

# Demographic Characterization of Patients Enrolled in the China Pituitary Disease Register Network

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To the Editor: Pituitary disease is a group of pituitary gland disorders, including pituitary adenoma and other lesions, in the sellar region.<sup>[1]</sup> Typical endocrine symptoms and mass effects are likely to have harmful results on patients, families, and society. Pituitary databases of various sizes and focuses have been established in the USA and Europe.<sup>[2-4]</sup> The vast territory, unbalanced economic development, uneven medical access, bias in awareness of the disease, and unsatisfactory data collection techniques have seriously affected the prognosis of patients with pituitary disease in China.<sup>[2]</sup> The China Pituitary Disease Register Network (CPDRN) was established in 2015 as the first multicenter, nationwide pituitary disease registry in China, aiming to resolve the abovementioned problems.<sup>[5]</sup> This article describes the establishment process and demographic baseline of the CPDRN.

The CPDRN was administered by the Peking Union Medical College Hospital (PUMCH) in 2015 and is accessible on the internet ([www.cpdn.cn](http://www.cpdn.cn)). As of February 2018, 32 provincial and national hospitals throughout China, which are all members of the Chinese Pituitary Adenoma Collaboration Group, have been enlisted. These are large pituitary centers performing over 100 pituitary operations annually.

The system is composed of software specifically designed based on the B/S structure and a database based on SQL Server 2012 software; the system can thereby support the automated data integration from third-party systems, including hospital information systems (HIS), laboratory information systems, radiology information systems, and electronic patient records. Case report forms (CRFs) were designed by the China Pituitary Adenoma Specialist Council.

The database permits patients who have undergone pituitary surgery and have been pathologically diagnosed since 2015 to be entered prospectively; the database also allows patient data to be entered retrospectively for cases diagnosed before 2015, via electronic medical records. The earliest case registered was diagnosed in 1978. Diagnoses include 14 categories of pituitary diseases.

Patients' demographics, diagnosis, initial evaluation, follow-up evaluation, details of treatment, and posttreatment evaluation have been uploaded. Laboratory and imaging findings included hormonal data, pituitary image findings, and visual acuity plus field. Treatment details included surgery, pathological results (pathological type, Ki-67, immunohistochemical staining, vimentin, CD34, p53, etc.), medical treatment, and radiotherapy. All clinical data were recorded in unified units. Data monitoring was done in the following two steps: an automatic logical audit carried out by software and a manual review carried out by experienced physicians.

We characterized the CPDRN patients according to their baseline demographics. Data were exported from the CPDRN database as Microsoft Excel files and were statistically analyzed using SPSS for Windows Version 22.0 (IBM Corp., NY, USA). Mean, standard deviation, median, minimum, and maximum values were calculated.

By March 2018, 14,414 patients from 32 centers were included in the analysis, among whom 42.78% (6167/14,414) were men and 57.22% (8247/14,414) were women, with the majority being Han Chinese (9282/9564, 95.99% among those recorded). The diagnosis dates ranged from 1978 to 2018, and age at diagnosis followed a normal distribution, with a mean age at initial diagnosis of  $44.2 \pm 14.3$  years and a follow-up time of 0.58 (0–35.68; median [range]) years.

The CPDRN database includes patients from 33 out of 34 of China's provinces. Among these, North China had the most

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patients (4215, 41.31%), while South China had the least patients (250, 2.45%). The geographical distribution of patients after 2008 gradually extended from North China to the other regions, consistent with an increasing number of centers.

Fourteen categories of pituitary disease were included in the CPDRN database. Pituitary adenoma was the most common diagnosis (14,193, 98.47%), among which nonfunctioning pituitary adenoma accounted for the largest proportion. Prolactin-secreting adenomas accounted for 15.02% of the total, which is lower than previously reported (44–59%). The initial treatment of prolactin-secreting adenomas was dopaminergic agonists, rather than neurosurgery.<sup>[6]</sup> Adrenocorticotropic hormone-secreting adenomas accounted for approximately 12.28% of all pituitary adenomas in the CPDRN, which is higher than the 1–7% reported in Finland; this outcome is related to PUMCH's expertise in Cushing's disease, which affects patients' choice of hospital.<sup>[6]</sup> Craniopharyngioma (95, 0.66%), Rathke's cleft cysts (74, 0.51%), hypophysitis (6, 0.04%), germinoma (3, 0.02%), pituitary carcinoma (44, 0.31%), and diabetes insipidus (1, 0.01%) were in the minority diagnoses, while no cases of histiocytosis have been entered in the registry [Table 1].

The registry is multicenter based instead of population based, and epidemiological data, including incidence and prevalence rates, cannot be obtained. Selection bias arises because those who volunteer to participate in a registry or who attend a specialty clinic that provides registry data may not be representative of the true population. Analytic techniques may be required to account for biases or for the complex sampling schemes encountered when using registry data. Other discrepancies come from variations in data quality acquired from the different centers. A total of 11,444 patients have no follow-up records, which points out insufficiencies in data collection. Requiring a follow-up plan being entered into the database after uploading the initial treatment is a promising solution. With a timespan from 1978 to 2018, the database contains changes not only in diagnostic criteria but also in diagnostic tools and all other aspects of medical care. Thus, we collected clinical data based on well-defined CRFs, including laboratory tests, imaging findings, and pathologic results, to make it possible to include cases with the original evidence.

In conclusion, as the first nationwide multicenter pituitary disease registry database, the CPDRN has effectively formed a network among Chinese centers to support the excellent medical treatment of pituitary disease; these centers now can serve the entire population and function at terminals or webnodes to recruit further neurosurgery and endocrinology centers from their respective parts of China.

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### Declaration of patient consent

The authors certify that they have obtained all appropriate consent

**Table 1: Etiological characteristics of patients from the CPDRN (N=14,412)**

Etiology	Male		Female		Total		
	n	Mean age (years)	n	Mean age (years)	Mean age (years)	n	Percentage (%)
Growth Hormone-Secreting Tumor	1377	40.0	1654	42.6	41.4	3031	21.03
Prolactin-Secreting Tumor	640	40.3	1492	33.4	35.5	2132	14.79
Gonadotropin-Secreting Tumor	368	53.7	170	52.3	53.3	538	3.73
ACTH-Secreting Tumor	349	33.1	1394	36.7	36.0	1743	12.09
Thyrotropin-Secreting Tumor	58	40.5	73	42.9	41.9	131	0.91
NFPA	3063	51.2	3089	49.1	50.2	6152	42.68
MEN	211	47.2	255	42.0	44.3	466	3.23
Hypophysitis	4	51.5	2	41.0	47.6	6	0.04
Rathke's Cleft Cyst	22	50.5	52	45.3	46.9	74	0.51
Craniopharyngioma	47	35.6	48	35.1	35.3	95	0.66
Pituitary Carcinoma	25	48.0	19	41.1	45.1	44	0.31
Germinoma	1	13.0	2*	17.0	38.3	3	0.02
Diabetes insipidus			1†	45.0	45.0	1	0.01

CPDRN: China Pituitary Disease Register Network; ACTH: Adrenocorticotrophic hormone; NFPA: Nonfunctioning pituitary adenoma; MEN: Multiple endocrine neoplasia. \*One of the germinoma patients was diagnosed Rathke's cleft cyst at the same time. †Diagnosed Rathke's cleft cyst at the same time.

forms from all patients. By signing the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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