

# Second trimester maternal serum screening test in China

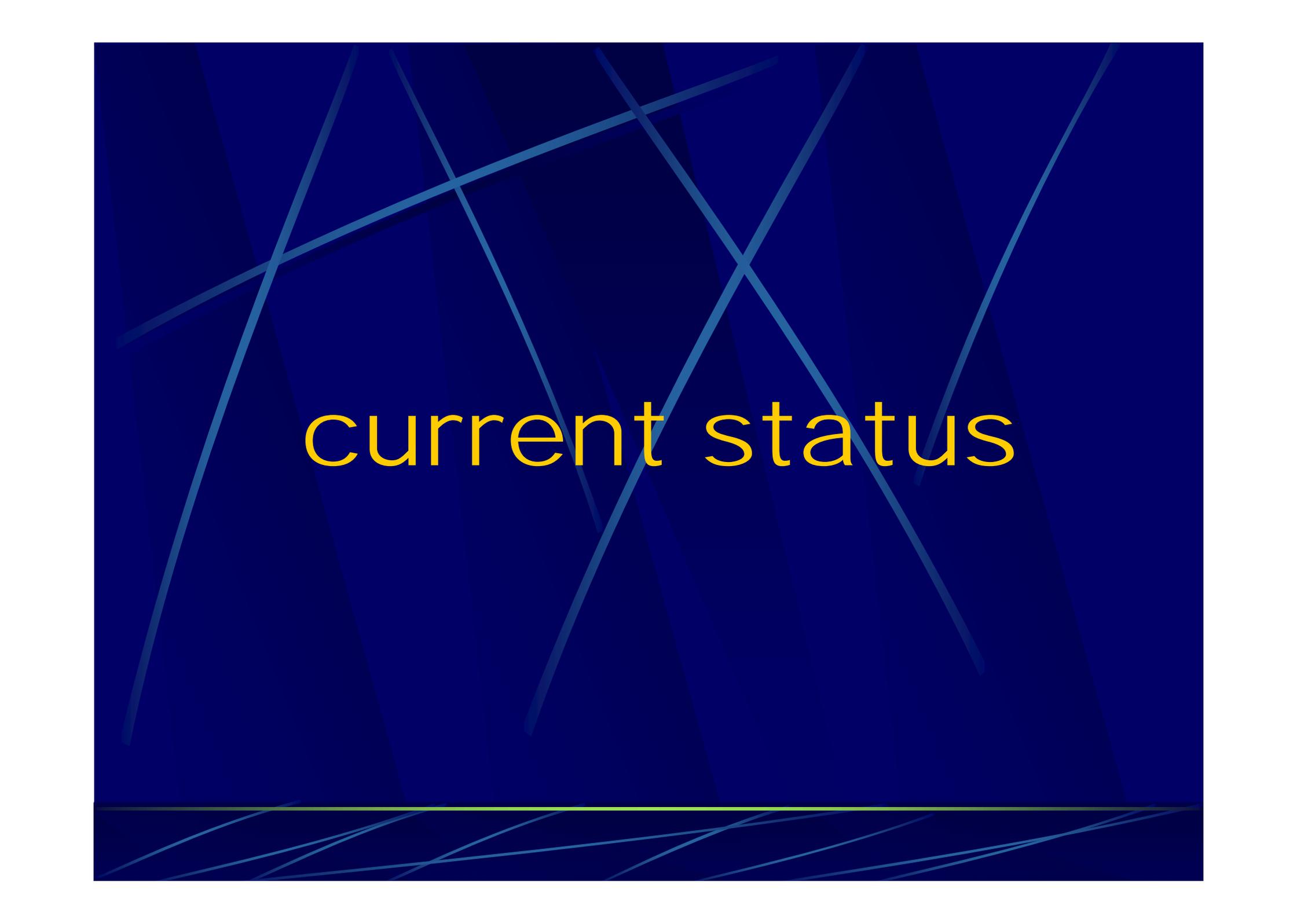
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# Background

- **The perinatal mortality rate kept decreasing in the last decade.**
- **Birth defects became the second main causes of perinatal mortality in China.**
- **There are about 1.2 million malformed newborns in China every year (20% of malformed newborns in the world ).**

# Government Policy

- Population growth rate kept in a stable low level in China in the last decade.
- In the 21<sup>st</sup> century, government's policy has changed from “control birth rate” to “**control birth rate and birth defects rate**”



current status

- **1998:** Second trimester maternal serum screening test started in a few hospitals in big cities
- **2002:** Second trimester maternal serum screening test is available in most of the province-level hospitals

## ● **Test markers:**

AFP + free  $\beta$  HCG

## ● **Methods**

About half of the facilities adopted the technique of time resolved fluorescence immunassay (TRFIA)

other techniques such as ELISA, GIA also being used in China.

## ● **Problems**

- **lack of protocols, standard and standardized methods**
- **Need normal ranges of every marker and MOM value in every gestation week for Chinese pregnant population**
- **Need cut-off value for high risk population**

# Tenth 5-years (10-5) program

● **objective:**

**Multiple-center clinical research to define**

- 1. normal ranges of AFP and free  $\beta$  HCG and MOM value in different gestation weeks for Chinese pregnant population**
- 2. cut-off value for high risk population**
- 3. protocols, standard and standardized methods**

# Group members

- **Peking Union medical college Hospital**
- **Preclinical medicine institute of Chinese academy of medical science**
- **Nanjing Gulou Hospital**
- **Nanjing Women and Children Health Care Hospital**
- **Women Hospital of Zhejiang University**
- **Guangzhou Women and Children Hospital**
- **Guangdong Province Women and Children Hospital**
- **The Second Huaxi Hospital of Sichuan University**
- **The Birth Defect Surveillance Center of China**
- **Jinan Women and Children Hospital**
- **Tianjing Women and Children Health Care Center**
- **The Women and Children Health Care Hospital of Hunan Province**
- **The First People's Hospital of Yunnan Province**

# methods

- makers: AFP + free  $\beta$  HCG
- gestation age: 14~20<sup>+6</sup> wk
- objects: singleton pregnancy
- total cases: 60,000
- methods: TRFIA
- cut-off value: 1/270 for trisomy 21  
1/350 for trisomy 18
- period: Jan. 2004 ~ Dec. 2005

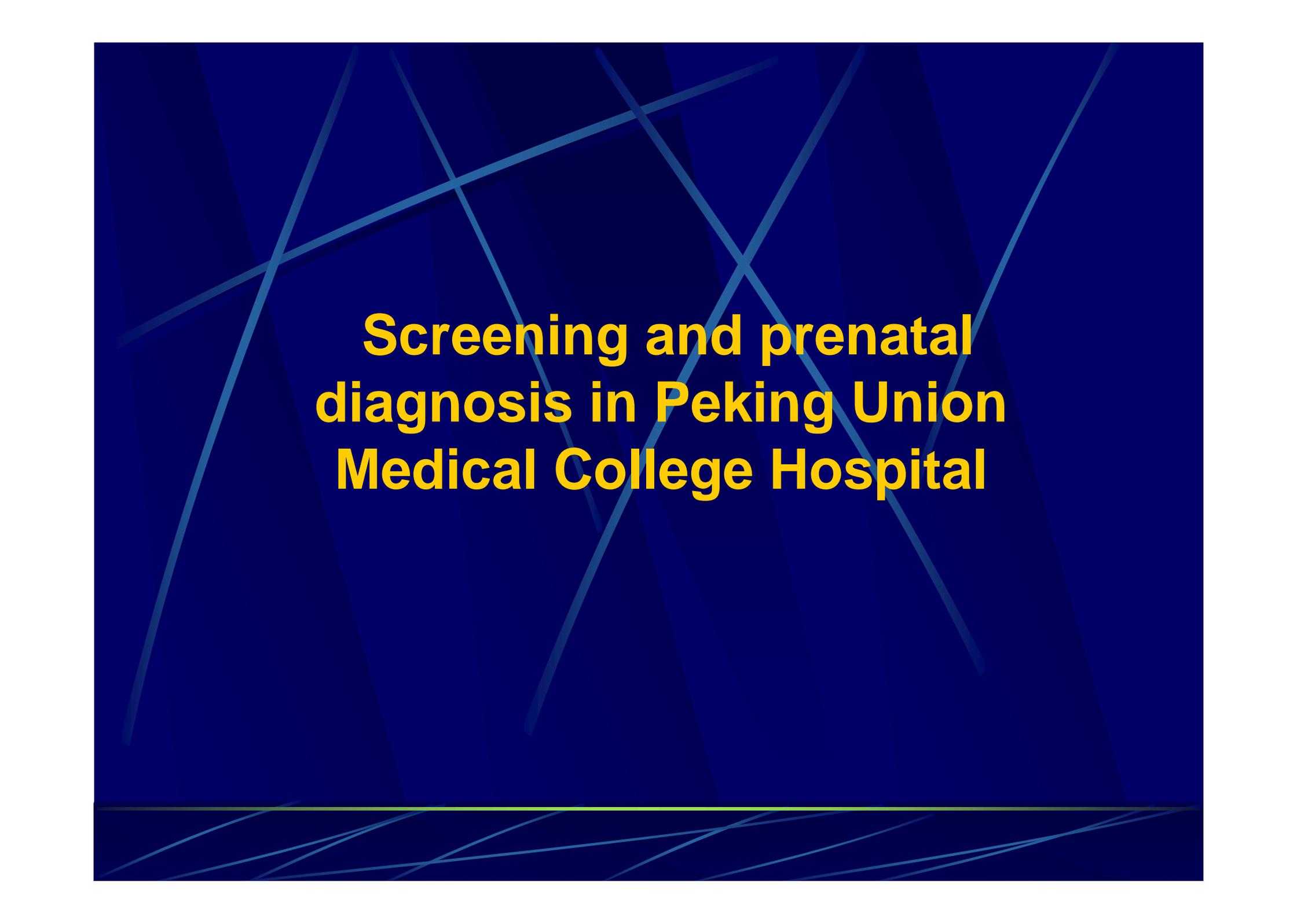
- **Preliminary results from a 20,000 case study using second trimester maternal serum screening test by Nanjing GuLou Hospital showed no difference**
  - **between urban and rural area**
  - **between North and South in China**

## **Author of the Protocol:**

- **Screening test: by the Nanjing Gulou Hospital and the Women Hospital of Zhejiang University**
- **Prenatal diagnosis: by Peking Union Medical College Hospital**
- **Follow Up: by The Birth Defect Surveillance Center of China.**
- **Quality Assurance: by the First People's Hospital of Yunnan Province**

## ● **Data Analysis**

- **A database system was created by PUMCH as a central location for all test results**
- **Capability available in local sites for electronic transfer of test results**
- **Collection and analysis of the data are ongoing**



**Screening and prenatal  
diagnosis in Peking Union  
Medical College Hospital**

- **Method :** AFP + free  $\beta$  HCG
- **Cut-off value:** 1/270 for trisomy 21  
1/350 for trisomy 18
- **Case number:** 6082
- **Time Period:** 01/2000- 09/2005 .
- **Patients:** Singleton  
Chinese  
14-20<sup>+6</sup> weeks of gestation  
on screening day

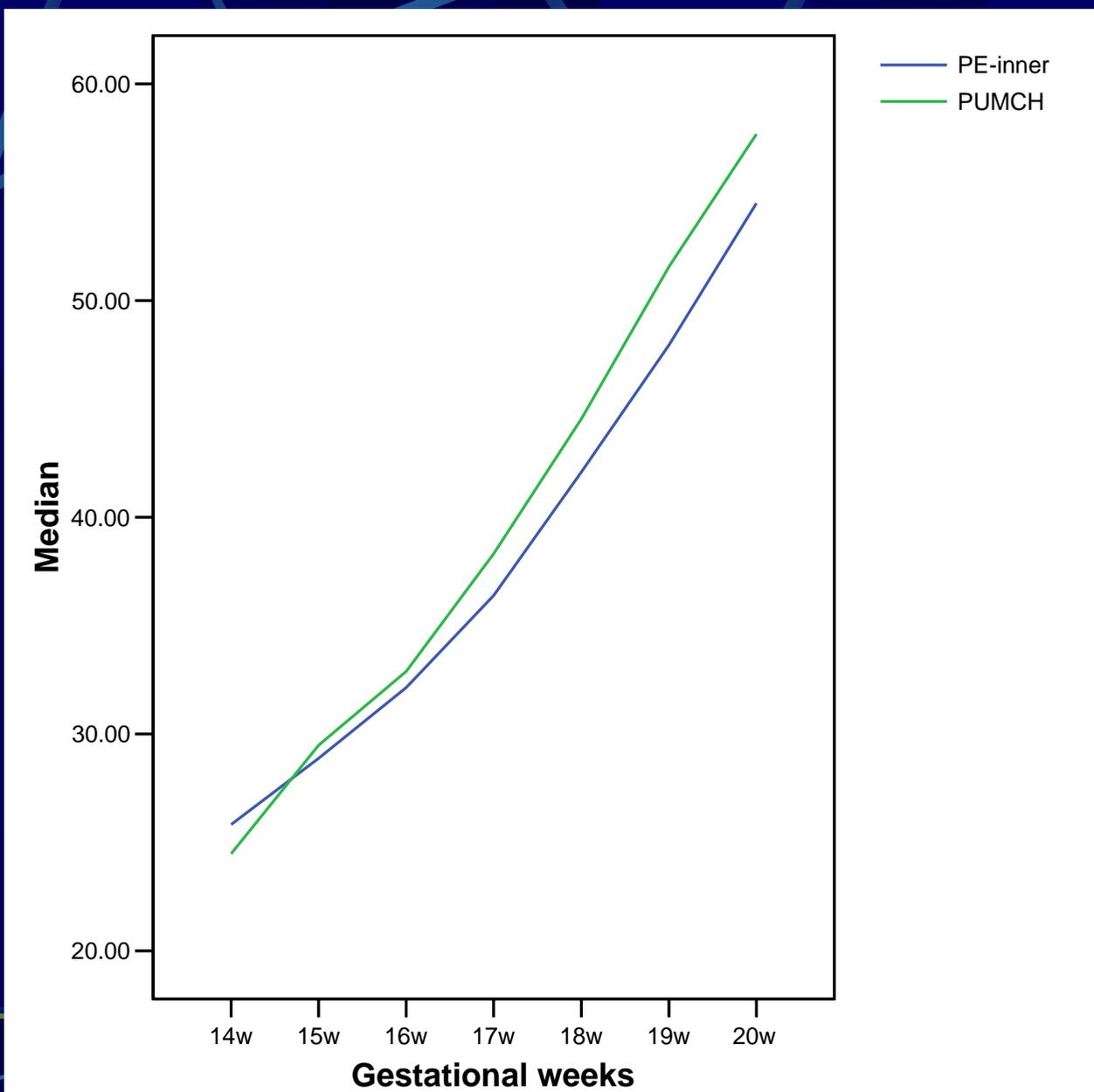
- **Instruments: time resolved fluorescence immunassay system (TRFIA) provided by PE company**
- **The risk calculation Software : 2T risk calculation system provided by PE company**
- **Statistics software : SPSS V13.0**

# Results

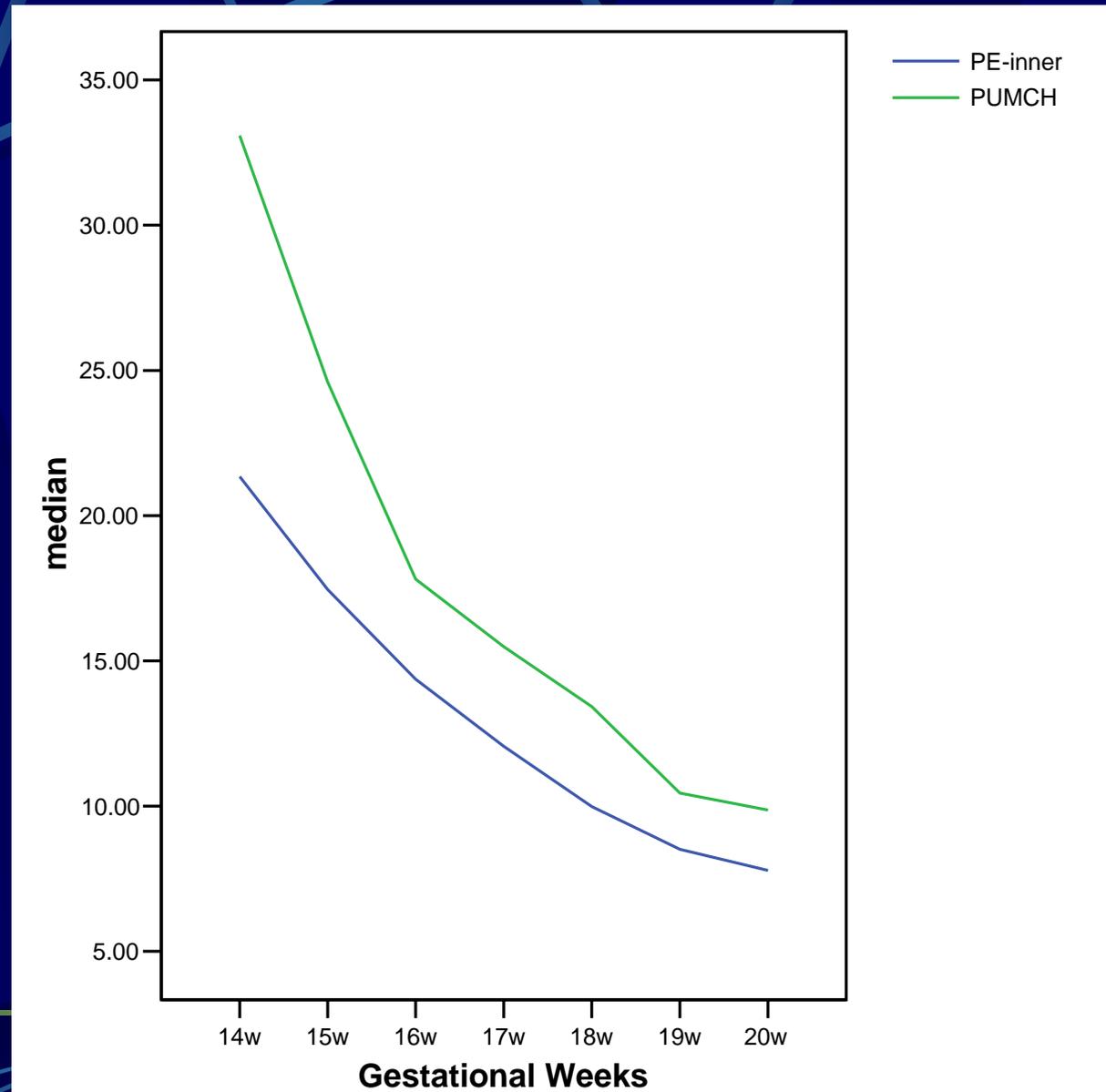
• **The median of AFP and free  $\beta$   
— HCG**

Gestation week	AFP		MOM	Gestation week	Free $\beta$ HCG		MOM
	PE - inner	PUMCH			PE - inner	PUMCH	
14w	25.83	24.48	0.95	14w	21.34	33.09	1.55
15w	28.89	29.49	1.02	15w	17.46	24.60	1.41
16w	32.14	32.89	1.02	16w	14.37	17.81	1.24
17w	36.39	38.32	1.05	17w	12.06	15.49	1.28
18w	42.09	44.54	1.06	18w	9.99	13.43	1.34
19w	47.94	51.56	1.08	19w	8.51	10.45	1.23
20w	54.49	57.68	1.06	20w	7.79	9.86	1.27

# Fig 1. The medians of AFP



**Fig 2. the median of free  $\beta$  -HCG**



## The maternal age and the high risk percentage

	<35 yrs	≥35 yrs	Total
<b>Case number</b>	<b>4976(81.8%)</b>	<b>1106(18.2%)</b>	<b>6082</b>
<b>High risk cases</b>	<b>587(11.8%)</b>	<b>375(33.9%)</b>	<b>962(15.8%)</b>
<b>Contribution of age groups to total risk case</b>	<b>61%</b>	<b>39%</b>	<b>100%</b>

# Amniocentesis

- The Number of screening cases: 6082
- High risk cases: 962
- The number of amniocentesis : 590
- The amniocentesis rate : 61.3%

# Results of amniocentesis

- **14 cases of chromosomal abnormality was found, including:**

**Trisomy 21 : 7 cases (including mosaicism )**

**Trisomy 18 : 2 cases**

**Abnormality of sex chromosome: 3 cases**

**Mosaic Tetraploid :1 case**

**Imbalanced translocation of chromosome: 1 case**

# False negative case

- 41 years old, risk of 1/280, amniocentesis still done, the fetal karyotype: trisomy 21
- 36 years old, risk of 1/1100, amniocentesis still done ,the fetal karyotype: trisomy 18
- 33 years old, low risk, B-us showed multiple malformation, TOP refused, karyotype of the neonate: trisomy 18



- **Discussion**

● **The factors that may affect the results:**

- **high percentage of the pregnant women older than 35**
- **more complicated pregnancy**

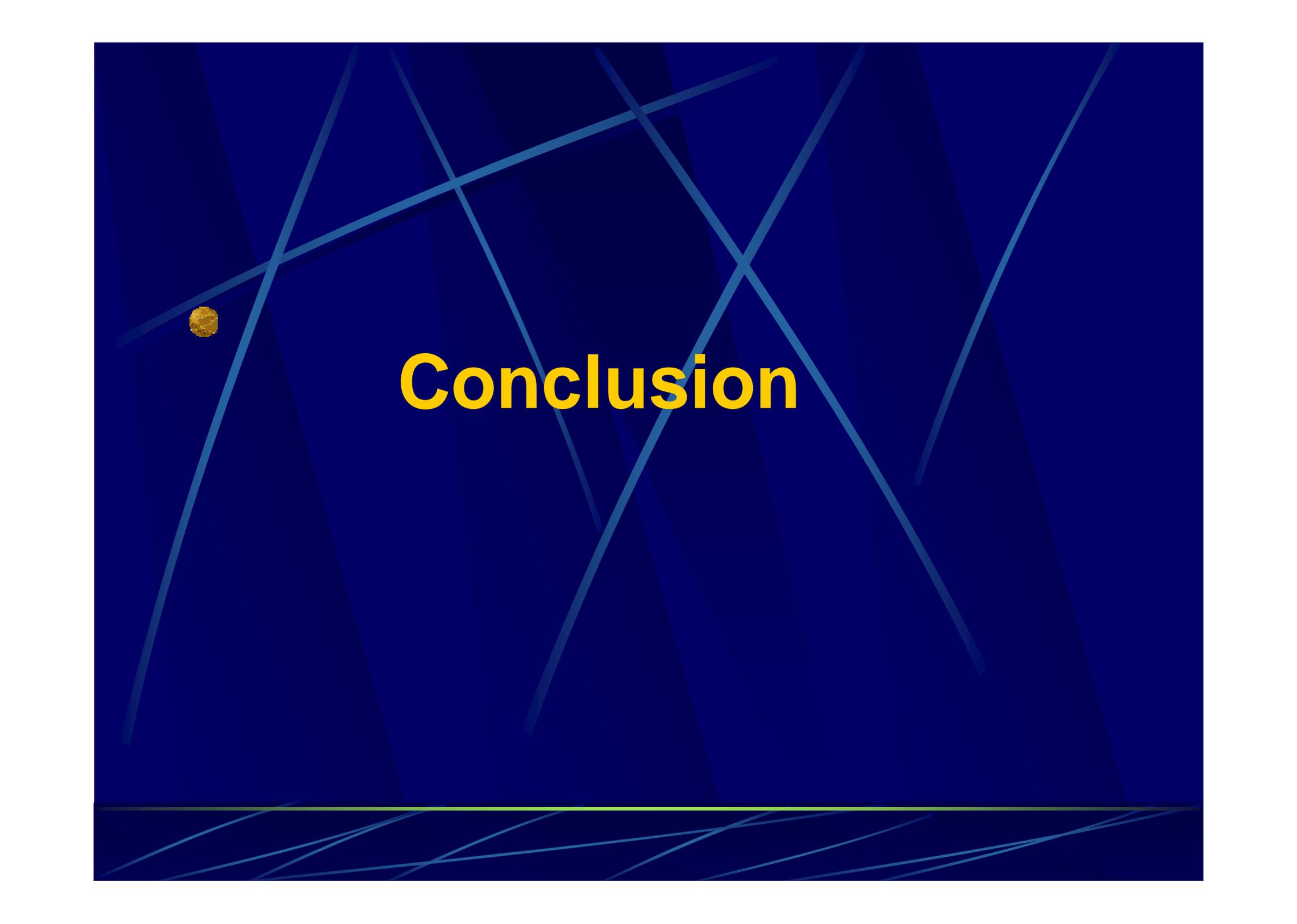
● **Calculation bias that may result in a high screening positive rate:**

High level of free  $\beta$  HCG

Low body weight

Low smoking rate

High pregnancy complication rate



# Conclusion

- **The Second trimester maternal serum screening test is effective to pick out high-risk pregnant women with Down's fetus, especially those younger than 35.**
- **In China, every pregnant woman older than 35 should be suggested for amniocentesis until the screening test system is more reliable.**