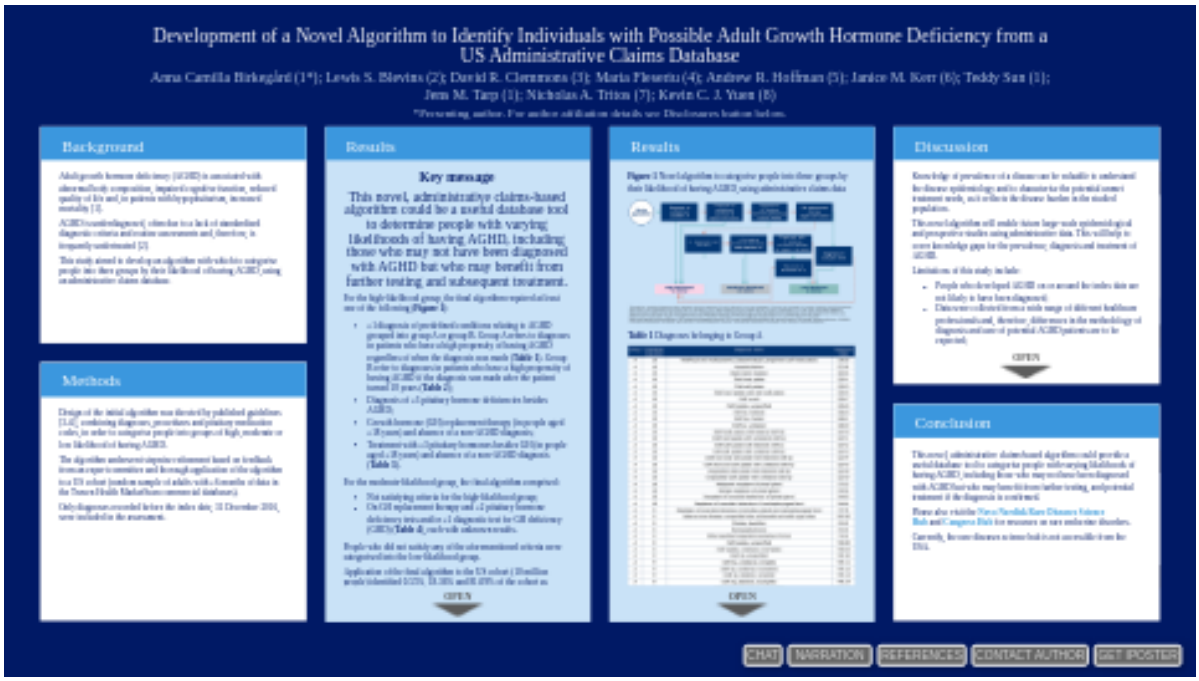
Development of a Novel Algorithm to Identify Individuals with Possible Adult Growth Hormone Deficiency from a US Administrative Claims Database



Anna Camilla Birkegård (1*); Lewis S. Blevins (2); David R. Clemmons (3); Maria Fleseriu (4); Andrew R. Hoffman (5); Janice M. Kerr (6); Teddy Sun (1); Jens M. Tarp (1); Nicholas A. Tritos (7); Kevin C. J. Yuen (8)

*Presenting author. For author affiliation details see Disclosures button below.

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BACKGROUND

Adult growth hormone deficiency (AGHD) is associated with abnormal body composition, impaired cognitive function, reduced quality of life and, in patients with hypopituitarism, increased mortality [1].

AGHD is underdiagnosed, often due to a lack of standardised diagnostic criteria and routine assessments and, therefore, is frequently undertreated [2].

This study aimed to develop an algorithm with which to categorise people into three groups by their likelihood of having AGHD, using an administrative claims database.

METHODS

Design of the initial algorithm was directed by published guidelines [3–6], combining diagnoses, procedures and pituitary medication codes, in order to categorise people into groups of high, moderate or low likelihood of having AGHD.

The algorithm underwent stepwise refinement based on feedback from an expert committee and thorough application of the algorithm to a US cohort (random sample of adults with ≥6 months of data in the Truven Health MarketScan commercial databases).

Only diagnoses recorded before the index date, 31 December 2016, were included in the assessment.

RESULTS

Key message

This novel, administrative claims-based algorithm could be a useful database tool to determine people with varying likelihoods of having AGHD, including those who may not have been diagnosed with AGHD but who may benefit from further testing and subsequent treatment.

For the high-likelihood group, the final algorithm required at least one of the following (**Figure 1**):

- ≥1 diagnosis of predefined conditions relating to AGHD grouped into group A or group B. Group A refers to diagnoses in patients who have a high propensity of having AGHD regardless of when the diagnosis was made (**Table 1**). Group B refer to diagnoses in patients who have a high propensity of having AGHD if the diagnosis was made after the patient turned 18 years (**Table 2**);
- Diagnosis of ≥3 pituitary hormone deficiencies besides AGHD;
- Growth hormone (GH) replacement therapy (in people aged ≥18 years) and absence of a non-AGHD diagnosis;
- Treatment with ≥3 pituitary hormones besides GH (in people aged ≥18 years) and absence of a non-AGHD diagnosis (**Table 3**).

For the moderate-likelihood group, the final algorithm comprised:

- Not satisfying criteria for the high-likelihood group;
- On GH replacement therapy and ≥2 pituitary hormone deficiency tests and/or ≥1 diagnostic test for GH deficiency (GHD) (**Table 4**), each with unknown results.

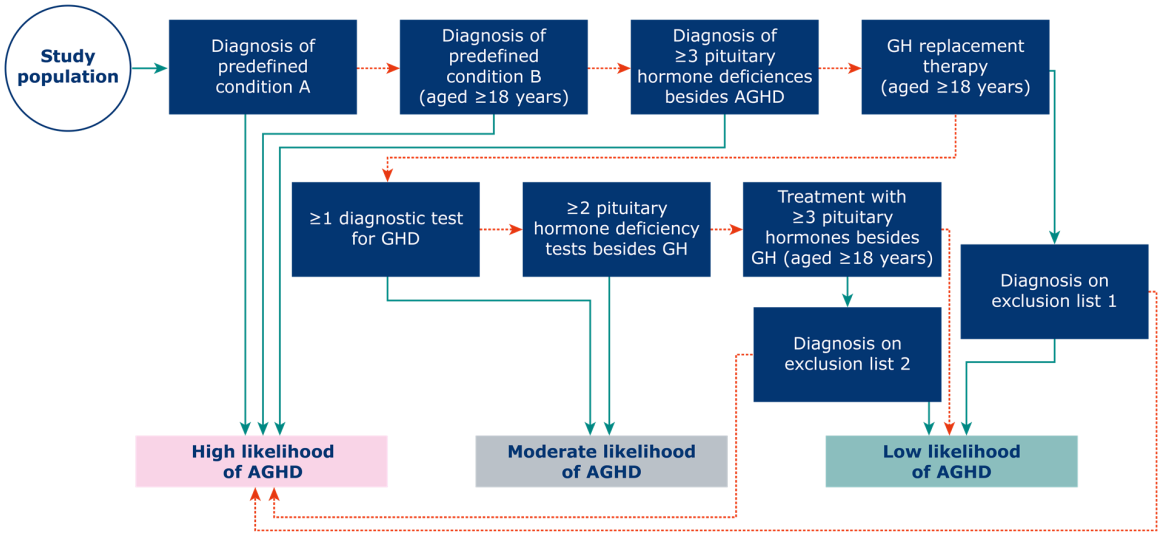
People who did not satisfy any of the aforementioned criteria were categorised into the low-likelihood group.

Application of the final algorithm to the US cohort (10 million people) identified 0.55%, 18.36% and 81.09% of the cohort as having a high, moderate or low likelihood of having AGHD, respectively.

Please follow this **link to view an infographic** (http://biopharmsites.novonordisk.com/content/dam/Global/AFFILIATE/biopharmsites-novonordisk-com/assets-biopharmsites-novonordisk-com/ispor-2020/AGHD%20infographic.pdf) summarising the study and results presented in posters PDB82 and PDB83

RESULTS

Figure 1 Novel algorithm to categorise people into three groups by their likelihood of having AGHD, using administrative claims data



The algorithm considered diagnosis codes, diagnostic tests and treatments for each individual in the study population. The flow chart consists of a number of guiding rules (blue squares), which result in the placement of each person into one of three groups by their likelihood of having AGHD. Each blue square is dependent on a set of codes (ICD10CM/ICD09CM for diagnoses, CPT for tests and ATC for treatments), which, combined with logical rules dependent on age, number of prescriptions or diagnoses, were used to determine whether each person answered yes (green arrow) or no (dashed red arrow). Predefined conditions (A or B) and diagnoses exclusion lists (1 or 2) are not shown in this poster.
AGHD, adult growth hormone deficiency; ATC, anatomical therapeutic chemical; CPT, current procedural terminology; GH, growth hormone; GHD, growth hormone deficiency; ICD09CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD10CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

Table 1 Diagnoses belonging to Group A

Group	ICD09CM/ ICD10CM	Diagnosis name	Diagnosis code
A	10	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis	C96.0
A	10	Hypopituitarism	E23.0
A	10	Septo-optic dysplasi	Q04.4
A	10	Cleft hard palate	Q35.1
A	10	Cleft soft palate	Q35.3
A	10	Cleft hard palate with cleft soft palate	Q35.5
A	10	Cleft uvula	Q35.7
A	10	Cleft palate, unspecified	Q35.9
A	10	Cleft lip, bilateral	Q36.0
A	10	Cleft lip, median	Q36.1
A	10	Cleft lip, unilateral	Q36.9
A	10	Cleft hard palate with bilateral cleft lip	Q37.0
A	10	Cleft hard palate with unilateral cleft lip	Q37.1
A	10	Cleft soft palate with bilateral cleft lip	Q37.2
A	10	Cleft soft palate with unilateral cleft lip	Q37.3
A	10	Cleft hard and soft palate with bilateral cleft lip	Q37.4
A	10	Cleft hard and soft palate with unilateral cleft lip	Q37.5
A	10	Unspecified cleft palate with bilateral cleft lip	Q37.8
A	10	Unspecified cleft palate with unilateral cleft lip	Q37.9
A	10	Malignant neoplasm of pineal gland	C75.3
A	10	Benign neoplasm of pineal gland	D35.4
A	10	Neoplasm of uncertain behaviour of pineal gland	D44.5
A	10	Neoplasm of uncertain behaviour of craniopharyngeal duct	D44.4
A	9	Neoplasm of uncertain behaviour of pituitary gland and craniopharyngeal duct	237.0
A	9	Letterer-siwe disease, unspecified site, extranodal and solid organ sites	202.50
A	9	Pituitary dwarfism	253.3
A	9	Panhypopituitarism	253.2
A	9	Other specified congenital anomalies of brain	742.4
A	9	Cleft palate, unspecified	749.00
A	9	Cleft palate, unilateral, incomplete	749.02
A	9	Cleft lip, unspecified	749.10
A	9	Cleft lip, unilateral, complete	749.11
A	9	Cleft lip, unilateral, incomplete	749.12
A	9	Cleft lip, bilateral, complete	749.13
A	9	Cleft lip, bilateral, incomplete	749.14
A	9	Cleft palate with cleft lip, unspecified	749.20
A	9	Cleft palate with cleft lip, unilateral, complete	749.21
A	9	Cleft palate with cleft lip, unilateral, incomplete	749.22
A	9	Cleft palate with cleft lip, bilateral, complete	749.23
A	9	Cleft palate with cleft lip, bilateral, incomplete	749.24
A	9	Personal history of irradiation, presenting hazards to health	V15.3
A	9	Malignant neoplasm of pineal gland	194.4
A	9	Benign neoplasm of pineal gland	227.4
A	9	Neoplasm of uncertain behavior of pineal gland	237.1

Table 2 Diagnoses belonging to Group B

Group	ICD09CM/ ICD10CM	Diagnosis name	Diagnosis code
B	10	Drug-induced hypopituitarism	E23.1
B	10	Hypothalamic dysfunction, not elsewhere classified	E23.3
B	10	Other disorders of pituitary gland	E23.6
B	10	Disorder of pituitary gland, unspecified	E23.7
B	10	Postprocedural hypopituitarism	E89.3
B	10	Iatrogenic pituitary disorders	253.7
B	9	Unspecified disorder of the pituitary gland and its hypothalamic control	253.9
B	9	Other anterior pituitary disorders	253.4
B	9	Other disorders of the pituitary and other syndromes of diencephalohypophyseal origin	253.8

Table 3 Algorithm structure: accepted pituitary hormones (other than GH)*

Group	ATC code	ATC name
Sex hormones	G03B	Androgens
Sex hormones	G03C	Oestrogens
Sex hormones	G03D	Progesterone
ACTH	H02	Corticosteroids for systemic use
Thyroxine	H03A	Thyroid preparations

*Only patients with at least two prescriptions of from at least two different groups within 1 year will be considered.
ATC, anatomical therapeutic chemical; ACTH, adrenocorticotropic hormone; GH, growth hormone.

Table 4 Algorithm structure: accepted tests for pituitary hormone deficiencies (other than GH)

Group	Test name	Hormone measured	CPT code
Sex hormone	LH	LH	83002
Sex hormone	FSH	FSH	83001
Sex hormone	LH/FSH	Gonadotropin panel	80426
ACTH	ACTH	ACTH	82024
ACTH	ACTH with cortisol	ACTH stim panel	80400/82533
TSH	TSH	TSH	84443
Combined	Combined anterior pituitary panel	ACTH, TSH, cortisol, LH, FSH, prolactin, hGH	80418
Sex hormone	Testosterone (done with LH/FSH) in men	Testosterone	80414/84403
Sex hormone	Oestradiol (done with LH/FHS) in women	Oestradiol	80415/82670
Sex hormone	Free testosterone	Testosterone	84402
Sex hormone	Bioactive testosterone	Testosterone	84410
TSH	Free T4	T4	84439
Sex hormone	Prolactin	Prolactin	84146

ACTH, adrenocorticotropic hormone; CPT, current procedural terminology; FSH, follicle-stimulating hormone; hGH, human growth hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

DISCUSSION

Knowledge of prevalence of a disease can be valuable to understand the disease epidemiology and to characterise the potential unmet treatment needs, as it reflects the disease burden in the studied population.

This novel algorithm will enable future large-scale epidemiological and prospective studies using administrative data. This will help to cover knowledge gaps for the prevalence, diagnosis and treatment of AGHD.

Limitations of this study include:

- People who developed AGHD on or around the index date are not likely to have been diagnosed;
- Data were collected from a wide range of different healthcare professionals and, therefore, differences in the methodology of diagnosis and care of potential AGHD patients are to be expected;
- The probability of having AGHD varies among the diagnoses, suggesting that the calculated proportion of people with moderate and high likelihood of AGHD might be overestimated.

CONCLUSION

This novel, administrative claims-based algorithm could provide a useful database tool to categorise people with varying likelihoods of having AGHD, including those who may not have been diagnosed with AGHD but who may benefit from further testing, and potential treatment if the diagnosis is confirmed.

Please also visit the **Novo Nordisk Rare Diseases Science Hub (http://www.novonordisk-rarediseaseshub.com/rare-endocrine-disorders/congresses)** and **Congress Hub** (http://biopharmsites.novonordisk.com/NN/ISPOR2020.html) for resources on rare endocrine disorders.

Currently, the rare diseases science hub is not accessible from the USA.

AUTHOR INFORMATION

1. Novo Nordisk A/S, Søborg, Denmark;

2. Department of Neurosurgery, University of California, San Francisco, CA, USA

3. Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, NC, USA

4. Departments of Medicine and Neurological Surgery, Northwest Pituitary Center, Oregon Health and Science University, Portland, OR, USA;

5. Stanford University, Stanford, CA, USA

6. Department of Endocrinology, University of Colorado Health Sciences Center, University of Colorado Denver, Anschutz Medical Campus, Aurora, CO, USA

7. Neuroendocrine Unit, Massachusetts General Hospital and Department of Medicine, Harvard Medical School, Boston, MA, USA

8. Barrow Pituitary Center, Barrow Neurological Institute and St. Joseph's Hospital and Medical Center, University of Arizona College of Medicine and Creighton School of Medicine, Phoenix, AZ, USA

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