Within-Trial Cost-Effectiveness of a Structured Lifestyle Intervention in Adults With Overweight/Obesity and Type 2 Diabetes: Results From the Action for Health in Diabetes (Look AHEAD) Study

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*Ping Zhang,[1] Karen M. Atkinson,[2] George A. Bray,[3] Haiying Chen,[4] Jeanne M. Clark,[5] Mace Coday,[6] Gareth R. Dutton,[7] Caitlin Egan,[8] Mark A. Espeland,[4] Mary Evans,[9] John P. Foreyt,[10] Frank L. Greenway,[3] Edward W. Gregg,[11] Helen P. Hazuda,[12] James O. Hill,[13] Edward S. Horton,[14] Van S. Hubbard,[9] Peter J. Huckfeldt,[15] Sharon D. Jackson,[14] John M. Jakicic,[16] Robert W. Jeffery,[17] Karen C. Johnson,[6] Steven E. Kahn,[2] Tina Killean,[18] William C. Knowler,[18] Mary Korytkowski,[19] Cora E. Lewis,[20] Nisa M. Maruthur,[5] Sara Michaels,[21] Maria G. Montez,[12] David M. Nathan,[22] Jennifer Patricio,[23] Anne Peters,[24] Xavier Pi-Sunyer,[23] Henry Pownall,[25] Bruce Redmon,[17] Julia T. Rushing,[4] Helmut Steinburg,[6] Thomas A. Wadden,[26] Rena R. Wing,[8] Holly Wyatt,[27] and Susan Z. Yanovski,[9] on behalf of the Look AHEAD Research Group**

OBJECTIVE

To assess the cost-effectiveness (CE) of an intensive lifestyle intervention (ILI) compared with standard diabetes support and education (DSE) in adults with overweight/obesity and type 2 diabetes, as implemented in the Action for Health in Diabetes study.

RESEARCH DESIGN AND METHODS

Data were from 4,827 participants during their first 9 years of study participation from 2001 to 2012. Information on Health Utilities Index Mark 2 (HUI-2) and HUI-3, Short-Form 6D (SF-6D), and Feeling Thermometer (FT), cost of delivering the interventions, and health expenditures was collected during the study. CE was measured by incremental CE ratios (ICERs) in costs per quality-adjusted life year (QALY). Future costs and QALYs were discounted at 3% annually. Costs were in 2012 U.S. dollars.

RESULTS

Over the 9 years studied, the mean cumulative intervention costs and mean cumulative health care expenditures were $11,275 and $64,453 per person for ILI and $887 and $68,174 for DSE. Thus, ILI cost $6,666 more per person than DSE. Additional QALYs gained by ILI were not statistically significant measured by the HUIs and were 0.07 and 0.15, respectively, measured by SF-6D and FT. The ICERs ranged from no health benefit with a higher cost based on HUIs to $96,458/QALY and $43,169/QALY, respectively, based on SF-6D and FT.

CONCLUSIONS

Whether ILI was cost-effective over the 9-year period is unclear because different health utility measures led to different conclusions.

For people with type 2 diabetes and overweight or obesity, modest and sustained weight loss can produce numerous clinical benefits, such as improving glycemic controls, lowering blood pressure, and improving quality of life (1,2). Weight loss can lead to economic benefits by reducing the need for health care and medications for

[1]*Centers for Disease Control and Prevention, Atlanta, GA*
[2]*VA Puget Sound Health Care System and University of Washington, Seattle, WA*
[3]*Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA*
[4]*Department of Biostatistics and Data Science, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC*
[5]*Division of General Internal Medicine, Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD*
[6]*Department of Preventive Medicine, The University of Tennessee Health Science Center, Memphis, TN*
[7]*Division of Preventive Medicine, School of Medicine, The University of Alabama at Birmingham, Birmingham, AL*
[8]*Weight Control and Diabetes Research Center, The Miriam Hospital, Providence RI*
[9]*National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD*
[10]*Department of Medicine, Baylor College of Medicine, Houston, TX*
[11]*Department of Epidemiology and Biostatistics, Imperial College London, London, U.K.*
[12]*Department of Medicine, The University of Texas Health Science Center at San Antonio, San Antonio, TX*
[13]*Department of Nutrition Sciences, The University of Alabama at Birmingham, Birmingham, AL*
[14]*Department of Medicine, Joslin Diabetes Center, Boston, MA*
[15]*Division of Health Policy and Management, School of Public Health, University of Minnesota, Minneapolis, MN*

glucose, lipid, and blood pressure control (3,4). Weight loss can be achieved with intensive behavioral lifestyle intervention programs that include counseling focused on diet and physical activity (1). The American Diabetes Association recommends diet, physical activity, and behavioral interventions designed to achieve 5% weight loss for people with type 2 diabetes and overweight or obesity (5). The U.S. Preventive Services Task Force recommends diet and physical activity counseling for people with unhealthy weight with known risk factors for cardiovascular disease (CVD), such as type 2 diabetes, high blood pressure, and unhealthy cholesterol levels, or with a previous CVD event (6).

Delivering behavioral lifestyle intervention programs to a targeted population, however, can be challenging and may require both health care and non–health care resources. For example, in the Diabetes Prevention Program (DPP), the intensive lifestyle program cost $2,780/person over the 3 years of the program. This did not include ancillary expenses such as transportation and childcare (7). Improving dietary intake and increasing physical activity could also incur additional costs to participants in term of food and exercise expenses (7). There is limited evidence on whether the benefits of lifestyle interventions in persons with type 2 diabetes are worth the costs.

Cost-effectiveness (CE) analysis is an analytical framework that weighs health and economic benefits with costs of an intervention relative to status quo or another intervention. Such analysis is often used to evaluate an intervention to see if it is worthwhile, as judged by the societal willingness to pay for a health outcome. The result of the CE analysis is often expressed as an incremental CE ratio (ICER), which is calculated as the difference in net costs measured in dollar terms divided by the gain in health outcomes such as quality-adjusted life years (QALYs). A QALY is a single global outcome measure that combines changes in both mortality (measured in life years) and morbidity (measured in patient health-related quality of life or health utility) due to the program. Health utility values normally range from 1, representing "full" health, to 0, representing death. A value of between 1 and 0 represents a "not full" health state. One QALY is equal to 1 year of life with full health. The purpose of the QALY method is to normalize health outcomes resulting from different interventions across diseases, thereby making it possible to compare interventions.

CE of behavioral lifestyle intervention programs designed to produce weight loss in people with type 2 diabetes is often evaluated based on a single short-term outcome such as body weight loss (8). Whether such programs are cost-effective based on global outcome measures like QALY is unclear. Only one study (9) estimated the CE of lifestyle modification in people with type 2 diabetes. This study projected the long-term health and economic consequences of seven lifestyle intervention programs using a computer simulation model in a Dutch setting. Two programs that aimed at weight reduction were found to be cost-effective at a cost of ≤€20,000 (~$23,000 U.S.)/QALY. However, the effectiveness of the two programs was based on data observed over 1 year. For the simulation, several assumptions had to be made on how the short-term effects on biomarkers would translate into long-term morbidity and mortality outcomes. Whether these assumptions can be supported by evidence from long-term clinical trials or follow-up of short-term trials is unclear. In contrast, CE analysis that uses data directly observed from long-term clinical trials does not require such assumptions and can also be used to validate the results from the modeling studies.

The 16-center Look AHEAD (Action for Health in Diabetes) study was a randomized, controlled clinical trial of 5,145 U.S. adults aged 45–76 years with type 2 diabetes and either overweight or obesity. Participants were randomized to an intensive lifestyle intervention (ILI) designed to induce and maintain weight loss through reduced energy intake and increased physical activity or standard diabetes support and education (DSE). The primary outcome was a composite of cardiovascular morbidity and mortality. The trial started in 2001 and was stopped for futility after a median (maximal) follow-up of 9.6 (11.5) years. In this report, we evaluate the CE of the ILI compared with DSE during the trial.

RESEARCH DESIGN AND METHODS

Study Population

Characteristics of the Look AHEAD study participants are detailed elsewhere (9). We used data from 4,827 participants over the first 9 years of the intervention period (cost data from one study site and outcome data at year 10 were not available for many study participants). Eligible participants had BMI >25 kg/m^2 (or >27 kg/m^2 if receiving insulin therapy). All participants signed a consent form approved by their local institutional review board.

[16]Department of Health and Physical Activity, University of Pittsburgh, Pittsburgh, PA
[17]Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, University of Minnesota Medical School, Minneapolis, MN
[18]National Institute of Diabetes and Digestive and Kidney Diseases, Phoenix, AZ
[19]Department of Medicine, University of Pittsburgh, Pittsburgh, PA
[20]Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL
[21]Indian Health Service, Shiprock, NM
[22]Diabetes Research Center, Massachusetts General Hospital, Boston, MA
[23]Department of Medicine, St. Luke's-Roosevelt Hospital Center, Columbia University, New York, NY
[24]Houston Methodist Research Institute, Baylor College of Medicine, Houston, TX
[25]Division of Endocrinology and Diabetes, Keck School of Medicine of the University of Southern California, Los Angeles, CA
[26]Center for Weight and Eating Disorders, University of Pennsylvania, Philadelphia, PA
[27]Department of Medicine, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO
Corresponding author: Ping Zhang, paz2@cdc.gov

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*A complete list of the members of the Look AHEAD Research Group can be found in the supplementary material online.

Interventions

The goal of the ILI was to achieve and maintain at least a 7% decrease in weight from baseline. Details of the intervention have been described previously (10). Briefly, for the first 6 months, participants attended one individual and three group sessions per month and were encouraged to replace two meals and one snack a day with liquid shakes and meal bars. During the second 6 months, they attended one individual and two group meetings per month and continued to replace one meal per day. In years 2–4, treatment was provided mainly on an individual basis and included at least one on-site visit per month and a second contact by telephone, mail, or e-mail. Short-term (6–8 weeks) refresher groups and motivational health promotion campaigns also were offered three times yearly to help participants reverse small weight gains. In subsequent years, participants were offered monthly individual visits, as well as one refresher group session and one campaign a year. To help participants achieve and maintain weight loss, a variety of diet strategies (e.g., prepared meals and liquid formula), exercise strategies, and the optional weight loss medication orlistat were used based on a preset algorithm and participant progress. Participants in DSE were offered three group sessions each year focusing on diet, physical activity, and social support. Regular medical care was provided by the participant's own physician in both groups.

CE Analysis

The ICER of ILI relative to DSE was calculated as the incremental cost divided by incremental effectiveness. The methods used and the findings related to both the incremental cost and incremental effectiveness have been published previously (4,11,12) and are described briefly below. We took a health care system perspective, considering the direct medical costs only. Analyses followed intention-to-treat principles and used all available data. Participants were included in their randomization group regardless of adherence. We estimated the 95% CI of ICER using bootstrapping method. We used a threshold of $100,000/QALY, an amount of willingness to pay for 1 year of life with "perfect" health (13), to judge the CE of ILI.

Incremental QALYs From ILI

As noted above, the methods and results of the comparison of ILI over DSE in health utility have been reported previously (11). In brief, four instruments were used to assess health utility value: the Feeling Thermometer (FT), Health Utilities Index Mark 2 (HUI-2), HUI-3, and Short-Form 6D (SF-6D). For FT scores, individual respondents were asked to rate their current health on a vertical thermometer-like scale with scores ranging from 0, representing worst possible health, to 100, representing best possible health. The reported minimally important difference (MID) for FT was between 0.061 and 0.074 (14). HUI-2 and HUI-3 used a 40-item questionnaire to assess participants' current physical and mental functions and published scoring rules to calculate health utility values. HUI-2 measures a total of 24,000 health states with scores ranging from −0.03 to 1.00. HUI-3 measures 972,000 health states with scores ranging from −0.36 to 1.00. The reported MID for the HUIs was between 0.02 and 0.04 (15). The SF-6D score was estimated based on data from selected items of the SF-36 and published scoring rule derived from a representative sample of 611 people from the general population of the U.K. SF-6D measures a total of 18,000 health states with scores ranging from 0.296 to 1.0. The MID for SF-6D was 0.035 (16,17).

FT was administered at baseline, quarterly during year 1, and semiannually in years 2 through 9. The HUI-2, HUI-3, and the SF-36 questionnaires were administered at baseline, quarterly during year 1, semiannually during years 2 through 4, and annually in years 5 through 9.

The predicted health utility by study year was estimated using generalized linear models to account for data skewness. Modified Park and Pregibon Link tests were used to select the best fitting distribution and link function. A β regression using binomial distribution with a logit link was used for FT. Poisson distributions with an identity link were used for HUI-2, HUI-3, and SF-6D. Additionally, since HUI-2 and HUI-3 scores were left-skewed, we first modeled the disutility score (1-utility score), then back-transformed to obtain the utility scores. Baseline age, sex, prior CVD, BMI, systolic blood pressure (SBP), clinic site, baseline health utility scores, intervention arm, year, and intervention arm by year interaction were used as predictors.

Survival probabilities by follow-up year were estimated using a parametric Weibull model, with adjustment for baseline age, sex, prior CVD, BMI, SBP, clinic site, and intervention arm. Mortality status was assessed every 6 months or by spontaneous report. Incremental QALYs were calculated as the difference in average QALYs across study participants between the ILI and DSE. Annual QALYs for each study participant were the product of predicated survival probability and predicted health utility in each year during the 9-year period. Annual QALYs from each of the four health utility measurements were added together over 9 years to get the cumulative QALY for that measure. Annual estimates of QALYs were discounted at 3% per year. Recycled prediction was used to obtain average QALY for DSE assuming all participants were from DSE and average QALY for ILI assuming all participants were from ILI. The 95% confidence level of QALY estimates for each intervention group and the difference between DSE and ILI were estimated using bootstrapping.

Incremental Cost of ILI

The incremental cost was calculated as the difference in the average total cost of ILI compared with DSE on a per-participant basis. The total cost for each participant was the sum of the costs associated with delivering the intervention and medical care over the study period. To estimate the accumulated costs over 9 years, annual estimates were adjusted for survival probabilities and were discounted at 3% per year and summed. All costs are reported in 2012 U.S. dollars.

Methods used for data collection and analysis for estimating the cost of intervention have been reported previously (12). In short, the intervention cost included time costs of staff who delivered the intervention and nonstaffing costs such as meal replacements, weight-loss medications, and diabetes-related educational materials. The data used to estimate personnel costs came from salary data for each type of staff member (e.g., registered dietitian, exercise specialist, and nurse) from study sites and periodic staff surveys on the amount of time spent delivering the intervention. Staffing cost data from one study site were not available because of privacy concerns. Nonstaffing costs were estimated from study records that included the number and type of visits each participant attended and, for participants in the ILI group, use

of meal-replacement products and orlistat weight-loss medication provided by the trial. Research-related staffing costs and facility (building/rent) costs were excluded. We used the predicted intervention cost for each participant to be consistent with the effectiveness data. Predictors were baseline age, sex, prior CVD, BMI, SBP, clinic site, intervention arm, year, and arm-by-year interaction.

Health care expenditures by study arm have also been reported previously (4). The health care expenditures for each study participant included costs associated with hospitalizations, outpatient visits (office, hospital clinic, or other), outpatient tests and procedures, rehabilitation/long-term care, and home care. Data on the use of each type of care were collected annually through face-to-face interviews at clinic visits and at 6-month intervals by telephone. Unit costs for each care category were obtained from various sources. Hospitalization costs were estimated based on regression models using data from the Nationwide Inpatient Sample (4). Outpatient care costs were based on the Medicare Physician Fee Schedule. Rehabilitation, long-term care, and home health services costs were based on Medicare Skilled Nursing Facility Prospective Payment System and National Home Health Utilization statistics for Medicare Parts A and B. Medication costs were based on adjusted average wholesale prices obtained from the Red Book (https://www.ibm.com/products/micromedex-red-book). We used the predicted health care expenditure for each participant to be consistent with the effectiveness data. A generalized linear model was fit with γ distribution and a log link. Baseline age, sex, prior CVD, BMI, SBP, clinic site, intervention arm, year, and arm-by-year interaction were included in the model as predictors.

Similar to analysis of QALY, recycled prediction was used to obtain survival-adjusted estimates for total cost for DSE and ILI. The incremental cost of ILI was estimated using bootstrapping method.

Table 1—Baseline characteristics of the Look AHEAD study participants by intervention arm

Baseline characteristics	DSE	ILI	*P* value*
N	2,416	2,411	
Age, years (%)			0.10
45–54	23.6	25.1	
55–64	53.8	54.8	
65–76	22.6	20.2	
Sex (%)			
Men	41.5	41.6	0.95
Women	58.5	58.4	
Race/ethnicity (%)			
White	67.3	67.1	0.98
African American	16.5	16.5	
Hispanic	7.9	7.8	
Other	8.3	8.6	
BMI, kg/m^2 (%)			0.23
25.0–29.9	13.7	15.4	
30.0–34.9	34.5	34.6	
35.0–39.9	28.8	26.8	
>40	23.1	23.2	
Duration of diabetes, years	6.8	6.7	0.83
Mean HbA_{1c} (%)	7.3	7.2	0.05
Hypertension (%)	83.3	84.2	0.37
Medication use (%)			
Antihypertensive	73.2	75.2	0.12
Diabetes	87.5	86.9	0.50
Lipid	52.3	51.8	0.75
Annual household income, U.S. dollars (%)	*n* = 248 missing	*n* = 254 missing	0.89
<$40,000	29.8	30.1	
$40,000 to <$80,000	38.7	39.0	
≥$80,000	31.6	30.9	

*χ^2 test.

RESULTS

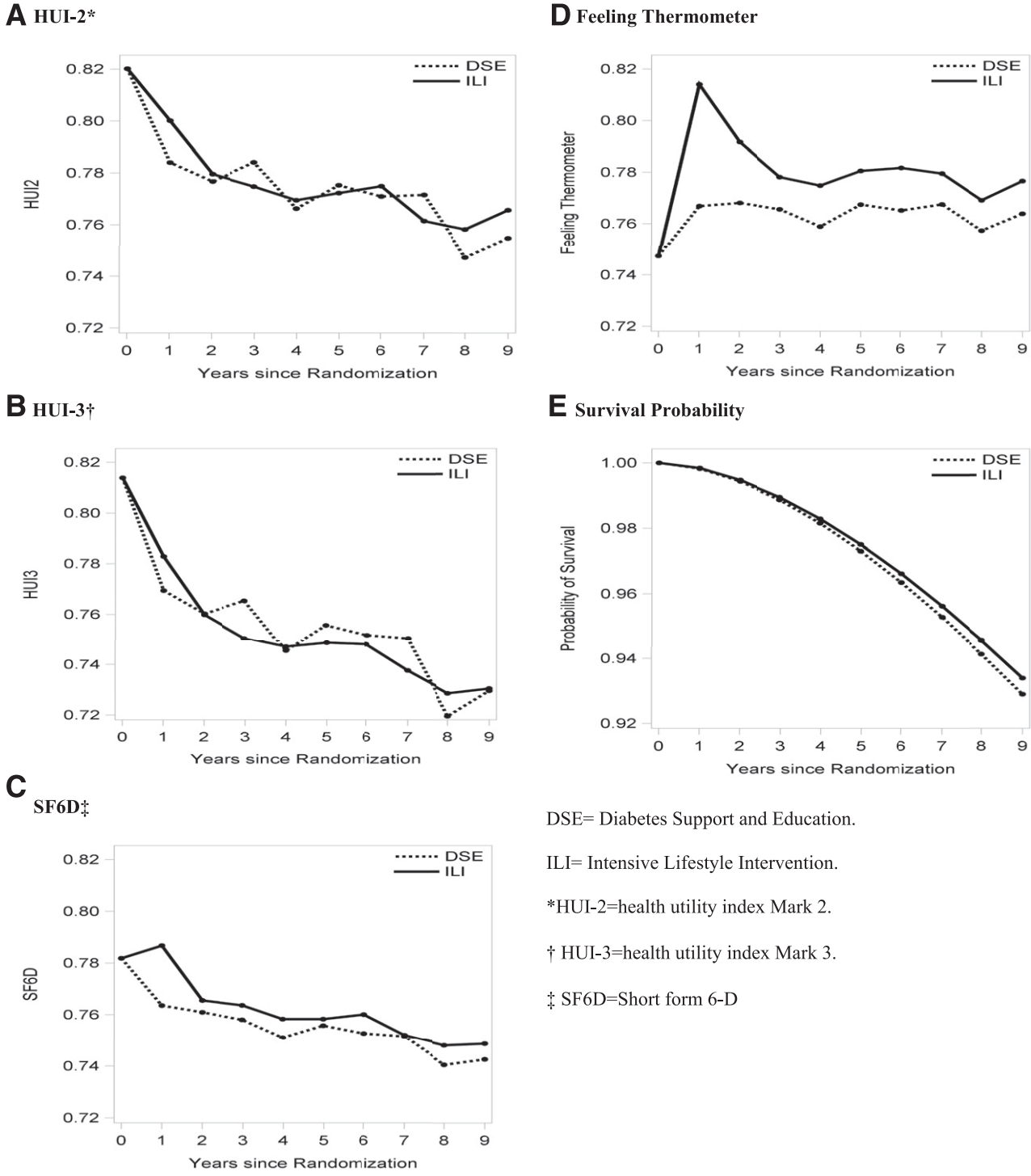
The major clinical and socioeconomic characteristics of study participants included in this study are presented in Table 1. There were no statistically significant differences in any of the characteristics between the intervention and control groups.

The predicted health utility values by measure and study arm are shown in Fig. 1. In year 1, the health utility values for all four instruments (FT, SF-6D, HUI-2, and HUI-3) were higher for the ILI group than for the DSE group. When evaluated over the full 9 years, ILI participants' mean FT and SF-6D scores were significantly higher than DSE participants' scores (0.02 [95% CI 0.015–0.026], $P < 0.001$ for FT; and 0.009 [95% CI 0.005–0.014], $P < 0.001$ for SF-6D). No significant differences were observed between the study groups for the HUI-2 or HUI-3 (−0.003 [95% CI −0.01 to 0.003], $P = 0.28$ for the HUI-2; and 0.00 [95% CI −0.008 to 0.008], $P = 0.99$ for the HUI-3). The survival probability declined over time for all study participants (Fig. 1*E*), with no significant difference between ILI and DSE participants ($P = 0.46$). The difference in survival probability at year 9 was 0.005 (−0.008 to 0.017).

Predicted intervention costs by intervention group over time are presented in Fig. 2 (Fig. 2*A* and Supplementary Table 1). The costs associated with both ILI and DSE declined over time. For the ILI participants, the cost was $2,891/participant in year 1, $1,946 in year 2, and decreased gradually to about $1,000/year in years 5–9. For DSE participants, the cost was $192/participant in year 1, $128 in year 2, and decreased to ∼$100/year in years 5–9.

The health care expenditure per study participant by study arm is presented in Fig. 2 (Fig. 2*B* and Supplementary Table 1). Health care expenditure increased over the study period for both ILI and DSE participants, starting at ∼$6,000 in year 1 and increasing to >$10,000 by year 9 for both ILI and DSE. The difference in health care expenditures between the two study groups by year varied, but the expenditure of DSE participants was always higher than that of ILI participants.

Cumulative QALYs by utility measurement by study group and cumulative total cost by intervention group are presented in Supplementary Fig. 1. Cumulative QALYs and total cost increased with time for all utility measurements and both intervention



DSE= Diabetes Support and Education.

ILI= Intensive Lifestyle Intervention.

*HUI-2=health utility index Mark 2.

† HUI-3=health utility index Mark 3.

‡ SF6D=Short form 6-D

Figure 1—Predicted health utility values with different measurements and survival probability by study arm: HUI-2 (*A*), HUI-3 (*B*), SF-6D (*C*), FT (*D*), and survival probability (*E*) in the ILI and DSE groups during the 9-year study period.

groups. There were no significant differences in QALYs between the two study groups as measured by HUI-2 and HUI-3 (Supplementary Fig. 1*A* and *B*). In comparison, ILI participants had a higher cumulative QALYs than DSE participants as measured by SF-6D and FT (Supplementary Fig. 1*C* and *D*). Cumulative total costs for ILI participants were higher than those for DSE participants in all study years (Supplementary Fig. 1*E* and Supplementary Table 1).

Incremental QALYs, incremental costs, and ICER of ILI over DSE are shown in Table 2. As ILI led to no increases in QALYs as measured by HUI-2 and HUI-3, the ICERs were not defined using these two utility measurements. The gains from ILI were 0.07 QALYs (i.e., 26 days with full health) for SF-6D and 0.15 QALYs (i.e., 55 days with full health) for FT, respectively. Over the study period, ILI participants cost an average of $10,388 more in intervention costs, $3,721 less in health

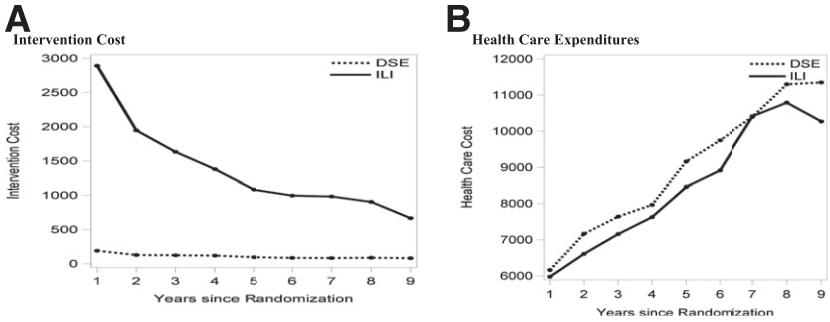


Figure 2—Predicted annual intervention cost and health care expenditures by study arm: intervention cost (*A*) and health care expenditures (*B*) in the ILI and DSE groups during the 9-year study period.

care expenditures, and $6,666 more in the incremental cost than DSE participants. The estimated ICERs were $96,458/QALY based on the SF-6D and $43,169/QALY based on FT.

CONCLUSIONS

Previous studies reported that lifestyle intervention is cost-effective for the purpose of preventing type 2 diabetes in persons with prediabetes (18,19). This analysis sought to determine whether a lifestyle intervention program designed to produce weight loss in people with overweight/obesity and type 2 diabetes is an efficient use of limited health care resources. No previous study has collected data on all components of a formal CE analysis over an extended period to answer this question. The Look AHEAD trial sought to answer this question through prospective collection of data on health utility scores, costs associated with delivering the intervention, general medical care use, and mortality over 9 years. Random assignment to ILI, compared with DSE, led to a higher overall cost of ~$6,700, little or no difference in health-related quality of life, and no significant improvement in mortality. The large variations in CE ratios of ILI by different health utility measures imply that there are some uncertainties associated with the CE of ILI. There is not a universally acceptable threshold to judge the CE of an intervention for adoption. Using $100,000/QALY as a threshold (13), only two of the four measurements showed that ILI was cost-effective. Thus, health care systems should be cautious about adopting the lifestyle intervention without further evidence from longer follow-up of Look AHEAD participants.

The ILI was not likely to be cost-effective for two main reasons. First, delivering ILI as implemented in the trial was resource intensive (12), with frequent treatment contact and individual sessions. Although ILI led to fewer hospitalizations, less use of medications, and lower total medical care costs (4), the savings in health care expenditures were not large enough to offset the costs of delivering ILI. Second, the intervention led to little or no gain in QALYs. The ILI participants had a better survival than DSE participants, but the difference was not significant. The gains from better health-related quality of life measured by health utility ranged from none as measured by HUI-2 and HUI-3 to small improvements as measured by SF-6D and FT.

The ILI did not lead to a lower incidence of the composite CVD outcome, the primary end point of the Look AHEAD trial. However, ILI improved other clinical outcomes or biomarkers. At 1 year of intervention, the ILI group lost an average of 8.6% of their initial body weight, while the DSE group lost 0.7% (20). Mean fitness levels improved by 20.4% in ILI and by 5% in DSE (14). At the end of the trial, ILI participants still had a mean 6% weight loss, while DSE participants had 3.5% (20). ILI also resulted in other clinical benefits, including improved glucose control, improved blood pressure, less sleep apnea, lower liver fat, less depression, less urinary incontinence, less severe kidney disease, less knee pain, improved sexual function, lowered inflammation markers (20), and higher disability-free years (21). However, these improved clinical outcomes and biomarkers did not translate into a higher score on all four health utility measurements used in our study.

Improvements in health utility scores resulting from ILI were small and statistically significant only using SF-6D and FT. In addition, the higher utility scores did not reach to the level of MID for either SF-6D or FT. The lack of or small significant effects might be due to effective clinical management of CVD risk factors in both study arms, which may limit the ability of the ILI to affect long-term QALYs. Reasons for the discordant scores by utility measure were unclear but could be due to a combination of factors. The four instruments are correlated with one another, but their scores are not interchangeable (22). The lack of significant effect measured by HUI-2 and HUI-3 over the 9-year study period could be due to: *1*) magnitude of improvements in health-related quality of life resulting from ILI was relatively small, and *2*) the two measures were not sensitive enough to capture these small improvements. Examining health utility scores by intervention year indicted ILI led to a statistically

Table 2—Total and incremental QALYs, total and incremental costs, and CE ratio ($/QALY) of ILI relative to DSE

Measurements	DSE (95% CI)	ILI (95% CI)	Δ ILI-DSE (95% CI)	CE ratio ($/QALY) (95% CI)
HUI-2 (QALYs)	6.08 (6.03, 6.13)	6.10 (6.05, 6.15)	0.03 (−0.04, 0.09)	—
HUI-3 (QALYs)	5.94 (5.88, 5.99)	5.94 (5.87, 5.99)	0 (−0.08, 0.07)	—
SF-6D (QALYs)	5.92 (5.88, 5.96)	5.99 (5.95, 6.03)	0.07 (0.02, 0.12)	96,458 (41,597, 2,95,448)
FT (QALYs)	6.03 (5.98, 6.06)	6.18 (6.14, 6.22)	0.15 (0.10, 0.21)	43,169 (23,053,76,588)
Intervention cost ($)	887 (877, 898)	11,275 (11,134, 11,405)	10,388 (10,247, 10,514)	—
Health care expenditures ($)	68,174 (66,305, 70,147)	64,453 (62,549, 66,375)	−3,721 (−6,273, −1,167)	—
Total cost ($)	69,062 (67,192, 71,038)	75,728 (73,864, 77,636)	6,666 (4,082, 9,203)	—

significant higher utility score measured by all four utility measures including HUI-2 and HUI-3 in the 1st year, which could be related to a larger body weight reduction in that year. Examining scores of individual domains included in HUI-2 and HUI-3 over the entire study period indicated that the ILI participants experienced small improvements in the cognition, mobility, and ambulation domains, but no improvements in other domains (11). These small positive effects in the three domains, however, were not large enough to lead to a significant change in overall utility scores. Health utility scores as measured by both FT and SF-6D were statistically significant in the 1st year and remained significant in later years. This result could imply that FT and SF-6D were more capable to detect the small changes in health domains affected by the ILI than HUI-2 and HUI-3. Previous studies also showed ability to detect difference in health utility improvement varies by utility measurement in persons with osteoporosis (23). HUIs may only be able to detect large improvements in health utility in patients with type 2 diabetes with overweight/obesity with little limitations in physical functions. The lack of ability to detect small improvements by HUIs could also limit interpretability of results measured by the two health utility instruments.

Lifestyle interventions among adults with overweight/obesity and type 2 diabetes could be cost-effective in a time span >9 years as clinical benefits of ILI, especially on hard health outcomes such as CVD, may take >9 years to be realized. Reducing weight and improving fitness, glucose, and blood pressure, as observed in the intervention period, may lead to reduction in diabetes-related complications and death later on. Results from the ongoing Look AHEAD Extension may be able to provide an answer regarding the long-term health benefit and CE of ILI for this population.

Whether the ILI used in this study would be cost-effective in a real-world setting is unknown. The cost associated with delivering the ILI could be lowered by using trained laypeople in group settings. A meta-analysis of this literature showed that there were no differences in weight loss achieved by trained professionals versus lay educators (24). A lifestyle intervention program used in the DPP study cost $1,399/person in year 1 and ~$700/person in years 2 and 3 (7); however, a similar program translated into community-based programs (e.g., YMCA) reduced the program cost over 1 year to $400–$600/participant, which was only about a third of the intervention cost as implemented in the DPP trial. The total cost to deliver the ILI over the 9-year study period was $11,275, $6,666 more than DSE (Table 2 and Supplementary Table 1). ILI participants, however, had a lower medical cost of $3,721 ($68,174 vs. $64,453). If the ILI in this study could be delivered in a community setting at one-third of the trial cost ($3,721 in 2012 U.S. dollars or $4,213 inflated in 2020 U.S. dollars) as the DPP lifestyle intervention or lower, the intervention would be cost-saving. Recently, other efforts to reduce the cost of lifestyle interventions, as provided in the DPP, have involved offering programs at community centers, using lay community intervention staff (24,25), or using digital media to deliver programs.

Our results should be interpreted with caution. While we showed some uncertainties associated with the CE of implementing ILI in all adults with overweight/obesity and type 2 diabetes, our results do not imply lifestyle modification should not be used as a weight-loss strategy in these patients. The American Diabetes Association recommends both lifestyle modification and medication for management of type 2 diabetes that is tailored to patient preferences. ILI is effective in improving HbA_{1c} and blood pressure, thereby reducing the medication needed for controlling those risk factors. For those people who prefer not to use medications, lifestyle modifications may offer an appealing option to reduce or eliminate the need for medications.

Our study had several limitations. First, although participants were geographically and demographically diverse and had a broad age distribution similar to people with type 2 diabetes in the U.S., the degree to which the findings may generalize to other populations is unclear because of the recruitment practices and enrollment criteria used in the study. Second, data for cost associated with intervention personnel time were based on cross-sectional surveys. The reported time could be affected by recall bias and be subject to respondents' interpretations of the survey questionnaires. Third, actual salary data of people who delivered the intervention instead of the national wage rates were used to estimate the unit cost of time for different type of personnel, which may also limit generalization. Fourth, use of outpatient care and the occurrence of hospitalizations were self-reported, which may be affected by recall bias. Finally, the HUI-2 and HUI-3 scoring algorithms were derived from general populations from Canada, whereas for the SF-6D, we used a U.K. scoring algorithm. If preference scores from the U.S. population differed from those from Canadian and U.K. populations, our estimated impact of ILI on health-related quality of life may be biased. However, there is no previous research to show the preference scores were different among the U.S., Canada, and the U.K.

In conclusion, this study found that the CE of ILI versus education and support was unclear over the first 9 years of the intervention. Different measures of health utilities led to different conclusions. Whether the ILI is a good use of health resources in the long term may need to be reevaluated based on health outcomes observed from the continued follow-up of the trial beyond the active intervention period.

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