ISRCTN10768387 https://doi.org/10.1186/ISRCTN10768387

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

Submission date 27/05/2020	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 16/06/2020	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 11/06/2020	**Condition category** Genetic Diseases	[ ] Individual participant data [ ] 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
daipu301@vip.sina.com
Prof. Yongyi Yuan
yyymzh@163.com

Contact information

Type(s)

Scientific

Contact name
Prof Pu Dai

Contact details
Fuxing Road 28
Beijing
China
100853
+86 (0)13910213511
daipu301@vip.sina.com

Type(s)
Scientific

Contact name
Prof Yongyi Yuan

Contact details
Fuxing Road 28
Beijing
China
100853
+86 (0)13811502776
yyymzh@163.com

Type(s)
Scientific

Contact name
Dr Bo Gao

Contact details
Fuxing Road 28
Beijing
China
100853
+86 (0)18515902036
imjd@163.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

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

Study type(s)
Screening

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(s)
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

Key secondary outcome(s))

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

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

Healthy volunteers allowed
No

Age group
All

Sex
All

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 Heath 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 Heath 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
China
310003

Study participating centre
Maternal and Child Health Hospital of Liuzhou
66 Sanzhong Road
Liuzhou City
China
545001

Study participating centre
The People‘s’ Hospital of Guangxi Zhuang Autonomous RegionDepartment of Otolaryngology Head and Neck
6 Taoyuan Road
Nanning City
China
530000

Study participating centre
Second Hospital of Shanxi Medical University
No. 382, Wuyi Road
Taiyuan City
China
030001

Study participating centre
Xinjiang Viger Municipal People's Hospital
No.91, Tianchi Road, Tianshan District
Urumqi City
China
830001

Study participating centre
Qinghai Provincial People's Hospital
2 Gonghe Road, Chengdong District
Xining
China
810007

Study participating centre
General Hospital of Ningxia Medical University
804 Shengli South Street, Xingqing District

Yinchuan
China
750004

Study participating centre
The Affiliated Hospital of Inner Mongolia Medical University
No.1, North Tongdao Road
Hohhot
China
010000

Study participating centre
The First Affiliated Hospital of Nanchang University
17 Yongwaizheng Street
Nanchang
China
330006

Study participating centre
The First Hospital Affiliated to AMUSouthwest Hospital
30 Yanzheng Street, Gaotan, Shapingba District
Chongqing
China
630038

Study participating centre
Guangdong Second Provincial General Hospital
466 Xingang Middle Road, Haizhu District
Guangzhou
China
510317

Study participating centre
Shenzhen Longgang Otolaryngology Hospital
No. 3004, Longgang Section, Longgang Avenue, Longgang District
Shenzhen
China
518001

Study participating centre
Ningbo Women and Children's Hospital, Department of Otolaryngology Head and Neck
266 cishui West Street, Cicheng new town, Jiangbei District
Ningbo
China
315031

Study participating centre
Shaoxing Women and Children's Hospital, Department of Children Healthcare
305 East Street
Shaoxing
China
312000

Study participating centre
Ningbo First Hospital, Molecular diagnostic center
59 Liuting Street
Ningbo
China
315010

Study participating centre
Women's Hospital School of Medicine Zhejiang University
No.1 Bachelor Road
Hanzhou
China
310006

Study participating centre
Zhejiang Provincial Hospital of TCM, Department of Otolaryngology Head and Neck
54 Youdian Road, Shangcheng District
Hanzhou
China
310006

Study participating centre
Henan Children's Hospital
No. 255, Gangdu Street
Zhengzhou
China
450007

Study participating centre
Qingdao Women and Children's Hospital
6 Tongfu Road, Shibei District
Qingdao
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
No. 58, Zhongshan 2nd Road
Guangzhou
China
510080

Study participating centre
Gansu maternity and child-care hospital
143 Qilihe North Street
Lanzhou
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
20 Huanghe South St, Huanggu District

Shenyang
China
110031

Study participating centre
Henan Institute of Reproductive Health Science And Technology
26 Jingwu Road, Jinshui District
Zhengzhou
China
450014

Study participating centre
The First Affiliated Hospital of Hainan Medical University
31 Longhua Road
Haikou
China
570102

Study participating centre
The Second Hospital of Shandong University
247 Beiyuan Street
Jinan
China
250033

Study participating centre
The First Affiliated Hospital of Soochow University
No. 899, Pinghai Road
Suzhou
China
215006

Study participating centre
The Affiliated Children's Hospital of Soochow University
No.92 Zhongnan street, Suzhou Industrial Park
Suzhou
China
215021

Study participating centre
Xuanwu Hospital Capital Medical University
45 Changchun Street, Xicheng District
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
China
050082

Sponsor information

Organisation
Chinese PLA General Hospital

ROR
https://ror.org/04gw3ra78

Funder(s)

Funder type
Other

Funder Name
National key research and development project (2016YFC1000700)

Results and Publications

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes