Cost-Effectiveness of the Interventions in the Primary Prevention of Diabetes Among Asian Indians

Within-trial results of the Indian Diabetes Prevention Programme (IDPP)

AMBADY RAMACHANDRAN, DSC[1]
CHAMUKUTTAN SNEHALATHA, DSC[1]
ANNASAMI YAMUNA, PHD[1]
SIMON MARY, BSC[1]
ZHANG PING, PHD[2]

OBJECTIVE — In the Indian Diabetes Prevention Programme (IDPP), a 3-year randomized, controlled trial, lifestyle modification (LSM) and metformin helped to prevent type 2 diabetes in subjects with impaired glucose tolerance (IGT). The direct medical costs and cost-effectiveness of the interventions relative to the control group are reported here.

RESEARCH DESIGN AND METHODS — Relative effectiveness and costs of interventions (LSM, metformin, and LSM and metformin) in the IDPP were estimated from the health care system perspective. Costs of intervention considered were only the direct medical costs. Direct nonmedical, indirect, and research costs were excluded. The cost-effectiveness of interventions was measured as the amount spent to prevent one case of diabetes within the 3-year trial period.

RESULTS — The direct medical cost to identify one subject with IGT was Indian rupees (INR) 5,278 ($117). Direct medical costs of interventions over the 3-year trial period were INR 2,739 ($61) per subject in the control group, INR 10,136 ($225) with LSM, INR 9,881 ($220) with metformin, and INR 12,144 ($270) with LSM and metformin. The number of individuals needed to treat to prevent a case of diabetes was 6.4 with LSM, 6.9 with metformin, and 6.5 with LSM and metformin. Cost-effectiveness to prevent one case of diabetes with LSM was INR 47,341 ($1,052), with metformin INR 49,280 ($1,095), and with LSM and metformin INR 61,133 ($1,359).

CONCLUSIONS — Both LSM and metformin were cost-effective interventions for preventing diabetes among high risk-individuals in India and perhaps may be useful in other developing countries as well. The long-term cost-effectiveness of the interventions needs to be assessed.

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The global burden of diabetes is increasing, and developing countries face a grave health care burden due to this disease (1). Although the clinical and economic benefits of good glycemic control of diabetes in preventing vascular complications are well known (2–5), prevention of diabetes may have more far-reaching benefits by curbing the epidemic. India is facing a huge burden owing to the emerging epidemic of diabetes, with the largest number of diabetic individuals in the world (1). In the context of primary prevention, the results of the Indian Diabetes Prevention Programme (IDPP) have great significance. This program has demonstrated that moderate but consistent lifestyle modification (LSM) or therapeutic intervention with metformin could prevent or delay progression of impaired glucose tolerance (IGT) to diabetes with relative risk reductions of 28.5 and 26.4%, respectively (6). Combining the two did not enhance the benefits. A few other studies in Western populations had also shown that intensive LSM and pharmacological interventions can delay or prevent progression of IGT to diabetes (7–10).

Assessment of the cost-effectiveness of the IDPP is relevant for two reasons. First, although the cost and cost-effectiveness of preventing diabetes among high-risk individuals have been evaluated in Western populations (11,12), the cost-effectiveness of preventing diabetes in developing countries is unknown. Second, health care resources are more limited in developing countries such as India than in developed countries. Although both LSM and metformin intervention were shown to be cost-effective in developed countries, it is not clear whether such interventions should be implemented with the limited health resources in developing countries. Differences in the effectiveness and particularly in the cost of the intervention and treatments of diabetes and its complications would lead to different cost-effectiveness ratios for developed and developing countries. Information on the cost-effectiveness of preventing diabetes in developing countries is needed to make policy decisions related to prevention programs in developing countries.

The objectives of this study were to estimate the cost of delivering the LSM and metformin and the cost-effectiveness of the two interventions related to the control group as implemented in the IDPP. Information resulting from the

From the [1]India Diabetes Research Foundation, and Dr. A. Ramachandran's Diabetes Hospitals, Chennai, India; and the [2]Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia.

Address correspondence and reprint requests to Prof. A. Ramachandran, India Diabetes Research Foundation and Dr. A. Ramachandran's Diabetes Hospitals, 28, Marshall's Road, Egmore, Chennai 600008, India. E-mail: ramachandran@vsnl.com.

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Abbreviations: DPP, Diabetes Prevention Program; IDPP, Indian Diabetes Prevention Programme; IGT, impaired glucose tolerance; LSM, lifestyle modification; NNT, number needed to treat; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Components of expenditure considered for direct medical costs incurred during the intervention period of 3 years in various arms of the study*

Item and provider	Units (*n*/3 years)			Time (h spent/3 years)			Total cost in INR		
	Control	LSM	Met	LSM + Met	Control	LSM	Met	LSM + Met	Control	LSM	Met	LSM + Met
Standard lifestyle cost												2,739
Expenditure—laboratories												
Drug cost											1,561	1,561
Visits											375	375
Physician	0	12	10	12	—	1.5	0.99	1.5		1,292	620	1,292
Social worker	4	12	7	12	0.83	2.25	0.66	2.25	47	504	93	504
Dietician	1	12	1	12	0.16	2.25	0.33	2.25	10	531	20	531
Helper	1	12	5	12	0.16	1.5	0.58	1.5	9	336	65	336
Technician	0	6	8	6	—	0.48	0.48	0.48		60	75	60
Phone calls												
Social worker	1	39	10	39	0.05	1.98	0.24	1.98	3	745	33	745
Dietician	0	39	0	39	—	1.98	—	1.98		777	—	777
Helper	2	0	48	0	0.10	—	0.41	—	6	—	263	—
Secretary	3	36	36	72	0.15	0.15	0.25	0.15	6	78	78	156
Overhead charges									813	900	846	894
Travel cost									1,845	4,913	3,113	4,913
Total INR (U.S. $)									2,739 (61)	10,136 (225)	9,881 (220)	12,144 (270)

Met, metformin.

study will help to answer two basic questions: *1*) Are the interventions used in the IDPP suitable for India, where limited health care resources are available? and *2*) What resources would be needed if interventions similar to those in the IDPP were implemented on a large scale in low-resource settings?

RESEARCH DESIGN AND METHODS

IDPP

Subjects aged 35–55 years and of both sexes with reproducible IGT, i.e., positive test results on two occasions, were selected. A total of 531 participants were individually randomly assigned in the four arms of the study: namely, group 1, subjects given standard health care advice (control); group 2, subjects advised on LSM; group 3, subjects treated with metformin; and group 4, subjects advised on LSM and treated with metformin in consecutive order.

The field team members included a physician, laboratory technicians, dietitians, social workers, and helpers. They were trained to conduct all of the test procedures. The team members visited the work site or the residence of the subjects for screening, random assignment, and follow-up. The intervention procedure was explained individually at the time of subject randomization and then again by telephone after 2 weeks or by letter. Personal sessions were conducted at 6-month intervals for assessing subjects' adherence and for continued motivation. The time spent by the dietitian, social worker, and physician with each participant ranged from 0.15 to 0.75 h/year. Monthly telephone contacts were maintained by the secretary and also by the helper, social worker, and dietitian for continued motivation (0.05–0.41 h/year) in addition to receiving participants' calls to respond to doubts. An office secretary helped for communication and correspondence. An oral glucose tolerance test (OGTT) and A1C measurements were done annually, and those who developed diabetes were advised on treatment by their physicians.

LSM included modification of diet and physical activity. Baseline physical activity was assessed using a validated methodology that took into account participants' occupations, mode of transportation to work, and leisure-time activities (4). Subjects who were already performing some form of physical exercise (>30

min/day) were asked to continue their routine activities. Subjects who were sedentary or doing light physical activity were advised to walk briskly for at least 30 min/day regularly. Diet modification included reduction in total calories consumed if necessary, reduction in refined carbohydrates and fats, avoidance of direct sugar, and inclusion of fiber-rich foods.

For the participants receiving metformin (metformin and LSM and metformin groups), the dose was 250 mg twice a day. The dose was adjusted by the physician. Motivation for participants in the respective groups was done by the dietitian and social worker. The secretary and helper were involved in contacting the participants. Details of the interventions were previously published (6).

Costs of the interventions

Direct medical costs for all the intervention groups were compared with those for the control group. The direct medical costs of intervention included both personnel and nonpersonnel costs associated with initial implementation and maintenance of the intervention. The personnel cost was calculated on the basis of the actual salary including fringe benefits paid to the different types of personnel by IDPP (for details see online Appendix 1 [available at http://dx.doi.org/10.2337/dc07-0150]). Routine laboratory tariff for the tests and the market cost of metformin were used for calculations. Cost of screening was the laboratory expense of identifying individuals with IGT, which was calculated by the cost of the total number of OGTTs performed, divided by the number of subjects randomly assigned.

Table 1 shows the components considered for the cost calculations. Personnel and transportation costs were included. Because the study team had to travel to the participants' home or work site to implement intervention, we considered the costs associated with these travels as direct medical costs. The numbers of visits and telephone calls either for confirmation of visits or for reinforcement of the intervention strategy had been recorded in the source document. The medication cost was derived on the basis of the dose and the unit cost of the metformin tablets used during the 3 years of the study. Unit costs of personnel were calculated as described above. The establishment charges were taken as overhead cost. The calculations were based on actual records. The cost analysis was performed for the 3-year study period. Cost are expressed in Indian rupees (INR) or the 2006 U.S. dollar equivalent. We did not discount the cost that occurred in the 2nd and 3rd years of the intervention.

Procedures that were not practiced in a routine clinical setting were considered as research procedures and were not included in the analysis. Details of the direct nonmedical and indirect costs during the intervention period were not collected and hence are not included in this report.

For the LSM group, the costs considered were the resources used for counselors on diet and lifestyle parameters. For the metformin group, the costs considered were the resources used for standard lifestyle recommendations, taking a baseline clinical history, supply of tablets, dose titration, counseling, and review visits to ensure adherence. Serum creatinine was measured at baseline and annually to ensure that the drug was not affecting renal function. For the LSM and metformin group, the time spent by the staff was greater because advice of both modalities of treatment was given. The costs considered were the resources used for supply of tablets, dose titration, counseling on diet and lifestyle practices, and review visits. The laboratory costs included were the same as those for the metformin group.

Effectiveness of the interventions

We measured the effectiveness of the intervention by the number needed to treat (NNT) to prevent or delay one incident case of diabetes during the study. NNT is calculated as 1 divided by the absolute risk reduction, i.e., the difference in risk between the experimental and control groups in a clinical trial (12,13).

Cost-effectiveness of the interventions

The incremental cost of intervention for 3 years for a participant in a study arm was calculated by subtracting the standard lifestyle cost in the control group from the cost of intervention. The incremental effectiveness of an intervention was equal to the NNT of that intervention. The cost-effectiveness of the interventions was measured by the incremental cost-effectiveness ratio of preventing or delaying one case of diabetes. This was calculated as the incremental cost multiplied by the incremental effectiveness (i.e., NNT).

The cost-effectiveness of interventions for the base case analysis was assessed using the actual expenses recorded for the study. We also did sensitivity analyses by using possible variations in the study protocol that may influence the outcome. Three such options were analyzed. The first option was that the interventions were delivered without a physician with an anticipated 10% reduction in effectiveness. This was done because a physician may not be available or may be too expensive in some areas of the country. The field staff may require advice from a medical consultant if an emergency situation occurs with metformin treatment. The second option was considered because of possible limitations in staff strength and their available time. This option was group sessions for advice and motivation instead of an individual approach, as reported in a previous study, which may not alter the effectiveness (14). The third option included group sessions, with a possible improvement of effectiveness by 10% because of enhanced motivation generated through group discussions.

RESULTS

Costs of the interventions

For randomly assigning one subject with persistent IGT, performance of 20 OGTTs was needed. The direct medical cost of screening to identify one randomly assigned subject was estimated to be INR 5,278 ($117) (online Appendix 1).

The breakdown of the cost by study arm and year is presented in online Appendix 2. Table 1 summarizes the total direct medical cost of intervention by study arm over the 3-year clinical trial period. The cost of intervention for LSM and metformin was the highest (INR 12,144 [$270]), followed by LSM (INR 10,136 [$225]) and metformin (INR 9,881 [$220]). The cost was the lowest in the control group (INR 2,739 [$61]). Year-wise and total direct medical costs per person in the control and various intervention groups of the study are listed in Table 2. From a health system perspective, the group that had both LSM and metformin interventions had the highest incremental cost (INR 9,405 [$209]) followed by the LSM group (INR 47,397 [$164]) and the metformin group (INR 7,142 [$159]).

Incremental cost-effectiveness ratio

The NNT to prevent one case of diabetes was 6.4 with LSM, 6.9 with metformin, and 6.5 with LSM and metformin. Relative to the control group, the incremental cost-effectiveness ratio over the 3-year

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Table 2—*Summary of the total and incremental costs of the interventions of IDPP and sensitivity analysis with hypothetical models*

Type of intervention	Cost of intervention			
	Control	LSM	Met	LSM + Met
1st year	939 (21)	3883 (86)	3,568 (79)	4,571 (102)
2nd year	900 (20)	2594 (58)	3,069 (68)	3,254 (72)
3rd year	900 (20)	3659 (81)	3,244 (72)	4,319 (96)
Total	2,739 (61)	10,136 (225)	9,881 (220)	12,144 (270)
No. needed to prevent one case of diabetes (NNT)	—	6.4	6.9	6.5
Incremental cost (IC)	—	7,397 (164)	7,142 (159)	9,405 (209)
CER: IC × NNT	—	47,341 (1,052)	49,280 (1,095)	61,133 (1,359)
Sensitivity analysis (CER)				
No physician, effectiveness 10% less		42,979 (955)	49,176 (1,093)	57,927 (1,287)
Group sessions, effectiveness same		37,670 (837)	47,886 (1,064)	51,311 (1,140)
Group sessions, effectiveness 10% more		33,903 (753)	43,444 (965)	46,259 (1,028)

Data are INR (U.S. $). CER, cost-effectiveness ratio; Met, metformin.

trial period was INR 47,341 ($1,052) for the LSM group, INR 49,280 ($1,095) for the metformin group, and INR 61,133 ($1,359) for the LSM and metformin group, respectively (Table 2).

Sensitivity analysis

The results of the sensitivity analysis are also shown in Table 2. The cost-effectiveness ratio was INR 42,979 ($955) for LSM, INR 49,176 ($1,093) for metformin, and INR 57,927 ($1,287) for LSM and metformin, respectively, with the option of having no physician and effectiveness being reduced by 10%. In the second option the cost-effectiveness ratios for all three interventions decreased. In the third option of having enhanced effectiveness, the cost-effectiveness was improved in all three groups (Table 2). LSM was found to be most cost-effective intervention in both the base case and the sensitivity analysis. Sensitivity analysis deleting travel cost was not done because compliance with the treatment is not assured without repeated visits to the participants' work sites or homes.

CONCLUSIONS — The data available on the cost and cost-effectiveness of preventing diabetes are few, and they are from developed countries (9,10,15). There is a paucity of data from developing countries. In this study, we estimated the cost and cost-effectiveness of interventions within the 3-year trial period used in the IDPP from a health system perspective. The major portion of expenditures incurred was personnel cost, especially for the group who required lifestyle changes. In addition, travel cost has been included in the direct cost calculation because the study team had to travel to the participants' work sites or homes. This travel was done to ensure compliance with the treatment procedures. Because the costs related to research for the trial were excluded, the estimates represent the costs that would occur in a routine clinical practice.

The cost of interventions was not evenly distributed over the 3-year study period. The 1st-year cost was higher in all intervention groups because it involved laboratory tests and repeated phone calls for fixing up reviews and also for motivation. The cost was less in the 2nd year and increased in the 3rd year as more phone calls and visits had to be made to continue to motivate participants. In the Diabetes Prevention Program (DPP) study, the cost was the highest in the 1st year, and expenditures were reduced in the following years (11,12). The cost of intervention in India was much lower than the cost involved in the DPP (DPP cost of intervention in the metformin group was $2,542 vs. IDPP cost of $220, and LSM cost was $2,780 vs. IDPP cost of $225). Although the cost of metformin itself was also lower in India, the lower intervention cost in the IDPP was mainly due to the lower personnel cost. The low labor cost also contributed to the lowest cost-effective ratio of the LSM intervention. Although we did not collect the direct nonmedical cost in the study, it might be much lower than that in the DPP because there was no additional expenditure associated with fitness equipment or alternate foods in the IDPP, which accounted for the major part of the nonmedical cost in the DPP (11).

LSM was the most cost-effective intervention, followed by metformin. The cost of intervention was the highest with LSM and metformin because both modalities of intervention had to be implemented. However, the efficacy of this combination was not superior to that of either of them used separately. Our results suggest that when resources are available for prevention, LSM should be implemented first because it represents the best use of the resources. In a subpopulation, when LSM fails, metformin should be the next intervention option. Because it showed the lowest cost-effectiveness, LSM and metformin is not the choice for preventing diabetes among high-risk individuals under any circumstances.

The DPP study group estimated that from the health care perspective to prevent a case of diabetes in the U.S., the intensive lifestyle intervention cost was $15,700 and the metformin cost was $31,000 (12). Cost-effectiveness ratios were better in the Indian scenario, which showed that it would cost much less to prevent a case of diabetes in developing countries than in developed countries. Lower cost-effectiveness ratios for both interventions are mainly due to the lower intervention costs. However, lack of resources is a major concern.

Sensitivity analysis indicated that the cost-effectiveness of the LSM was improved the most, followed by metformin, under the different scenarios. These results suggest that the LSM could be an even better intervention than metformin if it was implemented in a group setting.

Preventing diabetes is of enormous value in the Indian scenario because the cost of diabetes care is high. On average, an individual with diabetes spends INR 10,000 ($227) for medical care in an urban area per year (16). In our analysis, the LSM cost was $1,052 to prevent or delay a case of diabetes. If by LSM diabetes can be

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prevented or delayed at least for 4 years, the prevention program would result in a net gain in investment. Thus, diabetes prevention represents a good use of health care resources in India and perhaps in other developing countries too.

The major limitation of our study was that quality-of-life measures have not been analyzed. The study was not designed to collect relevant data at baseline. In addition, in our study the cost-effectiveness of the LSM and metformin was estimated over a short time and is only a within-trial estimate, similar to the DPP (12). Long-term cost-effectiveness estimates may be more advantageous than short-term estimates, as we are not aware of the treatment benefits beyond the trial period. However, estimating the long-term cost is beyond the purview of the IDPP trial. In the future, long-term cost-effectiveness of IDPP-like interventions should be assessed.

To summarize, our within-trial analysis demonstrated that both lifestyle and metformin interventions are cost-effective. The information on the costs of intervention from our study can be important for planning larger intervention strategies by health care system personnel. The financial and manpower resources required for larger studies can be projected using the data presented in the study.

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