

Effectiveness and Cost-Effectiveness of Diabetes Prevention Among Adherent Participants

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Objectives: We report the 10-year effectiveness and within-trial cost-effectiveness of the Diabetes Prevention Program (DPP) and its Outcomes Study (DPPOS) interventions among participants who were adherent to the interventions.

Study Design: DPP was a 3-year randomized clinical trial followed by 7 years of open-label modified intervention follow-up.

Methods: Data on resource utilization, cost, and quality of life were collected prospectively. Economic analyses were performed from health system and societal perspectives. Lifestyle adherence was defined as achieving and maintaining a 5% reduction in initial body weight, and metformin adherence as taking metformin at 80% of study visits.

Results: The relative risk reduction was 49.4% among adherent lifestyle participants and 20.8% among adherent metformin participants compared with placebo. Over 10 years, the cumulative, undiscounted, per capita direct medical costs of the interventions, as implemented during the DPP, were greater for adherent lifestyle participants (\$4810) than adherent metformin participants (\$2934) or placebo (\$768). Over 10 years, the cumulative, per capita non-intervention-related direct medical costs were \$4250 greater for placebo participants compared with adherent lifestyle participants and \$3251 greater compared with adherent metformin participants. The cumulative quality-adjusted life-years (QALYs) accrued over 10 years were greater for lifestyle (6.80) than metformin (6.74) or placebo (6.67). Without discounting, from a modified societal perspective (excluding participant time) and a full societal perspective (including participant time), lifestyle cost <\$5000 per QALY-gained and metformin was cost saving compared with placebo.

Conclusions: Over 10 years, lifestyle intervention and metformin were cost-effective or cost saving compared with placebo. These analyses confirm that lifestyle and metformin represent a good value for money.

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For author information and disclosures,
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Previously, we reported the clinical and economic outcomes of an intent-to-treat analysis of the combined 10 years of the Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study (DPP/DPPOS).^{1,2} In that analysis, participants were analyzed according to their randomized treatment group whether or not they adhered to their assigned treatment. In this paper, we report the results of an “on treatment” or “per protocol” analysis of DPP/DPPOS. We assess outcomes by treatment group for participants who were adherent to their randomized assignments and compare the effectiveness and cost utility of the intensive lifestyle intervention (lifestyle) and the metformin intervention (metformin) with the placebo intervention (placebo).

Our previously published 10-year intent-to-treat analysis of DPP/DPPOS used data from all randomized participants including those who did not adhere to their randomized treatments, and so likely underestimated both the effectiveness and the benefits of lifestyle and metformin. In real-world clinical practice, neither costs nor benefits are incurred by nonparticipants, but among participants, both intervention costs and benefits are likely to be greater. Our goal in this analysis of the DPP/DPPOS is to extend our previous analyses to estimate the clinical effectiveness and cost-effectiveness of diabetes prevention among metformin participants who remained on treatment with metformin and lifestyle participants who succeeded in losing weight.

METHODS

Screening

The DPP enrolled 3234 participants with impaired glucose tolerance and fasting hyperglycemia who were at least 25 years of age and had body mass index of 24 kg/m² or higher (22 kg/m² in Asian Americans).³ The protocol and informed consent procedures were approved by all responsible institutional review boards. Participants signed written consent forms after discussion of all aspects of the study with study staff. For this analysis, we assigned costs related to finding the participants randomized to lifestyle and

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metformin but not the participants randomized to placebo. In estimating the costs of finding participants, we assumed that 10.4% of adults aged 45 to 74 years would be eligible to participate.⁴ We further assumed that potentially eligible subjects would be tested with a random capillary glucose level.⁵ If the capillary glucose level was ≥ 110 mg/dL, an oral glucose tolerance test (OGTT) would be performed⁶ and those with abnormal OGTTs would have a 15-minute visit with a physician to discuss the results. Based on the sensitivity, specificity, and reproducibility of the tests, we estimated that 12.8% of subjects screened would be eligible to participate in the DPP and that the average cost per eligible participant identified would be \$173.

Interventions

DPP. The goals for participants randomized to lifestyle were to achieve and maintain a weight reduction of at least 7% of initial body weight through diet and physical activity of moderate intensity, such as brisk walking, for at least 150 minutes per week.⁷ A 16-session core curriculum (given approximately weekly in individual participant sessions) and subsequent individual sessions (usually monthly) and group sessions with case managers were designed to reinforce the behavioral changes. The medication interventions (metformin and placebo) were initiated at a dose of 850 mg taken orally once a day. At 1 month, the dose was increased to 850 mg twice daily. Adherence was reinforced during individual quarterly visits with case managers. Standard lifestyle recommendations were provided to all groups through written information and an annual 20-to-30-minute individual session that emphasized the importance of a healthy lifestyle. Mean follow-up at the end of DPP was 3.2 years. For the purposes of this analysis, we assumed that all subjects were enrolled in DPP for exactly 3 years.

DPP/DPPOS Bridge. At the end of the DPP, all participants, regardless of their random treatment assignment, were offered a group-implemented 16-session lifestyle intervention before their enrollment in the DPP Outcomes Study. During this bridge period, 40% of lifestyle, 58% of metformin, and 57% of placebo participants attended at least 1 session.⁸ The original lifestyle group was offered additional lifestyle support and was not encouraged to take metformin. The original metformin group was encouraged to continue metformin and to participate in the group lifestyle intervention. Those randomized to placebo stopped placebo and were encouraged to participate in the group lifestyle intervention. For the purposes of this analysis, we assumed that year 4 represented the DPP/DPPOS bridge.

Take-Away Points

Over 10 years, among adherent participants, lifestyle intervention and metformin were effective and cost-effective for diabetes prevention compared with placebo.

- Interventions to delay or prevent chronic diseases are often not cost saving in the short term, as intervention costs are incurred early and savings from complications averted accrue late in the natural history of disease.
- In real-world clinical settings, lifestyle and metformin interventions are likely to be more effective and more cost-effective than they were during the randomized controlled clinical trial and its observational follow-up study.
- Interventions for diabetes prevention represent a good value for money.

DPPOS Maintenance. All active participants were eligible for continued follow-up during the DPPOS maintenance phase and 2766 of 3150 (88%) enrolled.¹ These included 910 participants originally randomized to lifestyle, 924 to metformin, and 932 to placebo. For the purposes of this analysis, we assumed that years 5 to 10 represented DPPOS maintenance.

During DPPOS maintenance, the group lifestyle intervention was implemented as the Healthy Lifestyle Program (HELP) for all participants. HELP reinforced the original weight loss and physical activity goals and focused on current topics in nutrition, physical activity, stress management, and diabetes prevention. Although all participants were invited to attend all HELP sessions, many chose to attend fewer.

DPP participants initially randomized to lifestyle were also eligible to receive 2 BOOST sessions per year to reinvigorate their self-management behaviors for weight loss. Those randomized to metformin and placebo were excluded from BOOST sessions. The sessions reinforced specific behavioral self-management activities (eg, self-monitoring of fat, calories, and/or physical activity, as well as weight checks) important for weight loss and physical activity adherence and/or maintenance. In addition, the sessions promoted home-based behavioral self-management of weight and physical activity through the use of motivational campaigns.

Only metformin participants were encouraged to take metformin. One percent of non-diabetic participants in lifestyle and 3% of non-diabetic participants in placebo took metformin for diabetes prevention at any time during DPPOS maintenance.¹ Lifestyle and placebo participants who took metformin during DPPOS maintenance were not excluded from the analyses.

Interventions for Participants With Diabetes. Participants identified with glucose levels diagnostic of diabetes at their semi-annual visits were seen within 6 weeks for glucose testing to confirm the diagnosis. Participants with confirmed newly diagnosed diabetes received individual counseling focused on self-monitoring of blood glucose, were provided with meters and test strips and encouraged to monitor their glucose levels once daily, and, for purpose of analysis, were maintained in their randomized intervention groups. Treatment for

diabetes and surveillance for complications and comorbidities were performed by the participants' own healthcare providers. Medications used by DPP participants for management of diabetes were recorded every 6 months on a drug summary form.

Subjects. For these analyses, we wished to assess resource utilization, costs, and outcomes by treatment group among participants randomized to lifestyle and metformin who adhered to their randomized interventions. We assumed that all participants randomized to lifestyle and metformin were adherent during year 1, when the interventions were initially implemented. We defined adherent lifestyle participants as those without diabetes who achieved and maintained 5% weight loss at $\geq 50\%$ of their semi-annual visits beginning at the end of year 1. We defined adherent metformin participants as those without diabetes who took $\geq 80\%$ of their prescribed metformin based on pill counts at $\geq 80\%$ of their semi-annual follow-up visits beginning at the end of year 1. We defined adherent placebo participants as all those randomized to the placebo group regardless of their adoption of lifestyle or metformin treatments during DPP, DPPOS Bridge, or DPPOS maintenance. Of the 1079 participants randomized to lifestyle, 587 (54%) were defined as adherent at the end of DPP year 1. Of 1073 participants randomized to metformin, 666 (62%) were defined as adherent at the end of DPP year 1. Participants in the lifestyle and metformin groups were defined as adherent until the time they became nonadherent or developed diabetes. For the most part, participants who were adherent at the end of DPP year 1 remained adherent for the duration of follow-up.

Costs. We calculated the mean per capita direct medical costs associated with the DPP/DPPOS interventions for participants who remained adherent to their randomized treatment assignments over each of the 10 years after randomization. Direct medical costs of the interventions were estimated from the resources used and unit costs adjusted to 2010 US dollars. We have previously reported in detail how costs were calculated.² To estimate the cost of the lifestyle intervention if it had been administered in a group format rather than individually, we recalculated the costs of lifestyle assuming that the core curriculum and monthly follow-up visits with the lifestyle case managers, which were conducted individually during the 3 years of the DPP, were conducted as group sessions with 10 participants. Studies have shown that group lifestyle intervention programs for obesity are at least as effective as individual programs.^{9,10} Although metformin was implemented with brand name metformin (Glucophage), we assumed that it was implemented with generically priced metformin throughout the 10 years of DPP/DPPOS.

We also estimated the per capita direct medical costs of care outside the study for adherent participants.^{2,11} The direct

medical cost of care outside the study was estimated from case report forms and surveys administered every 6 months. Direct medical costs included the costs of hospital, emergency department, urgent care, and outpatient services, the cost of telephone calls to healthcare providers, and the cost of prescription medications.^{2,11}

Direct non-medical costs were assessed twice, once during DPP and once during DPPOS, and costs were annualized.² In estimating the direct non-medical costs of the interventions for adherent participants, we considered the cost of food, food preparation items, exercise classes, gym memberships, personal trainers, and exercise equipment.² We also considered the costs of transportation to study visits and to medical visits.² The value of the time that participants spent shopping, cooking, exercising, and traveling to and attending appointments was also assessed.² The costs of exercise were valued according to whether participants "disliked," were "neutral," or "liked" leisure time physical activity.^{2,12} Although direct non-medical costs are not usually paid by private insurers or government health programs, we included them in our cost calculations from a societal perspective.

Outcomes. We assessed outcomes for adherent participants as both incident diabetes and quality-adjusted life-years (QALYs).¹³ QALYs measure length of life adjusted for quality of life as assessed by the health utility score. By convention, health utility scores are placed on a continuum where perfect health is assigned a value of 1.0 and health judged equivalent to death is assigned a value of 0.0. We assessed health utilities annually using the Self-Administered Quality of Well-Being Index.¹⁴ Mathematically, QALYs are calculated as the sum of the product of the number of years of life and the quality of life, measured in health utilities, in each of those years.

Perspective. For the primary analysis, we followed the recommendations of the Panel on Cost-Effectiveness in Health in Medicine¹³ and took the perspective of a health system. Thus, we included only direct medical costs of the interventions and non-intervention-related medical care in our base-case analysis. We included direct nonmedical costs excluding participant time in a sensitivity analysis from a modified societal perspective and direct nonmedical costs including participant time in a sensitivity analysis from a full societal perspective. These sensitivity analyses assessed the impact of covering the cost of the interventions implemented by the study participants on society as a whole.

Analyses. The analyses of lifestyle and metformin were conducted for participants who adhered to the lifestyle intervention (as assessed by weight loss) and who regularly took metformin (as assessed by pill counts). The analyses of placebo were conducted for all participants randomized to the placebo group. For the DPP group lifestyle analysis, we esti-

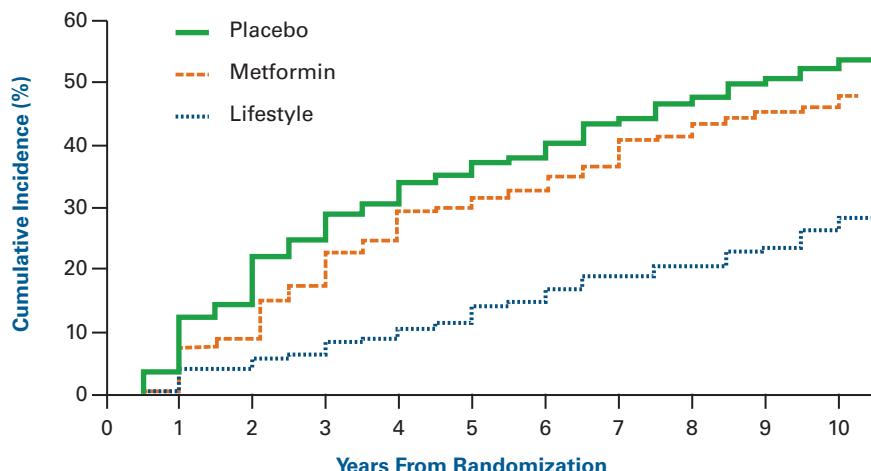
mated what the costs of lifestyle would have been during the 3 years of DPP if the 16-session core curriculum and monthly follow-up visits with the case managers had been conducted as closed-group sessions with 10 participants. We assumed that outcomes for DPP group lifestyle would have been the same as observed for the lifestyle intervention as originally implemented. We excluded from the analyses the costs of the research component of the DPP/DPPOS. All costs were expressed as year 2010 US dollars. Analyses were performed with a 10-year time horizon. Data on resource

utilization were aggregated using SAS (SAS Institute, Cary, North Carolina). The aggregated resource utilization data were then multiplied by the unit cost and by the probability that a participant was followed during the time period. The latter analyses and the tables and figures were generated using Excel (Microsoft Inc, Redmond, Washington). Initial analyses were performed without discounting. Subsequently, where noted, both costs and health outcomes were converted to net present value using a 3% discount rate.

RESULTS

At 10 years, the cumulative incidence of diabetes was 52.4% among participants originally randomized to the minimal intervention arm that included placebo medication and standard lifestyle recommendations (ie, the “placebo” group). The incidence of diabetes was 41.5% among metformin participants who regularly took metformin, and 26.5% among lifestyle participants who achieved and maintained a 5% reduction in initial body weight (Figure 1). Compared with placebo, the absolute risk reduction at 10 years was 25.9% with lifestyle and 10.9% with metformin. The relative risk reduction was 49.4% with lifestyle compared with placebo and 20.8% with metformin compared with placebo. Due largely to the reduced incidence of diabetes, quality of life, as assessed by health utility scores, was better among adherent lifestyle and adherent metformin participants than placebo participants. At 10 years, the mean undiscounted cumulative QALYs accrued were 6.80 for lifestyle, 6.74 for metformin, and 6.67 for placebo participants. Compared with placebo participants, adherent lifestyle participants accrued 0.13 more QALY (ie, years of perfect health) over 10 years and adherent metformin participants accrued 0.07 more QALY.

Figure 1. Cumulative Incidence of Confirmed Diabetes by Intervention Group and Study Year—Adherence Analysis



The annual undiscounted per capita direct medical costs of lifestyle, DPP group lifestyle, metformin, and placebo over 10 years for adherent participants are summarized in Table 1 and Figure 2a. The costs of lifestyle (\$3801) are \$1578, or over 70%, greater than the costs of offering lifestyle in a group format (\$2223) in DPP years 1 to 3 (DPP group lifestyle) because of the difference in resource utilization between an individual- and group-implemented intervention. The per capita costs of lifestyle were substantially lower during DPPOS than during DPP because of the change from an individual- to a group-implemented intervention, less frequent intervention sessions, and lower session attendance. The costs of placebo were slightly higher during DPPOS than during DPP because placebo participants engaged in the group lifestyle intervention.

The cumulative undiscounted per participant cost of the lifestyle intervention (\$4810) was substantially greater than the estimated cost of the DPP group lifestyle intervention (\$3232), the metformin intervention (\$2934), or the placebo intervention (\$768) (Figure 2b). Over 10 years, the cumulative undiscounted per capita incremental direct medical costs of the interventions were greater for adherent participants in lifestyle (\$4042), group lifestyle (\$2464), and metformin (\$2166) compared with placebo.

The cumulative undiscounted per capita direct medical costs of non-intervention-related medical care by intervention group and year following randomization for adherent participants are shown in Table 2 and Figure 2c. These are the costs of medical care received outside the DPP/DPPOS. The cumulative direct medical costs of non-intervention-related medical care (\$23,218 to \$27,468 per person over 10 years) were substantially greater than the costs of the interventions (\$768 to \$4810 per person over 10 years). Among all groups,

Table 1. Undiscounted Per Capita Direct Medical Costs of the DPP/DPPOS Interventions by Intervention Group and Study Year (\$)—Adherence Analysis

Year	Lifestyle	Metformin	Placebo	DPP Group Lifestyle ^a
Screening	173	173	0	173
1-DPP	1826	602	88	898
2-DPP	887	321	51	562
3-DPP	915	329	48	590
4 (Bridge)	175	355	221	175
5-DPPOS	119	190	58	119
6-DPPOS	124	190	57	124
7-DPPOS	142	188	56	142
8-DPPOS	146	188	55	146
9-DPPOS	145	189	57	145
10-DPPOS	158	209	77	158
Total	4810	2934	768	3232

DPP indicates Diabetes Prevention Program; OS, Outcomes Study.

^aSensitivity analysis. Assumes that DPP core curriculum and follow-up visits were conducted as group sessions with 10 participants.

the costs of non-intervention-related medical care increased over time. Over 10 years, the cumulative, per capita non-intervention-related direct medical costs were \$4250 greater for placebo participants compared with adherent lifestyle participants and \$3251 greater for placebo participants compared with adherent metformin participants.

By year 10, cumulative undiscounted per participant total direct medical costs of the DPP/DPPOS interventions and medical care received outside the DPP/DPPOS were higher for placebo (\$28,236) than for lifestyle (\$28,027), DPP group lifestyle (\$26,449), or metformin (\$27,150) (Figure 2d). Thus, when both intervention- and non-intervention-related medical costs were considered, all 3 interventions saved money relative to the placebo intervention.

Cumulative, 10-year, diet-, physical activity-, transportation-, and time-related costs were similar across treatment groups (\$147,704 for lifestyle, \$146,999 for metformin, and \$147,043 for placebo). Although adherent lifestyle participants spent more time exercising, the adjusted value of the time they spent exercising was not greater than for either metformin or placebo because of their greater enjoyment of leisure time physical activity and the lower opportunity cost.

Table 3 summarizes the differences in costs and QALYs and the incremental cost-effectiveness ratios of lifestyle, DPP group lifestyle, and metformin versus placebo and for lifestyle compared with metformin. From the health system perspective and without discounting, the total direct medical costs for the lifestyle, DPP group lifestyle, and metformin participants were less than for placebo participants and the interventions were more effective as assessed by QALYs gained.

In other words, all 3 interventions were cost saving compared with placebo. With discounting and compared with metformin, lifestyle cost \$2004 more but produced an additional 0.06 QALY over 10 years. From a health system perspective, with both costs and health outcomes discounted at 3% per year, the cost of lifestyle compared with placebo was \$19,988 per QALY gained, the cost of DPP group lifestyle compared with placebo was \$9688 per QALY gained, and the cost of metformin compared with placebo was \$20,183 per QALY gained. The cost of lifestyle compared with metformin was \$19,662 per QALY gained.

Without discounting, from both a modified societal perspective (excluding participant time) and a full societal perspective (including participant time), lifestyle cost <\$5000 per QALY gained and both DPP group lifestyle and metformin were cost saving compared with placebo. Compared with metformin, lifestyle cost <\$35,000 per QALY gained.

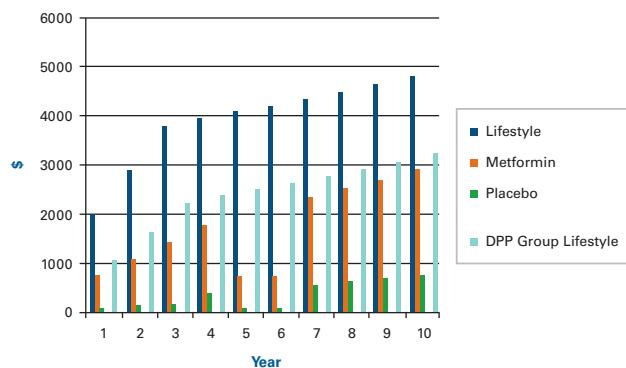
DISCUSSION

In this 10-year analysis of the combined Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study, the cumulative incidence of diabetes was 26.5% among lifestyle participants who adhered to the lifestyle intervention, 41.5% among metformin participants who adhered to metformin, and 52.4% among placebo participants. Compared with placebo, lifestyle reduced the absolute risk of diabetes by 25.9% and metformin reduced the absolute risk of diabetes by 10.9%. The relative risk reduction associated with lifestyle was 49.4% and that associated with metformin was 20.8%. In our previous intent-to-treat analysis, the risk of diabetes at 10 years was 42% with life-

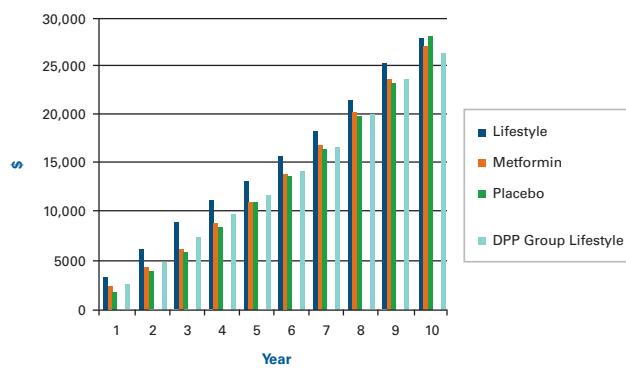
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■ Figure 2. Adherence Analysis for:

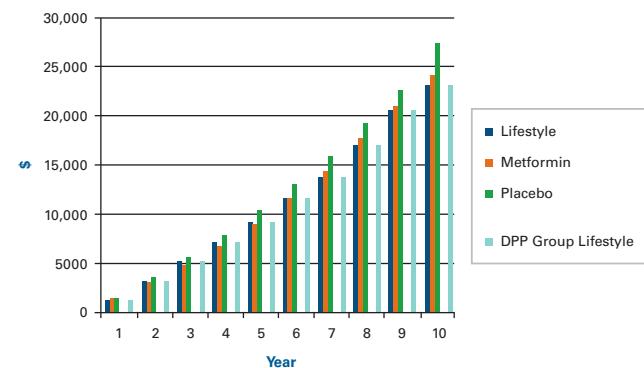
a. Cumulative, Undiscounted, Per Participant, Direct Medical Costs of the DPP/DPPOS Interventions by Intervention Group and Study Year



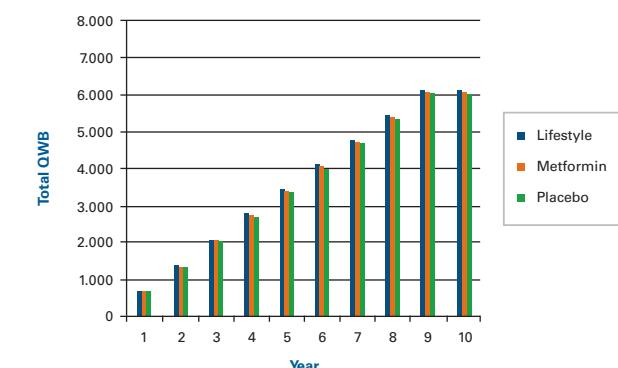
c. Cumulative, Undiscounted, Per Participant, Total Direct Medical Costs of the DPP/DPPOS Interventions and Medical Care Received Outside the DPP/DPPOS by Intervention Group and Study Year



b. Cumulative, Undiscounted, Per Participant, Direct Medical Costs of Medical Care Received Outside the DPP/DPPOS by Intervention Group and Study Year



d. Cumulative, Undiscounted, Per Participant, Total Quality of Well-Being Index by Intervention Group and Year



DPP indicates Diabetes Prevention Program; OS, Outcomes Study; QWB, quality of well-being.

style and 47% with metformin and 52% with placebo.² It is not surprising that lifestyle and metformin were substantially more effective among participants who adhered to the interventions.

The benefit of metformin as assessed by QALYs gained was also greater in this analysis than in the intent-to-treat analysis. In this analysis, lifestyle participants accrued 6.80 QALYs over 10 years, metformin participants accrued 6.74 QALYs, and placebo participants accrued 6.67 QALYs. In the intent-to-treat analysis, lifestyle participants accrued a similar number of QALYs (6.81 QALYs) but metformin participants accrued fewer QALYs (6.69 QALYs).² The lower QALYs gained in the intent-to-treat analysis of metformin participants may have been related to adverse events experienced by some metformin participants who subsequently were unable to remain adherent to therapy.

The cumulative undiscounted per capita direct medical costs of the DPP/DPPOS lifestyle and metformin interven-

tions were higher in participants who were adherent to treatment than in participants in the intent-to-treat analysis.² Lifestyle was approximately 5% more expensive (\$4810 vs \$4601), group lifestyle was 7% more expensive (\$3232 vs \$3023), and metformin was 28% more expensive (\$2934 vs \$2300). This likely reflects the greater adherence of participants to their interventions and greater resource utilization, especially in the case of metformin participants.

Undiscounted per capita direct medical costs of care outside the DPP/DPPOS were lower in lifestyle and metformin participants who were adherent to their randomized treatment assignments compared with intent-to-treat participants.² This could, in part, reflect the substantially lower incidence of diabetes among participants adherent to the lifestyle and metformin interventions. The undiscounted per capita 10-year cumulative direct medical costs of care outside DPPOS were 5% lower for adherent lifestyle partici-

■ Table 2. Undiscounted, Per Capita, Direct Medical Costs of Care Outside the DPP/DPPOS by Intervention Group and Study Year (\$)—Adherence Analysis

Costs by year	Lifestyle	Metformin	Placebo
1-DPP	1423	1517	1617
2-DPP	1909	1729	2045
3-DPP	1875	1671	2018
4 (Bridge)	2113	2056	2330
5-DPPOS	1865	2106	2543
6-DPPOS	2495	2665	2636
7-DPPOS	2306	2747	2875
8-DPPOS	3199	3400	3319
9-DPPOS	3460	3085	3265
10-DPPOS	2572	3241	4822
Total	23,218	24,217	27,468
Costs by category	Lifestyle	Metformin	Placebo
Outpatient visits	6741	6835	7325
Inpatient care	4748	4538	6856
ED visits	1855	1344	1825
Urgent care visits	1575	1836	1811
Calls to physicians	670	698	712
Prescription medications	6539	6972	6959
Self monitoring supplies and laboratory tests for diabetes	1090	1994	1978
Total	23,218	24,217	27,468

DPP indicates Diabetes Prevention Program; ED, emergency department; OS, Outcomes Study.

pants than intent-to-treat lifestyle participants (\$23,218 vs \$24,563) and 5% lower for adherent metformin participants than intent-to-treat metformin participants (\$24,217 vs \$25,615).²

In these analyses, from a health system perspective and without discounting, lifestyle, DPP group lifestyle, and metformin were all cost saving relative to placebo. In our previous undiscounted intent-to-treat analysis, lifestyle cost approximately \$6700 per QALY gained compared with placebo but both DPP group lifestyle and metformin were cost saving.² In both this analysis and our previous intent-to-treat analysis, lifestyle was more expensive than metformin but produced greater health benefits.² The undiscounted cost per QALY was \$14,213 and \$10,555, respectively.² In these analyses, from a health system perspective and with both costs and QALYs discounted at 3%, neither lifestyle, DPP group lifestyle, nor metformin was cost saving. These differences likely reflect the impact of discounting on early treatment costs. In these analyses, we assumed that all participants randomized to lifestyle and metformin remained adherent during the first year. Because early treatment costs were greater, discounting resulted in the early, relatively expensive preventive interventions being less cost-effective.

The results of this 10-year within-trial analysis demonstrate that lifestyle and metformin interventions are even more effective for diabetes prevention in DPP/DPPOS participants who are adherent to their randomized treatments than among the larger group of both adherent and nonadherent participants. In addition, the interventions are extremely cost-effective or even cost saving. These results are consistent with earlier analyses that assessed the cost-effectiveness of lifestyle and metformin interventions based upon the results of the Finnish Diabetes Prevention Study,¹⁵ the DPP,^{16,17} the DPP/DPPOS,¹⁸ and the Indian Diabetes Prevention Study.¹⁹ One study which did not find lifestyle intervention to be cost-effective²⁰ differed from the published lifetime cost-utility analyses¹⁶⁻¹⁸ in that it assumed that the lifestyle intervention continued over the participants' lifetimes even after they developed diabetes. It also assumed that when participants developed diabetes, their A1C remained <7.0% for the remainder of their lives. These assumptions led to potential overestimation of intervention costs and underestimation of the costs and quality-of-life impact of the complications and comorbidities of diabetes. Taken together, these assumptions likely account at least in part for the difference in results.

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Table 3. Differences in Costs and QALYs and Incremental Cost-Effectiveness Ratios for Lifestyle and Metformin Versus Placebo Over 10 Years From 3 Alternative Perspectives (\$)—Adherence Analysis

Differences in costs (Δ cost)	Lifestyle vs Placebo	Metformin vs Placebo	Lifestyle vs Metformin	DPP Group Lifestyle vs Placebo ^a
Health system perspective^b				
Undiscounted	-210	-1086	877	-1788
Discounted ^c	3007	1897	1110	1458
Modified societal perspective ^d (undiscounted)	579	-1465	2044	-999
Societal perspective ^e (undiscounted)	451	-1130	1581	-1126
Differences in QALYs (Δ QALY)				
Undiscounted	0.14	0.08	0.06	0.14
Discounted	0.15	0.09	0.06	0.15
Incremental cost-effectiveness ratios (Δ Cost / Δ QALY)				
Health system perspective ^b				
Undiscounted	Cost saving	Cost saving	14,213	Cost saving
Discounted ^c	19,988	20,183	19,662	9688
Modified societal perspective ^d (undiscounted)	4151	Cost saving	33,149	Cost saving
Societal perspective ^e (undiscounted)	3235	Cost saving	25,644	Cost saving

DPP indicates Diabetes Prevention Program; QALY, quality-adjusted life-year.

^aSensitivity analysis. Assumes that DPP core curriculum and follow-up visits were conducted as group session with 10 participants.

^bIncludes total direct medical costs.

^cBoth costs and QALYs discounted at 3%.

^dIncludes direct medical and direct nonmedical costs excluding participant time.

^eIncludes direct medical and direct nonmedical costs including participant time.

This analysis has a number of limitations. First, in defining participants as adherent to the lifestyle intervention, we used the outcome (weight loss) to define adherence. This was necessary because all lifestyle participants were strongly encouraged to attend lifestyle sessions and attendance was not a good marker of adoption of the behavioral intervention. Second, the simulated group lifestyle intervention was not empirically tested within the DPP. The decision to implement the lifestyle intervention individually within DPP was pragmatic. The study group was anxious to enroll participants and begin the interventions as quickly as possible. The literature suggests, however, that group-implemented lifestyle interventions are at least as effective as individually implemented interventions, largely due to the benefits of peer support. Third, we included all participants randomized to placebo in these analyses. During DPPOS, placebo participants were offered and participated in the group lifestyle intervention and 3% were prescribed metformin outside the study. If these interventions were effective in the placebo group, they would have reduced non-intervention-related resource utilization and costs. The relative impact of these potential biases is impossible to determine, but if the intervention costs were less than the savings resulting from a decreased incidence of diabetes, the bias would be

conservative, making lifestyle and metformin appear less cost-effective relative to placebo.

In summary, this assessment of outcomes among DPP/DPPOS participants who were adherent to their randomized treatment assignments indicates that lifestyle and metformin are likely to be even more effective in real-world clinical practice than they were during the randomized controlled clinical trial and its subsequent observational follow-up study. Perhaps not surprisingly, the costs of the interventions, especially the cost of the metformin intervention, were higher among adherent participants, but the benefits, assessed in terms of non-intervention-related direct medical costs, were also greater. Interestingly, the benefits in terms of QALYs gained were similar among adherent and intent-to-treat participants, perhaps reflecting the impact of non-diabetes-related comorbidities on quality of life. The impact of discounting on the cost-effectiveness equation highlights the fact that in chronic diseases, prevention is an important investment but often not cost saving in the short term.²¹ To the extent that intervention costs are accrued early in the natural history of disease and complications are accrued later, discounting tends to portray a less favorable cost-effectiveness picture. Nevertheless, these analyses confirm that lifestyle, group lifestyle, and metformin represent a good value for money.

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