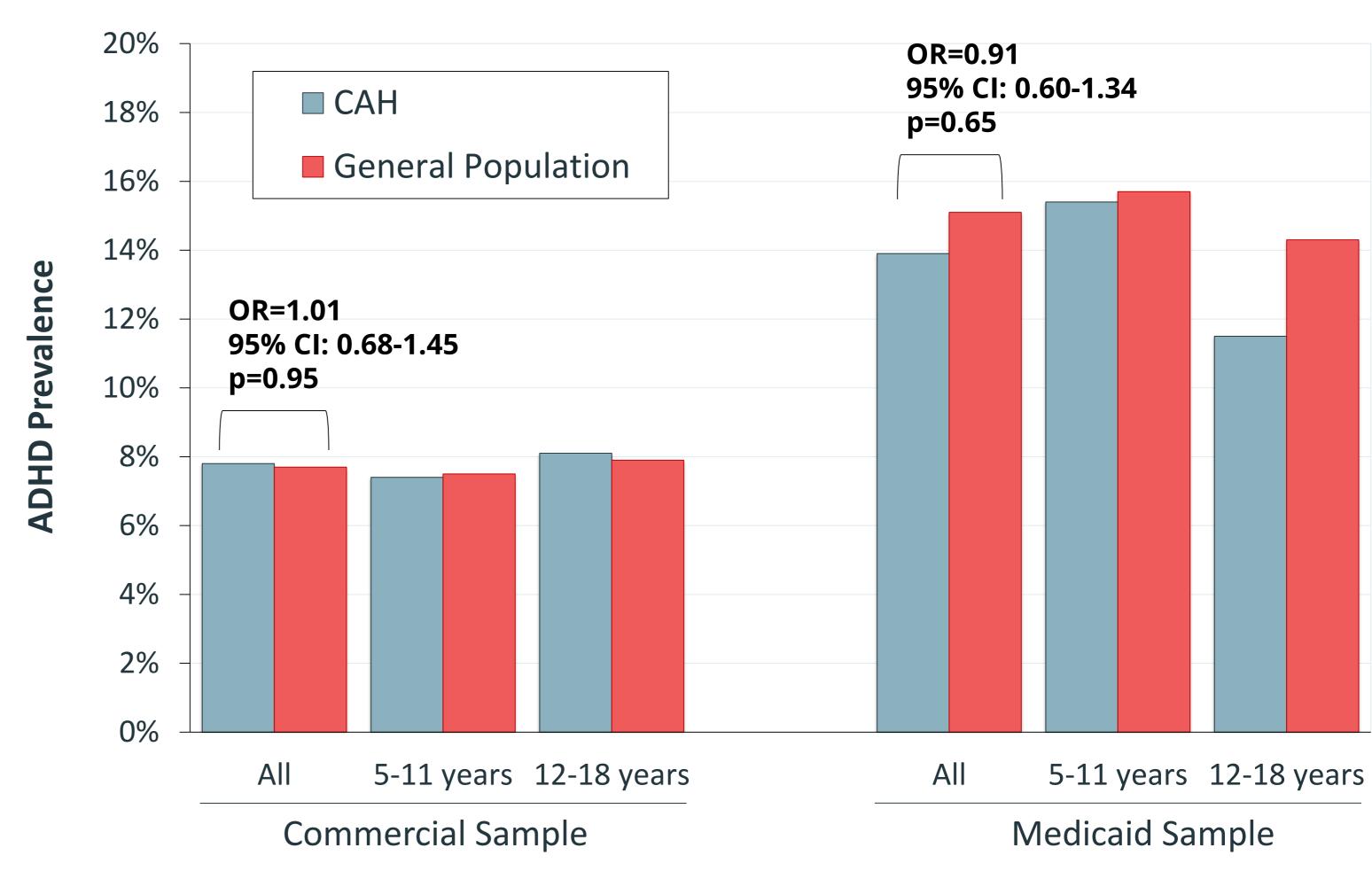
	Total Subjects	Met Criteria for ADHD	
General Population			
All	3,532,914	272,685	
5-11 years	1,655,679	123,987	
12-18 years	1,876,871	148,669	
CAH			
All	373	29	
5-11 years	176	13	
12-18 years	197	16	

Table 2. Medicaid sample

	Total Subjects	Met Criteria for ADHD	
General Population			
All	2,766,096	418,260	
5-11 years	1,602,812	252,351	
12-18 years	1,163,284	165,909	
CAH			
All	201	28	
5-11 years	123	19	
12-18 years	78	9	

- Overall, ADHD prevalence was higher in the Medicaid sample as compared to the Commercial sample.
- There was no increased risk for ADHD among those with CAH as compared to the general population in either sample (Figure 3).
- ADHD prevalence also did not differ significantly by age (Figure 3).

Figure 3. ADHD prevalence across study subsamples



# Conclusion

- Using two large national samples of privately and publicly -insured children and adolescents with CAH in the United States, we found that the prevalence of ADHD was comparable to that of the general pediatric population.
- These findings suggest that enhanced screening for ADHD among the pediatric CAH population may not be warranted.
- Our findings are limited by the smaller sample size of subjects who met criteria for CAH.
- Future studies will investigate the relationship between CAH and other common mental health comorbidities among children and adolescents, including depression and anxiety.

## References

- 1. Speiser PW, et al. Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103: 4043–4088.
- 2. van West D, et al. Differences in hypothalamic-pituitary-adrenal axis functioning among children with ADHD predominantly inattentive and combined types. Eur Child Adolesc Psychiatry. 2009;18(9):543-553.
- 3. Mueller, S. C., et al. (2010). Psychiatric characterization of children with genetic causes of hyperandrogenism. European journal of endocrinology, 163(5), 801–810.
- 4. Froehlich TE, et al. Prevalence, Recognition, and Treatment of Attention-Deficit/Hyperactivity Disorder in a National Sample of US Children. Arch Pediatr Adolesc Med. 2007;161(9):857–864.
- 5. Nyarko KA, et al. Treated Prevalence of Attention-Deficit/Hyperactivity Disorder Increased from 2009 to 2015 Among School-Aged Children and Adolescents in the United States. J Child Adolesc Psychopharmacol. 2017;27(8):731-734.





