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Cost-Utility Analysis of Intensive Blood Glucose Control with Metformin versus Usual Care in Overweight Type 2 Diabetes Mellitus Patients in Beijing, P.R. China

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ABSTRACT

Objective: The UKPDS 34 and 51 showed that intensive blood glucose control with metformin is cost-saving and increases life expectancy in overweight type 2 diabetic patients in the United Kingdom. Diabetes is becoming an important health problem in urban China. This study addresses the effects and costs of intensive blood glucose control in this setting, aimed at supporting decision-making on the allocation of scarce resources.

Methods: A decision analytic model was developed to estimate the costs and effectiveness of intensive blood glucose control in overweight type 2 diabetes patients in Beijing, compared with usual care in accordance with clinical practice. The analysis was carried out from a health-care perspective.

Results: The base-case analysis (3% discount rate) shows that the average incremental costs of 11 years of intensive treatment with metformin are 126.6 K RMB (16.4 K US$) per quality-adjusted life year (QALY) gained. The incremental cost-effectiveness ratio (ICER) is sensitive to the costs of medication alternatives for metformin in the intensive treatment group and to the discount rate used (0%: 105.6 K RMB (13.7 K US$) per QALY gained; 5%: 171.0 K RMB (22.2 K US$) per QALY gained). After 20 and 30 years (lifetime) follow-up, the ICERs become increasingly favorable, 90.1 K RMB (11.7 K US$) and 74.3 K RMB (9.6 K US$), respectively. The ICER is most sensitive to the costs of medication alternatives for metformin in the intensive treatment group, and to the discount rate.

Conclusions: Interpretation of the findings depends on the maximum willingness to pay for a QALY in China, which has not officially been defined. If this would be three times the gross domestic product per capita, a value that has been suggested in the literature, lifetime intensive blood glucose control is likely to be cost-effective. Our findings differ from the UKPDS studies and emphasize that generalizing the results of studies across countries requires considerable adaptation to the local context.

Keywords: cost-utility analysis, diabetes mellitus type 2, Markov modeling, P.R. China.

Introduction

According to a national health survey carried out in 2002, 22.8% of all Chinese adults are overweight and 7.1% are obese [1]. In absolute numbers, overweight and obesity affects 260 million Chinese, or 20% of the total population, and these numbers are expected to increase [2,3]. Obesity or being overweight are important risk factor for type 2 diabetes, 90% of type 2 diabetes patients are either overweight or obese [4]. Currently, there are about 20 million diabetes patients in China, a number that is expected to increase to 50 million in 2025 [5]. A total of 95% of all diabetes patients are diagnosed as having type 2 diabetes [5]. Compared to a national similar survey in 1996, focusing on the population of at least 20 years of age, in 2002 the prevalence of diabetes had increased from 4.6% to 6.4% in big cities and from 3.4% to 3.9% in medium and small cities [1]. In 2002, the direct health-care costs of type 2 diabetes were estimated to amount 18.6 billion Ren Min Bi (RMB, Chinese Currency; 1 RMB is about 0.101 EUR and about 0.125 US$) combining all cities in China, representing 3.94% of national health-care expenditure in China in that year [5].

The UKPDS 34 demonstrated that, compared to usual care, intensive blood glucose control with metformin decreases the risk of diabetes-related end points in overweight diabetic patients [6]. Furthermore, the UKPDS 51 showed that the intensive blood glucose control with metformin is cost-saving in the United Kingdom and extends life expectancy for overweight type 2 diabetic patients [7]. This article examines the generalizability of the UKPDS findings to China, to support decision-making on the allocation of scarce health-care resources in this country. Given the differences between the two settings, the data requirements

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Figure 1 The two blood glucose control policies under study: usual care versus intensive treatment. Node type: a square node represents a decision. A node with an "M" depicts a Markov node (two arms).

[2,8] and the predominantly urban location of the disease, the article follows a modeling approach focusing on a single big city, namely the capital, Beijing. The findings may be pertinent for use by health-care decision-makers now that the Chinese Government has recently published a plan to implement a health-care insurance scheme that should cover nearly all citizens before 2010 [9]. At the same time, this study allows discussion and incorporation of cost-effectiveness data in the Chinese clinical guideline for diabetes treatment, an activity which is supported by the research community [10].

Methods

To address the issue of the generalizability of the findings of the UKPDS 34 to the setting of Beijing, China, a Markov model has been developed [11]. The ingredients of the model are subsequently introduced, based on a general strategy to use the scientific literature to populate the model and, where this is impossible or inappropriate, supplement these data with data collected from clinical experts.

States and Probabilities

States of diabetes patients are distinguished on the basis of the long-term complications of the disease. This study takes the UKPDS 34 as a starting point, distinguishing 10 nonfatal disease states, of which seven are long-term and three are temporary [12]. Patients in the "Well"-state are defined as not suffering from any long-term complications. From this state, patients can enter into seven different long-term disease states. If patients suffer two or more long-term complications, they enter the "Severe Complications" state, the floor state. Finally, when patients die from any cause, they enter the "Death" state, which is an absorbing state. A 1-year cycle length was applied in this study.

Patients, both men and women, had to be newly diagnosed with type 2 diabetes, 25 to 65 years old, overweight (>120% of ideal bodyweight), and with fasting plasma glucose (FPG) above 6.0 m mol/l and below 15 m mol/l without symptoms of hyperglycaemia when following a diet [6]. Briefly, usual care policy was aimed at maintaining FPG below 15 m mol/l (6.1–15.0 m mol/l) and at avoiding symptoms of hyperglycaemia. Patients could use oral agents and insulin to control FPG. Intensive treatment policy was aimed at obtaining near-normal FPG (i.e., <6.0 m mol/l) with metformin. Other oral agents and types of insulin could be added with the aim of maintaining FPG below 6.0 m mol/l. It should be noted that at present only 11.5% of diabetes patients meet the target of an HbA1c level lower than 6.5% [13,14].

Based on the cohort and in- and exclusion criterion of the UKPDS, we assume that newly diagnosed diabetes patents do not have any long-term complications [15]. It is also assumed that transition probabilities are constant over time (the Markovian assumption) [16]. Transition probabilities in the "Well" state are calculated using the UKPDS 34 study. The probability of patients in the "Well" state and in the intensive treatment arm to suffer from any complications is regarded as a baseline probability. Clinical experts estimated the risk ratios of suffering other complications compared with a baseline. Transition probabilities in "Complication" states are derived from these baseline values multiplied by risk ratios. It was assumed that the transition probabilities and state costs in each of the complication states are the same in the two arms. The basic outline of the study is shown in Figure 1 and the structure of the model is shown in Figure 2.

Utilities of Health States

Given our focus on "value for money," it is appropriate to use "quality-adjusted life years (QALYs) gained" as the principle outcome in this study [17]. The utilities of the states are based on the UKPDS 62 [18]. Utilities of two other states, "Complication F: renal failure" and "Severe Complications" were derived from expert estimates.

Costs

This study applies a health-care perspective and is therefore limited to health-care costs. For modeling purposes, health-care costs are distinguished in two categories, transition (or event) costs of certain complications and state (or annual) costs in different states. Total costs are equal to the transition costs plus annual costs. There is a number of articles dealing with health-care expenditures of diabetes-related complications in China [19–33]. The remainder of the required cost data is based on estimates from eight selected experts in Beijing. Costs of metformin are derived from publications and from Intercontinental Marketing Services (IMS) (Norwalk, CT) data of all hospitals in Beijing,

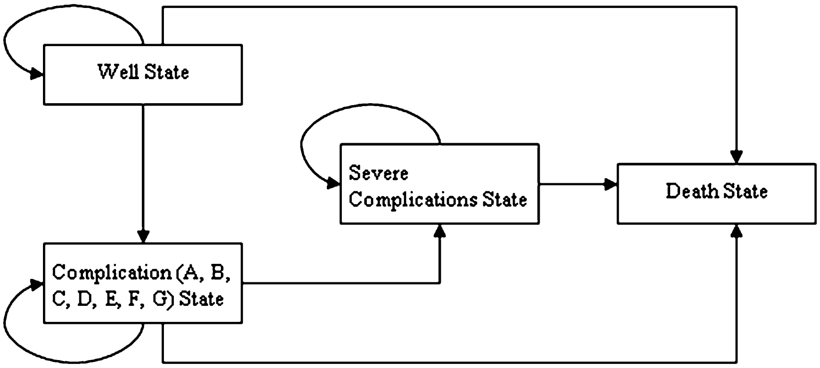

Figure 2 State-transition diagram. “Well,” “Complication” (seven states, A–G), “Severe complications,” and “Death” represent the Markov states. The arrows indicate pathways between the states.

which was provided by the Chinese branch of Novo Nordisk. Adverse events are not taken into account since the associated costs are only a minor part of the total costs [34].

Methodology of Expert Interviews

The interviews were carried out in the period between July 10 and July 26, 2006. All experts were interviewed individually at their hospital, seven by means of a face-to-face interview, and one by telephone. The experts were asked to answer questions on issues with which they were familiar. On average, each category of costs was based on five estimates.

Willingness to Pay for a QALY Gained

There is no documentation on the maximum willingness to pay (WTP) for a QALY gained in China. The Commission on Macroeconomics and Health of the World Health Organization estimated that the maximum value of one year of healthy life is about three times the annual earnings per capita [35]. Some studies are based on this approach [36,37], with one specifically referring to QALYs [37]. In 2005, the gross domestic product (GDP) per capita in Beijing was 44,969 RMB (5457 US$). Using this figure results in the assumption that the maximum WTP for a QALY gained in China might be about 134.9 K RMB [38].

Data Analysis

Based on the Markov model, the health economic analyses of usual care and intensive blood glucose control with metformin are carried out. Monte Carlo microsimulation was used in these analyses, and the number of trials is 10,000. Annual discount rates of 3% for both utilities and costs are applied in the base case analysis [39]. Univariate sensitivity analyses were performed to determine the main factors influencing the incremental cost-effectiveness ratio (ICER). All data were analyzed using TreeAge pro Suite 2007 (TreeAge Software, Williamstown, MA), and Excel 2003 (Microsoft, Redmond, WA). Figures were produced using SAS 9.1 (SAS, Cary, NC).

Results

Input for the Model

The transition probabilities in the “Well” state (for both intensive blood glucose control and usual blood glucose control) are derived from the UKPDS 34 (see Table 1). The transition probabilities in the complication states are equal to baseline values multiplied by ratios, which are derived from expert opinion (see Table 2). Costs were derived from selected articles in the literature and the remaining data are mainly based on estimates by experts (Tables 3–6). Generally, average unit cost estimates are used in our model. For certain items weighed costs are used, e.g., in case of myocardial infarction and renal failure. To simplify the calculation, we have used a fixed value of 16,961.5 RMB (2197.1 US$) to represent event costs of suffering long-term complications in any complication state [40]. This value is arrived at by weighing all event costs of long-term complications. Similar to this, event costs of “Temporary Complications” and “No Complications” are 1875.8 RMB (243.0 US$), and the event costs of all causes of death are 22,218 RMB (2878.0 US$). Utilities are mainly based on results of the UKPDS 62 (see Table 7). Utilities in any complication states are presented in absolute terms as well as in terms of the absolute loss compared with the “Well” state. Two utility values, “Complication F” (renal failure) and “Severe Complications,” are derived from expert opinion.

Base Case

To start with, the effects and costs of the two treatment strategies during a period of 11 years of follow-up are summarized in Table 8. At the end of this period, the intensive (metformin) control strategy results in an incremental gain of 0.25 QALYs, and the incremental cost is 33 K RMB compared to the usual care strategy. The associated ICER is 126.6 K RMB/QALY gained with intensive control with metformin versus usual care, which is a little lower than the (assumed) maximum WTP for a QALY gained, 134.9 K RMB

Table 1 Matrix of transition probabilities from the "Well" state to the other states in the model

Transition from Well state	To Com A: Nonfatal MI	Com B: Heart failure	Com C: Angina	Com D: Nonfatal stroke	Com E: Amputation	Com F: Renal failure	Com G: Blind in one eye	Severe complications	Death
Intensive care	0.006536992	0.003001444	0.005722211	0.001638270	0.001638270	0.000546388	0.003273855	0.000000000	0.013644000
Usual care	0.009054423	0.003858195	0.004990123	0.003631655	0.002044432	0.000454680	0.002951726	0.000000000	0.020186130

Com, complication; MI, myocardial infarction.

Table 2 Matrix of transition probabilities in complication states (both treatment arms)

Transition from complication state	To Severe complication state	Death
Complication A: nonfatal MI	0.053868250	0.047207379
Complication B: heart failure	0.074883354	0.062761255
Complication C: angina	0.084070055	0.039566878
Complication D: nonfatal stroke	0.073175883	0.045433691
Complication E: amputation	0.088909217	0.043932879
Complication F: renal failure	0.103493363	0.065490005
Complication G: blind in one eye	0.068375951	0.034928003
Severe complications*	0.103092619	0.063579880

*Patients with severe complications transiting to "Severe complications" here means that patients suffer another one or two long-term events in a single cycle. Although the state does not change, the events will incur costs, which are included in the model. MI, myocardial infarction.

(13.0 K Euro, 17.5 K US$). 126.6 K RMB/QALY gained is equal to 12.1 K Euro or 16.4 K US$/QALY gained [40].

At the end of follow-up, 11 years after initiating treatment, the probability of being in the "Well" state and "Death" state are 0.67 and 0.17 in the intensive control group, respectively, compared to 0.59 and 0.23 in the usual care group, respectively.

ICE Scatterplot and the Cost-Effectiveness Acceptability Curve (CEAC)

Each dot in the scatterplot represents a single result from the simulation, presenting the effects and costs of a comparator (intensive blood glucose control with metformin) relative to a baseline (usual care) (see Fig. 3). The ellipses represent a 95% confidence ellipse and 50% confidence ellipse, respectively. The adjusted CEAC is shown in Figure 4. In this analysis, the probability that the intervention would be cost-effective is maximally about 0.6, and the results are sensitive to the value of the WTP Max.

Sensitivity Analyses

Without discounting effects and costs, the intensive (metformin) control strategy leads to 0.28 QALYs gained, and the associated ICER is 105.6 K RMB/QALY gained, equal to 10.1 K EUR/QALY gained, or 13.7 K US$/QALY gained [40]. When a 5% discount rate of both costs and QALYs is applied, the intensive (metformin) control strategy leads to a gain of 0.20 QALYs, the ICER is then 171.0 K RMB/QALY gained, equal to 16.4 K Euro/QALY gained, or 22.2 K US$/QALY gained [40]. Other medicines' costs in the intensive treatment (metformin) group range from 1000 to 8000 RMB. Applying these values in a sensitivity analysis results in ICERs ranging from 46 K to 332 K RMB/QALY gained, so the ICER is most sensitive to this particular cost variable. The costs of General Diabetes Management ranged from 500 to 5000 RMB. Using these extreme values, the average ICER ranges

Table 3 Costs (RMB) of General Diabetes Management

Name	Unit costs in official documents [19]	Unit costs (expert opinion) Average (range)	Value used in the model	Frequency of use/ application per year Average (range)	Costs
Education and consultation	5–10	5.2 (0–10)	7.5	10.4 (1–24)	78.0
Visiting doctors/GPs	5–10	5.6 (4–9.5)	7.5	17.3 (8.5–24)	129.8
Monitoring blood glucose	4	5.6 (5–8)	4	155.2 (24–260)	620.8
Testing blood glucose	4	8 (8–8)	4	21.6 (18–24)	86.4
Testing HbA1c	25–70	63.8 (50–74)	63.8	4 (4–4)	255.2
Testing liver function	>20	45 (15–100)	45	2.1 (1.5–3)	94.5
Serum lipids test	21–128	117.5 (35–200)	117.5	1.8 (1.5–2)	211.5
Urine routine test	6–35	8 (8–8)	8	13.5 (12–15)	108.0
Renal function test	>20	52.5 (35–65)	52.5	1.75 (1.5–2)	91.9
Screening for foot diseases	>10	176.7 (90–240)	176.7	1.5 (1–2)	265.1
Screening for eye diseases	>10	23.3 (10–50)	23.3	1.6 (1–2)	37.3
Screening for microalbuminuria	70	46.7 (20–70)	70	4.4 (1–12)	308.0
Subtotal					2286.4

GP, general practitioner.

from 131 K to 161 K RMB/QALY gained. "Other medicines" costs in the usual care group ranged from 0 to 3000 RMB. Using these values the ICER varies from 76 K to 165 K RMB/QALY gained. The costs of metformin range from 113 to 1918 RMB. Based on these extreme values, the ICER ranges from 106 K to 170 K RMB/QALY gained. All state costs and event costs are tested as well, but these costs only have little influence on the ICER. The utility of the "Well" state is changed from 0.6 to 1 in the sensitivity analysis. The ICER ranges from 114 K to 182 K RMB/QALY gained. The incremental effectiveness increases from 0.18 QALY gained to 0.28 QALY (more than a 50% increase) gained with the increase of the utility value for the "Well" state from 0.6 to 1.

Second, we calculated lifetime costs and effectiveness of both treatment strategies. It was assumed that transition probabilities between states are constant over time. After 20 years, the intensive (metformin) blood glucose control strategy leads to 0.57 QALYs gained, and the associated ICER is 90.1 K RMB/QALY gained or 11.7 K US$/QALY gained. And after 30 years, the intensive (metformin) blood glucose control strategy leads to 0.94 QALYs gained with an associated ICER of 74.3 K RMB/QALY gained, or 9.6 K US$/QALY gained in 30 years.

Conclusion and Discussion

The results of the study show that lifetime intensive blood glucose control with metformin in overweight type 2 diabetes patients is likely to be cost-effective in Beijing if a maximum WTP for a QALY gained of three times the GDP per capita would serve as the principle criterion for decision-making. Although the estimates of QALYs gained and the associated ICERs at 20 or 30 years of follow-up are by necessity associated with a relatively high degree of uncertainty, there is a clear tendency toward increased cost-effectiveness of the intensive (metformin) control strategy with a longer time horizon. The sensitivity analysis showed that "other medicine's costs" in the intensive control (metformin) group is the most important variable influencing the ICER. Given the regular introduction of new pharmaceuticals in treatment of diabetes, this adds considerably to the uncertainty associated with

Table 4 Costs (RMB) of drugs and induced costs in the two treatment arms

Resource	Daily cost	Daily cost (IMS)[*]	Value used in the model	Costs (average)	Range	Annual costs
Metformin in the intensive treatment group	3.16 (1.57–5.52) [20]	2.9	3.16			1154
Additional tests related to metformin[†]				0		
Other medicines' costs in the intensive treatment group (expert opinion)[‡]				3380	(700–7800)	
Additional tests in the intensive treatment group				0		
Subtotal						4534
Other medicines' costs in the usual care group (expert opinion)[‡]				740	(0–3000)	
Additional tests in the usual care group				0		
Subtotal						740

[*] Based on weighed market share, and a daily dose of 1500 mg or 2550 mg.

[†] The test for monitoring drug-induced adverse effects.

[‡] To obtain near-normal FPG (i.e., <6.0 m mol/l) or <15.0 m mol/l, oral agents and different types of insulin will be added.

FPG, fasting plasma glucose; IMS, Intercontinental Marketing Services.

Table 5 Transition (event) cost (RMB) of complications

Event	Costs in literature or official document	Costs (expert opinion) Average (range)	Value used in the model
Fatal myocardial infarction	5,645–66,430 [21–24]	63,100 (10,000–130,000)	36,037.5
Nonfatal myocardial infarction	5,645–66,430 [21–24]	63,100 (10,000–130,000)	36,037.5
Sudden death		3,825 (800–7,500)	3,825
Heart failure		15,750 (8,000–25,000)	15,750
Angina		9,250 (4,000–15,000)	9,250
Fatal stroke	5,695–18,004 [21,22,25–27]	16,750 (10,000–30,000)	11,849.5
Nonfatal stroke	5,695–18,004 [21,22,25–27]	16,750 (10,000–30,000)	11,849.5
Death from peripheral vascular disease	16,521 [28]	18,000 (6,000–30,000)	16,521
Amputation	10,830–20,547 [28–31]	20,750 (10,000–30,000)	15,688.5
Death from renal disease	16,219 [28]	23,333 (10,000–40,000)	16,219
Renal failure*		0	0
Retinal photocoagulation	10,366 [28,31]	4,000 (1,000–7,000)	10,366
Vitreous hemorrhage	10,366 [28]	6,250 (5,000–7,500)	10,366
Blind in one eye	10,366 [28]	6,000 (6,000–6,000)	10,366
Cataract extraction	10,366 [21,28]	8,250 (6,500–10,000)	10,366
Death from hyperglycemia		6,000 (4,000–7,500)	6,000
Death from hypoglycemia		4,667 (3,000–7,500)	4,667
Fatal accident		5,167 (1,500–8,000)	5,167
Death from cancer		25,625 (6,500–50,000)	25,625
Death from any other specified cause		9,500 (8,500–10,000)	9,500
Death from unknown cause		7,500 (5,000–10,000)	7,500
Suffering long-term complications in complication states[†]			16,961.5
Suffer temporary complications or not suffering complications in complication states[‡]			1,875.8
Death in complication states[§]			22,218

*Annual costs are counted here. So, there are no event costs.

[†] We weigh the costs of long-term complications.

[‡] We weigh the costs of temporary complications and no complications.

[§] We weigh the costs of all causes of death.

the ICER. The cost-effectiveness ratio was also sensitive to the costs of metformin, "other medicine's costs" in the usual care group, the discount rate, and the utility value of the "Well" state. Most analyses indicate a potential for the intervention to be cost-effective, but the study does not allow for definitive conclusions.

The Model

The model that we developed was applied to assess both the 11-year follow-up and the lifetime effects and costs of the interventions studied. The former was chosen to allow a comparison with the UKPDS 34 study, the latter was chosen as it represents the recommended approach for modeling studies of chronic disease to be most useful for policymaking purposes. Other modeling studies have presented lifetime health effects and costs of diabetes treatment as well [41]. Any model is a simplification of reality. And although we have tried to go beyond minimum requirements, the model in our study does not include all complications, e.g., diabetic foot (or foot ulceration) has not been included. In theory, health economic studies

Table 6 State (annual) costs (RMB) of complications

State name	Costs in literature	Costs (expert opinion) Average (Range)	Value used in the model
Complication A: nonfatal MI	17,521–47,225 [31]	13,120 (7,500–25,000)	32,873
Complication B: heart failure	10,887 [31]	13,500 (7,000–35,000)	10,887
Complication C: angina	8,576 [31]	11,900 (7,500–25,000)	8,576
Complication D: nonfatal stroke	18,405 [31]	9,875 (7,000–15,000)	18,405
Complication E: amputation	10,998–14,012 [31]	12,000 (5,000–25,000)	12,505
Complication F: renal failure*	Hemeodialysis (HD) 75,865–98,204 Peritoneal dialysis (CAPD) 76,775–84,141 Kidney transplant (KT) 150,107 (First year) 54,078 (second year) [32,33]	106,650 (98,500–114,800) 99,150 (92,000–10,630)	102,000
Complication G: blind in one eye[†]	34,125 (blind in two eyes) [31]	6,500 (5,000–10,000)	8,000
Severe complications	With macro- and microvascular complication: 38,580 [31]	26,250 (15,000–30,000)	38,580
Death		0	0

*We weigh the costs of three main treatment alternatives, haemeodialysis (70%), peritoneal dialysis (20%), and kidney transplantation (10%). The differences in costs in the first year and the second year are relatively modest. To simplify the calculation, we apply a fixed value of 102,000 RMB.

[†] Based on expert opinion, the average costs are 6500 RMB. But the costs of general diabetic management plus intensive blood glucose control are nearly 7000 RMB. Due to this and because the highest value of the estimates is 10,000 RMB, we decided to apply an estimate of 8000 RMB here.

MI, myocardial infarction.

Table 7 State utility values based on UKPDS 62* [18]

State name	Value loss after the events (range)	State utility values
Well: no long-term complication (metformin group)	0	0.785
Well: no long-term complication (usual care group)	0	0.785
Complication A: nonfatal MI	–0.055	0.73
Complication B: heart failure	–0.108	0.677
Complication C: angina	–0.09	0.695
Complication D: nonfatal stroke	–0.164	0.621
Complication E: amputation	–0.28	0.505
Complication F: renal failure†	–0.21 (–0.082–0.35)	0.575
Complication G: blind in one eye	–0.074	0.711
Severe complications†	–0.27 (–0.084–0.4)	0.518
Death		0

*The UKPDS 62 used the EQ-5Q, and a Tobit Model in its estimates of utilities, with a mean tariff of 0.785.
†Estimated by experts.
Intensive blood glucose control does not influence utility values here.
MI, myocardial infarction.

should record all consequences of interventions and we know that diabetes can induce many long-term complications. But it is nearly impossible to follow up and register all of these in one clinical trial, and the UKPDS 34 only focused on a limited number of complications as end points. Basically, severe long-term complications are regarded as end points and minor ones are ignored in the UKPDS 34. For example, renal disease has four stages, but only the last stage, renal failure, was defined as an end point in this study. Because of limitations like these, we may have underestimated the total costs of treatment in both arms during follow-up.

The Role of Experts

In this study, estimates provided by eight clinical experts served as an important source of input for the model, and this may have introduced bias. All experts were interviewed individually, we did not inform the interviewees about other experts' estimates as part of the process because we were most interested in collecting their independent judgments. We dealt with the variety in responses by using the average value of each estimate provided and by including the ranges in the sensitivity analyses. We are aware of the fact that interviews are not the only method available to collect expert data. Examples of other methods for soliciting expert opinion include, e.g., the Delphi method and other formal consensus development methods, which have been widely used in the USA and the EU [42].

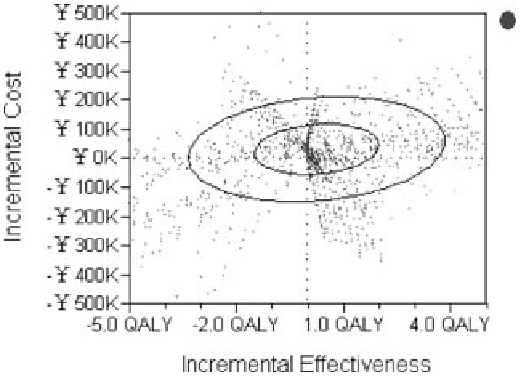

Figure 3 ICE scatterplot of intensive blood glucose control (metformin) versus usual care. ICE, incremental cost-effectiveness; QALY, quality-adjusted life year.

Ideally, of course, we would not have needed any expert opinion at all, but we were forced to use this approach due to a paucity of relevant, up to date and reliable data in the literature.

The Choice for Beijing as the Relevant Setting for the Study

Why was the study limited to a single city in China? First, at a general level, the choice for an urban setting can be justified by the fact that the prevalence of diabetes increases most rapidly in China's big cities. Second, the tremendous differences in economic development across China prevent using national level data, favoring a choice for a specific setting with relatively high-quality documentation. Third, although there are important differences between the patient population in the UK and China as a whole, these may not be as prominent when focusing on Beijing alone. To illustrate this latter point, life expectancy in the UK is about 5 or 6 years higher than in China in general [2,8] but, based on data from 2000, these differences were markedly reduced when specifically comparing the life expectancy of men and women in Beijing and the UK (Beijing: 74.3 [men], 78.0 [women]; UK: 74.7 [men], 79.7 [women]) [2].

Generalizability of the Findings to Other Cities in China

One of the consequences of the regional differences in economic development in China is that data collected in different regions of the country can hardly be generalized to the national level [2]. Clearly, the potential

Table 8 Main results of cost-utility analyses

Strategy	Cost (RMB)	Incremental costs	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
Usual care	56 K		6.59 QALY		8.6 K	
Intensive (metformin)	88 K	32 K	6.84 QALY	0.25 QALY	12.9 K	126.6 K

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

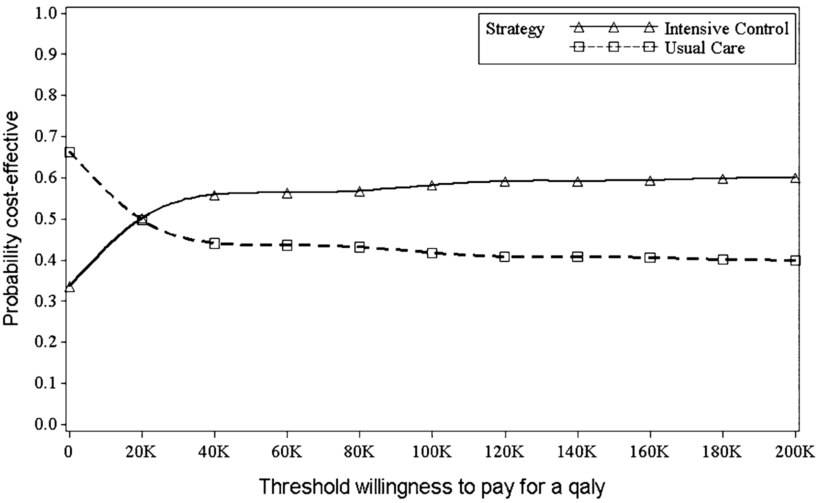

Figure 4 Adjusted cost-effectiveness acceptability curve (willingness to pay from 0 to 200 K RMB).

for generalizing the results of this study is limited to major urban areas. A number of considerations seem important here. First, citizens in only a few other regions, like Shanghai and Tianjin, are known to have a similar life expectancy as those living in Beijing, which is about five years longer compared to the average citizen [2]. In other major cities, e.g., Guangdong and Shenzhen, data on life expectancy are lacking. We stress this point because life expectancy, age-related morbidity/mortality rates, transition probabilities and QALYs gained are all linked. Third, and related to the former point, clinical practice and its variations are associated with levels of economic development and prosperity. Chinese national statistical reports show that the national annual expenditure per capita on medicine and medical services was 430 RMB (55.7 US$) for urban residents in 2002, but that this figure is 950 RMB (123.0 US$) for Beijing, which ranks highest in China [2]. Compared with the national level, Shanghai and Tianjin also have higher per capita expenditure on medicine and medical services than the national average, confirming their status as cities where the findings of this study might apply.

The International Level

Internationally, a few economic evaluations have been carried out which are linked to the UKPDS 34, including the UKPDS 51, UKPDS 72, and an application of the UKPDS 34 to Switzerland [6,7,13,43]. Those studies all report similar results in the sense that the intensive blood glucose control strategy dominates usual care (meaning that intensive treatment is less costly and more effective). The results for China are essentially different from those in Western countries, with increased effectiveness associated with increased costs of the intervention, but with as yet limited generalizability. It seems that there still is a long way to go before results obtained in Western countries, no matter the sophistication of the underlying models, can be reliably transferred to (parts of) developing countries like China. With this study we have tried to contribute to this development.

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