

# Multicenter study on the genetic screening and diagnosis of deafness in China

<b>Submission date</b> 27/05/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/06/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 11/06/2020	<b>Condition category</b> Genetic Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

According to the data of the national survey in 2006, there are about 27.8 million hearing and speech-disabled people in China, and about 700,000-800,000 hearing-impaired children under 7 years old. One in every 500 newborns has bilateral permanent deafness. Before the age of 5, the incidence of deafness increases to 2.7%, and to 3.5% in adolescence. Research shows that more than 60% of pre-lingual deafness is caused by genetic factors, and the rest is caused by environment or other unknown genetic factors.

As the first genetic hearing loss molecular diagnosis center in China, the genetic deafness molecular diagnosis center of PLA General Hospital has been established for 15 years. A series of achievements have been made in the research of the causes of deafness, discovery of new genes, the molecular epidemiology of deafness in the Chinese population, clinical gene diagnosis and prenatal diagnosis.

The emergence of next-generation sequencing has achieved high throughput and low cost, which brings a broad prospect for the field of gene diagnosis. At present, many gene testing institutions in China have carried out deafness gene testing services, mainly for the most common 3-4 hotspot mutation chips of deafness gene in Chinese population, and 129-167 deafness gene sequencing services. According to the research results of the researchers' center, four common gene mutations can explain about 40% of the causes of deafness, while the detection rate can rise to about 50% - 55% when the detection range is extended to more than 129 deafness genes by high-throughput sequencing technology. Although the improvement of diagnosis rate makes more deaf families or high-risk families obtain genetic consultation and prevention guidance, the promotion and implementation of deafness gene diagnosis and prenatal diagnosis in China still face a series of problems. The testing quality level of testing institutions is uneven, with a lack of standards. The testing report has not yet formed a standard, and the interpretation of variants is not clear. Testing institutions and clinical doctors give inaccurate genetic consultations. There is a lack of a referral and consultation system and process for difficult cases, and a lack of a biological database for deafness in China. The above deficiencies have greatly affected the summary of deafness molecular big data, the guidance of deafness family reproduction and the accurate treatment evaluation of deaf patients. Therefore, the PLA general hospital takes the lead in launching the clinical multicenter research project of deafness gene diagnosis, cooperating with domestic deafness gene testing institutions such as the medical institutions of major provinces and autonomous regions,

MyGenostics Inc.; GrandOmics Inc.; WuXi NextCODE Inc.; Capital Genomics Inc. This multicenter study aims to draw a gene map of Chinese people by collecting 10,000 genetic samples; develop clinical consensus/guidelines for the diagnosis of genetic deafness; standardize deafness gene test, report interpretation and genetic consultation; and upgrade the deafness gene test panel.

**Who can participate?**

Patients with congenital hearing loss or late-onset hearing loss and their families, or patients with acquired sensorineural hearing loss and their families, and hearing normal individuals with a family history of deafness.

**What does the study involve?**

Patients will take hearing tests, a CT scan and, if necessary, a general examination (thyroid ultrasound, kidney ultrasound, electrocardiogram, chest, abdomen, limbs X-ray, cranial MRI, etc). The researchers collect patients' and their family's medical record information, and collect their blood samples. The genetic testing institution completes the gene test and preliminary data analysis, and the original data will be sent to the designated cloud platform of multicenter for verification and further analysis. The test report will be issued by the testing institution, and approved by the PLA General Hospital and/or qualified sub-centre experts. The PLA General Hospital and the clinical experts of the sending unit will jointly provide patients with genetic consultation. For the cases with suspected pathogenic mutations, the testing institution will provide follow-up research programs. For the cases with no or suspected pathogenic mutation, the leading units of multiple centers will analyze the data again, and discuss the follow-up research plan through regular case discussion and academic activities.

**What are the possible benefits and risks of participating?**

Taking part in this study can help patients to reduce the risk of deafness in their offspring. It should be noted that this study can not completely exclude the risk of deafness in the next generation, such as pregnancy infection, other environmental factors or rare unknown deafness caused by genetic defects. If the report result is negative, senior experts will re-analyze the report, except for false negatives. If it is positive, it will be verified free of charge, except for false positives. Difficult and complex cases will be provided with priority referral and consultation channels.

**Where is the study run from?**

Genetic Deafness Molecular Diagnosis Center, PLA General Hospital, Beijing, China

**When is the study starting and how long is it expected to run for?**

September 2018 to August 2022

**Who is funding the study?**

Investigator initiated and funded

**Who is the main contact?**

Prof. Pu Dai

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Prof. Yongyi Yuan

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**Study website**

Nil known

# Contact information

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# Additional identifiers

## EudraCT/CTIS number

Nil known

## IRAS number

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

ChiCTR1800018223

## **Study information**

**Scientific Title**

Clinical demonstration for three-level prevention intervention of birth defect on monogenic disease (deafness)

**Study objectives**

The main purpose of this multicenter study is to draw a gene map of Chinese people by collecting 10,000 genetic deafness samples and develop clinical consensus/guidelines for the diagnosis of genetic deafness.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 26/7/2018, ethical review board of PLA General Hospital (Fuxing Road 28, Beijing, China; +86 (0)10 66937166; 301irb@sina.com), ref: S2018-088-01

**Study design**

Multicenter observational epidemiological study

**Primary study design**

Observational

**Secondary study design**

Epidemiological study

**Study setting(s)**

Hospital

**Study type(s)**

Screening

**Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

**Health condition(s) or problem(s) studied**

Genetic deafness

**Interventions**

The patients and their families will provide blood samples. Next-generation sequencing and Sanger sequencing will be carried out on the samples. The testing institution will analyze

preliminary data. The PLA General Hospital and the clinical experts of the sending unit will jointly provide patients with genetic consultation. For the cases with suspected pathogenic mutations, the testing institution will provide follow-up research programs. For the cases with no or suspected pathogenic mutation, the leading units of multiple centers will analyze the data again, and discuss the follow-up research plan.

## **Intervention Type**

Other

## **Primary outcome measure**

1. Number of cases in the database of genetic deafness patients in China at 5 years
2. Gene map of genetic deafness patients in China measured using the coverage of pathogenic variant on genetic deafness in the public database at 5 years

## **Secondary outcome measures**

1. Genetic deafness panel measured using coverage and accuracy of pathogenic variant on genetic deafness in the public database at 5 years
2. Guidelines of screening and diagnosis for genetic deafness patients in China measured using the published journal articles at 5 years

## **Overall study start date**

09/01/2018

## **Completion date**

31/08/2022

# **Eligibility**

## **Key inclusion criteria**

1. Congenital hearing loss or late-onset hearing loss and their families
2. Patients with congenital malformation of auditory organ and their families
3. Acquired sensorineural hearing loss patients and their families
4. Hearing normal individuals with a family history of deafness

## **Participant type(s)**

Mixed

## **Age group**

All

## **Sex**

Both

## **Target number of participants**

10000

## **Key exclusion criteria**

1. The patients and their families who refused to participate in the program after receiving the education by doctors
2. The patients with deafness caused by non-genetic factors were definitely diagnosed

**Date of first enrolment**

09/01/2018

**Date of final enrolment**

31/08/2022

## **Locations**

**Countries of recruitment**

China

**Study participating centre****Chinese PLA General Hospital**

Fuxing Road 28, Haidian District

Beijing

China

100853

**Study participating centre****China Rehabilitation Research Center for Hearing and Speech Impairment**

A 8 Huixinli, Chaoyang District

Beijing

China

100029

**Study participating centre****The General Hospital of the PLA Rocket Force**

16 xinjiekouwei st, Xicheng District, Beijing

Beijing

China

100088

**Study participating centre****Beijing Children's Hospital of Capital Medical University**

56 Nanlishi Road, Xicheng District

Beijing

China

100045

**Study participating centre**

**China-Japan Friendship Hospital**

Yinghuayuan East st, Chaoyang District  
Beijing  
China  
100029

**Study participating centre**

**Beijing Tongren Hospital of Capital Medical University**

1 Dongjiaomin Lane, Dongcheng District  
Beijing  
China  
100730

**Study participating centre**

**Peking University First Hospital**

8 Xishiku St, Xicheng District  
Beijing  
China  
100034

**Study participating centre**

**Bo GaoPeking University Third Hospital**

49 Huayuan North Road, Haidian District  
Beijing  
China  
100191

**Study participating centre**

**Peking Union Medical College Hospital**

41 Damucang Hutong, Xicheng District  
Beijing  
China  
100032

**Study participating centre**

**Beijing Friendship Hospital of Capital Medical University**

95 Yong'an Road, Xicheng District  
Beijing  
China  
100050

**Study participating centre**

**Shanghai Ninth People's Hospital**

No. 639, Manufacturing Bureau Road, Huangpu District  
Shanghai  
China  
200011

**Study participating centre**

**Fujian Medical University ShengLi Clinical College, Fujian Provincial Hospital**

134 East Street  
Fuzhou  
China  
350001

**Study participating centre**

**Union Hospital Tongji Medical College Huazhong University of Science and Technology**

1277 Jiefang Avenue  
Wuhan  
China  
430022

**Study participating centre**

**The First Affiliated Hospital of UTSCAnhui Provincial Hospital**

17 Lujiang Road  
Hefei  
China  
230001

**Study participating centre**

**XiangYa Hospital CentralSouth University**

87 Xiangya Road  
Changsha  
China  
410008

**Study participating centre**

**Nanfang Hospital**

1838 North Guangzhou Avenue  
Guangzhou



China  
510515

**Study participating centre**

**Maternal and Child Health Care Hospital of Guangdong Province**

521 Xingnan Avenue, Panyu District

Guangzhou

China

511400

**Study participating centre**

**Tianjin First Central Hospital**

24 Fukang Road, Nankai District

Tianjin

China

300192

**Study participating centre**

**Precision medicine research center of Zhengzhou University / precision medicine application center of the Second Affiliated Hospital of Zhengzhou University**

No. 40, Daxue Road, Erqi District

Zhengzhou

China

450000

**Study participating centre**

**Henan Provincial People's Hospital, Department of Otolaryngology Head and Neck**

No.7, Weiwu Road

Zhengzhou

China

450003

**Study participating centre**

**Hebei Medical University Second Hospital**

215 Heping West Road

Shijiazhuang

China

050000

**Study participating centre**  
**Maternal and Child Health Care Hospital of Tangshan**  
1 Hetai Road, Lunan District  
Tangshan  
China  
63017

**Study participating centre**  
**Children's Hospital of Hebei Province**  
133 Jianhua South Street, Yuhua District  
Shijiazhuang  
China  
050030

**Study participating centre**  
**Shandong ENT Hospital Affiliated to Shandong University**  
4 Duanxing West Road, Huaiyin District  
Jinan  
China  
250022

**Study participating centre**  
**Jinan Maternal and Child Care Hospital**  
No.2, Jianguo Xiaojing 3rd road  
Jinan  
China  
250000

**Study participating centre**  
**Children's Hospital of Nanjing Medical University**  
72 Guangzhou road, Gulou District  
Nanjing  
China  
210000

**Study participating centre**  
**Zhenjiang Maternal and Child Care Hospital**  
20 Zhengdong Road  
Zhenjiang  
China  
212001

**Study participating centre**  
**The Affiliated Hospital of Guizhou Medical University**  
28 Guiyi street  
Guiyang  
China  
550004

**Study participating centre**  
**First Affiliated Hospital of Kunming Medical University**  
295 Xichang Road  
Kunming  
China  
650032

**Study participating centre**  
**Lanzhou University Second Hospital**  
No. 82, cuiyingmen, Chengguan District  
Lanzhou  
China  
730030

**Study participating centre**  
**First Affiliated Hospital of Air Force Military Medical University**  
169 Changle West Road  
Xian  
China  
710032

**Study participating centre**  
**First Affiliated Hospital of Anhui Medical University**  
218 Jixi Road  
Hefei  
China  
230000

**Study participating centre**  
**Hefei BOE Hospital**  
Intersection of Dongfang Avenue and Wenzhong Road, Xinzhan District

Hefei  
China  
230013

**Study participating centre**

**Second Affiliated Hospital of Anhui Medical University**

No. 678, Furong Road, Hefei Economic and Technological Development Zone  
Hefei  
China  
230601

**Study participating centre**

**Jilin University Second Hospital**

218 Ziqiang street, Nanguan District  
Changchun  
China  
130041

**Study participating centre**

**The Fourth Affiliated Hospital of China Medical University**

4 Chongshan East Road, Huanggu District  
Shenyang  
China  
110032

**Study participating centre**

**Yanbian University Hospital**

Juzi Street 1327  
Yanji  
China  
100191

**Study participating centre**

**Shenyang Women's and Children's Hospital**

No. 87, Danan street, Shenhe District  
Shenyang  
China  
110011

**Study participating centre**

**The First Affiliated Hospital of China Medical University**

No. 155, Nanjing North Street, Heping District

Shenyang

China

110001

**Study participating centre**

**The Children's Hospital, Zhejiang University School of Medicine**

57 Zhugan lane

Hangzhou

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310003

**Study participating centre**

**Maternal and Child Health Hospital of Liuzhou**

66 Sanzhong Road

Liuzhou City

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**Study participating centre**

**The People's Hospital of Guangxi Zhuang Autonomous Region**  
**Department of Otolaryngology**  
**Head and Neck**

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Nanning City

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**Study participating centre**  
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2 Gonghe Road, Chengdong District  
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810007

**Study participating centre**  
**General Hospital of Ningxia Medical University**  
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**The Affiliated Hospital of Inner Mongolia Medical University**  
No.1, North Tongdao Road  
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**Study participating centre**  
**The First Affiliated Hospital of Nanchang University**  
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Nanchang  
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**Study participating centre**  
**The First Hospital Affiliated to AMUSouthwest Hospital**  
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Chongqing  
China  
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**Study participating centre**

**Guangdong Second Provincial General Hospital**

466 Xingang Middle Road, Haizhu District

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No. 3004, Longgang Section, Longgang Avenue, Longgang District

Shenzhen

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Ningbo

China

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**Study participating centre**

**Shaoxing Women and Children's Hospital, Department of Children Healthcare**

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China

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**Ningbo First Hospital, Molecular diagnostic center**

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Ningbo

China

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**Women's Hospital School of Medicine Zhejiang University**

No.1 Bachelor Road

Hanzhou

China

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**Study participating centre**

**Zhejiang Provincial Hospital of TCM, Department of Otolaryngology Head and Neck**

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**Study participating centre**

**Henan Children's Hospital**

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**Study participating centre**

**Qingdao Women and Children's Hospital**

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China

266034

**Study participating centre**

**Ningxia Rehabilitation Center for the Disabled**

115 Hupan Road, Jinfeng District

Yinchuan

China

750002

**Study participating centre**

**Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University**

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Guangzhou

China

510080

**Study participating centre**

**Gansu maternity and child-care hospital**

143 Qilihe North Street



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China  
730050

**Study participating centre**  
**Haidian Maternal and Child Health Hospital**  
33 Haidian South Road, Haidian District  
Beijing  
China  
100080

**Study participating centre**  
**Shenyang No.4 People's Hospital**  
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China  
110031

**Study participating centre**  
**Henan Institute of Reproductive Health Science And Technology**  
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450014

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China  
570102

**Study participating centre**  
**The Second Hospital of Shandong University**  
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Jinan  
China  
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**The First Affiliated Hospital of Soochow University**  
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Suzhou  
China  
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China  
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**Xuanwu Hospital Capital Medical University**  
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Beijing  
China  
100053

**Study participating centre**  
**Baoding Children's Hospital**  
103 Baihua East Road  
Baoding  
China  
071051

**Study participating centre**  
**Qilu Hospital of Shandong University**  
107 Wenhua West Road  
Qingdao  
China  
250012

**Study participating centre**  
**The Affiliated Hospital of Qingdao University**  
16 Jiangsu Road, Shinan District  
Qingdao  
China  
266000

**Study participating centre**

**980 Hospital of the joint service support force of the Chinese People's Liberation Army**

398 Zhongshan West Road, Qiaoxi District

Shijiazhuang

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## **Sponsor information**

**Organisation**

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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.plagh.cn>

**ROR**

<https://ror.org/04gw3ra78>

## **Funder(s)**

**Funder type**

Other

**Funder Name**

National key research and development project (2016YFC1000700)

## **Results and Publications**

**Publication and dissemination plan**

1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website

**Intention to publish date**

01/09/2023

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Pu Dai (daipu301@vip.sina.com), Prof. Yongyi Yuan (yyymzh@163.com) and Dr Bo Gao (imjd@163.com). The next-generation sequencing data for genetic deafness can be shared with groups who would like to participate in the trial during the research, and all data will be submitted to the public database (e.g ClinVar) in 3 years after the the end of the trial.

**IPD sharing plan summary**

Data sharing statement to be made available at a later date