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Cost-effectiveness analysis of prenatal diagnosis intervention for Down's syndrome in China

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Objectives: The cost-effectiveness of prenatal diagnosis intervention for Down's syndrome (DS) in China was assessed and evidence-based information for policy makers and providers is presented.
Methods: Based on field surveys in four selected cities in China and a literature review, the economic evaluation of prenatal diagnosis for DS from a societal perspective is conducted by cost-effectiveness analysis.
Results: In current clinical practice, for a cohort of 10,000 pregnant women, the strategy that delivers karyotyping by chorionic villus sampling (CVS) or amniocentesis (AC) only to those pregnant women 35 years of age and older (maternal age screening strategy) can detect .67 DS births. The strategy that offers the diagnostic test after maternal serum screening with α-fetoprotein and human chorionic gonadotrophin (maternal serum screening strategy) can detect 1.41 DS births. The cost per prevented DS birth by the maternal age screening strategy and maternal serum screening strategy is US$13,091 and US$56,048, respectively. Sensitivity analysis shows that the maternal serum screening strategy can be cost-effective if uptake rate of CVS or AC for patients with positive serum tests increase while the cost of serum screening decreases.
Conclusions: Although, in general, serum screening has been found to be more cost-effective than maternal age screening, this appears not to be the case in China. The reasons appear to be low uptake rate of the maternal serum strategy, low uptake rate of CVS or AC, and the high price of serum screening. Our findings are that health system factors concerning technology utilization are important determinants of the technology's efficiency.

Keywords: Cost-effectiveness analysis, Prenatal diagnosis, Down's syndrome

Down's syndrome (DS), trisomy chromosome 21, is one of the common birth defects associated with chromosome malformation. A DS patient is characterized by congenital low intelligence, mental retardation, and physical dysfunctions, which are always accompanied with other congenital abnormalities. The disease heavily influences the patient's ability of self-care, social adaptability, and productivity and also leads to a huge economic burden to the patient, the patient's family, and society. The incidence of DS births ranges from 1/700 to approximately 1/1,000 worldwide (17). It is estimated there were 16,000 to 20,000 newborn infants with DS in 2003 in China, based on Chinese population statistics information (16).

At present, there is no effective curative therapy for DS patients, and the only way to control DS is to prevent it by prenatal diagnosis. The diagnosis of DS is made by chromosome analysis, which can be initiated prenatally by chorionic villus

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sampling (CVS) or amniocentesis (AC). In view of the risk of invasive procedures, prenatal screening for DS has developed rapidly over the past 20 years. In 1988, maternal age screening was improved by the second trimester triple test, which measures the level of α-fetoprotein (AFP), unconjugated estriol (uE_3), and human chorionic gonadotrophin (hCG) in the maternal serum. Some centers adopted the double test without uE_3 (21). Gilbert notes that there are nine maternal screening strategies for DS (8), which can be followed by prenatal cytogenic diagnosis, if indicated.

In China, maternal serum screening for DS was traced back to 1996 (15). Only a few Chinese studies have reported the effectiveness of the maternal serum screening strategy with a large sample size. Most papers have studied the double test in the second trimester, in Beijing, Guangzhou, Quanzhou, Shanghai, and other cities in the eastern areas (13;20;27;29). Clearly, maternal serum screening is not widespread in China, and its coverage is quite low in general, even in large cities. To improve the population's health status and quality of life, it is undoubtedly necessary to develop and implement prenatal screening followed by more definitive diagnosis; however, little information of this strategy's effectiveness and cost-effectiveness is provided to policy makers and healthcare providers to make decisions. This study intends to assess the cost-effectiveness of prenatal diagnosis interventions for DS in China from a societal perspective, and provide evidence-based information to health policy makers and providers.

METHODS

Field Survey

Shanghai, Shijiazhuang and Tangshan in Hebei, and Xi'an in Shaanxi were selected to be study sites. Seven healthcare institutions with the capacity to perform 500 prenatal screens annually were surveyed in 2004. Data collected included volume of services, uptake rate, and price of health services related to prenatal diagnosis. Consultation with physicians complemented our field survey to provide additional information about prenatal screening and diagnosis.

Literature Review

A literature review of Chinese papers was carried out to gain a solid understanding of safety, effectiveness, and uptake rate of prenatal diagnosis for DS in China. Literature retrieval was done by CBMDisc, and key words were "Down's syndrome," "prenatal diagnosis," or "prenatal screening." If related parameters are not available in Chinese, we mainly depended on the HTA report and the systematic review in English.

Economic Evaluation

Decision Model. This study simulates expected health outcomes of different prenatal diagnosis interventions in a cohort of 10,000 pregnant women. The first strategy is no prenatal screening and diagnosis at all. This model is called "without intervention." The second strategy assumes that karyotyping by CVS or AC is delivered only to those pregnant women 35 years of age and older. This approach is called "maternal age screening strategy." The third strategy models maternal serum screening with the AFP and hCG double test to pregnant women in the second trimester, which is widely used in China, then the diagnostic test is only for high-risk women. We term this approach the "maternal serum screening strategy." We did not include the triple test in the model because it is not widely used in China.

We include five health outcomes in the model. These outcomes are averted DS birth by diagnosis, undiagnosed DS live birth, fetal loss due to CVS or AC, spontaneous miscarriage, and normal live birth.

Determination of Costs, Effectiveness, and Benefits

Costs Measurement and Valuation. From the societal standpoint, health services costs calculated on the basis of charges are equal to real costs born by patients and third payers, so this study treats health service expenses as costs. Direct medical costs include screening, genetic counseling, AC, karyotype analysis, and pregnancy termination of a DS fetus. Direct nonmedical costs, productivity loss, and intangible costs are not included in the study. There are few additional costs of nonmedical and productivity, because prenatal screening and diagnosis occur when pregnant women receive their routine prenatal care checkup. All measured costs occurred within 1 year; therefore, there is no need to discount over time. Costs in yuan were converted into U.S. dollars at the exchange rate current at the time of the data collection, 8.28 yuan = US$1.00.

The following models were used:

$$\begin{aligned}\text{CMAS} = {} & (\text{NPW\_35} \times \text{PG}) + (\text{NPW\_35} \times \text{URD} \times \text{PD}) \\ & + (\text{NDS\_35} \times \text{RP} \times \text{PT}) + (\text{NFL\_35} \times \text{PM})\end{aligned}$$

Where CMAS is societal costs for maternal age screening strategy; NPW_35 is the number of pregnant women older than 35 years of age; PG is the price of genetic counseling; URD is the uptake rate of diagnosis in women 35 and older; PD is the price of diagnosis; NDS_35 is the number of DS diagnosed after uptake diagnosis in pregnant women older than 35 years; RP is the rate of termination of pregnancy after DS diagnosed; PT is the price of termination; NFL_35 is the number of fetuses lost due to an invasive diagnostic procedure in pregnant women older than 35 years; and PM is the price of miscarriage.

$$\begin{aligned}\text{CMSS} = {} & (\text{NPW} \times \text{URPS} \times \text{PS}) + (\text{NP} \times \text{PG}) \\ & + (\text{NP} \times \text{URDP} \times \text{PD}) + (\text{NDS} \times \text{RP} \times \text{PT}) \\ & + (\text{NFL} \times \text{PM})\end{aligned}$$

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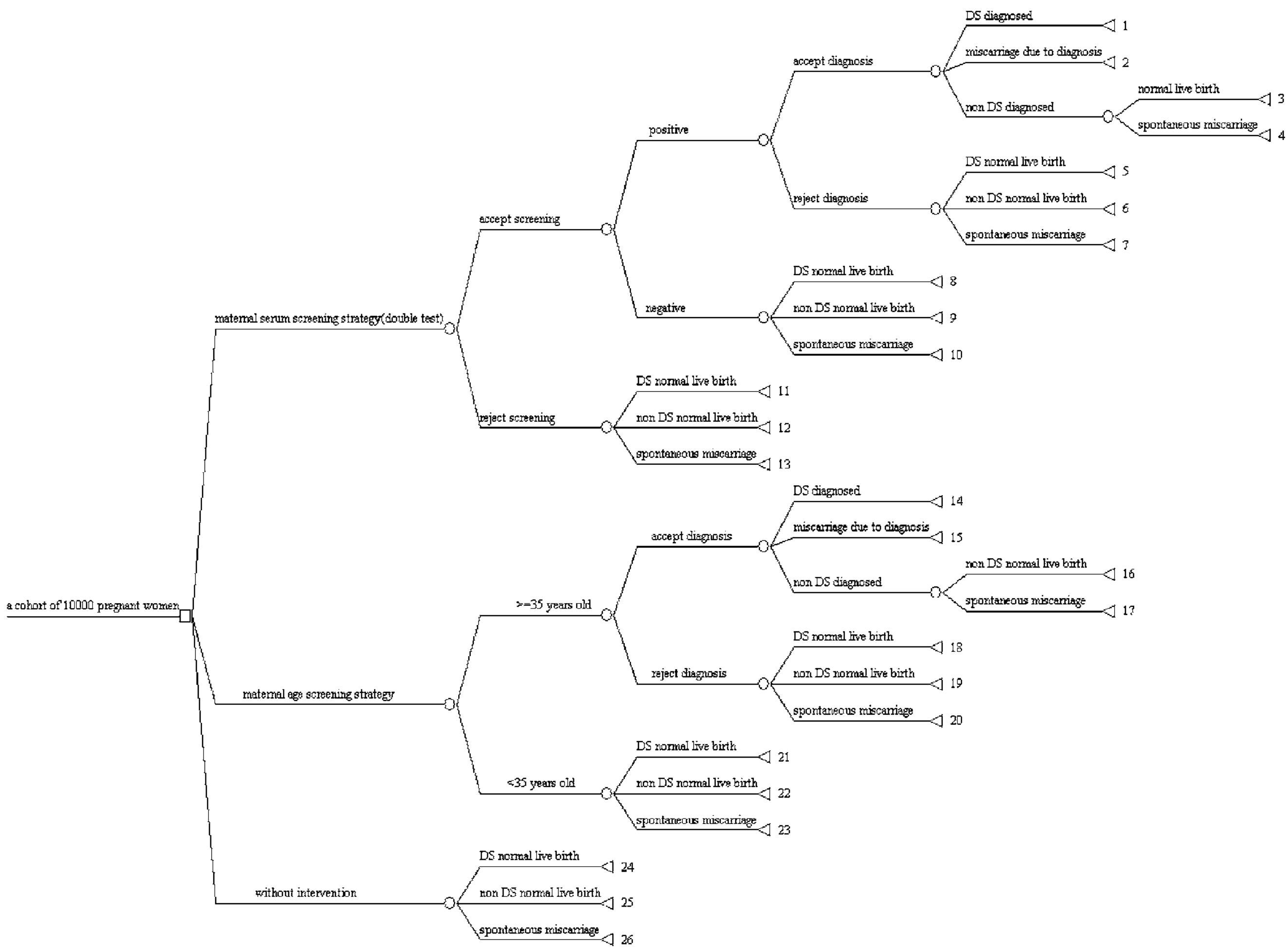

Figure 1. Decision model of three prenatal diagnosis strategies.

Where CMSS is the societal costs for maternal serum screening strategy; NPW is the number of pregnant women; URPS is the uptake rate of prenatal screening (maternal serum); PS is the price of prenatal screening (maternal serum); NP is the number of positive pregnant women after screening; URDP is the uptake rate of prenatal diagnosis in the screened people with positive value; NDS is the number of DS diagnosed after uptake diagnosis in pregnant women; and NFL is the number of fetuses lost due to an invasive diagnostic procedure in pregnant women.

Our indicator of the effectiveness of each strategy is the number of prevented DS births (diagnosed DS cases). The safety of the strategy is measured as the normal fetal loss per DS birth prevented. The smaller this index is, the safer the strategy (22).

Cost-Effectiveness Analysis

The three screening strategies can be compared by the costs per DS case prevented. Incremental cost-effectiveness analysis is also used to demonstrate the additional effectiveness resulting from marginal additional inputs.

Sensitivity Analysis

One-way sensitivity analysis is used to evaluate the robustness of the results. The key factors that influence the economic evaluations are identified and are allowed to vary to see how sensitive the program evaluations are to each of these variables.

RESULTS

Decision Model of Prenatal Diagnosis Interventions for DS

The decision tree of the three prenatal diagnosis interventions is shown in Figure 1.

Model Parameters

The values for all of the model parameters are derived from the literature, field survey, and expert opinion. They are reflections of the current screening picture in China to some extent. These values, together with the sources on which they are based, are shown in Table 1.

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Table 1. Main Model Parameters and Sources

Description of parameters	Initial value	Range	Sources
Incidence of DS(‰)			
-All pregnant women	1.117	.64–1.8	(3;9;11;18;25;28)
-Pregnant women 35 years of age and older	5.32	2.59–15.1	(2;7;26)
-Pregnant women younger than 35	.88	.576–2.02	(1;7;10)
Sensitivity of the double test (%)	70	60–80	(1;8;10;18;20;27, a, b)
False-positive rate of the double test (%)	5	3–12	(1;18;20;27, a, b)
Sensitivity and specificity of AC (%)	100	98–100	(8;27, a, b)
Miscarriage rate due to AC (%)	.9	.5–1.5	(8;19)
Uptake rate of serum screening (%)	50	30–80	(a, b)
Uptake rate of AC among screened people with positive value (%)	36	21–50	(5;10;18;27;28, a, b)
Uptake rate of AC in pregnant women 35 years of age and older (%)	25	10–50	(a, b)
Termination rate after diagnosed with DS (%)	100	90–100	(3;8;11, a)
Percent of pregnant women 35 years of age and older among all pregnant women (%)	5	3–10	(4;6;23;27;28)
Spontaneous miscarriage (%)	4.26	4.26	(14)
Price of the double test ($)	14.5	7.2–21.7	b
Price of genetic counseling ($)	1.4	.5–2.2	b
Price of prenatal diagnosis (AC and karyotype included) ($)	60.4	36.2–96.6	b
Price of termination ($)	241.5	181.2–301.9	a
Price of miscarriage ($)	241.5	120.8–362.3	a

DS, Down's syndrome; AC, amniocentesis; a, expert opinion/consultation; b, data from field survey.

Table 2. Simulated Effectiveness of the Three Strategies in a Cohort of 10,000 Pregnant Women

Expected outcome	Without intervention	Maternal age screening strategy	Maternal serum screening strategy
DS diagnosed	.00	.67	1.41
DS live births	11.17	10.36	9.76
Fetal losses due to AC	.00	1.13	.82
Spontaneous miscarriages	426.00	426.00	425.91
Unaffected DS live births	9,562.83	9,561.84	9,562.10
Total	10,000.00	10,000.00	10,000.00
Safety index	–	1.69	.58

DS, Down's syndrome; AC, amniocentesis.

Simulated Effectiveness

The decision model shows that maternal age screening strategy and maternal serum screening strategy could prevent .67 and 1.41 DS births in the cohort of 10,000 pregnant women, respectively, compared with no intervention. The risk of the maternal age screening strategy and maternal serum screening strategy could induce 1.13 and .82 fetal losses, respectively, due to invasive diagnostic procedures, and the safety index for the latter is better (see Table 2).

One-way sensitivity analysis demonstrates that the effectiveness of maternal serum screening is better than that of the age strategy if the uptake rate of serum screening is over 24 percent and other factors hold constant. If the uptake rate of prenatal diagnosis in the pregnant women 35 years of age and older is over 52 percent, or the percentage of pregnant women 35 years of age and older in all pregnant women is over 10.4 percent, or the incidence of pregnant women 35 years of age and older is over 11.1 per thousand, the age strategy could be superior to the serum strategy; however, the likelihood of those thresholds occurring is very small. We conclude that the serum strategy dominates the age strategy.

Cost-Effectiveness Analysis of the Three Strategies

The costs per DS birth prevented for the three interventions are US$0; US$13,091, and US$56,048, respectively, with the maternal age screening strategy apparently much more cost-effective than the maternal serum screening strategy. Compared with the maternal age screening strategy, the incremental cost-effectiveness ratio of the maternal serum screening strategy is US$94,526 per DS birth averted (see Table 3).

Our results indicate that the traditional maternal age screening strategy is more cost-effective than the newer maternal serum screening strategy. One-way sensitivity analysis showed that there are many factors that influence the efficiency of maternal serum screening strategy, including the false-positive rate of the double test, the detection rate of the double test, the price of the double test, the uptake rate of AC among people screened positively, and the incidence

Table 3. Cost-Effectiveness Analysis of the Three Strategies

Strategies	Costs (US$)	Effectiveness (DS prevented)	Costs-Effectiveness (US$)	ICER (US$)
Without intervention	0	.00		
Maternal age screening strategy	8,705	.67	13,091	
Maternal serum screening strategy	78,884	1.41	56,048	94,526

DS, Down's syndrome; ICER, incremental cost-effectiveness ratio.

Table 4. Comparison of Incremental Cost-Effectiveness Ratios of Different Scenarios (Program Costs and DS Cases Detected in a Cohort of 10,000 Pregnant Women)

Scenarios	Costs (US$)		Effectiveness		ICER
	Age strategy	Serum strategy	Age strategy	Serum strategy	(US$)
Initial model[a]					
URPS=50%,URDP=36%,URD=25%,PS=14.5	8,705	78,884	.67	1.41	94,526
Uptake rate of AC					
URPS=50%,URDP=46%,URD=35%,PS=14.5	11,898	80,565	.93	1.80	79,167
URPS=50%,URDP=56%,URD=45%,PS=14.5	15,090	82,246	1.20	2.19	67,676
URPS=50%,URDP=66%,URD=55%,PS=14.5	18,282	83,927	1.46	2.58	58,755
URPS=50%,URDP=76%,URD=65%,PS=14.5	21,474	85,608	1.73	2.97	51,628
Uptake rate of screening and AC					
URPS=60%,URDP=46%,URD=35%,PS=14.5	11,898	96,678	.93	2.16	69,093
URPS=70%,URDP=56%,URD=45%,PS=14.5	15,090	115,144	1.20	3.07	53,561
URPS=80%,URDP=66%,URD=55%,PS=14.5	18,282	134,283	1.46	4.13	43,521
URPS=80%,URDP=80%,URD=80%,PS=14.5	26,263	138,049	2.13	5.00	38,866
Price of screening					
URPS=50%,URDP=36%,URD=25%,PS=12.1	8,705	66,806	.67	1.41	78,259
URPS=50%,URDP=36%,URD=25%,PS=9.7	8,705	54,729	.67	1.41	61,991
URPS=50%,URDP=36%,URD=25%,PS=8.5	8,705	48,690	.67	1.41	53,858
URPS=50%,URDP=36%,URD=25%,PS=7.2	8,705	42,652	.67	1.41	45,724
URPS=50%,URDP=36%,URD=25%,PS=4.8	8,705	30,574	.67	1.41	29,456
Ideal scenario					
URPS=60%,URDP=46%,URD=35%,PS=12.1	11,898	82,185	.93	2.16	57,282
URPS=70%,URDP=56%,URD=45%,PS=9.7	15,090	81,328	1.20	3.07	35,458
URPS=80%,URDP=66%,URD=55%,PS=7.2	18,282	76,312	1.46	4.13	21,771
URPS=80%,URDP=80%,URD=80%,PS=4.8	26,263	60,754	2.13	5.00	11,992

[a] The model's initial values are URPS = 50%, URDP = 36%, URD = 25%, PS = US$ 14.5.
URPS, uptake rate of prenatal screening (maternal serum); URDP, uptake rate of prenatal diagnosis among screened women with positive value; URD, uptake rate of prenatal diagnosis in women aged 35 and above; PS, price of prenatal screening (maternal serum); AC, amniocentesis.

of DS. The robustness of the maternal age screening strategy is influenced by the incidence of DS in pregnant women 35 years of age and older and the price of prenatal diagnosis. Other parameters are shown to have little impact on the cost-effectiveness ratio of the two strategies. These parameters include the uptake rate of maternal serum screening, the price of genetic counseling, and the uptake rate of diagnosis of pregnant women 35 years of age and older.

Varying the values of various parameters tips the cost-effectivness determination from maternal age screening to maternal serum strategy in Table 4. For example, if the uptake rate of prenatal diagnosis is increased both in the positively screened women and women 35 years of age and older, the incremental cost-effectiveness ratio would decrease, holding constant the uptake rate of serum screening and the price of serum screening. Similarly, if the uptake rate of serum screening, the uptake of prenatal diagnosis both in positively screened women and women 35 years of age and older are increased, with the price of serum screening held constant, the incremental cost-effectiveness ratio would be reduced. If the price of serum screening decreased while the other three factors are held constant, the incremental cost-effectiveness ratio is also reduced. In the ideal context in which uptake rates are increased and the price of serum screening are reduced, the incremental cost-effectiveness ratio would be dramatically better. This observation demonstrates how the efficiency of the maternal serum screening strategy can be improved in China in the future.

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DISCUSSION

Cost-Effectiveness of Prenatal Diagnosis for DS in China

The literature on prenatal diagnosis generally supports the serum screening strategy preventing DS births. Most studies have suggested that the serum screening strategy is better than the age screening strategy in terms of effectiveness and cost-effectiveness (8;21;22).

Our research, however, finds that the serum screening strategy is not as cost-effective as the maternal age screening strategy in China. Comparing the international and domestic clinical practice experiences, we found several explanations why the maternal serum screening strategy is not as cost-effective as it was thought to be in China.

Justification of Serum Screening

It is well known that the incidence of DS is associated with maternal age, and incidence in pregnant women 35 years of age and older is considerably higher than that of women younger than 35. However, the proportion of pregnant women 35 years of age and older ranges from 3 to 10 percent of total pregnant women in China, rather low. Pregnant women younger than 35 constitute a dominant share, and probably produce many DS cases even though the incidence rate of DS is relatively low. So it is necessary to provide the prenatal screening in pregnant women based on informed consent, not only to women older than 35, but also to those below the age of 35.

Health technology is always the combination of efficacy and safety. The choice of adopting health technology is a balance of potential benefits and risks, as safety is an important concern. If the CVS or AC had been recommended to all pregnant women, the miscarriage rate attributed to invasive procedures would increase dramatically. With regard to safety, serum screening followed by a diagnosis strategy is safer than age screening plus diagnosis strategy. Also, more DS cases are detected by serum screening than from age screening. So the serum strategy is safer and more effective, but it needs more resource inputs for better outcomes.

Efficacy and Effectiveness

One factor influencing the cost-effectiveness of DS prevention is the gap between efficacy and effectiveness of intervention. Theoretically, the double test is a good option with acceptable efficacy and 60–80 percent sensitivity and 95 percent specificity. Given the incidence of DS of 1.117 per thousand, if the screening sensitivity is 70 percent, one should detect at least 7.8 DS cases before birth. However, in fact, only 1.39 DS cases are identified by serum screening in actual screening programs. We next look for the underlying reasons why this gap is so large.

If we increase the uptake rate of serum screening, and other factors are held constant, the sensitivity analysis results show that the cost-effectiveness ratio is only slightly changed. Therefore, the uptake rate does not appear to explain the poor effectiveness of screening.

The uptake rate of AC in pregnant women with a positive serum screening value is assumed as 36 percent initially, which is dramatically lower than the rate reported in Western journals, around 80 percent. This makes a big difference in the results because many high-risk pregnant women do not accept or do not believe the results of the diagnosis, which defeats the purpose of screening. Undoubtedly, there is a declining trend in cost-effectiveness when the uptake increases. There are two reasons that explain the low acceptability of intrusive diagnosis for pregnant women. First, the traditional culture influencing compliance of prenatal diagnosis is the Chinese population's traditional attitude about pregnancy. In general, women are afraid of accepting intrusive interventions such as CVS and AC when they are pregnant, even if there is clear evidence demonstrating high risks. Second, the procedure-related miscarriage rate due to CVS or AC in China is higher than that of Western countries because only a few specialty hospitals have the capacity to do the test well; the number of CVS or AC procedures is quite low. Therefore, increasing the uptake rate of AC is crucial to improving the cost-effectiveness of maternal serum screening.

Costs

Based on the sensitivity analysis, cost-effectiveness will be more cost-effective when the price of screening declines. When the price of screening is cut by half, the ICER drops by 48 percent. When the price of screening decreases by a third, the ICER drops by 31 percent.

We also found that the price ratio between serum screening and AC in China is quite different from that of the United Kingdom. Gilbert showed that the unit cost of AC was £208, and the unit cost of the double test in the second trimester was £10, so the price ratio is over 20 (8). However, the price ratio between the two services in China is low, with AC costing 500 yuan, and the double test screening 120 yuan. The different price ratio also influences the cost-effectiveness. If the AC is not very expensive relative to that of the double test, there is less financial incentive to choose serum screening over the diagnostic procedure. If the screening is relatively costly, there is less justification to implement it in a large population. In developed countries, such as the United Kingdom, the price ratio of diagnostic service and screening is high, so screening is favored from the economic viewpoint. If the price ratio is quite low, on the other hand, the price of screening is closer to that of diagnostic services, and so diagnostic procedures tend to be more efficient.

The price ratio in China's health service industry reflects the country's pricing mechanism. In the past, in a deliberate attempt to make healthcare services affordable, the prices of most medical services were kept low. So prices did not reflect either actual costs or market behavior driven by supply and demand. From the 1980s, government subsidies to providers decreased, but prices of basic health services still could not reflect actual costs. As a supplementary policy, the government permitted pricing based on costs for new health services, mainly high-technology services. In general, new services now have higher prices than costs. The above policies lead to the distortion of prices in health care, in which overpriced services and underpriced services coexist. Of course, providers are inclined to overuse overpriced services. We did cost accounting of all related services in our study program, and we found that prenatal diagnosis and genetic counseling tend to be underpriced services, whereas serum screening is one of the overpriced services (12). The price ratio is also a factor that pushes providers to use screening rather than diagnosis.

POLICY IMPLICATIONS

Improvement of the efficiency of serum screening depends on improving the effectiveness of screening and lowering its price. How can screening's effectiveness be improved? The key drivers are changes in pregnant women's knowledge, attitude, and behavior. Knowledge of Down's syndrome, its disease burden, and prevention strategy should be transferred to the pregnant woman and her family by health promotion programs, premarital care, voluntary pregnancy courses, or routine early pregnancy check-ups. These activities will encourage pregnant women to opt for screening. Qualified genetic counseling to high-risk pregnant women will help patients to understand the significance and value of further testing, and reduce the likelihood of poor advice, so that the uptake of diagnosis would be increased. In addition, the mechanism of avoiding the risk of prenatal diagnosis should be established, mainly for miscarriage due to invasive diagnostic procedures and DS live births due to technology's false-negative defects.

Of course, it is mandatory to ensure informed consent and pregnant women's autonomy at all stages according to Chinese regulations, rules, and ethical guidelines. According to the proposed ethical guidelines for prenatal diagnosis by the World Health Organization, prenatal diagnosis should be voluntary in nature, and the woman's and/or couple's choices in a pregnancy with an affected fetus should be respected and protected, within the framework of the family and of the laws, culture, and social structure of the country (24).

The second way is to look for new interventions that are more cost-effective in other countries to see if they would fit within the Chinese context. Clinical efforts now focus on improvement of the sensitivity and specificity of serum screening tests, more markers, or including ultrasound testing, so that the probability of women needing an invasive diagnostic test would be reduced or eliminated (17). Such practice meets the needs of providers and patients for highly effective, low risk, cost-effective services.

How can the price of screening be reduced or the price ratio among related clinical services be changed? Setting a rational price is very important because it affects incentives. The health authority and pricing authority should set the price of health services based on unit costs, so that the price ratio is rational. Our study showed it is necessary for the government to reduce the price of serum screening test, and raise the prices of prenatal diagnostic procedures; which will bring about a rational stimulant for the provider. If the price of the serum screening test were reduced, it would make the prenatal screening for Down's syndrome affordable for the urban vulnerable population and rural pregnant women.

LIMITATIONS

Taking Drummond's guideline for assessing economic evaluation as a criterion, the main issue of this study is that cost measurement was based on charges rather than unit costs; however, it brings a unique contribution to the study. The main barrier to the research is that data on unit costs of health services or other goods or services are not readily available. From the societal viewpoint, charges are equal to the real "costs" for the pregnant women and the third payer. Furthermore, it leads us to perform the sensitivity analysis of prices (charges) of services, because the efficiency of the maternal serum screening strategy in China is not consistent with that of the other countries. In addition, our findings are important in that the price and price ratio of prenatal screening and diagnosis should be adjusted so they are based on the unit costs so as to reflect their actual resource cost.

Some argue that our study's parameters are not homogeneous, and some parameters are of weak evidence. With regard to the parameters of the model, our principle is to use the Chinese parameters as much as possible, including information from Chinese literature review, field survey, and expert opinion. However, we had to make use of the Western parameters to some extent because some Chinese data were unavailable. In addition, we conducted sensitivity analysis to solve these issues to some extent.

We recognize that the generalizability of this study throughout China is questionable. In view of the diversity of the country, such as urban and rural, east and west, developed and developing, there are factors that make our findings more applicable to some areas of China than to others. However, the study provides the information on prenatal diagnosis for Down's syndrome to policy makers and providers throughout the country and will facilitate additional analysis to expand its geographic scope.

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