Genetic services and testing in China

Xinliang Zhao · Peirong Wang · Xuguang Tao ·
Nanbert Zhong

Received: 2 October 2012 / Accepted: 22 February 2013 / Published online: 18 April 2013
© Springer-Verlag Berlin Heidelberg 2013

Introduction

China is the most populous country in the world, with over 1.3 billion citizens. Public health care in China has been rapidly improved during the last 30 years. Health care in China became largely public and easy accessible. Despite significant improvements in health care and the introduction of western style medical facilities, China has several emerging public health difficulties, including respiratory disorders as a result of widespread air pollution and unbalanced distribution and development of public health care facilities.

X. Zhao · P. Wang · X. Tao · N. Zhong
Peking University Center of Medical Genetics,
Peking University Health Science Center, Beijing, China

X. Zhao
Department of Biochemistry, PLA General Hospital, Beijing,
China

P. Wang
Institute of Biophysics, Chinese Academy of Sciences, Beijing,
China

X. Tao
Institute of Basic Theory,
China Academy of Chinese Medicine Science, Beijing, China

N. Zhong
Shanghai Children's Hospital, Shanghai, China

N. Zhong
New York State Institute for Basic Research in Developmental
Disabilities, Staten Island, NY, USA

N. Zhong (✉)
Department of Human Genetics, New York State
Institute for Basic Research in Developmental Disabilities,
1050 Forest Hill Road,
Staten Island, NY 10314, USA
e-mail: nanbert.zhong@opwdd.ny.gov

Demography and population health indicators

China ranges from mostly plateaus and mountains in the west to lower lands in the east. The economy of China is the world's second largest after the USA, with a nominal gross domestic product (GDP) of \$4.99 trillion and purchasing power parity (PPP) of \$8.77 trillion in 2009. China is the world's fastest-growing major economy, with an average growth rate of 10 % for the past 30 years (China 2010c).

China consists of 23 provinces, 4 municipalities, and 5 autonomous regions (ATR), and 2 special administrative regions that are Hong Kong and Macao. China has been the world's most populous nation for many centuries. When China took its first post-1949 census in 1953, the population stood at 582 million (China 1954); by the fifth census in 2000, the population had more than doubled, reaching 1.3 billion (China 2001). The demographics of China are identified by a large population with a relatively small youth division (Table 1), which is partially a result of the Chinese one-child policy (Silva 2006).

By 2005, the life expectancy increased to 70 for males and 74 for females (China 2006). The adult mortality rate has dropped from 35 per 1,000 in 1990 to 7.06 per 1,000, while the neonatal mortality rate has dropped to 8.74 per 1,000 live births (China 2008), and the mortality of children under 5 has also been reduced to 10.2 per 1,000 (China 2009a).

Health expenditures and financing

As the overall health market in China quickly grew to 161 billion USD by 2007 (China 2007a), the public expenditure for health care in 2009 was 18 billion USD. This constitutes 2.9 % of total government expenditures (China 2010b). Private expenditure on health care contributed 45.2 % of the total expenditure on health in 2007. Forty-five percent of health care costs was provided by private funds, 34.5 % by

Table 1 Demographical information

Population		1,346,227,885 (China 2009d)
Population density		137.0 people per km ² (China 2009d)
Age structure (China 2009d)	0–14	19.8 % (male 140,877,745/female 124,290,090)
	15–64	72.1 % (male 495,724,889/female 469,182,087)
	65 and over	65 years and over 8.1 % (male 51,774,115/female 56,764,042)
Population growth rate		0.606 % (China 2007d)
Birth rate		13.45 births/1,000 population (China 2007a)
Death rate		7 deaths/1,000 population (China 2007a)
Net migration rate		–0.39 migrant(s)/1,000 population (China 2007a)
Sex distribution		Male 51.53 %; female 48.47 % (China 2007a)
Sex ratio	At birth	1.11 male(s)/female (China 2007a)
	Under 15 years	1.134 male(s)/female (China 2007a)
	15–64 years	1.057 male(s)/female (China 2007a)
	65 years and over	0.914 male(s)/female (China 2007a)
	Total population	1.06 male(s)/female (China 2007a)
Infant mortality	Total	22.12 deaths/1,000 live births (China 2007a)
	Male	20.01 deaths/1,000 live births (China 2007a)
	Female	24.47 deaths/1,000 live births (China 2007a)

insurance, and 20.5 %, by central/local government funds (China 2008).

Antenatal medical care coverage 99.99 % of the population in 2009, 78 % of mothers received postnatal care in 2009. The deliveries (5.51 %) were home deliveries or carried out in unregistered clinics. The women (90.96 %) made at least 1 visit to hospitals before delivery, and 3.53 % of pregnant women delivering at hospitals never visited hospitals during pregnancy. Total births (94.49 %) were attended by skilled health professionals in 2008. The attended delivery rate was 97.45 % in the urban areas, and it was 92.32 % in rural areas (China 2009a).

Indicators of congenital/genetic “disease burden”

There are three national surveillance programs for birth defects and maternal and neonatal health: National Statistic of Health (assessed annually by the Ministry of Health), National Birth Registry (assessed by the Ministry of Public Security annually), and National birth defect registry (assessed by the Ministry of Health and National Population and Family Planning Commission annually). These surveillance networks were established in 1986. The information collected by these databases includes basic health indicators for infants and mothers. The period monitored by the National birth defect registry is from 7 days to 28 weeks after birth.

Nationwide population-based figures for all monitored birth defects was 5.6 % for 2011, and the overall number of birth defects identified during neonatal period rose from 109.79/10,000 for the year 2000 to 153.23/10,000 for 2011 (China 2012c). As shown in Table 2, congenital heart disorder (CHD), polydactyly, cleft lip/palate, neural tube defect, and

hydrocephaly were included in the top ten common malformations between years 2000 and 2011. Notably, CHD accounts for 26.7 % of all birth defects identified (China 2012c).

The incidence for these common malformations differs between urban and rural areas (Table 3). Unlike the situation for NTD and limb reduction, the urban incidence of CHD is nearly twice as high as the rural.

The commonly occurring single gene recessive disorders for China include phenylketonuria (PKU), congenital hypothyroidism (CH), glucose-6-phosphate dehydrogenase (G6PD) deficiency, and thalassemia.

PKU and CH are the two conditions in the national mandatory newborn screening program of China. Two separate large scale epidemiological research studies revealed similar results regarding the incidences of PKU which are 1/13,699 (Wang 2011) and 1/11680 (Li 2011). The national neonatal screening unit also published that the incidence of CH is higher in China (1/2,033) than in the USA (1/3,000–4,000), and Japan (1/7,000; Li 2011).

G6PD deficiency and thalassemia exhibited huge geographical variation. The China Ministry of Health (MOH) has not published national incidence or prevalence of these disorders, as the prevalence is much higher in southern China (Guangxi, Hainan, Yunnan, Guangdong and Guizhou province). Many studies has shown that the carriers for either G6PD deficiency and thalassemia weight 5 % or more in southern China (Table 4), and in some areas the carrier frequency can be over 20 % (China 2012c).

Generally chromosomal abnormalities are responsible for about 85 % of miscarriages in China (Zhang et al. 2009). The most common chromosomal disorder in live births in China is Down syndrome (Zhu 2011). The national incidence for

Table 2 The incidence of major congenital malformations in China (China 2012c)

Order	Year		2000		2005		2010		2011	
	Type	In	Type	In	Type	In	Type	In	Type	In
1	Cleft lip/palate	14.50	Cleft lip/palate	14.04	CHD	23.96	CHD	28.82	CHD	40.95
2	NTD	13.60	Polydactyly	12.45	Polydactyly	14.66	Polydactyly	15.91	Polydactyly	16.73
3	Polydactyly	9.20	NTD	11.96	Cleft lip/palate	13.73	Cleft lip/palate	13.17	Cleft lip/palate	11.43
4	Hydrancephaly	6.50	CHD	11.40	NTD	8.84	NTD	6.48	Hydrancephaly	5.47
5	CHD	6.20	Hydrancephaly	7.10	Hydrancephaly	7.52	Hydrancephaly	6.00	Club foot	5.17
6	Limb reduction	5.21	Limb reduction	5.79	Limb reduction	5.76	Club foot	5.08	Hypospadias	5.03
7	Club foot	4.69	Club foot	4.97	Hypospadias	5.24	Hypospadias	4.87	Dactylosymphysis	4.88
8	Hypospadias	3.08	Hypospadias	4.07	Club foot	5.06	Dactylosymphysis	4.81	NTD	4.50
9	Dactylosymphysis	3.08	Dactylosymphysis	3.95	Dactylosymphysis	4.94	Limb reduction	4.74	Limb reduction	4.09
10	Microtia	2.86	ARMS	3.43	Microtia	3.60	Microtia	3.09	Microtia	2.79

In incidence, in 1/10,000 units, CHD congenital heart disorder, NTD neural tube defect, ARMS anorectic malformations

Down syndrome 4.7/10,000. The incidence of Down syndrome seems higher in urban areas than rural and mountainous areas (Xia et al. 2006), and this is due to low recognition, resulting from limited healthcare and diagnostic service in rural and mountainous areas, especially in south-western China. Mid-term maternal screening and ultrasound screening for Down syndrome and other severe congenital malformations are performed for every pregnant woman in developed regions as a national mandatory program that allows 65 % (on average speaking) of Down syndrome identification during pregnancy (Zhu 2011). Although advanced maternal age greatly increases the incidence of Down syndrome, over half of the babies with Down syndrome were born to mothers under 30 (Rosen and D'Alton 2005).

Various disorders that have a genetic component only become apparent later in life. Due to the lack of awareness and incompetence in recognition, little data are available on these conditions, locally; Table 5 shows the prevalence of a few such disorders in China.

Percentage of all infant deaths due to congenital/genetic disorders

The overall rate of infant death in China is 0.9 % and for children under 5, the rate is 1.72 % (China 2010a). The detailed percentage of all infant deaths due to congenital/genetic disorders is shown in Table 6 (China 2012c).

Estimated potential for reducing the proportion of infant deaths due to congenital and genetic disorders

Dietary supplementation of folic acid greatly reduced incidence of NTD by over 62.3 % in China, especially in rural areas (72.7 %; China 2012c). Additionally salt iodinate supplementation also resulted in a drop of thyroid disease. Prenatal detection of CHD by ultrasonography allows early intervention via surgery. Newborn screening for PKU also allows early intervention of dietary treatment. The government initiated the PKU medical care scheme, providing free phenylalanine-free food for affected children.

Increased exposure to known risk factors that impact the incidence of congenital/genetic disorders at birth

One of the most common teratogens identified in the country is cigarette smoke. The males (52.9 %) and 2.4 % of females are addicted to cigarette smoke, and 72 % of the non-smokers are endangered by passive smoking (China 2010a). It has been clearly shown that both active and passive smoke could link to still birth, miscarriage, cleft lip, and/or palate (China 2010a). Other teratogens associated with birth defects include syphilis, rubella infection, pesticides, epilepsy medications, radiation, and various chemical pollutions.

Table 3 The differences of incidence of common malformations between urban and rural areas (China 2012c)

Birth defects	2000			2011		
	Urban	Rural	National	Urban	Rural	National
NTD	6.82	24.28	11.96	2.42	6.61	4.50
CHD	12.30	9.22	11.44	54.30	27.38	40.95
Limb reduction	5.60	6.31	5.81	3.61	4.57	4.09

The incidence is in 1/10,000 units

Estimate of how (increased) life expectancy, changes in life styles etc. will impact the prevalence of chronic diseases with a known genetic component

According to the annual MOH 2008 report, 98 % (China 2009a) of the urban people older than 65 was suffering from one or several chronic disorders. Comparatively, the figure was 82 % in 1993 (China 1994a).

Availability of genetic services

Initially, prenatal and cytogenetic diagnostic programs began to be developed in the 1960s but were suspended by the riot of The Great Cultural Revolution until the 1970s. By then, advanced cytogenetic and molecular genetic services were gradually developed. Informal genetic counseling services began in the Hunan Province of China in 1973. At about the same time, chromosome laboratory studies had been initiated, and thereafter, genetic research laboratories were developed in some institutes and universities (Li et al. 1983). In 1978, a series of training sessions for chromosome testing were held, and many cytogenetic laboratories were established afterwards. The first practice for molecular genetic diagnosis occurred in the mid 70s in Shanghai. This was the 1st stage of the development of medical genetic service in China. The second period was around the 1990s, when many institutions began to establish genetic laboratories. By the time of the 2nd national conference for medical genetics in 1992, genetic tests were available for over 20 genetic disorders, including Down

syndrome and other chromosomal abnormalities, thalassemia, hemophilia, Huntington Disease, Duchene muscular dystrophy, spinal muscular atrophy, spinal cerebellum atrophy, and: PKU. The 3rd stage of development was after 2000, with the promotion of government regulations and many professional guidelines which standardize the medical genetic services. In this period, the style of development shifted from non-governmental voluntary to governmental mandatory. To comply with governmental regulations, the diagnostic service provider was changed from institutions to the public health system. Currently, nearly all maternal and child health hospitals and all tier three hospitals are able to perform karyotyping and provide basic genetic counseling services. Some major metropolitan area hospitals utilized their financial and technical resources to set up genetic labs for indigenous diseases. In recent years, research institutions and universities are also joining in to play a role of developing new approaches and technology for detecting genetic diseases.

The increasing governmental awareness of prevention/intervention of birth defects and nation-wide surveillance will lead to faster development in the area of medical genetic service, and thus greatly benefit the public. Table 7 below shows the key genetic services available in China for different health purposes and in different types of settings. Genetic testing is now available for many common genetic disorders.

Although population and family planning clinics and maternal and child health hospitals are available throughout the country, and preconception tests are free of charge for

Table 4 The prevalence of thalassemia, PKU, and G6PD in China

Defects	Regions	Prevalence (1/1,000)	Period	Reference
Thalassemia (Carrier)	Guangdong	88.5	2004–2009	(Shen et al. 2010)
	Guangxi	79.7	–	(Zhang et al. 2006)
	Guizhou	39.4	2003	(He et al. 2004)
PKU	National	0.09	1985–2001	(Wang 2011)
G6PD (Carrier)	Shanghai	8.6	1991	(Xu et al. 2008)
	Hainan	37.3	–	(Huang et al. 2007)
	Guangdong	40.2	–	(Mao et al. 2005)

Table 5 Prevalence of some common late-onset disorders

Disorder	Prevalence/prevalence (per 100,000)	Reference
Breast cancer	Female, 5.90	(China 2010a)
Colorectal cancer	Male, 8.19; female, 6.26	(China 2010a)

everyone, the rate of using the services is very disappointing. There are three reasons:

1. The lack of governmental support for molecular genetic diagnosis: To ensure the service standard and coverage of neonatal screening, carrier screening and cytogenetic diagnosis, MOH has issued many guidelines and regulations (China 1995, 2002b, 2007c, 2011a, 2003a, 2009c), but none of these was specific for molecular genetic diagnosis, which is thought to be the most integral component of genetic healthcare service. Without standards and increased governmental support, molecular genetic diagnostic services would be illegal. Such tests can only be carried out in academic institutions for non-clinical use.
2. The shortage in technical personnel: Unlike the developed countries, there is no education program designed for the training of medical genetic professionals. The technical personnel carrying out molecular genetic tests in the institutions are mostly educated overseas. It is impossible to gather a sufficient amount of highly educated professionals from abroad.
3. The lack of public awareness: In urban areas, most of the people are well educated. It is easy for them to understand and realize the usefulness of genetic service(s). But for those in rural areas and migrating working populations whose primary focus has been subsistence, intensive education and guidance are required.

The government of China has become well aware of the problems mentioned above. It has promulgated the existence of comprehensive genetic services and is committed to the perfection of comprehensive genetic services by establishing a nationwide network for the prevention and intervention of genetic

disorders. It will implement effective measurements and procedures especially for the rural areas, and promote relative research and its translation to clinical use (China 2012c).

Total number of genetic service facilities in the different health care settings

The maternal and child health care system has been successfully established in all areas of China. In this system, a provincial maternal and child health hospital, which is normally located in the capital city of the province, is in charge of other sub-level maternal and child health hospitals. According to the 2010 MOH annual report (China 2010a), there are 3,018 maternal and child health hospitals (clinics) throughout the country.

There are 10,801 general hospitals (China 2010a) with experts in gynecology, obstetrics and pediatrics who are providing genetic service(s) for the public. By 2012, over 600 prenatal screening/diagnosis centers, 185 neonatal metabolic disorder screening units, and 22,598 new-born blood spots sampling centers have been established nationwide (China 2012c).

Other than the above clinical services, most of the molecular genetic tests were performed in academic settings. Nine institutions were able to provide such genetic service in China by 2008. The earliest was in Changsha, Hunan Province (Central South University); for Beijing and Shanghai, two were present in each city which are the Beijing Union Medical College, Peking University Center of Medical Genetics, Shanghai Medical Genetics Institute and Shanghai Tongji University. In Liaoning Province, two academic departments are offering genetic services, one was in Shenyang (National University in Medicine), and the other was in Dalian (Dalian Medical University). A center in Hangzhou, Zhejiang Province (University of Zhejiang) is also providing genetic services for the public, but all for non-clinical use.

Access to genetic services

Costs and reimbursement systems for genetic services available in China

The ordinary reimbursement system for health care services in China is the national social health insurance, which is still under development. It covers 97 % of the employed (including self-employment) population, all the elders and children. The insurance reimburses 80–90 % of the cost if the service is approved by the insurance authority when the tests and treatment were carried out in the local public health system. In such cases, the reimbursement is transferred to the clinical center instantly and directly, and the patients only have to pay for the rest. The percentage reimbursement depends on the type of the insurance. If the tests and the treatment were taken at a clinical center in a different city from the one registered in the

Table 6 Percentage of all infant deaths due to congenital/genetic disorders (China 2012c)

	2000		2011	
	Mortality	Percentage	Mortality	Percentage
Urban	11.8	25.5	5.8	23.7
Rural	37	11.5	14.7	18.3
National	32.2	12.5	12.1	19.1

Mortality: the mortality rate of defined areas, unit at 1/1,000. Percentage: the percentage of all infant deaths due to congenital/genetic disorders

Table 7 Availability of specific services in China

Type of service available	Types of setting					Locations	
	Public domain			Private domain		Urban areas	Rural areas
	Primary care (community)	Secondary care (Tier 2)	Tertiary care (Tier 3)	Commercial	Charity		
Pre-implantation genetic diagnosis	×	×	○	○	×	○	×
Prenatal genetic diagnosis	×	×	○	×	×	○	×
Newborn screening	×	○	○	×	○	○	○
Genetic Screening	×	×	○	×	○	○	○
Carrier testing	×	×	○	○	○	○	×
Diagnostic testing	×	×	○	○	○	○	×
Predictive testing	×	×	○	○	○	○	×
Pharmacogenetic testing	×	×	○	○	○	○	×
Molecular testing for viral infections	×	○	○	×	×	○	○
Genetic counselling services	○	○	○	○	○	○	○
Abortion services	○	○	○	×	×	○	○

○ available, × absent

insurance, the patient is then required to pay the full cost before claiming reimbursement. Molecular genetic tests are new to the insurance authority and are not yet approved by MOH; thus they are not paid by the insurance. Most of the molecular genetic tests carried in an academic institution are free for the patients, as they are covered by research grants. But such test results are unacceptable by clinical professionals; and the test itself is unsustainable, once the research project is done, the test service will also be terminated, due to lack of funding.

Most of the genetic counseling, prenatal and neonatal screening, prenatal ultrasound examination, and karyotyping for birth defects are approved by the insurance. The social health insurance system started working from the 1990s and was originally a designated health service for adults having a long-term employment. Since 2007, the social health insurance has been expended to all citizens, including children and elders. In less developed areas (mostly in the middle and west part of China), hospitals and clinic posts are providing free routine health check-ups for pregnant women when they are enrolled in the prenatal healthcare system that has been a local health promotion plan in most provinces. The pre-marital health examination is free to all, and in some provinces (e.g., Beijing and Guangdong) a preconception health examination is also fully covered by the government.

The potential barriers have been identified for people to access to genetic services within China

The potential barriers have been identified for people to access to genetic services within China. In addition, financial difficulty is a major barrier without doubt, particularly where the genetic tests are too costly for the patient and no

medical aid covers the cost. The typical charge of a single molecular genetic test is 1,000–2,000 CNY, which is over half of the average monthly salary. Unbalanced distribution of genetic services and the large size of the country have resulted in that traveling to major hospital/institutions, a costly and time-consuming process for lower income families thus constituting a geographical and fiscal barrier. The ignorance of both health professionals and the public regarding the available genetic services and their value, may present a barrier to access, since the benefits may not be understood and referrals may not be made appropriately or may be made late. Lack of local expertise hinders the development of genetic services to the public; therefore sometimes the sample for molecular diagnosis has to be sent out to other centers for molecular diagnosis. Besides the above, a cultural issue is also a factor that should not be forgotten. For example, patients with a fatalistic attitude (faithful Buddhist and many other Chinese local beliefs) toward their health and pregnancy may prevent some Chinese people from utilizing genetic services. In addition, many patients use both Western medical and traditional Chinese herbal services (in some cases, spirit healer might also be a choice). In these situations, they may reject genetic services. The detailed barriers are listed below.

- (a) Language—the official language of China is Mandarin, but only 53.06 % Chinese can communicate by Mandarin fluently; 86.38 % can speak one of seven very distinct accents. Fifty-three ethnic groups have their own language and written characters. Most of the languages for small ethnic groups are rich in daily life and psychology, but lack scientific words. The language

barrier greatly reduces the promotion of reproductive health care services (Xu 2002; Qian et al. 2011).

- (b) Life style—life style of people also differs between ethnic groups, e.g., people of Mongolian Minority are nomads and good at keeping livestock. However, Tibetan has a completely different lifestyle and language (Xu 2002; Wu et al. 1999; Qiu et al. 2003).
- (c) Belief—Apart from three major beliefs (Buddhism, Christianity, Islamism) of the world, which are present in China, Taoism is also a large belief group in China (Baidu 2012). Some ethnic groups may also have their own figure of belief. Belief deeply influencing life styles, behavior, and dietary structures; and thus, may also affect the acceptability of the prevention and intervention procedures for genetic disorders (Dou 1991).
- (d) Tendency—Although Chinese herbal medicine is deeply rooted in the population, the majority of people would like to consult both Western medical health professionals and traditional Chinese herbal medical doctors. This is particularly obvious in the older generation and in ethnic minorities, which resulted in difficulty to implement genetic services (Xu 2002).
- (e) Physical status and genetics—Due to the large land and variety of ethnic background, physical status varies from the northern to southern areas of the country. For example, thalassemia and G6PD are the most common genetic conditions in the provinces of Guangdong and Guangxi on the south coast of China (China 2012c), while clubfoot is much higher in Tibet Autonomous Region than other areas of the country although the underlying genetic mechanism is yet to be identified (Zhong and Zhao, unpublished data).

State of genetic services

Human resources, education, and training

The number of registered medical professionals are accessed and published annually by MOH (Table 8). According to the governmental media's news, over 280 universities/colleges are qualified for giving 5–8 years higher education for the students who will be a medical doctor, and another 350 institutions are qualified for providing the training for nurses and technicians (Wu 2012). In 2012, 1.76 million students

were enrolled in undergraduate medical-related courses (Wu 2012). For all these medical students basic genetics is compulsory; some top universities (Peking University, Tsinghua University, Zhejiang University, Tongji University and Shanghai Communication University) also have a specially designed medical genetics program instead of biological genetics for the medical students, for whom the advanced medical genetics courses are implemented, as we have experienced, by adapting the current medical genetics textbook used for medical students and for medical genetics trainees in the medical schools of the USA (Zhong 2006). Since 1999, the Chinese government has increased its investment in education, thus the number of medical graduates has grown from 12,207 in 2003 to 55,458 in 2009 (China 2010a).

As mentioned above, MOH does not recognize genetic professionals as a unique type of occupation, there are no official statistics for the number of doctors, nurses, and lab technicians who are providing genetic services.

The brain drain/emigration of high-end health care personnel working in all fields of medical services is a problem for the country. Many outstanding doctors decided to move to developed countries for better working opportunities and higher salaries. In the top university like Peking University Health Center, at least 1/10 students go abroad after the completion of their education. On the other hand, scientists or medical doctors with a degree awarded by an overseas university cannot be accepted by MOH, and therefore, are not allowed to perform medical practice for the public.

Workload

The exact number of medical genetic centers in China is unavailable, as there is no official data available. By an Internet search, only nine university-bound medical genetic centers were found. In addition, most of the provinces have established at least one prenatal screening and one diagnostic center in major hospitals. These centers are regionally distributed throughout the country and communications are usually established on a basis of personal relations. Genetic counseling and karyotyping are routinely provided by all these centers either in universities or hospitals, but nearly all the DNA level genetic tests were performed in universities. The workload in all the centers is extremely heavy because of a lack of qualified staff. China has 13 billion people but is grossly understaffed in the field of medical genetics resulting in many unmet genetic health needs in local communities, although WHO has suggested that two medical geneticists and four genetic counselors are required to provide an adequate genetic service to every one million people (Wertz and Fletcher 2004). Clinical genetic services, although limited, have been integrated into the public health system, in and around the academic centers of the universities and hospitals. Most genetic counseling clinics are held

Table 8 Available health workforce (China 2009a)

Job title	Number
Physicians	1,905,436
Nursing and midwifery personnel	1,854,818
Community health workers	295,125
Village health workers	1,050,991

in public hospitals, especially maternal and child health hospitals. The medical genetic staff hardly ever undertake outreach visits due to limited resources, which have resulted in the majority of the population remaining underserved. The universal systematized prevention and surveillance of birth defects has been implemented since 1994.

An efficient maternal and child healthcare system has been established from small towns to metropolitan cities, and the right to receive routine medical examination before/during pregnancy is protected by law and various regulations (China 1994b, 1995, 2003a). Facilities for general prenatal care, including karyotyping, biochemical tests, ultrasonography screening, microbiological tests are present in all-level hospitals; however, authorized prenatal screening and prenatal diagnosis is only available in qualified centers that are evaluated and authorized by the government, such as The Department of Health at provincial level.

Laboratories for genetic services

Diagnostic genetic testing is performed mainly through the laboratories at the major hospitals that are affiliated with top-ranked universities such as Peking University, Peking Union Medical College, Fudan University, etc. Although the service is fully available and accessible, the majority of specimens processed by these laboratories are usually from the university-affiliated hospitals. Unlike in developed countries, specimens are not sent directly to the appropriate and centralized laboratory for genetic testing in China, even though the local laboratory may not be capable of performing the tests. Genetic testing is offered as part of a research program in medical schools in a certain number of universities. As the school research laboratory is not a government-approved diagnostic laboratory, no diagnostic result is authorized to be reported. However, the research-based result is always confused with the diagnostic report. To overcome this, the Chinese MOH founded a National Center of Reproduction Technology in 2009, which will become a central diagnostic laboratory for genetic diseases. There are more than 60+ centers, with academic affiliations, performing diagnostic genetic testing services, on a service basis.

Along with the growing economy, hospital-based genetic testing is far behind market demands. For example, prenatal karyotyping of amniotic fluid has to be delayed for three months in quite a lot of prenatal centers even though the laboratory staff has to finish seven to eight patients' specimens per day routinely. The increased market demands have stimulated development of private laboratories, through which genetic tests, including cytogenetic, molecular, and metabolic tests, are offered. Postnatal specimens can be processed but only on a basis of a subcontract with a government-authorized prenatal center. Most of private independent laboratories are in central cities, like in Beijing,

Shanghai, and Guangzhou, or in a science-park of national, provincial, or municipal developing zones. These private laboratories usually provide the services that are not covered by public centers for primary healthcare facilities that lack facilities and capacities. Although the money spent for the genetic testing in private services is usually not be reimbursed by social health insurance and the charge is usually higher than public services, it seems that out-of-pocket payment is affordable for those who are willing to proceed with the test. In fact, the number of people who are voluntarily looking for accurate and efficient genetic service is growing, which has stimulated Chinese healthcare reform and opened new revenue for economic development.

Paternal testing is a specialized service in China. It was initially performed by genetic laboratories in 1991 but centralized under the National Public Security system. Nowadays, without certification and authorization by this system, no laboratory is able to perform legally recognized paternal testing (China 2007b).

Quality assurance of medical genetic services

Quality assessment schemes are available and the centers in hospitals are exposed to regular peer review and inspection. All clinical laboratories offering genetic diagnosis are required to meet the various standards of issued by MOH (China 1994c, 2002a, 1995, 2002b, 2003a, 2003b). 103 clinical testing departments gained approval of ISO15189 (Accreditation Criteria for the Quality and Competence of Medical Laboratories) and a few them obtained credentials from American College of Pathologists (CAP) (China 2012b). The documentation of testing process and data outcome generated from genetic services are handled individually by the providers.

National policies and legal frameworks

In the current existing national policy guidelines (China 1981, 2011b), reducing birth defects and improving the birth quality have become the priority in maternal and child health services in China. The Law of the Peoples Republic of China on Maternal and Infant Health Care (China 1994b) clearly states a priority of healthcare for preconception, perinatally, pregnancy, at birth, infancy, and childhood. The Maternal and Child Health Law also guaranteed that everyone has access to health care.

The use of blood products, tissue, stem cells and gametes and zygotes in humans is carefully regulated. Any use or research of these materials requires written application to a local ethics committee.

Cultural and social issues pertaining to medical genetic services in China.

Research priorities in genetics/genomics

Current national policies for funding research in genetics/genomics, priorities for funding, and funding mechanisms

There is no policy in China specifically covering the funding for research in human/medical genetics. Governmental funding is channeled through Natural Science Foundation of China (NSFC) and the Ministry of Science and Technology (MOST). For 2009, the NSFC distributed 18.275 billion RMB (about 3 billion USD) (China 2012a). The full funding scheme of NSFC consists of three groups: research projects (funding is limited to an individual project, similar to NIH RO1 mechanism), research scientist developmental project (funding is limited to a person or a group for a specific research project, similar to NIH R29 mechanism), and environment condition projects (funding is limited for improving and investigating laboratory's hardware condition, e.g., equipment). All three schemes are not specifically allocated to fund medical genetic research, but on a basis of scientific merit. The funding level differs by application and schemes. The financial support for an individual project is likely to range from 200 to 500 k RMB (30–70 k USD), including those projects considered as a priority and key research. Some large projects combine several key research institutions and involved a greater level of funding, such as “863 National Research Foundation” (National Advanced Technology Developmental Plan) and “973 National Research Foundation” (National Major Basic Research Developmental Plan), are funded directly by MOST. Both 863 and 973 are similar to NIH program project with U mechanism, which budget may be up to 50 million RMB and considered as the top funds in the country. Before the 863 and 973 program was released, lobbying of MOST was quite important. The MOST would also invite chief scientists to propose priority, on an annual basis, for 863 and 973 program. Once the proposal is received, MOST will organize a series of evaluations to decide the research priority to fund. Announcement of funding opportunity will be released after the priority is identified and a decision is made, but unfortunately it is very short notification and tightly close to the deadline of application submission. The applicant has to construct their research proposal according to the format of MOST within a very short time frame, which explains why so many applications do not consist of well developed scientific ideas and well designed approaches. For those applications that have been approved, funding to the investigators who need money to conduct their research, could be delayed. Usually the delay period could be from 6 to 12 months or longer. Occasionally, one could be notified with “surprising money” that suddenly becomes available and the investigators are required to submit their application

within a few days. This type of funding usually does not require peer review, and grantees are usually the ones who have a strong connection with the funding agency. These abnormal processes are being corrected and the peer review process is improved, although a few unusual tracts are still influencing the review process. Generally speaking, the application could be awarded only if the application has been scored with three “A” or five “A,” depending on whether there are three or five reviewers during the first round scientific review process. The second or third round is usually only for the large size collaborative projects such as 863 or 973 funds. MOH only functions as an agency to identify the clinical research priority, and not many medical geneticists are involved in the decision-making group. Local government agencies may also provide funds with a relative small budget, ranging from a few thousand to 50,000 RMB and the amount hardly goes over 100,000 RMB (~15,000 USD) except for research that has been identified as a “key” project that could benefit the local or regional communities or economic development. The total amount may then reach 300,000 RMB (~45,000 USD) for a 3-year project.

Research funding by private parties

Generally, private funding is not available to support research, except if it is contracted research for the funding agency. Most of time, the funds come from therapeutic or pharmaceutical companies for conducting clinical trials. There is almost no funding at all for medical genetics.

Known collaboration with international funding agencies

Chinese researchers in human genetics collaborate with international research teams and have received international funding from bodies such as the WHO, UNICEF, National Institute of Health (USA), Center for Disease Control (USA), the March of Dimes Foundation, Bill Gates Foundation, Wellcome Trust, and the European Union.

Current centers of excellence in genetics/genomics research

There are several centers of excellence in the field of human genetics or medical genetics at present, most of which are located in metropolitan cities such as Beijing, Shanghai, Guangzhou, Chongqing, and other provincial capital cities. Almost all the centers are affiliated with either universities, China Academy of Medical Science, or China National Academy of Sciences. The most sounding genome center is the Beijing Institute of Genomics (BIG, <http://www.big.ac.cn>), the driving force for the human genome project in China, now moving towards translational medicine.

Regulation of translation of new genetic tests into health care practice

The Chinese Government always welcomes application of new technology. There is much funding available for the development of new technology and for translation to clinical fields. For example, on the national level, “863 Project” and “Natural Science Foundation of China (H20).” All the technology and instruments used in clinical areas are required to be approved by MOH, but a period of scientific and clinical trial is allowed, and the trial must comply with “The Regulation for Medical Equipment Clinical Trial” published by State Food and Drug Administration (China 2004). Clinical technology itself has been classified into three groups by MOH, according to the safety, effectiveness, complexity, and level of ethical issue involvement of each technology. The higher level means more strict regulation. Despite the more complicated application progress, level two and three technologies are also required report the comprehensive progress of application to the approval issuing body (China 2009b). As genetic testing is a level technology, the application procedure may only consist of clinical trial and evaluation. The typical length of time for obtaining an approval is 1.5–2 years.

Patient organizations and public education in genetics: The availability and structure of parent/patient organizations, including funding, objectives and provision of services

Apart from China Foundation for Birth Defect Intervention and Aid, there is no official patient association organized by the government. There are over 30 national patient/family organizations for genetic disorders. All the organizations were registered as non-governmental and non-profit entities, which were then under the administration of the National Bureau of Public Organization, Ministry of Civil Affairs. Each organization consists of an operative board, which is formed by key and active members. Some groups (e.g., Autism Association, <http://app.autism.com.cn/enterprise/jsp/special/autism.com.cn/index.jsp>) also have a medical advisory board formed by medical professional and a few of them had a subcommittee of fundraising. The size of associations and groups vary largely due to the prevalence of disorders.

The purposes of most of the support groups are very similar, including raising public/government awareness, fundraising, offering support, providing suggestions, advice, and literature to affected individuals and their families, and supporting and stimulating relevant research.

The objectives of the supporting groups are very similar, and generally, they aim to: seek political legislation/policy support, raise awareness about the condition in the community; offer support, advice, and literature to affected individuals and their families; supporting and stimulating relevant research (mostly in academic centers, PKU Union, e.g., <http://pkuunion.org/>),

where possible; training support parents; gaining support from interested medical experts; and making appropriate referrals.

The sources of funding and main activities of these organizations: Fund raising is generally undertaken in a very limited way, unless the association is well recognized and a financial professional is involved in the actual operation/organization of the association. Most support groups receive very little funds though various sources. Government seldom funds small public organizations. The majority of the funding is membership fees and donations. Where fundraising is undertaken, most funding comes from private businesses, corporate and individual donors, and in a few cases from international parties. Some large associations may have their own retailing or publishing company as their continuous solid source of funding.

The services offered by the groups/associations are generally appropriate to their objectives and include but not limited to:

- a. providing condition-relevant literature and educating their members and the public
- b. organizing support group meetings
- c. giving training to patients or their parents to improve the quality of life
- d. providing psychosocial support, telephone/internet consultations
- e. raising funds to support more activities

Relationship with clinical genetics community/health service: The National Bureau of Public Organization does not have any direct connection with clinical genetic services, rather through help from MOH. Individual associations usually have their own communication with either local clinical genetics and health service or higher-level facilities. Often, professionals of the clinical genetic services are invited to attend the association meetings. On the other hand, clinical geneticists and genetic counselors also keep in contact with the groups. Leaflets on the conditions are often produced in collaboration with the supporting parties; referrals are made to and from association members. So the relationship between the voluntary groups and the genetics professionals is generally good and that between the groups and the health department appears to be smooth and effective, particularly when a special clinic is dedicated to the management of a common condition in a tertiary public hospital setting.

Availability of primary prevention of congenital/genetic disorders via combinations of public and professional education programs

Due to the increased awareness by the government, protocols have been developed to tackle congenital/genetic disorders. Unlike some countries, China supplies fortified basic food, including free folic acid supplement to women from 3 months

before to 3 months after the beginning of pregnancy. The procedure has been carried out and carefully monitored for years and as a result, the incidence of neural tube defects has fallen by 62.3 % nationally, and by 70 % in some provinces with a higher incidence previously (China 2012c). Also, salt has been iodized for many years thus preventing most cases of postnatal iodine deficiency disorders and goiter.

The National Population and Family Planning Commission has established an effective network deeply rooted in the public, even available in undeveloped areas. This network was originally founded for implementation of the “One Child Policy.” But as the governmental attention shifted to birth defect prevention, the network was involved in many projects. By carefully designing the course, the network can maximize the effectiveness in the public education programs.

Professional and public education, covering recognition and prevention of congenital disorders, takes place at many levels. Medical/clinical professionals, including nurses, are all college/university graduates, which receive basic teaching in medical genetics during their degree and diploma studies, as well as in-service training held by individual hospitals during their employment.

Lay public groups, such as labor unions or women’s unions in large entities or residential societies, patient organizations, may routinely organize talks from human genetics professionals. Although there is no proper genetic counseling as a profession currently in China, an obstetrician and gynecologist would take the role to give educational lectures to a number of professionals and the general public. Maternal and child health hospitals and other healthcare professional and governmental groups, such as voluntary groups like the Best Baby Association organized by the Peking University Center of Medical Genetics and the China National Commission of Population and Family Planning may compile leaflets for distribution on a number of common disorders, as well as on prenatal genetic diagnosis and genetic counseling services.

Conclusion

China is a fast-developing country with the largest population in the world. The economics and lives of people have been improved dramatically in the last 20 years. The Chinese government has given a great deal of attention since the founding of the Republic in 1949 to maternal and child health in the interest of protecting the health of mothers and children. In the last two decades, China has made substantial progress in reducing maternal, infant, and under-five mortalities.

Nevertheless, national figures for maternal and infant health indicators mask large disparities, which exist between urban and rural populations, and across different regions of China. Due to the limited access to the medical genetic service

and antenatal/preconception care, maternal and infant death rates are highest among the rural, poor, and migrant populations, and in those regions, such as the western regions of China, with least access to antenatal and preconception care. The government needs to be better informed about the shortage of medical genetic professionals and the blanks in molecular genetic diagnostic service.

To tackle the problems above, the national government should take advantage of “single-party state,” and provide more financial and technical support to less-developed areas, establish medical genetics occupation groups, including medical geneticists, genetic counselors, diagnostic laboratory personnel, and supporting personnel and launch-related education programs, speed up the approval progress for molecular diagnosis and encourage the positive activities of the patient organizations, and promote direct research support in medical/clinical genetics.

The big gap between China and well-developed countries in genetic services cannot be filled in a short period time, but it is widely believed that that strong governmental support can effect rapid changes to benefit all of the people.

Acknowledgments The authors would like to thank members of Best Baby Association of Peking University, who contributed their time and effort to assist in compiling this report. The survey was supported by (a) the European Commission’s Joint Research Centre “Institute for Health and Consumer Protection,” Ispra, Italy; (b) the Department of Human Genetics, Hannover Medical School, Hannover, Germany; and (c) the Unit of Women’s Health Research, Medical School, Westfälische Wilhelms-Universität Münster, Münster, Germany.

References

- Baidu (2012) Taoism. Baidu encyclopedia. <http://baike.baidu.com/view/6683.htm>
- China (1954) The report for national census. Ministry of Public Security, Beijing
- China (1981) Marriage Law. China National People’s Congress, Beijing
- China (1994a) 1993 China health statistics yearbook. Ministry of Health, Beijing
- China (1994b) Law of the Peoples Republic of China on Maternal and Infant Health Care. National People’s Congress of China, Beijing
- China (1994c) The regulations on the administration of medical institutions. The Central People’s Government of the People’s Republic of China, Beijing
- China (1995) The regulation of special technical service and personnel for maternal & infants health. Ministry of Health, Beijing
- China (2001) The report for national census. Ministry of Public Security, Beijing
- China (2002a) Clinical gene amplification testing laboratory management measures. Ministry of Health, Beijing
- China (2002b) The guidelines for providing premarital medical service. Ministry of Health, Beijing
- China (2003a) The regulation for prenatal diagnosis. Ministry of Health, Beijing
- China (2003b) Technical specifications for fetal karyotype analysis. Ministry of Health, Beijing

- China (2004) The regulation for medical equipment clinical trial. State Food and Drug Administration, Beijing
- China (2006) 2006 China health statistics yearbook. Ministry of Health. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/http://www.moh.gov.cn/publicfiles/business/htmlfiles/zwgkzt/ptjnj/year2006/index.html>
- China (2007a) 2007 China health statistics yearbook. Ministry of Health. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohbgt/s8274/200807/37168.htm>
- China (2007b) Basic principles of the criminal judicial appraisal. China Ministry of Justice, Beijing
- China (2007c) The guidelines for providing preconception medical service. Ministry of Health, Beijing
- China (2007d) The report of national census. Ministry of Public Security, Beijing
- China (2008) 2008 Chinese health statistical digest. Ministry of Health. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohbgt/s8274/200805/35671.htm>
- China (2009a) 2009 Chinese health statistical digest. Ministry of Health. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohbgt/s8274/200905/40765.htm>
- China (2009b) The measures for the administration of the clinical application of medical technology. Ministry of Health, Beijing
- China (2009c) The regulation for neonatal screening Ministry of Health, Beijing
- China (2009d) The report of national census. Ministry of Public Security, Beijing
- China (2010a) 2010 Chinese health statistical digest. Ministry of Health. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/publicfiles/business/htmlfiles/zwgkzt/ptjnj/year2010/index2010.html>
- China (2010b) Annual report for year 2009. Ministry of Finance, Beijing
- China (2010c) The report on the national GDP for 2009 (revised). Bureau of Statistics, Beijing
- China (2011a) The guidelines for providing health care service during pregnancy and delivery Ministry of Health, Beijing
- China (2011b) Judicial Interpretation of Marriage Law. Judicial Interpretation No. (2011) 18. The Supreme People's Court, Beijing
- China (2012a) Annual report for Year 2011. National Natural Science Foundation of China, Beijing
- China (2012b) The list of CNAS certified laboratories. National Accreditation Service for Conformity Assessment, Beijing
- China (2012c) The report on birth defect prevention and treatment in China. Ministry of Health, Beijing
- Dou G (1991) The report of 2 cases fetal alcohol syndrome. Qinghai Med J 1:52–54
- He Y, Shan K, Xie Y, Wu C, Zhao Y, Xiu J, Qi X, Ren X (2004) A Screening for Thalassemia among 545 Pregnant Women and Their Spouses in Guiyang Area. Journal of Guiyang Medical College 2:18–20
- Huang C, Wang J, Zhao Z, Yang C (2007) Analysis of results in screening of neonatal G6PD in Hainan Province. China Tropical Medicine 7:2095–2096
- Li L (2011) Neonatal screening. Paper presented at the National conference on early pregnancy and prenatal screening and birth defect prevention, Kunming, Yunnan Province, China
- Li L, Xia J, Dai H, Xu J, Xu F, He X (1983) The chromosomal analysis of 1168 patients from genetic counseling. Bull Hunan Med Coll 2:121–128
- Mao W, Ye S, Gong W (2005) The neonatal screening of G6PD deficiency in 3030 infants of Shenzhen. Chinese Journal of Birth Health and Heredity 12:78–79
- Qian G, Liu H, Zhong N, Wang R, Zou H, He J, Yu W (2011) The analysis of birth defects for different ethnic groups in the Xinjiang Uygur Autonomous Region. J Clin Rehabilitative Tissue Eng Res 15(20):3797–3800
- Qiu X, Jia D, Zeng X, Zhong X, Lin M, Zhang H, Zhang Z, Tang Z, Huang D (2003) The evaluations of risk factors for birth defect in Guangxi minor ethnic populations. Chin J Birth Health Hered 25(2):138–141
- Rosen T, D'Alton ME (2005) Down syndrome screening in the first and second trimesters: what do the data show? Semin Perinatol 29(6):367–375. doi:10.1053/j.semperi.2006.01.001
- Shen Y, Li Z, Pan G (2010) Molecular Epidemiological Study on A-Thalassemia among the New lyweds in Foshan City. Chinese Journal of Family Planning 3(18):160–162
- Silva PRD (2006) La politique de l'enfant unique en République populaire de Chine
- Wang Y (2011) Intervention of birth defect. Paper presented at the National conference on early pregnancy and prenatal screening and birth defect prevention. Kunming, Yunnan Province, China
- Wertz DC, Fletcher JC (2004) Genetics and ethics in global perspective. Kluwer Academic Publishers, Netherlands
- Wu J (2012) China now has over 600 institutions providing education for health care professionals. Xinhua News. http://news.xinhuanet.com/edu/2012-01/24/c_111459291.htm. Accessed 3-Jan-2013 2012
- Wu L, Wu K, Chen H, Xu C, Li S, Yang Y, Wang X (1999) The study of birth defect in children of Ningxia province. Ningxia Med J (1):51–52
- Xia J, Zhao Q, Li B, He S (2006) The epidemic trend and preventive strategy of Down syndrome in Guangdong Province. Matern Child Health Care China 1:80–82
- Xu D (2002) The eugenic analysis of Tibetan traditional reproductive custom. Tibetan Res 3:97–103
- Xu H, Wang Y, Tian G (2008) Epidemiological Investigation of Glucose-6-phosphate Dehydrogenase (G6PD) Deficiency in Shanghai. Shanghai Journal of Preventive Medicine 20(6):285–286
- Zhang X, Zhou Y, Li P, Luo R, Ruan L, Wang R, Wu Z, Li M, Huang Y (2006) Study On the screening program of thalassemia and the genotype and hematologic parameter among people of productive age in a village of Nanning Guangxi. Chinese Journal of Epidemiology 9(27):769–772
- Zhong N (2006) Peking University Center of Medical Genetics (PUCMG): a comprehensive medical genetics program in China. J Peking Univ (Health Sci) 38(1):6–7
- Zhu J (2011) Genetic counseling and birth defect prevention. Paper presented at the National conference on early pregnancy and prenatal screening and birth defect prevention, Kunming, Yunnan Province, China