A Long-Term Intensive Lifestyle Intervention and Physical Function: The Look AHEAD Movement and Memory Study

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Objective: To assess the long-term effects of an intensive lifestyle intervention on physical function using a randomized post-test design in the Look AHEAD trial.

Methods: Overweight and obese (BMI ≥ 25 kg m⁻²) middle-aged and older adults (aged 45-76 years at enrollment) with type 2 diabetes (n = 964) at four clinics in Look AHEAD, a trial evaluating an intensive lifestyle intervention (ILI) designed to achieve weight loss through caloric restriction and increased physical activity compared to diabetes support and education (DSE), underwent standardized assessments of performance-based physical function including an expanded short physical performance battery (SPPBexp), 20-m and 400-m walk, and grip and knee extensor strength 8 years post-randomization, during the trial’s weight maintenance phase.

Results: Eight years post-randomization, individuals randomized to ILI had better SPPBexp scores [adjusted mean (SE) difference: 0.055 (0.022), P = 0.01] and faster 20-m and 400-m walk speeds [0.032 (0.012) m s⁻¹, P = 0.01, and 0.025 (0.011) m s⁻¹, P = 0.02, respectively] compared to those randomized to DSE. Achieved weight loss greatly attenuated the group differences in physical function, and the intervention effect was no longer significant.

Conclusions: An intensive lifestyle intervention has long-term benefits for mobility function in overweight and obese middle-aged and older individuals with type 2 diabetes.

Introduction

Limitations in physical function predict future disability, greater healthcare costs, and mortality (1,2). Obesity is a strong predictor of limitations in physical function and appears to operate through both direct pathways (e.g., lower extremity pain, biomechanical changes) and indirect pathways (e.g., obesity-related comorbidities) (3,4).

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Type 2 diabetes further accelerates declines in physical function and increases the risk of disability (5,6).

Over the short term, physical function can be improved through lifestyle change. In overweight and obese persons, participation in weight loss and exercise interventions lasting up to 18 months improved performance-based physical function measures with both weight loss and exercise conferring benefit (7-9). In the Look AHEAD trial, randomization to an intensive lifestyle intervention that included both weight reduction and increased physical activity was associated with a slower rate of self-reported limitations in mobility over a 4-year period compared to randomization to a diabetes support and education control group (10).

While these results are encouraging, the ultimate public health benefit of such interventions depends on their sustainability. Furthermore, weight loss reduces skeletal muscle mass (11), which in turn may induce weakness and is associated with impaired physical function and disability (12). Thus, whether potential benefits of lifestyle change on physical function are sustainable over the long term is unknown. To address this issue, we obtained performance-based measures of physical function 8-9 years after randomization to a lifestyle intervention designed to promote and maintain weight loss through caloric restriction and increased physical activity in four of the Look AHEAD clinic sites using a randomized post-test design. We hypothesized that individuals randomized to a long-term intensive lifestyle intervention would have better physical function compared to those randomized to a diabetes support and education control group.

**Methods**

The design and methods of the Action for Health in Diabetes (Look AHEAD) trial have been published previously (13). In brief, Look AHEAD recruited individuals who were 45-76 years of age and had a body mass index ≥25 kg m⁻² (≥27 kg m⁻² in participants on insulin), HbA1c <11%, systolic blood pressure <160 mmHg, diastolic blood pressure <100 mmHg, and triglycerides <600 mg dl⁻¹. These individuals underwent a maximal graded exercise test to ensure that exercise could be safely prescribed, completed 2 weeks of self-monitoring, and attended a diabetes education session prior to randomization.

The Look AHEAD Movement and Memory (Look AHEAD M&M) ancillary study enrolled Look AHEAD participants at four clinic sites to assess physical and cognitive function at either the Year 8 or 9 examination, during the weight maintenance phase of the trial. Only Look AHEAD participants who were currently active (i.e., had not died, been lost to follow-up, or refused further Look AHEAD activity) at the Baton Rouge, Denver, Memphis and Pittsburgh clinics and who provided separate informed consent were eligible to enroll. This ancillary study was approved by local Institutional Review Boards.

**Interventions**

At enrollment into the Look AHEAD trial, participants were randomly assigned by center to an Intensive Lifestyle Intervention (ILI) or a diabetes support and education (DSE) control condition. The ILI included diet modification and physical activity and was designed to achieve and maintain weight loss of at least 7% (14). ILI participants were assigned a calorie goal (1200-1800 kcals day⁻¹ based on initial weight), with <30% of total calories from fat and a minimum of 15% of total calories from protein. The physical activity goal was ≥175 min of unsupervised moderately intense physical activity per week and focused on activities similar in intensity to brisk walking. ILI participants were seen weekly for the first 6 months and three times per month for the next 6 months, with a combination of group and individual sessions. During Years 2-4, participants were seen individually at least once per month and had a minimum of one additional contact by phone, mail or email per month. During Years 5+, participants were encouraged to continue individual monthly sessions and annual campaigns were used to promote adherence.

DSE participants were invited to three group sessions focused on diet, physical activity, or social support each year for the first 4 years and one session annually thereafter (15). Information on behavioral strategies was not presented.

**Physical function**

The Look AHEAD M&M ancillary study assessed performance-based physical function at a clinic exam in the 8th or 9th year of follow-up. Certified clinic staff masked to intervention assignment conducted all physical function measures. The sample sizes for each of the performance-based functional measures vary based on specific participant safety exclusions (see online Supporting Information).

The Short Physical Performance Battery (SPPB) was administered to assess lower extremity physical function (16). The SPPB consists of standing balance tasks (side-by-side, semi- and full-tandem stands for 10 seconds each), a 4-m walk to assess usual gait speed, and time to complete five repeated chair stands. Each of the three performance measures is assigned a score ranging from 0 (inability to perform the task) to 4 (the highest level of performance) and summed to create an SPPB score ranging from 0 to 12 (best). The SPPB was modestly expanded (SPPBexp) to minimize ceiling effects of the SPPB when used in well-functioning populations (17). The SPPBexp increased the holding time of the standing balance tasks to 30 seconds and added a single leg stand. The SPPBexp component scores are calculated as the ratio of observed performance to the best possible performance and summed to provide a continuous score ranging from 0 to 3, with higher scores indicative of better performance.

Usual walking speed over 20 m and walking endurance over 400 m were measured (18). The course was 20-m long and marked by cones at each end. Participants were instructed to walk at their usual pace, and time to complete the first 20 m and the longer 400 m was recorded.

Grip strength (kg) was measured twice in each hand using an isometric Hydraulic Hand Dynamometer (Jamar, Bolingbrook, IL). The maximum force from two trials for the stronger hand was used in the analyses. Maximum knee extensor strength (kg; one repetition maximum) was assessed on a Nautilus One™ Leg Extension machine. The right leg was tested unless there was a contraindication (e.g., prior knee surgery). If participants experienced knee pain during the test and there were no contraindications to test the other leg, the other leg was tested.

**Physical activity**

The RT3 triaxial accelerometer (StayHealth®, Monrovia, CA) worn during waking hours on at least 5 out of 7 days was used to provide...
an objective measure of physical activity at Year 8/9. Daily energy expenditure for periods of moderate to vigorous physical activity using the criteria of bouts of ≥3.0 metabolic equivalents (METs) lasting ≥10 min (MET-min day⁻¹) were quantified (19).

Weight and cardiorespiratory fitness
Clinic staff masked to intervention assignment collected annual measures of weight throughout the trial using a digital scale. A maximal graded exercise test was administered at baseline and a submaximal graded exercise test at 1- and 4-year follow-up (20). Cardiorespiratory fitness was estimated in METs.

Baseline assessment of potential risk factors for physical function
Self-reported characteristics and conditions were assessed using standardized questionnaires at the baseline visit. Participants brought current prescription medications to the baseline visit. The Short Form-36 Health Survey (SF-36) was used as a measure of health status (21). The SF-36 measures 8 health domains with domain subscale scores ranging from 0 to 100 (higher scores indicating better functioning or well-being). The Beck Depression Inventory (BDI) was used to measure depressive symptom burden. A BDI score ≥10 was used as a marker for symptoms of mild to moderate depression (22). Height was measured in duplicate using a stadiometer. Blood specimens were collected after a 12-h fast and were analyzed by the Central Biochemistry Laboratory (Northwest Lipid Research Laboratories, University of Washington, Seattle, WA) using standardized laboratory procedures for measuring HbA₁c.

Statistical analyses
Initial analyses involved descriptive statistics. Comparisons between groups were done using chi-square tests for proportions and t tests or ANOVA for continuous variables. Analysis of covariance models were used to contrast the Year 8 (or Year 9) values of performance-based physical function (SPPB and SPPBexp, 20-m and 400-m walk speed, and grip and knee extensor strength) among participants grouped by intervention assignment. Two sets of models were fitted for each measure: a minimal model including baseline age, gender, race/ethnicity, education level, and clinic site as covariates; and a fully adjusted model including baseline age, gender, race/ethnicity, education level, and clinic site as covariates; and a fully adjusted model including baseline BMI, HbA₁c, insulin use, diabetes duration, hypertension status, prior CVD, depressive symptoms, smoking status, cardiorespiratory fitness, SF-36 Physical Functioning and Bodily Pain subscales, and year of visit. To account for selection bias, we calculated the conditional probability to be included in the Look AHEAD M&M ancillary study for each active participant at the participating clinics based on their baseline characteristics, i.e., all the covariates in the fully adjusted model except year of visit and intervention assignment. Then a sensitivity analysis was performed that included the calculated conditional probability as an additional covariate in the full ANCOVA model described above. The consistency of the intervention effect across pre-specified interactions between intervention group and baseline age, gender, BMI, cardiorespiratory fitness, and diabetes duration was examined in the ANCOVA models. Pre-planned analysis stratified by age group (<60 vs. ≥60 years) was done to examine the effects of the intervention on those at higher risk of mobility disability due to age. We also examined the effects by magnitude of weight loss (<7 vs. ≥7%) and the potential mediating effects of the individual intervention components. All analyses were performed in SAS 9.3 (Cary, NC).

Results
Recruitment into the Look AHEAD M&M ancillary study occurred from September 2009 through June 2012. The four clinics enrolled 1,331 participants into the Look AHEAD trial at baseline. When Look AHEAD M&M enrollment started, 30 of the original participants had withdrawn from Look AHEAD, 65 had died, and 4 were lost to follow-up, leaving 1,232 participants who attended a Year 8 or 9 visit during the Look AHEAD M&M enrollment period. Of these, 1,092 (89%) consented to enroll in the Look AHEAD M&M ancillary study, of which 1,081 were seen either at the clinic (n = 979) or assessed by telephone (n = 102). Data for the performance-based physical function measures presented here are from 964 participants who were assessed in the clinic with complete covariate data, 72% of the original Look AHEAD enrollees.

Compared to the original Look AHEAD cohort at the four participating clinics, participants in the Look AHEAD M&M ancillary study who were included in these analyses were less likely to be African-American and have hypertension, more likely to have a college degree, and had higher baseline cardiorespiratory fitness and SF-36 General Health scores (all P < 0.05), but did not differ by any other risk factors for physical function that we considered including baseline BMI and SF-36 Physical Functioning subscale nor was there a difference in the distribution of intervention assignments between enrollees and non-enrollees. The risk factor distribution was balanced between groups (Table 1), except that a greater percentage of ILI participants had elevated BDI scores compared to DSE participants.

The ILI intervention produced substantial differences in weight loss and cardiorespiratory fitness compared to the DSE condition among the participants included in our analyses (P < 0.001). Differences were largest after the first year of intervention, but remained through Year 8 for weight change (Figure 1) and through Year 4 (when it was last measured) for cardiorespiratory fitness. The ILI group lost a mean (SD) 9.4% (7.1%) of their weight at Year 1 and maintained a 6.0% (8.6%) mean weight loss through Year 8. In contrast, weight loss in the DSE group was 0.7% (4.7%) at Year 1 and 2.3% (9.4%) at Year 8. The ILI group had a mean (SD) 24.3% (31.3%) increase in cardiorespiratory fitness at Year 1 and maintained a 5.5% (26.3%) increase in cardiorespiratory fitness at Year 4. In contrast, the DSE group had a 5.4% (21.1%) increase in cardiorespiratory fitness at Year 1 but a 2.9% (24.0%) decrease in cardiorespiratory fitness at Year 4.

The physical function data were collected an average (range) of 8.1 (7.8-9.3) years after randomization. Table 2 shows the distribution of physical function test scores grouped by intervention assignment. ILI participants had higher SPPBexp scores and faster 20-m gait speed than the DSE participants. Table 3 shows the associations between the intervention and physical function for the minimally and fully adjusted models. In the fully adjusted models, participants randomized to ILI had higher SPPBexp scores (P = 0.01) and faster gait speed on both the 20-m (P = 0.01) and 400-m walk (P = 0.02). Analyses using the conditional probability of being included
TABLE 1 Characteristics at the time of enrollment into the Look AHEAD trial of participants who provided data on physical function by intervention assignment: the Look AHEAD Movement and Memory Study

| Characteristic                          | Diabetes support and education (DSE); N = 472 | Intensive lifestyle intervention (ILI); N = 492 | P value |
|----------------------------------------|-----------------------------------------------|-----------------------------------------------|---------|
| Age (years)                            | 58.9 (6.8)                                    | 58.8 (6.8)                                    | 0.67    |
| < 60 yrs                               | 258 (54.7)                                    | 279 (56.7)                                    | 0.52    |
| ≥ 60 yrs                               | 214 (45.3)                                    | 213 (43.3)                                    |         |
| Gender, N (%)                          |                                               |                                               | 0.88    |
| Female                                 | 269 (57.0)                                    | 278 (56.5)                                    |         |
| Male                                   | 203 (43.0)                                    | 214 (43.5)                                    |         |
| Race/ethnicity, N (%)                  |                                               |                                               | 0.95    |
| African-American                       | 95 (20.1)                                     | 100 (20.3)                                    |         |
| Non-Hispanic white                     | 338 (71.6)                                    | 354 (72.0)                                    |         |
| Other/multiple                         | 39 (8.3)                                      | 38 (7.7)                                      | 0.08    |
| Education, N (%)                       |                                               |                                               |         |
| HS or less                             | 69 (14.6)                                     | 71 (14.4)                                     | 0.06    |
| Post HS                                | 200 (42.4)                                    | 191 (38.8)                                    |         |
| College/graduate                       | 188 (39.8)                                    | 224 (45.5)                                    |         |
| Other                                  | 15 (3.2)                                      | 6 (1.2)                                       |         |
| Body mass index (kg m\(^{-2}\))        |                                               |                                               |         |
| Mean (SD)                              | 35.7 (5.6)                                    | 35.6 (6.0)                                    | 0.90    |
| N (%)                                  | 25-29                                          | 93 (18.9)                                     | 0.06    |
| ≥ 30                                   | 404 (85.6)                                    | 399 (81.1)                                    |         |
| Weight (kg), mean (SD)                 | 101.2 (18.5)                                  | 102.1 (19.1)                                  | 0.45    |
| HbA1c (%)\(^{a}\), N (%)               |                                               |                                               | 0.96    |
| < 7.0                                  | 226 (47.9)                                    | 231 (47.0)                                    |         |
| 7.0-8.9                                | 202 (42.8)                                    | 215 (43.7)                                    |         |
| 9.0-11.0                               | 44 (9.3)                                      | 46 (9.3)                                      |         |
| Insulin use, N (%)                     |                                               |                                               | 0.55    |
| No                                     | 399 (84.5)                                    | 409 (83.1)                                    |         |
| Yes                                    | 73 (15.5)                                     | 83 (16.9)                                     |         |
| Diabetes duration, N (%)               |                                               |                                               | 0.78    |
| < 5 yrs                                | 224 (47.5)                                    | 238 (48.4)                                    |         |
| ≥ 5 yrs                                | 248 (52.5)                                    | 254 (51.6)                                    |         |
| Hypertension, N (%)                    |                                               |                                               | 0.53    |
| No                                     | 84 (17.8)                                     | 80 (16.3)                                     |         |
| Yes                                    | 388 (82.2)                                    | 412 (83.7)                                    |         |
| Prior cardiovascular disease, N (%)    |                                               |                                               | 0.41    |
| No                                     | 408 (86.4)                                    | 416 (84.6)                                    |         |
| Yes                                    | 64 (13.6)                                     | 76 (15.4)                                     |         |
| Depressive symptoms,\(^{b}\), N (%)   |                                               |                                               | 0.04    |
| BDI score ≤ 10                         | 434 (91.9)                                    | 433 (88.0)                                    |         |
| BDI score > 10                         | 38 (8.1)                                      | 59 (12.0)                                     |         |
| Smoking status, N (%)                  |                                               |                                               | 0.29    |
| Never                                  | 255 (54.0)                                    | 241 (49.0)                                    |         |
| Former                                 | 197 (41.7)                                    | 229 (46.5)                                    |         |
| Current                                | 20 (4.2)                                      | 22 (4.5)                                      |         |

*Glycated haemoglobin.

*Beck Depression Inventory.

*Short Form-36 Health Survey.

The intervention effect did not appear to vary by baseline age (P values for interaction terms, P ≥ 0.32), gender (P ≥ 0.16), BMI (P ≥ 0.11), cardiorespiratory fitness (P ≥ 0.10), or diabetes duration (P ≥ 0.28 except for grip strength, P = 0.01). We further examined the associations between the intervention and physical function stratified by age. For those who were ≥60 years at randomization, ILI participants had higher SPPBexp scores than DSE participants [adjusted mean (SE): 1.53 (0.03) vs. 1.44 (0.03), P = 0.02]. For those who were <60 years at randomization, ILI participants had faster 20-m and 400-m gait speed compared to DSE participants [adjusted mean (SE): 1.21 (0.01) vs. 1.17 (0.01), P = 0.03, respectively].

The intervention effect did not appear to vary by baseline age (P values for interaction terms, P ≥ 0.32), gender (P ≥ 0.16), BMI (P ≥ 0.11), cardiorespiratory fitness (P ≥ 0.10), or diabetes duration (P ≥ 0.28 except for grip strength, P = 0.01). We further examined the associations between the intervention and physical function stratified by age. For those who were ≥60 years at randomization, ILI participants had higher SPPBexp scores than DSE participants [adjusted mean (SE): 1.53 (0.03) vs. 1.44 (0.03), P = 0.02]. For those who were <60 years at randomization, ILI participants had faster 20-m and 400-m gait speed compared to DSE participants [adjusted mean (SE): 1.21 (0.01) vs. 1.17 (0.01), P = 0.03, respectively].

To better understand the effect of weight loss on the physical function measures that were significantly different by intervention group, we examined the outcomes within each intervention group stratified by whether or not participants achieved the target weight loss goal (≥7%). ILI participants who achieved ≥7% weight loss at Year 8/9 had higher SPPB exp scores and faster 20-m and 400-m gait speed (all P ≤ 0.001) compared to those who did not; there was a similar trend for those in the DSE group who achieved ≥7% weight loss (Table 4).

To explore the individual components of the intervention (weight loss and physical activity) on physical function and their possible role in mediating the intervention effect, Year 8/9 weight change from baseline and Year 8/9 physical activity were individually added to the fully adjusted model for the physical function measures.
that were significantly different by intervention group. The group differences were attenuated by at least 40% when weight change was added to the model and the intervention effect was no longer significant (Table 5). Although objectively measured moderate to vigorous physical activity at Year 8/9 differed by intervention group [mean (SD): 63.5 (105.7) vs. 47.4 (84.7) MET-min day$^{-1}$ for ILI vs. DSE, $P = 0.01$], group differences were attenuated by no more than 16% when physical activity was included in the model and the intervention effect remained statistically significant.

**Discussion**

After at least 8 years of randomization to an intensive lifestyle intervention, middle aged and older adults with type 2 diabetes had better mobility and lower extremity physical performance compared to those randomized to a diabetes support and education control group. Neither upper nor lower extremity strength differed between the intervention groups, suggesting that weight loss did not lead to declines in strength despite anticipated declines in muscle mass. The intervention effect did not appear to vary by baseline age, gender, BMI, cardiorespiratory fitness, or diabetes duration.

Both intervention groups likely included individuals who intentionally lost weight and who experienced unintentional weight loss; however, almost twice as many individuals in the ILI group achieved and maintained $\geq 7\%$ weight loss at Year 8. In the ILI group, individuals who achieved $\geq 7\%$ weight loss had better lower extremity function and mobility than those who did not. Furthermore, when we accounted for achieved weight loss, the intervention effect was greatly attenuated and no longer significant. When we accounted for current physical activity however, the intervention effect remained significant. This suggests that much of the benefit observed was related to the direct effects of weight loss. This does not preclude an effect of the physical activity component of the intervention since persons losing the most weight may also have engaged in more physical activity. Both weight loss and improvements in cardiorespiratory fitness were previously reported to mediate the intervention effect on self-reported limitations in mobility over the first 4 years in the Look AHEAD trial (10). Cardiorespiratory fitness was not measured after Year 4 which prevented us from examining change in cardiorespiratory fitness as a potential mediator.

There are several potential mechanisms by which weight loss may improve physical function in obese individuals. Obesity is associated with reduced gait efficiency related to biomechanical changes (23). In addition, the loss of total mass without the loss of strength may have also improved gait efficiency by reducing the effort of movement. Weight loss reduces systemic markers of inflammation (24-26), which are also strongly associated with impaired physical function and mobility disability (27-29).

Previous trials assessing the functional benefits of lifestyle interventions in overweight and obese middle aged and older persons have been of shorter duration (12-18 months) (7-9). In these prior studies (7-9), achieved weight loss was of similar magnitude (ranging from 5.7% to 9%) to the initial weight loss achieved at 1 year in Look AHEAD (9.4%). The end-of-study between-group weight loss

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**Figure 1** Mean (SE) changes in weight from baseline for participants grouped by intervention assignment: the Look AHEAD Movement and Memory Study.

**TABLE 2** Average physical function for participants at their Year 8/9 visit grouped by intervention assignment: the Look AHEAD Movement and Memory Study

| Physical function measure                              | Diabetes support and education (DSE) | Intensive lifestyle intervention (ILI) | $P$ value |
|--------------------------------------------------------|-------------------------------------|--------------------------------------|-----------|
|                                                        | N  | Mean (SD)         | N  | Mean (SD)         |             |
| SPPB score (range 0-12)                                | 468| 10.0 (2.1)        | 486| 10.1 (1.9)        | 0.27       |
| SPPB$\text{exp}$ (range 0-3)                            | 468| 1.62 (0.41)       | 485| 1.68 (0.40)       | 0.03       |
| 20-m walk speed (m s$^{-1}$)                            | 449| 1.12 (0.22)       | 469| 1.16 (0.22)       | 0.02       |
| 400-m walk speed (m s$^{-1}$)                           | 422| 1.05 (0.19)       | 447| 1.07 (0.19)       | 0.07       |
| Grip strength (kg)                                     | 445| 30.7 (10.7)       | 462| 31.0 (10.2)       | 0.71       |
| Knee extensor strength (maximum weight lifted; kg)     | 342| 23.4 (12.5)       | 359| 23.4 (11.9)       | 0.99       |

*Unadjusted.

Abbreviations: SPPB, Short Physical Performance Battery; SPPB$\text{exp}$, Expanded Short Physical Performance Battery.
TABLE 3 Mean differences between intensive lifestyle intervention (ILI) and diabetes support and education (DSE) participants on physical function measures: the Look AHEAD Movement and Memory Study

| Physical function measure      | Minimal adjustment modela   | Full modelb   |
|-------------------------------|-----------------------------|---------------|
|                               | Mean (SE) difference:       | Mean (SE) difference: |
|                               | I LI minus DSE | P value | I LI minus DSE | P value |
| SPPB score (range 0-12)       | 0.092 (0.118) | 0.44    | 0.132 (0.113) | 0.24    |
| SPPBexp score (range 0-3)     | 0.048 (0.023) | 0.04    | 0.055 (0.022) | 0.01    |
| 20-m walk speed (m s\(^{-1}\)) | 0.028 (0.013) | 0.03    | 0.032 (0.012) | 0.01    |
| 400-m walk speed (m s\(^{-1}\)) | 0.019 (0.012) | 0.11    | 0.025 (0.011) | 0.02    |
| Grip strength (kg)            | −0.022 (0.474) | 0.96    | 0.027 (0.470) | 0.95    |
| Knee extensor strength (max weight lifted; kg) | −0.419 (0.605) | 0.49 | −0.340 (0.604) | 0.57 |

aAdjusted for age, gender, race/ethnicity, education, and clinic site.
bAdditional adjustment for baseline BMI, HbA1c, insulin use, diabetes duration, hypertension status, prior CVD, depressive symptoms, smoking, cardiorespiratory fitness, and SF-36 Physical Functioning and Bodily Pain subscales, and year of visit.
Abbreviations: SPPB, Short Physical Performance Battery; SPPBexp, Expanded Short Physical Performance Battery.

Differences ranged from 4.5 to 8% (7-9). In Look AHEAD, the ILI group sustained a mean weight loss of 6.0% 8 years post-randomization, while the DSE group lost 2.3%. The difference in gait speed (at fast pace) between weight loss plus exercise and control groups in the shorter trials ranged from 0.06 to 0.13 m s\(^{-1}\) (7-9). In Look AHEAD, the ILI group’s mean gait speed (at usual pace) was 0.02 to 0.03 m s\(^{-1}\) better than the DSE group; a difference equivalent to being ~3.5 years younger. Furthermore, among the ILI group, the difference in gait speed was 0.05 to 0.08 m s\(^{-1}\) between those who achieved and maintained the 7% weight loss target compared to those who did not. Perera et al. have previously reported that a difference of 0.05 m s\(^{-1}\) represents a small albeit clinically meaningful difference (30). Thus, while the sustained difference in physical function is modest in individual terms, the potential impact of weight loss on a population basis could be substantial. A recent data pooling effort showed that each 0.1 m s\(^{-1}\) difference in gait speed is associated with a 12% difference in total mortality (31).

Concerns regarding the functional consequences of the loss of lean mass have deterred some physicians from recommending weight loss for older adults (32-34). According to the sarcopenia hypothesis (12), lower lean mass leads to weakness which is a hallmark of disability. In the Health ABC study, the loss of total mass was associated with a 30-40% loss of lean mass (35). We did not observe differences in upper or lower extremity strength between the ILI and DSE groups. Because body composition was only assessed in a subset of participants, we cannot directly examine whether change in lean mass was associated with the functional outcomes. The lack of a relationship between short-term changes in lean mass and strength has also been observed in other studies examining both intentional and unintentional weight loss (36-38).

This study has notable strengths and limitations. Although these analyses are based on a post-test design, the comparisons are based on randomization assignment, thereby accounting for potential unmeasured confounders between the groups strengthening the basis for drawing causal inferences from these data. Participation in the ancillary study was high, exceeding 85% of the eligible population. Losses to follow-up were not associated with predictors of impaired physical function at baseline and sensitivity analyses applying

TABLE 4 Mean physical function by achieved weight loss at Year 8/9 visit within intervention assignment: the Look AHEAD Movement and Memory Studya

| Physical function measure      | Diabetes support and education (DSE) | Intensive lifestyle intervention (ILI) |
|-------------------------------|---------------------------------------|---------------------------------------|
|                               | Year 8/9 achieved weight              | Year 8/9 achieved weight              |
|                               | loss <7% (n = 374): mean (SE)         | loss >7% (n = 145): mean (SE)         | P value |
| SPPBexp score (range 0-3)     | 1.60 (0.02)                           | 1.66 (0.03)                           | 0.07    |
| 20-m walk speed (m s\(^{-1}\)) | 1.12 (0.01)                           | 1.15 (0.02)                           | 0.11    |
| 400-m walk speed (m s\(^{-1}\))| 1.04 (0.01)                           | 1.07 (0.01)                           | 0.08    |
|                               | Year 8/9 achieved weight              | Year 8/9 achieved weight              |
|                               | loss <7% (n = 293): mean (SE)         | loss >7% (n = 250): mean (SE)         | P value |
| SPPBexp score (range 0-3)     | 1.63 (0.02)                           | 1.73 (0.02)                           | 0.001   |
| 20-m walk speed (m s\(^{-1}\)) | 1.12 (0.01)                           | 1.20 (0.01)                           | <0.0001 |
| 400-m walk speed (m s\(^{-1}\))| 1.05 (0.01)                           | 1.10 (0.01)                           | 0.0009  |

aAdjusted for age, gender, race/ethnicity, education, clinic site, year of visit, and baseline BMI, HbA1c, insulin use, diabetes duration, hypertension status, prior CVD, depressive symptoms, smoking, cardiorespiratory fitness, and SF-36 Physical Functioning and Bodily Pain subscales.
Abbreviations: SPPBexp, Expanded Short Physical Performance Battery.
statistical techniques to account for differential participation provided similar results. The intervention itself was successful in achieving sustained long-term weight loss in a substantial proportion of the study sample providing a unique opportunity to examine the long-term benefits of weight loss on physical function. However, the DSE group also lost weight over the course of the trial which may have attenuated differences observed in physical function. Physical function was only measured 8 years post-randomization so we cannot assess the extent to which change in weight was associated with change in physical function. Furthermore, had physical function been measured earlier in the study when there was greater separation of weight loss between the two groups, we may have observed greater differences in physical function. Physical activity was only measured in a subset of participants at baseline; thus, we were unable to examine change in physical activity as a potential mediator of the intervention effect. Finally, multiple comparisons were made on several measures of physical function which may increase the probability of type I error, thus, caution should be used when interpreting the P values.

In conclusion, individuals randomized to a long-term intensive lifestyle intervention designed to achieve 7% weight loss had modest but significant benefits in performance-based physical function 8 years later. Despite losing a significant amount of body weight, differences in strength were not observed between the randomized groups. Intentional weight loss through dietary modification and increased physical activity may be useful in preventing or delaying the onset of impaired physical function and mobility disability in overweight and obese middle aged and older individuals with type 2 diabetes.

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TABLE 5 Mean differences between intensive lifestyle intervention (ILI) and diabetes support and education (DSE) participants on physical function measures adjusting for intervention measures: the Look AHEAD Movement and Memory Study

| Physical function measure | N   | Mean (SE) | Full model | Mean (SE) | Full model + achieved weight loss at Year 8/9 | Mean (SE) | Full model + physical activity at Year 8/9 |
|---------------------------|-----|----------|------------|----------|--------------------------------------------|----------|------------------------------------------|
|                           |     | difference: |            |          | DSE                                         |          |                                          |
|                           |     | ILI minus DSE | P value |         | ILI minus DSE                                 | P value  | ILI minus DSE                                  | P value |
| SPPB exp score (range 0-3)| 953 | 0.055 (0.022) | 0.01 |        | 0.032 (0.022)                                 | 0.14 | 0.048 (0.021)                                 | 0.03 |
| 20-m walk speed (m s⁻¹)  | 918 | 0.032 (0.012) | 0.01 |        | 0.019 (0.012)                                 | 0.13 | 0.026 (0.012)                                 | 0.04 |
| 400-m walk speed (m s⁻¹) | 869 | 0.025 (0.011) | 0.02 |        | 0.014 (0.011)                                 | 0.17 | 0.021 (0.011)                                 | 0.04 |

*aAdjusted for age, gender, race/ethnicity, education, clinic site, year of visit, and baseline BMI, HbA1c, insulin use, diabetes duration, hypertension status, prior CVD, depressive symptoms, smoking, cardiorespiratory fitness, and SF-36 Physical Functioning and Bodily Pain subscales.

*bModerate to vigorous physical activity in MET-min day⁻¹.

Abbreviations: SPPB exp, Expanded Short Physical Performance Battery.

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