



Impact of Intensive Lifestyle Intervention on Disability-Free Life Expectancy: The Look AHEAD Study

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OBJECTIVE

The impact of weight loss intervention on disability-free life expectancy in adults with diabetes is unknown. We examined the impact of a long-term weight loss intervention on years spent with and without physical disability.

RESEARCH DESIGN AND METHODS

Overweight or obese adults with type 2 diabetes age 45–76 years ($n = 5,145$) were randomly assigned to a 10-year intensive lifestyle intervention (ILI) or diabetes support and education (DSE). Physical function was assessed annually for 12 years using the 36-Item Short Form Health Survey. Annual incidence of physical disability, mortality, and disability remission were incorporated into a Markov model to quantify years of life spent active and physically disabled.

RESULTS

Physical disability incidence was lower in the ILI group (6.0% per year) than in the DSE group (6.8% per year) (incidence rate ratio 0.88 [95% CI 0.81–0.96]), whereas rates of disability remission and mortality did not differ between groups. ILI participants had a significant delay in moderate or severe disability onset and an increase in number of nondisabled years ($P < 0.05$) compared with DSE participants. For a 60-year-old, this effect translates to 0.9 more disability-free years (12.0 years [95% CI 11.5–12.4] vs. 11.1 years [95% CI 10.6–11.7]) but no difference in total years of life. In stratified analyses, ILI increased disability-free years of life in women and participants without cardiovascular disease (CVD) but not in men or participants with CVD.

CONCLUSIONS

Long-term lifestyle interventions among overweight or obese adults with type 2 diabetes may reduce long-term disability, leading to an effect on disability-free life expectancy but not on total life expectancy.

Type 2 diabetes increases the risk of microvascular and macrovascular morbidity, leading to a 60% increased risk of cardiovascular disease (CVD), 6 times the risk of end-stage kidney disease, and 10 times the risk of amputation relative to people without diabetes (1,2). Although rates of diabetes complications have declined in the U.S., accompanying increases in lifetime risk of diabetes and life span have increased the total number of years that the average American lives with the disease (2). Diabetes more than doubles the incidence of physical disability, hastens its onset by 6–7 years, and has a greater effect on disability-free years of life than total years of life

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*A complete list of the Look AHEAD Study Group can be found in the Supplementary Data online.

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(3,4). Disability affects quality of life, increases risk for further morbidity, and dramatically increases the need for subsequent health services (4–6). Furthermore, the lack of clear evidence of reductions in national disability prevalence levels over time among adults with diabetes raises the question of whether current clinical and public health approaches to reduce morbidity are effective (7,8).

Given the concern about the impact of diabetes and its complications in the older diabetic population, the Look AHEAD (Action for Health in Diabetes) trial found that overweight adults with type 2 diabetes assigned to an intensive lifestyle intervention (ILI) had a 48% reduced risk of mobility loss over 4 years compared with adults receiving the diabetes support and education (DSE) control condition (9). The large magnitude of this effect combined with the high absolute incidence of physical disability among adults with diabetes suggest that lifestyle interventions could have a substantial effect on the number of years spent in a disabled versus non-disabled state (3,6). A multifactorial behavioral intervention featuring caloric restriction and increased physical activity may affect mechanisms underlying functional decline and may have the greatest potential for affecting complex conditions such as disability. However, accurate estimation of the impact of an ILI on the remaining years of active and disabled life also depends on the concurrent associations of intervention with disability, remission from disability, and mortality risk.

As a 10-year lifestyle-based weight loss intervention, Look AHEAD is one of the longest lifestyle intervention trials to be conducted and presents a unique setting to examine the extended impact of lifestyle on healthy aging (10). In this study, we examine the impact of the Look AHEAD intervention on physical disability, remission from physical disability, and mortality. We then incorporate these findings into a lifetime progression model to estimate the impact of this ILI on the number of years spent with and without physical disability among adults with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Study Design and Population

Look AHEAD is a multicenter randomized controlled trial that tested the impact of an ILI on CVD incidence and diabetes-

related morbidity (11,12). The study enrolled 5,145 overweight and obese adults with type 2 diabetes age 45–76 years across 16 research centers. Participants were randomly assigned with equal probability to either an ILI designed to achieve sustained weight loss or DSE. Inclusion criteria included a BMI ≥ 25 kg/m² or ≥ 27 kg/m² among those receiving insulin therapy. Exclusion criteria included hemoglobin A_{1c} >11%, systolic blood pressure >160 mmHg, diastolic blood pressure >100 mmHg, plasma triglyceride levels >600 mg/dL, inability to complete a maximal graded exercise test, and inability to complete 2 weeks of diet and activity self-monitoring. Recruitment occurred during 2001–2004. All participants signed an informed consent approved by local institutional review boards. These analyses excluded eight individuals with missing data, leaving an analytic sample of 5,137 (99.8%) adults (Supplementary Fig. 1).

Intervention

Details of the ILI have been published previously (12,13). The intervention included weekly group and individual sessions for 6 months followed by two group sessions and one individual session per month for the second 6 months, twice-monthly contact for years 2–4, and monthly contact for years 5 and beyond to prevent weight regain. The intervention also included refresher sessions throughout years 4–10. The ILI sought to reduce total caloric intake to 1,200–1,800 kcal/day on the basis of initial weight and to limit total fat and saturated fat content to <30% and 10% of the diet, respectively. Participants were counseled to achieve a goal of 175 min of physical activity per week using strategies such as brisk walking. Behavioral strategies included self-monitoring, goal setting, and problem solving. Dietary change was further supported through calorie counting and provision of meal replacements (12).

DSE participants were offered three group sessions each year that focused on diet, physical activity, and social support. Medical and pharmacological risk factor management for hyperglycemia, lipids, and blood pressure was provided by the participant's physician independent of the Look AHEAD trial for both groups. Interventions continued through 14 September 2012. The median intervention length was 9.9 years (interquartile range 9.2–10.4), and follow-up ranged from 0 to 11 years.

Assessments

Participants attended annual clinic visits for assessments conducted by centrally trained staff masked to intervention assignment. Body weight was measured with a digital scale. Physical function was assessed using items from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) physical functioning subscale (14). The mobility items included activities such as pushing a vacuum cleaner or playing golf; climbing one flight of stairs; bending, kneeling, or stooping; walking more than a mile; and walking 100 yards.

Statistical Analysis and Modeling

The analyses involved three stages. First, we defined stages of physical disability using hidden Markov models. Second, we estimated incidence of physical disability, mortality, and remission after disability by intervention group. Finally, we incorporated incidence estimates into a five-stage Markov model to project the number of years spent with and without disability over the lifetime by intervention group.

Hidden Markov Models

Hidden Markov models were used to define states of physical disability and to classify individuals according to states over the duration of the study (15,16). These models used information from six variables of the SF-36 physical function items (vigorous activities; moderate activities; climbing one flight of stairs; bending, kneeling, or stooping; walking more than a mile; walking 100 yards) collected at each of the 11 visits to examine the dynamics and transitions of underlying latent states and to cluster participants according to these states. Participants were asked the following questions: "Does your health now limit you in these activities? If so, how much?" For each variable, responses were yes, limited a lot; limited a little; or not limited at all. The number and structure of states are determined by a goodness-of-fit index and are assumed to be constant over time. Participants were then classified in the state for which they had the greatest likelihood (15,16).

The hidden Markov models process led to 13 discrete states that were subsequently collapsed into three categories of no disability, moderate disability, and severe disability. Specific characteristics of each state are shown in Supplementary Fig. 2. In brief, participants classified as

Table 1—Incidence of disability and remission from physical disability according to intervention group: the Look AHEAD study

	Intervention condition		IRR (95% CI)	P value
	DSE	ILI		
Overall population (n = 5,137)	2,570	2,567	—	
Moderate/severe disability cases	980	930	—	
Moderate/severe per 100 person-years	6.8 (5.8–7.9)	6.0 (5.6–6.4)	0.88 (0.81–0.96)	< 0.01
Severe per 100 person-years	2.5 (1.9–3.2)	2.2 (2.0–2.4)	0.87 (0.75–1.01)	0.07
Disability remission per 100 disabled persons/year*	30.1 (23.6–38.5)	34.8 (31.4–38.5)	1.06 (0.92–1.23)	0.42
Deaths (n, %)	199 (7.7)	171 (6.7)	—	
Yearly mortality rate per 100 person-years	0.96 (0.67–1.36)	0.81 (0.69–0.94)	0.86 (0.70–1.06)	0.15
Men (n = 2,079)	1,037	1,042	—	
Moderate/severe disability cases	345	346	—	
Moderate/severe per 100 person-years	5.2 (4.0–6.6)	5.1 (4.6–5.7)	0.99 (0.85–1.15)	0.91
Severe per 100 person-years	2.1 (1.4–3.2)	1.9 (1.6–2.3)	0.96 (0.75–1.21)	0.70
Disability remission per 100 disabled persons/year	24.1 (16.0–36.3)	32.5 (27.5–38.4)	1.23 (0.96–1.56)	0.10
Deaths (n, %)	117 (11.3)	93 (8.9)	—	
Yearly mortality rate per 100 person-years	1.4 (0.9–2.3)	1.1 (0.9–1.4)	0.79 (0.60–1.03)	0.08
Women (n = 3,058)	1,533	1,525	—	
Moderate/severe disability cases	635	584	—	
Moderate/severe per 100 person-years	8.2 (6.7–9.9)	6.7 (6.2–7.3)	0.81 (0.73–0.91)	< 0.01
Severe per 100 person-years	2.8 (2.0–3.9)	2.3 (2.0–2.7)	0.81 (0.67–0.99)	0.04
Disability remission per 100 disabled persons/year	34.4 (25.3–46.6)	36.3 (31.9–41.2)	0.98 (0.82–1.17)	0.81
Deaths (n, %)	82 (5.4)	78 (5.1)	—	
Yearly mortality rate per 100 person-years	0.6 (0.4–1.0)	0.6 (0.5–0.8)	0.96 (0.70–1.30)	0.77
No CVD (n = 4,424)	2,223	2,201	—	
Moderate/severe disability cases	842	786	—	
Moderate/severe per 100 person-years	8.2 (6.9–9.6)	7.1 (6.6–7.6)	0.87 (0.79–0.95)	< 0.01
Severe per 100 person-years	2.4 (1.8–3.2)	2.0 (1.8–2.3)	0.83 (0.71–0.98)	0.02
Disability remission per 100 disabled persons/year	34.2 (26.4–44.3)	37.9 (34.1–42.2)	1.05 (0.90–1.22)	0.56
Deaths (n, %)	138 (6.2)	116 (5.3)	—	
Yearly mortality rate per 100 person-years	0.8 (0.5–1.2)	0.6 (0.5–0.8)	0.84 (0.66–1.08)	0.17
CVD (n = 713)	347	366	—	
Moderate/severe disability cases	138	144	—	
Moderate/severe per 100 person-years	9.9 (6.7–14.7)	9.8 (8.4–11.5)	0.98 (0.78–1.24)	0.87
Severe per 100 person-years	2.9 (1.6–5.5)	3.2 (2.5–4.1)	1.14 (0.78–1.65)	0.50
Disability remission per 100 disabled persons/year	15.3 (7.3–31.7)	21.0 (15.5–28.4)	1.17 (0.75–1.82)	0.49
Deaths (n, %)	61 (17.6)	55 (15.0)	—	
Yearly mortality rate per 100 person-years	2.4 (1.3–4.6)	2.0 (1.6–2.6)	0.86 (0.60–1.25)	0.43

Data are n or n (95% CIs) unless otherwise indicated. *Analyses of disability incidence excluded persons with disability at baseline.

ILI group and ranged from 5.8% at age 60 to 8.8% at age 75 in the DSE group (Supplementary Fig. 4). For women, incidence ranged from 7.6% per year at age 60 to 11.5% at age 75 in the ILI group and from 8.7% at age 60 to 13.0% at age 75 in the DSE group. Incidence of remission for men ranged from 25.7% per year at age 60, declining to 15.0% at age 75 in the ILI group (vs. 23.1% and 13.4% for ages 60 and 75, respectively, in the DSE group) (Supplementary Fig. 5). For women, incidence of remission ranged from 23.1% per year at age 60, declining to 13.4% at age 75 in the ILI group (vs. 22.1% and 12.7% for ages 60 and 75, respectively, in the DSE group). However, the overall differences in rates of remission between ILI and DSE were not statistically significant. Similarly, no significant differences were found in rates of mortality between

ILI and DSE participants overall or in any strata.

Disability-Free Life Expectancy

Across all ages, ILI participants were estimated to have a 0.8–0.9-year delay in the age of onset of moderate/severe physical disability and an equivalent increase in the number of nondisabled years of life (Table 2) while having no significant difference in the total years of life. The impact on active years of life was significant from age 50 and 60 years, but not from age 70 years. For example, from age 50, the average ILI participant had 15.3 nondisabled years, became disabled at age 65.3, and then spent 20.7 years disabled before death. The same-aged counterparts in the DSE group had 14.4 nondisabled years, became disabled at age 64.4, and spent 21.5 years disabled before death. In stratified

analyses, the ILI intervention was associated with an increase in the number of nondisabled years in women and those without CVD but not in men or those with CVD. Age of disability onset was younger for women than for men and for those with CVD than for those without CVD.

When disability-free life expectancy was estimated using the severe disability definition instead of the moderate/severe definition (Table 3), the difference in disability onset and years of life spent with disability between ILI and DSE participants was ~30% less than in the primary analysis and was no longer statistically significant. A 60-year-old in the ILI group had 16.7 nondisabled years of life (vs. 16.1 in the DSE group), became severely disabled at age 76.7 years (vs. 76.1 in DSE), and spent 10.4 years with disability before death (vs. 10.7 in the DSE group).

Table 2—Number of years with and without physical disability (moderate or severe), according to intervention group: the Look AHEAD study

Age (years)	DSE				ILI			
	Age at disability onset (years)	Nondisabled years (n)	Disabled years (n)	Total years (n)	Age at disability onset (years)	Nondisabled years (n)	Disabled years (n)	Total years (n)
Total								
50	64.4 (63.7–65.1)	14.4 (13.7–15.1)	21.5 (19.3–23.7)	35.8 (33.8–38.1)	65.3 (64.8–65.8)§	15.3 (14.8–15.8)§	20.7 (18.7–22.9)	36.0 (34.1–38.2)
60	71.1 (70.6–71.7)	11.1 (10.6–11.7)	15.7 (13.7–18.0)	26.9 (24.8–29.2)	72.0 (71.5–72.4)§	12.0 (11.5–12.4)§	15.2 (13.2–17.3)	26.8 (24.8–29.0)
70	78.4 (77.8–79.0)	8.4 (7.8–9.0)	10.2 (8.0–12.5)	18.6 (16.4–21.0)	79.2 (78.6–79.8)	9.2 (8.8–9.8)	9.9 (7.8–12.2)	18.7 (16.5–21.1)
Men								
50	67.0 (66.0–67.9)	17.0 (16.0–17.8)	16.8 (14.5–19.3)	33.7 (31.5–36.2)	67.9 (67.1–68.6)	17.9 (17.3–18.5)	16.1 (14.0–18.5)	34.0 (31.8–36.3)
60	72.8 (72.0–73.5)	12.8 (8.7–10.1)	12.3 (10.3–14.7)	25.1 (23.0–27.4)	73.7 (73.0–74.3)	13.7 (13.3–14.5)	11.8 (9.8–14.0)	25.5 (23.4–27.8)
70	79.4 (78.7–80.1)	9.4 (8.7–10.1)	7.8 (5.9–11.1)	17.2 (15.1–19.7)	80.2 (79.5–80.9)	10.2 (9.5–10.8)	7.6 (5.7–9.8)	17.8 (15.6–20.3)
Women								
50	63.0 (62.3–63.6)	13.0 (12.3–13.6)	25.6 (22.7–28.2)	38.5 (35.8–41.1)	63.9 (63.3–64.4)	13.9 (13.3–14.4)§	24.8 (22.0–27.4)	38.7 (35.9–41.4)
60	69.8 (69.2–70.4)	9.8 (9.2–10.4)	19.7 (17.0–22.3)	29.4 (26.7–32.1)	70.6 (70.1–71.1)	10.6 (10.1–11.1)§	19.1 (16.5–21.6)	29.7 (27.0–32.3)
70	77.3 (76.7–77.9)	7.3 (6.7–7.9)	13.6 (10.9–16.3)	20.9 (18.2–23.6)	78.0 (77.5–78.7)	8.0 (7.5–8.7)	13.3 (10.6–15.9)	21.4 (18.7–24.0)
No CVD								
50	64.7 (64.0–65.4)	14.7 (14.0–15.4)	23.7 (21.0–26.2)	38.0 (35.6–40.3)	65.6 (65.1–66.2)*	15.6 (15.1–16.2)*	22.9 (20.3–25.3)	38.5 (35.8–41.0)
60	71.5 (70.9–72.1)	11.5 (10.9–12.1)	17.8 (15.3–20.3)	29.0 (26.6–31.3)	72.4 (71.9–72.9)†	12.4 (11.9–12.9)†	17.3 (14.7–19.7)	29.7 (27.1–32.1)
70	78.9 (78.3–79.6)	8.9 (8.3–9.6)	12.1 (9.4–14.6)	20.7 (18.1–23.1)	79.7 (79.1–80.4)§	9.7 (9.1–10.4)§	11.7 (8.2–14.3)	21.5 (18.7–24.0)
CVD								
50	62.0 (60.9–63.2)	12.0 (10.9–13.2)	18.2 (15.6–20.9)	30.2 (27.7–32.9)	63.0 (61.9–64.1)	13.0 (11.9–14.1)	17.7 (15.3–20.2)	30.6 (28.3–33.1)
60	69.3 (68.4–70.1)	9.3 (8.4–10.1)	12.8 (10.7–15.3)	22.1 (19.9–24.5)	70.1 (69.3–70.9)	10.1 (9.3–10.9)	12.5 (10.5–14.8)	22.6 (20.7–24.9)
70	77.0 (76.4–77.7)	7.0 (6.4–7.7)	7.9 (6.0–10.3)	14.9 (12.9–17.6)	77.7 (77.1–78.5)	7.7 (7.1–8.5)	7.9 (6.0–10.2)	15.6 (13.7–18.1)

Data are n in years (95% CIs). *P < 0.001, †P < 0.01, §P < 0.05 for comparison between the ILI and DSE groups.

In sensitivity analyses of the primary outcome (moderate/severe disability), if the relative effect of ILI on disability and remission was assumed to be maintained after the completion of the intervention for the remainder of life (i.e., instead of return to no difference between groups as in the primary analyses), the difference in disabled and nondisabled life-years between ILI and DSE is ~50% greater than in primary analyses. There is a 1.6-year difference between ILI and DSE in estimated nondisabled years from age 50 years and a 1.0-year difference from age 70 years (Table 4). If the intervention effect was assumed to last 4 or 8 years beyond the period of intervention, the estimated benefits are intermediate between the primary analyses and those assuming a lifetime continued effect.

CONCLUSIONS

The combination of high rates of diabetes prevalence, increasing longevity of adults with type 2 diabetes, and high incidence of disability has increased the need for interventions that reduce morbidity and increase the number of years spent in an active, healthy state (2,3). In these analyses of adults with type 2 diabetes, ILI for weight loss resulted in significant delays in the onset of physical disability and significant increases in disability-free life expectancy in the overall population and in stratified analyses among women and those without CVD. Given the large increases in life span observed and the continued high national prevalence of type 2 diabetes in older adults, these findings indicate that lifestyle interventions can play an important role in compressing population morbidity.

Obesity and diabetes have each been consistently associated with an increased risk of physical disability, including mobility loss and loss of independence in instrumental and basic activities of daily living (5,18,19). Disability is a core element of morbidity, affects quality of life, and is a potent predictor of subsequent use of health services and mortality. However, few studies have examined the impact of lifestyle interventions on disability incidence. In prior analyses from Look AHEAD, participants randomly assigned to ILI had reduced disability prevalence after 4 and 8 years (9,20), consistent with other studies showing that exercise and weight loss programs reduce mobility loss in older adults with osteoarthritis (21,22). The

present analyses extend those findings to 12 years and incorporate data on remission from disability and mortality risk to provide the first estimates, to our knowledge, of the long-term impact of a lifestyle intervention on disability.

The multicomponent, lifestyle-based Look AHEAD intervention could have affected disability-free life expectancy in several ways. First, intervention participants had significant improvements in physical fitness as measured by treadmill walking capacity after 4 years, likely resulting from a combination of improved muscle strength, cardiorespiratory fitness, and reduced fat mass (23,24). Studies of the specific domains of quality of life in Look AHEAD have shown that the primary benefits have been in the areas of mobility and ambulation as well as global feelings of health on the basis of the Feeling Thermometer Scale (25). An improved lean-to-fat mass ratio associated with the intervention was further confirmed at 8 years (24). Second, other analyses from Look AHEAD have demonstrated benefits on depressive symptoms and sleep apnea that also could have translated into improved physical functioning (26,27). Finally, other observed benefits on health reported for the Look AHEAD ILI, including reduced chronic kidney disease, inflammation, and overall hospitalizations, possibly have indirect effects on daily functioning (28–30).

We observed variation in the effects by age, sex, and CVD history. First, the effects of ILI on disability-free life expectancy were significant from age 50 and 60 years but not from age 70 years, which was not due to an observed difference in the ILI effect on disability incidence but, rather, because the number of years of expected life remaining (18 years) for a 70-year-old was only one-half that of a 50-year-old (36 years) (3). Second, ILI was associated with a significant reduction in physical disability incidence in women and those without prior CVD but not among men or those with CVD. The more robust effect among women may be because they become disabled earlier and live longer than men, providing a greater potential for benefit of lifestyle intervention. Similarly, people without CVD may be more apt to benefit from lifestyle intervention as a result of a better physical capacity to maintain changes in physical activity habits. We note, however, that the magnitude of difference between ILI and DSE did

Table 3—Number of years with and without physical disability (severe) according to intervention group: the Look AHEAD study

Age (years)	DSE				ILI			
	Age at disability onset (years)	Nondisabled years (n)	Disabled years (n)	Total years (n)	Age at disability onset (years)	Nondisabled years (n)	Disabled years (n)	Total years (n)
Total								
50	71.4 (70.5–72.3)	21.4 (20.5–22.3)	14.4 (12.4–16.6)	35.8 (33.7–38.0)	72.0 (71.3–72.6)	22.0 (21.3–22.6)	14.1 (12.2–16.1)	36.0 (34.0–38.2)
60	76.1 (75.3–77.0)	16.1 (15.3–17.0)	10.7 (8.8–12.9)	26.9 (24.8–29.2)	76.7 (76.0–77.5)	16.7 (16.0–17.5)	10.4 (8.7–12.5)	27.2 (25.2–29.4)
70	81.6 (80.7–82.6)	11.6 (10.7–12.6)	6.9 (5.1–9.1)	18.6 (16.3–21.0)	82.3 (81.4–83.1)	12.3 (11.4–13.1)	6.8 (5.0–8.9)	19.1 (16.9–21.4)
Men								
50	73.4 (72.1–74.6)	23.4 (22.1–24.6)	10.4 (8.5–12.6)	33.7 (31.5–36.2)	73.9 (72.8–75.0)	24.2 (23.0–25.3)	9.3 (7.7–11.4)	33.6 (31.5–35.9)
60	77.3 (76.2–78.4)	17.3 (16.2–18.4)	7.8 (6.1–9.9)	25.1 (22.9–27.5)	77.9 (76.9–78.9)	18.2 (17.2–19.3)	6.8 (5.3–8.7)	25.0 (23.0–27.3)
70	82.2 (81.2–83.3)	12.2 (11.2–13.3)	5.0 (3.5–7.0)	17.2 (15.0–19.7)	82.8 (81.8–83.9)	13.0 (11.9–14.1)	4.3 (3.0–6.1)	17.3 (15.2–19.8)
Women								
50	70.2 (69.2–71.1)	20.2 (19.2–21.1)	18.4 (15.7–21.1)	38.5 (35.7–41.2)	70.8 (69.2–71.1)	20.8 (20.0–21.5)	18.0 (15.4–20.5)	38.7 (36.0–41.3)
60	75.1 (74.2–76.0)	15.1 (14.2–16.0)	14.3 (11.7–16.9)	29.4 (26.7–32.0)	75.7 (75.0–76.5)	15.7 (15.1–16.8)	14.0 (11.4–16.5)	29.7 (27.0–32.3)
70	81.0 (80.0–81.9)	11.0 (10.0–11.9)	11.0 (10.0–11.9)	20.9 (18.1–23.7)	81.6 (80.7–82.5)	11.6 (10.7–12.5)	9.8 (7.3–12.3)	21.4 (18.6–24.0)
No CVD								
50	72.4 (71.3–73.4)	22.4 (21.3–23.4)	15.6 (13.3–18.0)	38.0 (35.6–40.3)	72.9 (72.1–73.6)	22.9 (22.1–23.6)	15.7 (13.3–18.0)	38.5 (35.8–41.0)
60	77.3 (76.3–78.3)	17.3 (16.3–18.3)	11.7 (9.5–14.0)	29.0 (26.6–31.3)	77.8 (76.9–78.6)	17.8 (16.9–18.6)	11.9 (9.6–14.2)	29.7 (27.1–32.1)
70	82.9 (81.9–84.0)	12.9 (11.9–14.0)	7.8 (5.6–10.1)	20.7 (18.1–23.1)	83.4 (82.4–84.3)	13.4 (12.4–14.3)	8.1 (5.8–10.3)	21.5 (18.7–24.0)
CVD								
50	67.6 (66.1–69.0)	17.6 (16.1–19.0)	12.6 (10.3–15.3)	30.2 (27.7–32.9)	68.3 (66.9–69.6)	18.3 (16.9–19.6)	12.4 (10.2–14.8)	30.6 (28.3–33.1)
60	73.1 (72.0–74.2)	13.1 (12.0–14.2)	9.0 (7.1–11.2)	22.1 (19.9–24.5)	73.8 (72.8–74.9)	13.8 (12.8–14.9)	8.8 (7.0–11.0)	22.6 (20.7–24.9)
70	79.4 (78.5–80.3)	9.4 (8.5–10.3)	5.5 (4.0–7.8)	14.9 (12.9–17.6)	80.1 (79.1–81.0)	10.1 (9.1–11.0)	5.5 (4.0–7.7)	15.6 (13.7–18.1)

Data are n in years (95% CIs).

Table 4—Number of disabled and nondisabled years (moderate or severe) according to intervention group and duration of effect after end of intervention: the Look AHEAD study

	DSE				ILI			
	Age at disability onset (years)		Total years (n)		Age at disability onset (years)		Total years (n)	
	Nondisabled years (n)	Disabled years (n)	Disabled years (n)	Total years (n)	Nondisabled years (n)	Disabled years (n)	Disabled years (n)	Total years (n)
0 years								
50	64.4 (63.7–65.1)	14.4 (13.7–15.1)	21.5 (19.3–23.7)	35.8 (33.8–38.1)	65.3 (64.8–65.8)§	15.3 (14.8–15.8)§	20.7 (18.7–22.9)	36.0 (34.1–38.2)
60	71.1 (70.6–71.7)	11.1 (10.6–11.7)	15.7 (13.7–18.0)	26.9 (24.8–29.2)	72.0 (71.5–72.4)§	12.0 (11.5–12.4)§	15.2 (13.2–17.3)	26.8 (24.8–29.0)
70	78.4 (77.8–79.0)	8.4 (7.8–9.0)	10.2 (8.0–12.5)	18.6 (16.4–21.0)	79.2 (78.6–79.8)	9.2 (8.8–9.8)	9.9 (7.8–12.2)	18.7 (16.5–21.1)
4 years								
50	64.4 (63.7–65.1)	14.4 (13.7–15.1)	21.5 (19.3–23.8)	35.8 (33.8–38.1)	65.4 (64.9–65.9)§	15.4 (14.9–15.9)§	20.7 (18.6–22.9)‡	36.1 (34.0–38.2)
60	71.1 (70.6–71.7)	11.1 (10.7–11.7)	15.7 (13.7–18.0)	26.9 (24.8–29.1)	72.0 (71.6–72.5)§	12.0 (11.6–12.5)§	15.2 (13.2–17.4)*	27.2 (25.2–29.4)
70	78.4 (77.9–79.1)	8.4 (7.9–9.1)	10.2 (8.0–12.6)	18.6 (16.3–21.1)	79.2 (78.6–79.8)	9.2 (8.6–9.8)	9.9 (7.8–12.3)	19.1 (17.0–21.6)
8 years								
50	64.4 (63.7–65.1)	14.4 (13.7–15.1)	21.5 (19.4–23.7)	35.8 (33.8–38.1)	65.5 (64.9–66.0)§	15.5 (15.0–16.1)§	20.6 (18.6–22.8)‡	36.1 (34.1–38.2)
60	71.1 (70.6–71.7)	11.1 (10.6–11.7)	15.7 (13.7–18.0)	26.9 (24.8–29.1)	72.1 (71.6–72.6)§	12.1 (11.6–12.6)§	15.2 (13.2–17.4)	27.3 (25.3–29.5)
70	78.4 (77.9–79.0)	8.4 (7.9–9.0)	10.2 (8.0–12.5)	18.6 (16.3–21.1)	79.3 (78.7–79.9)	9.3 (8.7–9.9)	10.0 (7.9–12.3)	19.2 (17.1–21.6)
Lifetime								
50	64.4 (63.7–65.1)	14.4 (13.7–15.1)	21.5 (19.4–23.7)	35.8 (33.8–38.0)	66.0 (65.3–66.7)*	16.0 (15.3–16.7)*	21.2 (18.9–23.6)	37.2 (35.0–39.6)
60	71.1 (70.6–71.7)	11.1 (10.6–11.7)	15.7 (13.7–18.0)	26.9 (24.8–29.1)	72.4 (71.8–73.0)‡	12.4 (11.8–13.0)‡	15.7 (13.5–18.2)	28.1 (25.8–30.5)
70	78.4 (77.9–79.1)	8.4 (7.9–9.1)	10.2 (8.0–12.6)	18.6 (16.3–21.0)	79.4 (78.8–80.1)§	9.4 (8.8–10.1)§	10.3 (8.0–12.7)	19.7 (17.3–22.2)

Data are n in years (95% CIs). *P < 0.001, †P < 0.01, ‡P < 0.05 for comparison between the ILI and DSE groups.

not differ appreciably across the strata and that the sample sizes and number of events were considerably smaller among men and those with CVD. Thus, variation in statistical power was likely the primary factor driving different conclusions across strata. Significant benefits also were limited to moderate/severe disability because disability-adjusted life-years defined by the more severe threshold were not significant. Although this finding may be a function of less statistical power for the less frequent outcome, severe disability possibly is affected by different mechanisms that are less influenced by ILI.

The current study differs from prior intervention studies in terms of the metric under investigation. Whereas prior studies evaluated changes in physical function, our analyses incorporate effects on remission from disability as well as mortality and take a lifetime perspective. In general, lower incidence of disability, higher remission from disability, and a more favorable mortality rate in adults without versus with disabilities will contribute to a delay in disability and a greater disability-free life expectancy. The large reductions in mortality and macrovascular complications of diabetes in the U.S. during the 1990s and 2000s is likely to place a greater emphasis on this and similar metrics that capture the impact of diabetes on quality of life (2,3).

This analysis had several limitations. First, our definition of disabled and nondisabled life-years ultimately depends on a subjective selection of a threshold for physical disability. However, we used an objective, data-driven approach to select the most appropriate threshold by using all the information available in the SF-36 items before calculating incidence or testing primary comparisons. Second, our physical function assessments are based on self-report and not validated by objective, physical performance measures. However, the SF-36 has strong psychometric properties, has been extensively validated, and is well-accepted for quality-of-life measurements in clinical trials (14). Third, the analyses modeled life expectancy beyond the trial time frame and years of age. However, our primary analysis used a conservative assumption that there was no intervention effect beyond the period of intervention. Finally, the analysis did not permit a determination of factors influencing the association between lifestyle intervention and years of

life with and without disability. Nevertheless, this study is the first we are aware of to directly estimate the impact of a long-term lifestyle intervention on active and disabled life expectancy in overweight and obese adults with type 2 diabetes.

In summary, these findings indicate that an ILI that focuses on caloric restriction and increased physical activity can reduce long-term physical disability and has an impact on disability-free life expectancy despite not affecting total life expectancy. Given the continued high prevalence of diabetes in the U.S. and the increasing life spans of adults with diabetes, these findings have important implications for the compression of morbidity and improvement of quality of life among overweight and obese adults with type 2 diabetes.

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References

- Nathan DM. Long-term complications of diabetes mellitus. *N Engl J Med* 1993;328:1676–1685
- Gregg EW, Zhuo X, Cheng YJ, Albright AL, Narayan KM, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985–2011: a modelling study. *Lancet Diabetes Endocrinol* 2014;2:867–874
- Bardenheier BH, Lin J, Zhuo X, et al. Disability-free life-years lost among adults aged ≥ 50 years with and without diabetes. *Diabetes Care* 2016;39:1222–1229
- Wong E, Backholer K, Gearon E, et al. Diabetes and risk of physical disability in adults: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* 2013;1:106–114
- Lu FP, Lin KP, Kuo HK. Diabetes and the risk of multi-system aging phenotypes: a systematic review and meta-analysis. *PLoS One* 2009;4:e4144
- Guralnik JM, Fried LP, Salive ME. Disability as a public health outcome in the aging population. *Annu Rev Public Health* 1996;17:25–46
- Fries JF. Measuring and monitoring success in compressing morbidity. *Ann Intern Med* 2003;139:455–459
- Centers for Disease Control and Prevention. Diagnoses diabetes [article online], 2016. Available from <https://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html>. Accessed 23 February 2018
- Rejeski WJ, Ip EH, Bertoni AG, et al.; Look AHEAD Research Group. Lifestyle change and mobility in obese adults with type 2 diabetes. *N Engl J Med* 2012;366:1209–1217
- Wing RR, Bolin P, Brancati FL, et al.; Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145–154
- Ryan DH, Espeland MA, Foster GD, et al.; Look AHEAD Research Group. Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of

cardiovascular disease in type 2 diabetes. *Control Clin Trials* 2003;24:610–628

- Wadden TA, West DS, Delahanty L, et al.; Look AHEAD Research Group. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity (Silver Spring)* 2006;14:737–752
- Wesche-Thobaben JA. The development and description of the comparison group in the Look AHEAD trial. *Clin Trials* 2011;8:320–329
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473–483
- Ip EH, Zhang Q, Rejeski WJ, Harris TB, Kritchevsky S. Partially ordered mixed hidden Markov model for the disablement process of older adults. *J Am Stat Assoc* 2013;108:370–380
- Zhang EH, Rijmen F, Ip EH. Multivariate discrete hidden Markov models for domain-based measurements and assessment of risk factors in child development. *J Graph Comput Stat* 2010;19:746–765
- Ross S. *Introduction to Probability Models*. Oxford, UK, Academic Press, 2014
- Bianchi L, Zuliani G, Volpato S. Physical disability in the elderly with diabetes: epidemiology and mechanisms. *Curr Diab Rep* 2013;13:824–830
- Volpato S, Ferrucci L, Blaum C, et al. Progression of lower-extremity disability in older women with diabetes: the Women's Health and Aging Study. *Diabetes Care* 2003;26:70–75
- Rejeski WJ, Bray GA, Chen SH, et al.; Look AHEAD Research Group. Aging and physical function in type 2 diabetes: 8 years of an intensive lifestyle intervention. *J Gerontol A Biol Sci Med Sci* 2015;70:345–353
- Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum* 2004;50:1501–1510
- Ettinger WH Jr, Burns R, Messier SP, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277:25–31
- Jakicic JM, Egan CM, Fabricatore AN, et al.; Look AHEAD Research Group. Four-year change in cardiorespiratory fitness and influence on glycemic control in adults with type 2 diabetes in a randomized trial: the Look AHEAD Trial. *Diabetes Care* 2013;36:1297–1303
- Pownall HJ, Bray GA, Wagenknecht LE, et al.; Look AHEAD Research Group. Changes in body composition over 8 years in a randomized trial of a lifestyle intervention: the Look AHEAD study. *Obesity (Silver Spring)* 2015;23:565–572
- Zhang P, Hire D, Espeland MA, et al.; Look AHEAD Research Group. Impact of intensive lifestyle intervention on preference-based quality of life in type 2 diabetes: results from the Look AHEAD trial. *Obesity (Silver Spring)* 2016;24:856–864
- Rubin RR, Wadden TA, Bahnson JL, et al.; Look AHEAD Research Group. Impact of intensive lifestyle intervention on depression and health-related quality of life in type 2 diabetes: the Look AHEAD trial. *Diabetes Care* 2014;37:1544–1553
- Foster GD, Borradaile KE, Sanders MH, et al.; Sleep AHEAD Research Group of Look AHEAD Research Group. A randomized study on the effect of

weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med* 2009;169:1619–1626

28. Look AHEAD Research Group. Effect of a long-term behavioural weight loss intervention on nephropathy in overweight or obese adults with type 2 diabetes: a secondary analysis of the

Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol* 2014;2:801–809

29. Espeland MA, Glick HA, Bertoni A, et al.; Look AHEAD Research Group. Impact of an intensive lifestyle intervention on use and cost of medical services among overweight and obese adults with type 2 diabetes: the action for health in diabetes. *Diabetes Care* 2014;37:2548–2556

30. Belcazar LM, Reboussin DM, Haffner SM, et al.; Look AHEAD Research Group. A 1-year lifestyle intervention for weight loss in individuals with type 2 diabetes reduces high C-reactive protein levels and identifies metabolic predictors of change: from the Look AHEAD (Action for Health in Diabetes) study. *Diabetes Care* 2010;33:2297–2303