INCREASED MORBIDITY AND HOSPITAL ADMISSIONS IN PATIENTS WITH ADRENAL INSUFFICIENCY

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INTRODUCTION

- Patients with adrenal insufficiency (AI) (primary [PAI], secondary to pituitary disease [PIT] and congenital adrenal hyperplasia [CAH]) have reduced life expectancy with reported standardized mortality ratios of ~2:1 but given the rarity of AI, the underlying explanation remains largely unknown.

AIMS

- The objective of this study was to evaluate patient characteristics and morbidity (prevalence of concomitant conditions and hospitalization incidence) in patients with AI compared with a general population sample.

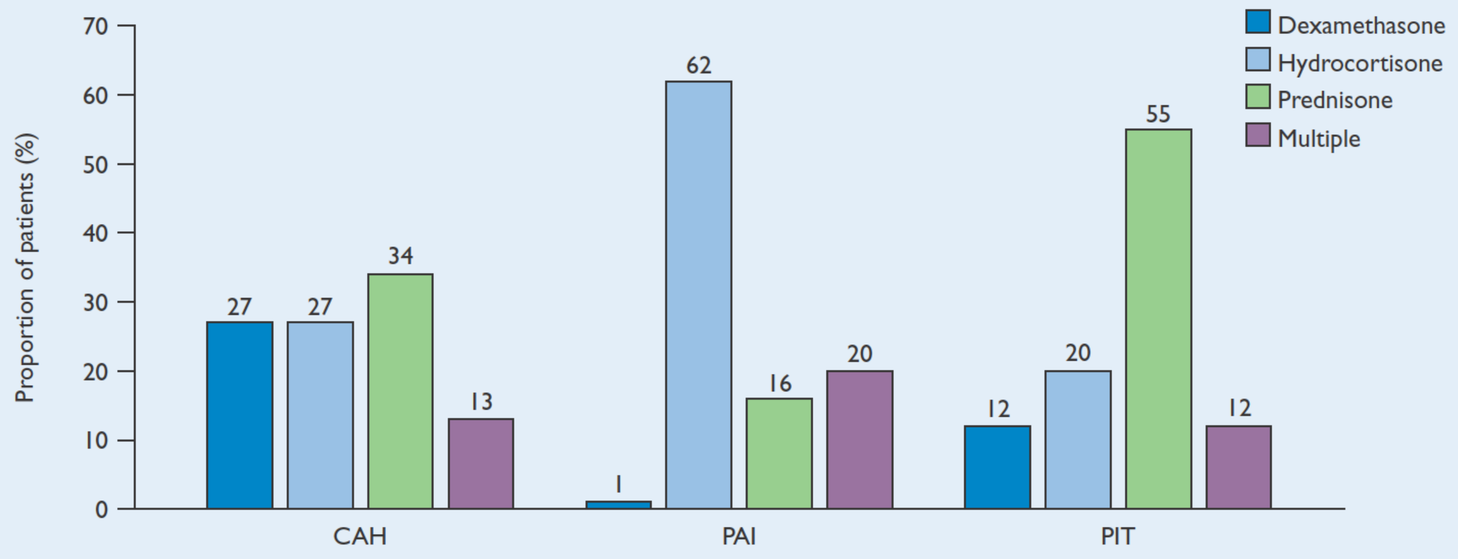
METHODS

- United States administrative health claims data from Truven Health MarketScan® Commercial and Medicare databases (January 2006 to June 2011, including 108,271,287 records) were used.
- Patients were classified into three cohorts based on type of adrenal disorder: secondary AI (PIT) due to pituitary disorder (n = 8818), primary AI (PAI) (n = 1014), and congenital adrenal hyperplasia (CAH) (n = 551) (Figure 1).
- **Inclusion criteria:** within each cohort, patients had to have (1) a minimum of two diagnosis codes on different days (see Figure 1 for coding algorithm) and (2) continuous health and pharmacy coverage starting at least 6 months before and for at least 12 months after index diagnosis.

Analysis

- **Matched control:** Each patient meeting inclusion and exclusion criteria within each AI cohort (PAI, CAH and PIT) were matched using the greedy algorithm 1:1 on age (within 5 years), gender, insurance type and region to a general population control group in the same insurance database (matched control).
- **Probability of comorbidities:** Separate logistic regression models were used to estimate the probability of having each comorbid condition (diabetes, depression, anxiety, hyperlipidaemia and hypertension) for each AI cohort (PAI, CAH, and PIT) compared with their matched control. For these models covariates included the year of index diagnosis and patient demographics.
- **Inpatient admissions:** A multivariable regression model was generated to estimate the total number of annual inpatient admissions for each AI cohort (PAI, CAH, and PIT) compared with their matched control. For this model, covariates included the year of index diagnosis, patient demographics and patient comorbidities.

Figure 2. Steroid usage in the 6–12 month period after diagnosis of AI.



RESULTS

- All results are based on matched AI and general population cohorts.
- Compared with controls, patients with AI had higher odds of diabetes mellitus, hypertension, hyperlipidaemia, depression and anxiety ranging from an odds ratio (OR) of 1.51 for hyperlipidaemia in PAI and CAH to 3.85 for diabetes in CAH (Table 1).
- Patients with PIT had higher odds of having hyperlipidaemia and hypertension (OR = 1.98 and 2.24) in comparison with controls (Table 1).
- For every 1 inpatient admission for the matched cohort, there were an estimated 4.6 inpatient admissions for the PAI cohort (Table 2).
- For every 1 inpatient admission for the matched cohort, there were an estimated 4 inpatient admissions for the PIT cohort (Table 2).
- The PIT cohort used prednisone more frequently than other steroids; in the PAI cohort, hydrocortisone was used more frequently. Steroid use in the CAH cohort was more evenly distributed (Figure 2).
- PAI and PIT have a greater probability of inpatient admission with infection compared with their matched cohorts.

LIMITATIONS

- There are many limitations to the use of claims databases (lack of generalizability to non-insured populations, lack of laboratory values, lack of physician notes with clinical details) but the large numbers of available patients allow characterization of clinical care in patients with rare diseases beyond controlled clinical trials.

Table 1. Odds ratios of comorbid conditions in AI cohorts compared with matched controls.

	Comparison	Odds ratio (95% CI)	p value
Diabetes*	PAI vs controls	**1.75 (1.35–2.25)**	< 0.0001
	CAH vs controls	**3.85 (2.52–5.90)**	< 0.0001
	PIT vs controls	**1.87 (1.72–2.04)**	< 0.0001
Depression	PAI vs controls	**2.40 (1.97–2.91)**	< 0.0001
	CAH vs controls	**1.89 (1.40–2.56)**	< 0.0001
	PIT vs controls	**2.55 (2.38–2.72)**	< 0.0001
Anxiety	PAI vs controls	**2.62 (2.09–3.30)**	< 0.0001
	CAH vs controls	**2.99 (2.02–4.42)**	< 0.0001
	PIT vs controls	**2.80 (2.59–3.02)**	< 0.0001
Hyperlipidaemia	PAI vs controls	**1.51 (1.23–1.84)**	< 0.0001
	CAH vs controls	**1.51 (1.04–2.19)**	0.0320
	PIT vs controls	**1.98 (1.84–2.12)**	< 0.0001
Hypertension	PAI vs controls	**1.53 (1.25–1.88)**	< 0.0001
	CAH vs controls	**2.03 (1.49–2.75)**	< 0.0001
	PIT vs controls	**2.24 (2.10–2.40)**	< 0.0001

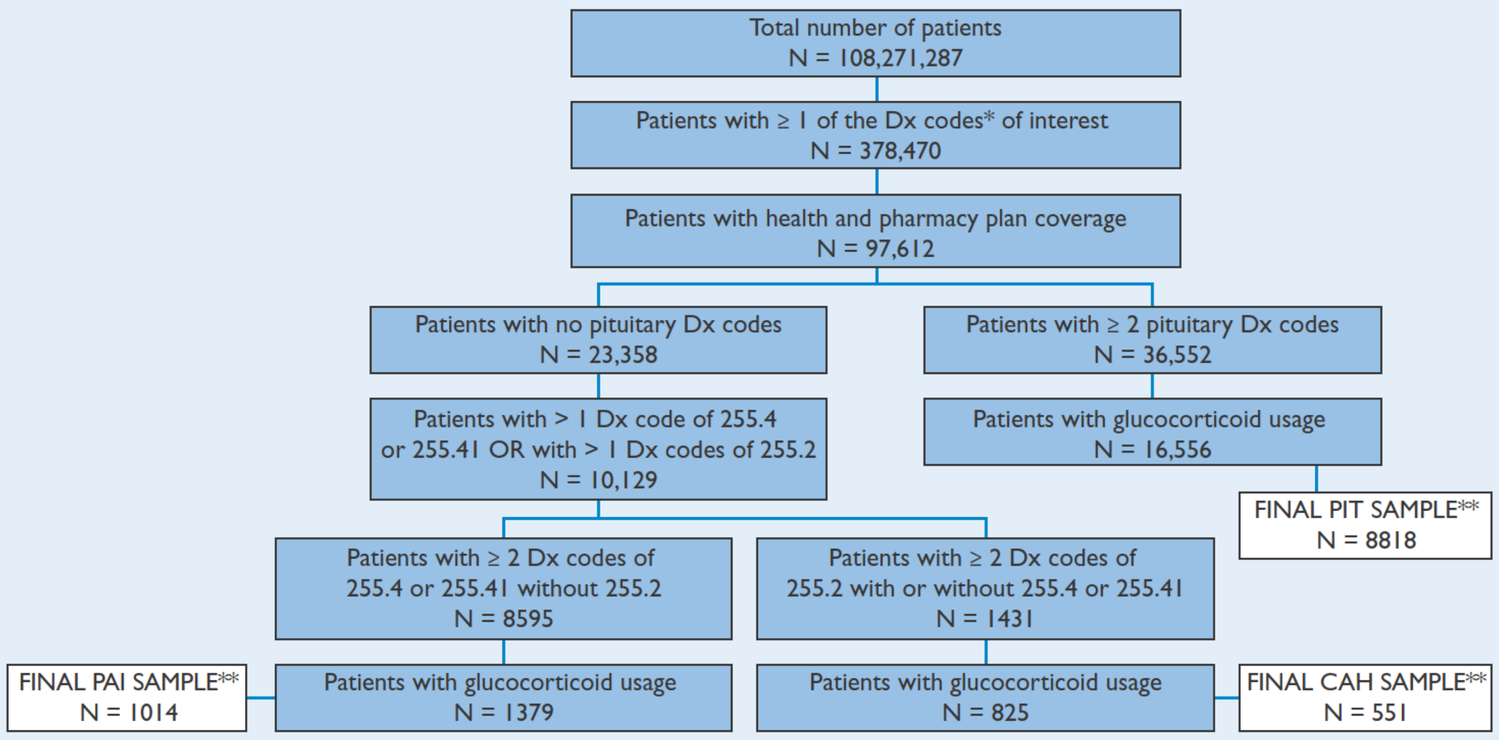
*Diabetes includes Type I or Type II.

Table 2. Inpatient admissions for AI cohorts compared with matched controls.

Comparison	AI estimate	Matched control estimate	Ratio
PAI vs controls*	0.69	0.15	4.64:1
PIT vs controls*	0.63	0.16	4:1

*p < 0.0001.
Inpatient admissions were not estimated for CAH owing to small sample size.

Figure 1. Attrition diagram.



*ICD-9 diagnosis (Dx) codes: 227.3, benign neoplasm of pituitary gland and craniopharyngeal duct; 237.0, neoplasm of uncertain behaviour of pituitary gland and craniopharyngeal duct; 239.7, neoplasm of unspecified nature of endocrine glands and other parts of nervous system; 253.2, panhypopituitarism; 253.4, other anterior pituitary disorders; 253.7, iatrogenic pituitary disorders; 253.8, other disorders of the pituitary and other syndromes of diencephalohypophyseal origin; 253.9, unspecified disorder of the pituitary gland and its hypothalamic control; 255.2, adrenogenital disorders; 255.4, corticoadrenal insufficiency; 255.41, glucocorticoid deficiency.
**Final AI samples matched to a general population cohort by age, gender, insurance type and region.

CONCLUSIONS

- Using data from > 10,000 adults with AI, the results of our study suggest that all types of AI carry a significant metabolic and psychiatric burden, with higher risk of comorbidities and hospital admissions compared with the general population sample.

Disclosures

PMS has received speaker fees from Shire and Novartis. BMKB has nothing to disclose. CM is an employee of Shire International GmbH. CG and MR are employees of CTI Clinical Trial and Consulting Services Inc., which is a paid consultant to Shire. GJ has received speaker's honoraria and grants from Novartis, Novo Nordisk, Pfizer and Sandoz, speaker's honoraria from Merck Serono and Otsuka, and consultancy fees from AstraZeneca and Shire.

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