Cost-Minimization Analysis of Metformin and Acarbose in Treatment of Type 2 Diabetes

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ABSTRACT

Background: Metformin is the first-line oral hypoglycemic agent for type 2 diabetes mellitus (T2DM) per international guidelines with proven efficacy, safety, and cost-effectiveness. However, little information comparing it with acarbose exists. Objective: To study the cost-effectiveness of metformin and acarbose—two extensively adopted agents—in treating T2DM. Methods: Cost-minimization analysis was conducted on the assumption that metformin and acarbose have equivalent clinical effectiveness. The cost of treatment was detected and evaluated from a payer's perspective. In sensitivity analyses, several clinical scenarios were developed according to clinical practices and physicians' prescribing behaviors in China. Results: Metformin can save annual treatment costs by 39.87% to 40.97% compared with acarbose. Under a wide range of assumptions on utilization profile and physician prescribing behavior, it saves costs by 19.83% to 40.97% in patients whose weight is 60 kg or less and by 39.87% to 70.49% in patients whose weight is more than 60 kg, which corroborates the results that metformin is more cost-effective than acarbose. Conclusions: Metformin appears to provide better value for money than does acarbose. Findings from this study are consistent with those from previous studies that metformin is undoubtedly the first choice in the management of T2DM, with significant glucose-lowering effects and low treatment costs. Keywords: acarbose, cost-minimization, metformin, type 2 diabetes.

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Introduction

Diabetes is one of the common chronic diseases worldwide [1]. China leads among the countries with the highest prevalence of diabetes. In 2010, the prevalence of diabetes in Chinese adults 18 years and older was 11.6% (113.9 million) [2]. Because of the long duration and expensive treatment, diabetes not only affects patients' quality of life but also brings a heavy economic burden to both the family and the society. A study on the epidemic and economic burden of diabetes in China [3] indicates that the average annual growth rate of direct medical cost of diabetes was 19.9% in recent years, which was higher than the gross domestic product and national health care expenditure growth was 19.9% in recent years, which was higher than the gross domestic product and national health care expenditure growth.
carbohydrate diet, such as Chinese [10]. Little information exists, however, comparing metformin with acarbose in both clinical effectiveness and cost-effectiveness.

After a meta-analysis, it was found that glucose-lowering effects of metformin monotherapy and acarbose monotherapy are the same by direct comparison, while metformin monotherapy is a little better by indirect comparison [11]. This means that glucose-lowering effects of metformin monotherapy are at least as good as those of acarbose monotherapy. Thus, this study aimed to make an economic evaluation by using a cost-minimization analysis technique to see which drug is more cost-effective.

**Methods**

**Estimation of the Cost**

The perspective of the payer was used in this study because both drugs are covered by the payer. Cost was estimated on the basis of treatment schedules from the literature [12–19] and prices of both drugs in China; only direct medical costs were included. For metformin (brand name Glucophage, specification 500 mg × 20 tablets), the highest price set by the government is ¥29.2 and the lowest set by the market is ¥24.82; for acarbose (brand name Glucobay, specification 50 mg × 30 tablets), the highest and the lowest price is ¥74.2 and ¥61.92, respectively [20–23]. Both the lowest and highest prices were used to estimate the annual average treatment cost. Because both drugs are common oral hypoglycemic agents and tolerated well and have similar treatment efficacy and gastrointestinal adverse reactions, which can be alleviated by starting at a low dose and escalating the dose gradually [7,11,24–26], we, therefore, assume that patients taking both drugs have the similar frequency of doctor visits. Thus, we assume that the relevant costs in treating T2DM, such as doctors visit, diagnostic, inspection, and hospitalization cost, and so forth [27], can be set to be equivalent and not included in this study. All costs were based on 2014 prices and expressed in Renminbi (¥).

**Base-Case Identification**

There is no fixed dosage regimen for the management of hyperglycemia in patients with T2DM with metformin or acarbose or any other pharmacologic agents [24,25]. Data on medication use and average dosage were derived from the direct comparison section of the meta-analysis [11–19], which directly compared the treatment effect of metformin and acarbose and showed their comparable efficacy in the Chinese population (1500 mg/d for metformin and 150 mg/d for acarbose).

**Sensitivity Analysis**

Because physicians’ compliance with drug’s instruction recommendations or national guidelines with regard to the initiation and monitoring of drug dosage in treating T2DM is unknown, in sensitivity analysis, several different clinical scenarios were developed after interviews with physicians treating diabetic patients, to illustrate potential clinical situations as well as to analyze the difference in annual average treatment costs with metformin and acarbose.

Based on physicians’ prescribing behaviors in China and the potential increased risk for elevated serum transaminases in patients with low body weight [25], the usual maximum dose of acarbose is slightly different in different weight groups (150 mg/d for weight < 60 kg and 300 mg/d for weight > 60 kg) [28–30]. Meanwhile, because of the difference in clinical prescribing habits and cognition of physicians in China, metformin also has two usual maximum doses (1500 and 2000 mg/d) in clinical practice, which is not strongly associated with patients’ weight. Eight clinical scenarios, therefore, were developed according to different therapeutic regimens for patients with T2DM with different body weights to model different clinical conditions that may reflect real-world usage patterns of patients with T2DM. Scenario 1 considered all patients treated using only one oral drug (metformin or acarbose) at the initial dose. Scenarios 2, 5, and 6 involved patients who received only one oral drug (metformin or acarbose) at the usual maximum dose. Scenarios 3, 4, 7, and 8 simulated a situation that both drugs were titrated from the initial dose to the usual maximum dose gradually in patients with different body weights (Table 1). The common characteristics of scenarios 2 to 4 are that patients’ weight is 60 kg or less and that of scenarios 5 to 8 is that patients’ weight is more than 60 kg. Moreover, scenario 1 includes both weight groups (Table 1).

**Results**

**Annual Average Treatment Cost of Metformin and Acarbose at Base Case**

In base-case cost analysis, the annual treatment cost of metformin was ¥1558.90 while that of acarbose was ¥2260.08 when referring to the lowest price; the annual treatment cost of metformin and acarbose was ¥1598.70 and ¥2708.30 referring to the highest price, respectively. Under the same level of glycemic control, metformin could achieve annual cost savings by 39.87% (lowest price) or 40.97% (highest price) compared with acarbose (Table 2).

**Annual Average Treatment Cost of Metformin and Acarbose at Different Scenarios**

The annual treatment cost of metformin ranged from ¥452.97 to ¥2131.60 whereas that of acarbose ranged from ¥753.36 to ¥2708.30 at the four different scenarios (scenarios 1–4) in which patients’ weight is 60 kg or less. Under these assumptions, metformin also minimizes the cost in all the four scenarios regardless of changes in daily dosage or medication cost, remaining a cost-saving strategy of 19.83% to 40.97% (Table 2). The annual treatment cost of metformin ranged from ¥452.97 to ¥2131.60 whereas that of acarbose ranged from ¥753.36 to ¥5416.60 at the five different scenarios (scenario 1, and 5–8) in which patients’ weight is more than 60 kg. For all the five scenarios, metformin administration was the lower cost strategy compared with acarbose, for which savings ranged from 39.87% to 70.49% (Table 2).

**Discussion**

Economic evaluation refers to the comparative analysis of alternative projects in terms of their costs and consequences by using principles and methods of economics. In the context of current health policy, with more and more governments trying to limit the escalation in health expenditure, there is an increasing need to find medical treatment strategies that are as effective but less costly. A pharmacoeconomic approach is commonly used to evaluate the health benefit of drug treatments to gain good value for money. Economic evaluation of medical products is particularly important in a country such as China, where for the inclusion of a drug in the national essential drugs list, the call in and out of a drug in the National Reimbursement Drug List, and the pricing of new drugs, patent medicines, and other drugs,
### Table 1 - Clinical scenarios for patients with T2DM with different body weight.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Patient Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All weights</td>
<td>Metformin is maintained in initial dose (500 mg/d); acarbose is maintained in initial dose (50 mg/d).</td>
</tr>
<tr>
<td>2</td>
<td>Weight ≤ 60 kg</td>
<td>Metformin is maintained in usual maximum dose (2000 mg/d, given in divided doses); acarbose is maintained in usual maximum dose (150 mg/d, given in divided doses).</td>
</tr>
<tr>
<td>3</td>
<td>Weight ≤ 60 kg</td>
<td>Metformin is started at 500 mg/d for the first week and titrated up to 1000 mg/d given in divided doses in the second week and to 1500 mg/d given in divided doses from the third week onwards. Acarbose is started from 50 mg/d during the first week and titrated up to 100 mg/d given in divided doses in the second week and to 150 mg/d given in divided doses from the third week onwards.</td>
</tr>
<tr>
<td>4</td>
<td>Weight ≤ 60 kg</td>
<td>Metformin is started at 500 mg/d for the first week and titrated up to 1000 mg/d given in divided doses in the second week, to 1500 mg/d given in divided doses in the third week, and to 2000 mg/d given in divided doses from the fourth week onwards. Acarbose is started from 50 mg/d during the first week and titrated up to 100 mg/d given in divided doses in the second week and to 150 mg/d given in divided doses from the third week onwards.</td>
</tr>
<tr>
<td>5</td>
<td>Weight &gt; 60 kg</td>
<td>Metformin is maintained in usual maximum dose (1500 mg/d, given in divided doses); acarbose is maintained in usual maximum dose (300 mg/d, given in divided doses).</td>
</tr>
<tr>
<td>6</td>
<td>Weight &gt; 60 kg</td>
<td>Metformin is started at 500 mg/d for the first week and titrated up to 1000 mg/d given in divided doses in the second week and to 1500 mg/d given in divided doses from the third week onwards. Acarbose is started from 50 mg/d during the first week and titrated up to 100 mg/d given in divided doses in the second week, to 150 mg/d given in divided doses in the third week, and to 300 mg/d from the fourth week onwards.</td>
</tr>
<tr>
<td>7</td>
<td>Weight &gt; 60 kg</td>
<td>Metformin is started at 500 mg/d for the first week and titrated up to 1000 mg/d given in divided doses in the second week, to 1500 mg/d given in divided doses in the third week, and to 2000 mg/d given in divided doses from the fourth week onwards. Acarbose is started from 50 mg/d during the first week and titrated up to 100 mg/d given in divided doses in the second week, to 150 mg/d given in divided doses in the third week, and to 300 mg/d from the fourth week onwards.</td>
</tr>
</tbody>
</table>

T2DM, type 2 diabetes mellitus.

### Table 2 - The annual treatment cost of metformin and acarbose in patients with T2DM.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Price</th>
<th>Annual treatment cost (¥)</th>
<th>Cost difference (¥)</th>
<th>Saving in annual cost (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Acarbose</td>
<td>Metformin</td>
<td>Cost difference</td>
</tr>
<tr>
<td>Base case</td>
<td>Lowest</td>
<td>2260.08</td>
<td>1358.90</td>
<td>901.18</td>
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<tr>
<td></td>
<td>Highest</td>
<td>2708.30</td>
<td>1598.70</td>
<td>1109.6</td>
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<tr>
<td>Patients with T2DM with weight ≤ 60 kg</td>
<td>Scenario 1</td>
<td>Lowest</td>
<td>753.36</td>
<td>452.97</td>
</tr>
<tr>
<td></td>
<td>Highest</td>
<td>902.77</td>
<td>532.90</td>
<td>369.87</td>
</tr>
<tr>
<td></td>
<td>Scenario 2</td>
<td>Lowest</td>
<td>2260.08</td>
<td>1811.86</td>
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<tr>
<td></td>
<td>Highest</td>
<td>2708.30</td>
<td>2131.60</td>
<td>576.7</td>
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<td></td>
<td>Scenario 3</td>
<td>Lowest</td>
<td>2216.74</td>
<td>1332.83</td>
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<tr>
<td></td>
<td>Highest</td>
<td>2656.36</td>
<td>1568.04</td>
<td>1088.32</td>
</tr>
<tr>
<td></td>
<td>Scenario 4</td>
<td>Lowest</td>
<td>2216.74</td>
<td>1759.74</td>
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<tr>
<td></td>
<td>Highest</td>
<td>2656.36</td>
<td>2070.28</td>
<td>586.08</td>
</tr>
<tr>
<td>Patients with T2DM with weight &gt; 60 kg</td>
<td>Scenario 1</td>
<td>Lowest</td>
<td>753.36</td>
<td>452.97</td>
</tr>
<tr>
<td></td>
<td>Highest</td>
<td>902.77</td>
<td>532.90</td>
<td>369.87</td>
</tr>
<tr>
<td></td>
<td>Scenario 5</td>
<td>Lowest</td>
<td>4520.16</td>
<td>1358.90</td>
</tr>
<tr>
<td></td>
<td>Highest</td>
<td>5416.60</td>
<td>1598.70</td>
<td>3817.9</td>
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<tr>
<td></td>
<td>Scenario 6</td>
<td>Lowest</td>
<td>4520.16</td>
<td>1811.86</td>
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<tr>
<td></td>
<td>Highest</td>
<td>5416.60</td>
<td>2131.60</td>
<td>3285</td>
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<td></td>
<td>Scenario 7</td>
<td>Lowest</td>
<td>4346.78</td>
<td>1332.83</td>
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<tr>
<td></td>
<td>Highest</td>
<td>5208.84</td>
<td>1568.04</td>
<td>3640.8</td>
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<td></td>
<td>Scenario 8</td>
<td>Lowest</td>
<td>4346.78</td>
<td>1759.74</td>
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<td></td>
<td>Highest</td>
<td>5208.84</td>
<td>2070.28</td>
<td>3138.56</td>
</tr>
</tbody>
</table>

T2DM, type 2 diabetes mellitus.

* Lowest, the lowest set by market; highest, the highest price set by government.

1 Cost difference = annual cost of acarbose – annual cost of metformin.

2 Saving in annual cost = (annual cost of acarbose – annual cost of metformin) × 100/annual cost of acarbose.
it is now, by law, recommended that technical evaluation for the drugs be conducted by using evidence-based medicine and pharmacoeconomic approaches [31–34].

This study examined the costs of metformin and acarbose in the treatment of patients with T2DM. We used the cost-minimization analysis technique under the hypotheses that key clinical outcomes and adverse effects of both drugs are effectively equivalent based on results from a previous meta-analysis study [13]. Our results show that metformin seems to be more cost-effective than acarbose.

In economic evaluation, it is difficult to accurately measure the study variables, and each medication therapy may bring different treatment costs when applied among different populations or medical institutions; therefore, it is important to verify the effect of basic assumptions on study results. Thus, we developed eight scenarios, in sensitivity analyses, to mirror the real-life cost profile. The results are consistent with the base-case analysis, corroborating that metformin is more cost-effective than acarbose. Our results, however, may represent a cost-effective advantage for metformin only if differences in dosage adjustment and monitoring were observed in a real clinical practice and underlying hypotheses mentioned above are true.

Results from this study confirm findings from several economic evaluation studies conducted in China, comparing metformin monotherapy with acarbose monotherapy in the treatment of T2DM. The studies reported that metformin was cost-effective than acarbose for treating T2DM [35–41], and particularly, it was superior to acarbose in controlling fasting blood glucose [42–46]. As the course of T2DM prolongs, any single therapy may find it difficult to effectively control the blood glucose level of patients with T2DM, and then there is a need to use combination therapies to strengthen glycemic control in clinical practice. In this context, several studies assessing the comparative efficacy and cost of metformin and acarbose from the perspective of drug combination also indicate that metformin combination therapy is still a preferable therapeutic regimen compared with acarbose combination therapy [47–50]. Nevertheless, the reliability of these evaluation results might be constrained attributable to small sample sizes (range 87–705) in their basal clinical trials; thus, these findings should be considered with caution. Furthermore, a review of the economic evaluation of metformin hydrochloride and acarbose suggests that they have a similar role in prolonging the life of patients, improving the cardiovascular disease, and preventing or delaying the onset of T2DM [51]. Metformin hydrochloride is a preferred treatment for patients with T2DM, with a higher efficiency in reducing fasting blood glucose and minimum cost compared with other hypoglycemic drugs. Although acarbose is good at reducing postprandial blood glucose, it has a higher cost [51]. Moreover, in patients with impaired glucose tolerance, metformin demonstrates a better value for money [51]. Metformin is more cost-effective not only in treating T2DM but also in preventing the onset of diabetes compared with acarbose [52,53].

This study was conducted from a payer’s perspective, and the indirect cost related to the T2DM treatment was not taken into account. Direct medical costs theoretically consist of fees for doctor visit, medication cost, diagnostic cost, inspection cost, hospitalization cost, transport cost, and so forth [27]. However, in this study, we estimated only the drug cost, not other costs because we assumed that other costs are the same in the two treatment groups. This study, furthermore, considers only a single monotherapy for 1 year; however, in clinical practice, because of the complexity of diabetes, drug combination therapy is common and patients may switch drugs, which can have an impact on the cost; over a longer period, more complications related to diabetes, including microvascular and macrovascular disease, may occur [6], which can also add treatment costs. Thus, more studies are needed to understand the comprehensive annual costs to provide disease burden information for guiding decision making of resource allocation.

Regardless of these limitations, our study has a noteworthy strength that it is the first economic evaluation focusing on the comparison of metformin with acarbose in T2DM treatment, which is conducted on the basis of results from a meta-analysis study with large sample sizes and adequate clinical data.

Conclusions
Metformin appears to provide better value for money than does acarbose. Findings from this study are consistent with previous studies that metformin is undoubtedly the first choice in the management of T2DM, with significantly glucose-lowering effects and low treatment costs.

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REFERENCES


