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Research Article

Impact of Multidomain Lifestyle Intervention on Frailty Through the Lens of Deficit Accumulation in Adults with Type 2 Diabetes Mellitus

Felicia R. Simpson, PhD,[1] Nicholas M. Pajewski, PhD,[2] Barbara Nicklas, PhD,[3] Stephen Kritchevsky, PhD,[3] Alain Bertoni, MD,[4] Frank Ingram, PhD,[1] Daniel Ojeranti,[1] and Mark A. Espeland, PhD[2,*]; for the Indices for Accelerated Aging in Obesity and Diabetes Ancillary Study of the Action for Health in Diabetes (Look AHEAD) Trial

[1]Department of Mathematics, Winston-Salem State University, North Carolina. [2]Department of Biostatistics and Data Science, [3]Department of Internal Medicine, and [4]Department of Epidemiology and Prevention, Wake Forest School of Medicine, Winston-Salem, North Carolina.

*Address correspondence to: Mark A. Espeland, PhD, Department of Biostatistics and Data Science, Wake Forest School of Medicine, One Medical Center Boulevard, Winston-Salem, NC 27157. E-mail: mespeland@wakehealth.edu

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Abstract

Background: Type 2 diabetes and obesity increase the accumulation of health deficits and may accelerate biological aging. Multidomain lifestyle interventions may mitigate against this.

Methods: Within a large, randomized clinical trial of intensive lifestyle intervention including caloric restriction, increased physical activity, dietary counseling, and risk factor monitoring compared with diabetes support and education, we examined the accumulation of health deficits across 8 years. We used two complementary frailty indices (FIs) based on deficit accumulation, one modeled on work in the Systolic Blood Pressure Intervention Trial and the other including additional deficits related to obesity and type 2 diabetes mellitus. Differences between intervention groups and their consistency among subgroups were assessed with re-randomization tests.

Results: Data from 4,859 adults (45–76 years at baseline, 59% female) were analyzed. Random assignment to intensive lifestyle intervention was associated with lower FI scores throughout follow-up as captured by areas under curves traced by longitudinal means ($p \leq .001$), over which time mean (*SE*) differences between intervention groups averaged 5.8% (0.9%) and 5.4% (0.9%) for the two indices. At year 8, the percentage of participants classified as frail (FI > 0.21) was lower among intensive lifestyle intervention (39.8% and 54.5%) compared with diabetes support and education (42.7% and 60.9%) for both FIs (both $p < .001$). Intervention benefits were relatively greater for participants who were older, not obese, and without history of cardiovascular disease at baseline.

Conclusions: Eight years of multidomain lifestyle intervention create a buffer against the accumulation of age-related health deficits in overweight or obese adults with type 2 diabetes.

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Keywords: Multidomain lifestyle intervention, Aging, Diabetes mellitus, Obesity

Diabetes and obesity are often described as accelerators of biological aging due to associations with decreased life span, increased risk of disability, and reductions in health-related quality of life with increasing age (1–3). The accumulation of age-related deficits in health and functional outcomes, that is, the deficit accumulation model of frailty, serves as a marker of an individual's "aging-related health state" (4) and is recognized as a major risk factor for poorer function, disability, and death, in general and specifically within the context of diabetes (5–7). This has spurred interest in developing interventions that might slow or even reverse the progression of frailty, including multidomain lifestyle interventions that simultaneously target multiple behaviors, including diet, physical activity, and risk factor monitoring.

The strongest evidence that such lifestyle interventions can reduce frailty, quantified via deficit accumulation, is from the Multidomain Alzheimer's Preventive Trial (MAPT), which reported that lifestyle intervention targeting nutrition, physical activity, and cognitive training slowed the increase in a deficit accumulation frailty index (FI) over 3 years in a cohort of older individuals at enhanced risk for cognitive decline (8). The Action for Health in Diabetes (Look AHEAD) trial provides the opportunity to assess whether a multidomain intervention targeting weight loss and increased physical activity slows the accumulation of health deficits over 8 years in a cohort of individuals with diabetes and overweight/obesity aged 45–76 years (9).

Methods

The Look AHEAD design, methods, and CONSORT diagram have been published previously (9,10). It was a multisite, single-blind RCT that recruited 5,145 individuals (during 2001–2004) who were overweight or obese and had type 2 diabetes. At enrollment, participants were 45–76 years of age with body mass index (BMI) > 25 kg/m^2 (>27 kg/m^2 if on insulin), glycated hemoglobin (HbA1c) < 11%, systolic/diastolic blood pressure < 160/<100 mm Hg, and triglycerides <600 mg/dL. Protocols and consent forms were approved by local Institutional Review Boards.

Interventions

Participants were randomly assigned with equal probability to intensive lifestyle intervention (ILI) or the control condition of diabetes support and education (DSE). The multidomain ILI included diet modification and increased physical activity designed to induce weight loss to an average >7% at 1 year and maintain this over time (11). ILI participants were assigned a daily calorie goal (1,200–1,800 based on initial weight), with <30% of total calories from fat (<10% from saturated fat) and a minimum of 15% of total calories from protein. The physical activity goal was >175 min/wk through activities similar in intensity to brisk walking. Measurements of blood pressure, lipids, glycosolated hemoglobin (HbA1c) were obtained: participants were provided results of these tests, and when levels did not conform to clinical guidelines, data were shared with their clinicians. During the first 6 months of ILI, participants attended three group meetings and one individual session per month. For the remainder of the first year, participants were provided two groups and one individual meeting per month. In months 13–48, participants attended monthly individual meetings that were followed approximately 14 days later with phone calls or e-mails from interventionists. Optional monthly group meetings were also offered. After this, ILI participants were encouraged to continue individual monthly sessions and annual campaigns were used to promote maintenance of weight loss.

DSE participants were invited to attend group sessions focused on diet, physical activity, and social support (12). Four meetings were offered in year 1, three per year in years 2–4, and one meeting per year thereafter. Attendance at these meetings was optional. Participants did not receive specific diet, activity, or weight goals or information on behavioral strategies; however, risk factor monitoring was identical in both interventions.

Relative to the DSE, the ILI produced sustained weight losses and increases in physical function (10). Interventions were terminated September 2012, after an average of 10 years (range 8–11). This manuscript is limited to the first 8 years of Look AHEAD to compare ILI and DSE during delivery.

Frailty Indices Based on Deficit Accumulation

The deficit composition of FIs has varied widely among studies. It is recommended that they include 30 or more components, each related to aging, with the deficits not being overly redundant or exceedingly rare (13). We constructed an FI modeled after the Systolic Blood Pressure Intervention Trial (SPRINT; Supplementary Table S1) (14). Its FI included 37 health factors, 8 of which were not directly available in Look AHEAD (self-reported atrial fibrillation, potassium, sodium, blood urea nitrogen, orthostatic hypotension, Montreal Cognitive Assessment Orientation Score, and the Logical Memory Delayed Recall task). It also included deficits related to being underweight (BMI < 18.5 kg/m^2) and diabetes, both of which are not applicable as all Look AHEAD participants had diabetes and none reached the cut point for underweight. Look AHEAD did not have an objective measure of global cognitive function: instead, we used self-reported abilities on thinking, memory, and decision making (15). It also had no objective measure of physical function (eg, gait speed): instead, we used a self-report assessment of walking ability. We refer to this index with the above modification as FI_{SPR}.

SPRINT excluded individuals with type 2 diabetes. Thus, it may not be as sensitive to diabetes-related aging as an index including additional components related to diabetes and obesity in older individuals. Conversely, if such additional components do not materially affect the performance of the index in Look AHEAD, this reinforces the generalizability of indices across diverse cohorts. We augmented the FI_{SPR} with nine additional deficits related to diabetes and obesity to create a 38-item FI, which we label FI_{AUG} (Supplementary Table S2): self-reports of sleep apnea, body stiffness after sleep or rest, urinary incontinence, worsening eyesight or hearing, poorly healing wounds, diabetic nephropathy, and use of insulin determined by audits of prescription medications. We further categorized each FI as fit (FI ≤ 0.10), pre-frail (0.10 < FI ≤ 0.21), or frail (FI > 0.21) (14,16): we use these classifications as a convenient ordering rather than diagnostic criteria. At baseline, the distribution among these groupings in the SPRINT cohort was 19% fit, 54% pre-frail, and 28% frail (14).

Collection of FI Components During Follow-up

At enrollment and annual follow-up visits, self-reported lifestyle characteristics, health conditions, and clinical histories were assessed using standardized questionnaires (9). Prescription medications were verified, and weight and blood pressure were measured. Following 12-hour fasting, metabolic risk factors (lipid/lipoproteins, glucose, and creatinine) were measured annually through year 4 and every other year thereafter. History of cardiovascular disease at baseline was based on self-report of prior myocardial infarction, coronary artery bypass, angioplasty/stent procedures, peripheral vascular disease, stroke, stable angina, and class I/II heart failure. Hypertension was defined by current treatment or measured blood pressure ≥ 140/90 mm Hg. Depressive symptoms were assessed with the Beck Depression Index.

Statistical Analysis

Our analyses used de-identified data developed for investigators outside of the core Look AHEAD study group. Of the 5,145 Look AHEAD participants, 4,901 (95.3%) provided consent for this data sharing. Forty-two did not provide sufficient follow-up data to compute the FIs, resulting in our analytical cohort of 4,859. Baseline characteristics between intervention groups were compared using *t*-test and chi-square test. We calculated FIs at each annual visit when

at least 80% of their deficits were evaluable. Rates of individuals lost to follow-up or for whom we were otherwise unable to compute FIs increased over time. At year 1, these were 5% (DSE) and 3% (ILI); at year 8, these were 15% (DSE) and 13% (ILI).

The covariance structure of the longitudinal assessments was complex, depending on both historical self-reported events (eg, history of stroke) and current measures (eg, obesity status) and the nature of any missing data. Because of this, we used re-randomization tests for inference, which while potentially yielding less statistical power than other approaches, required few assumptions about the distribution of data (17). To capture differences between groups, we computed the mean FI value at each year of follow-up and the area under the curve traced by these means across 8 years. This measure can be thought of as a cumulative summary of the average FI values over time. To generate a sampling distribution for this statistic under the null hypothesis of no differences between groups, we randomly assigned participants to intervention groups 1,000 times, preserving the observed sample sizes, and recorded the proportion that yielded more extreme (positive or negative) summary measures than observed as the two-sided *p* value for the inference. We report *SE* as the *SD* of this sampling distribution. We repeated this approach for predefined subgroups based on baseline characteristics: age, sex, BMI, duration of diabetes, and history of cardiovascular disease. We also compared the distribution of frailty status (fit, pre-frail, or frail) between the intervention groups at baseline and year 8 using chi-square tests.

Results

Table 1 describes baseline characteristics of the cohort. The balance afforded by the randomization was preserved, and both FI_{SPR} and FI_{AUG} were similar between intervention groups ($p > .35$). Figure 1 portrays the distribution of the two FIs, which were highly correlated ($r = .90$).

Table 2 provides mean baseline FI_{SPR} and FI_{AUG} scores for subgroups based on traditional risk factors for aging. Although some differences include contributions of factors included as deficits in the indices (eg, obesity, hypertension, and smoking), the overall patterns are not unexpected. Racial/ethnic minorities, obese individuals, smokers, and those with poorer diabetes control, longer durations of diabetes, and hypertension had significantly higher mean baseline FI than those without these characteristics.

Figure 2A portrays mean 8-year trajectories of FI_{SPR} by intervention assignment. Within the DSE cohort, mean scores dipped slightly from baseline to year 1, but then rose gradually through the remainder of follow-up. Mean scores for the ILI cohort dropped more markedly between baseline and year 1, and then rose steadily, narrowing the gap between intervention groups. Overall, mean trajectories varied markedly between groups ($p \leq .001$). Averaged over time, the mean (*SE*) FI_{SPR} scores for the ILI cohort were 5.8% (0.9%) lower than those for the DSE cohort. Relative to DSE, the year 8 distributions of scores among ILI participants were shifted towards lower levels of frailty ($p < .001$).

Figure 2B is a parallel presentation for scores from the FI_{AUG}. With inclusion of additional obesity- and diabetes-related deficits, there was less of an initial buffer induced at year 1 between the two groups than for FI_{SPR}, but also slightly less attenuation of differences between groups across follow-up. Differences between intervention groups were highly statistically significant ($p \leq .001$) and, averaged over time, were 5.4% (0.9%) lower among ILI participants and shifted toward less frailty at year 8.

Table 1. Characteristics at Look AHEAD Enrollment Grouped by Intervention Assignment: *N* (%) or Mean (*SE*)

	Diabetes Support and Education	Intensive Lifestyle Intervention	
	N = 2,432	*N* = 2,427	*p* Value[a]
Age, y			
45–59	1,341 (55.2)	1,375 (56.6)	.30
60–76	1,090 (44.8)	1,052 (43.4)	
Sex			
Female	1,427 (58.7)	1,420 (58.5)	.90
Male	1,005 (41.3)	1,007 (41.5)	
Race/ethnicity			
African American	399 (16.4)	396 (16.3)	.86
Hispanic	337 (13.9)	336 (13.8)	
Non-Hispanic White	1,615 (66.4)	1,603 (66.0)	
Other, multiple	81 (3.3)	92 (3.8)	
BMI, kg/m^2			
Overweight: 25–29	342 (14.1)	374 (15.4)	.18
Obese: ≥30	2,089 (85.9)	2,051 (84.6)	
HbA1c, %			
<7.0	1,104 (45.4)	1,136 (46.8)	.47
7.0–8.9	1,240 (51.0)	1,196 (49.3)	
9.0–11.0	88 (3.6)	95 (3.9)	
Insulin use, missing = 178			
No	1,962 (83.7)	1,989 (84.6)	.43
Yes	381 (16.3)	362 (15.4)	
Diabetes duration, y			
0–4	1,092 (45.1)	1,125 (46.7)	.28
≥5	1,327 (54.9)	1,285 (53.3)	
Hypertension			
No	405 (16.6)	393 (16.2)	.66
Yes	2,027 (83.4)	2,034 (83.8)	
Smoking missing = 11			
Never	1,218 (50.2)	1,188 (49.0)	.64
Former	1,107 (45.6)	1,127 (46.5)	
Current	100 (4.1)	108 (4.5)	
History of cardiovascular disease			
No	2,102 (86.4)	2,077 (85.6)	.40
Yes	330 (13.6)	350 (14.4)	
SPRINT Frailty Index (FI_{SPR}), mean	0.200 (0.064)	0.201 (0.067)	.43
≤0.10	44 (1.8)	58 (2.4)	
>0.10 to ≤0.20	1,465 (60.2)	1,457 (60.0)	.37
>0.21	923 (38.0)	912 (37.6)	
Augmented Frailty Index (FI_{AUG}), mean	0.202 (0.062)	0.211 (0.065)	.37
≤0.10	20 (0.8)	16 (0.7)	
>0.10 to ≤0.20	1,333 (54.8)	1,296 (53.4)	.46
>0.21	1,079 (44.4)	1,115 (45.9)	

Notes: BMI = body mass index. [a]Chi-square or *t*-test.

Table 3 examines whether differences between interventions varied among important subgroups. Listed are mean differences in areas under the trajectories for the DSE minus ILI intervention groups, with positive values indicating a relative benefit for ILI compared with DSE. Results are fairly consistent for FI_{SPR} and FI_{AUG}. ILI benefits were comparable for women and men and independent of diabetes duration. However, overall relative benefits of ILI were greater for older participants, with interaction $p = .023$ (FI_{SPR}) and $p = .031$ (FI_{AUG}). Similarly, ILI appeared to provide relatively greater

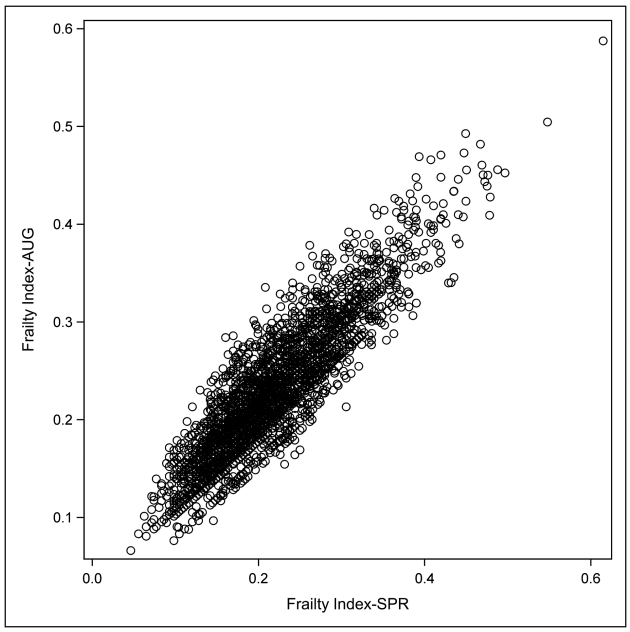

Figure 1. Scatterplot of the FI_{SPR} and FI_{AUG} deficit accumulation frailty indices at baseline ($r = .90$).

benefit for FI_{SPR} among overweight compared with obese individuals (interaction $p = .023$), and for those without baseline history of cardiovascular disease: interaction $p = .020$ (FI_{SPR}) and $p = .016$ (FI_{AUG}). Supplementary Exhibit 3 portrays the mean trajectories of FI_{SPR} for participants grouped by intervention assignment for subgroups based on age, baseline BMI, and history of cardiovascular disease.

Among all deficits included in the FI_{SPR} and FI_{AUG}, those that increased most across 8 years are reflective of diabetes and obesity: neuropathy, insulin usage, and sleep apnea. The prevalence of participants reporting stopped breathing during sleep increased from 12% to 33% in DSE participants and from 13% to 30% among ILI participants. The prevalence of insulin use increased from 16% to 37% in DSE individuals and from 15% to 31% in ILI individuals. The prevalence of participants reporting a diagnosis of diabetic neuropathy increased from 12% to 25% in DSE participants and from 13% to 26% in ILI participants.

Discussion

We showed that a multidomain lifestyle intervention administered to overweight and obese adults with type 2 diabetes in midlife and early late-life appears to buffer against the accumulation of age-related deficits when compared with diabetes support and education. This benefit was apparent irrespective of the precise composition of deficits used in the two FIs we explored. Adding components sensitive to diabetes and obesity did not materially improve the performance of the FI: this provides support that the precise composition of FIs may not be as important as having sufficient numbers of nonoverlapping components, whose incremental increases over time collectively contribute to changes in the FI. The overall magnitude of the benefit was not large, at least compared with the range of FI scores at baseline. Across follow-up, FI scores for ILI participants were 5%–6% lower, and at year 8, the prevalence of frailty was 3%–6% lower. The significant intervention effects documented in Look AHEAD for disability-free life years (6%–8%, depending on age) and all-cause hospitalizations (11%) were also modest but important (18,19).

Table 2. Differences in Baseline Deficit Accumulation Frailty Indices Among Subgroups

Baseline Characteristic	FI_{SPR} Mean (*SE*)[a]	FI_{AUG} Mean (*SE*)[a]
Age, y		
45–59	0.202 (0.002)	0.211 (0.002)
60–76	0.199 (0.002)	0.210 (0.002)
	$p = .392$	$p = .785$
Sex		
Female	0.200 (0.002)	0.206 (0.002)
Male	0.202 (0.002)	0.216 (0.002)
	$p = .430$	$p < .001$
Race/ethnicity		
African American	0.205 (0.002)	0.216 (0.002)
Hispanic	0.206 (0.003)	0.210 (0.002)
Non-Hispanic White	0.198 (0.001)	0.210 (0.001)
Other, Multiple	0.193 (0.005)	0.208 (0.005)
	$p < .001$	$p < .001$
BMI, kg/m^2		
Overweight: 25–29	0.171 (0.003)	0.181 (0.003)
Obese: ≥30	0.207 (0.002)	0.217 (0.002)
	$p < .001$	$p < .001$
HbA1c, %		
<7.0	0.190 (0.002)	0.200 (0.002)
7.0–8.9	0.210 (0.002)	0.220 (0.002)
9.0–11.0	0.198 (0.005)	0.208 (0.005)
	$p < .001$	$p < .001$
Insulin use		
No	0.196 (0.002)	0.200 (0.002)
Yes	0.226 (0.003)	0.259 (0.002)
	$p < .001$	$p < .001$
Diabetes duration, y		
0–4	0.194 (0.002)	0.200 (0.002)
≥5	0.206 (0.002)	0.219 (0.002)
	$p < .001$	$p < .001$
Hypertension		
No	0.178 (0.003)	0.190 (0.003)
Yes	0.205 (0.002)	0.215 (0.002)
	$p < .001$	$p < .001$
Smoking		
Never	0.188 (0.002)	0.200 (0.002)
Former	0.210 (0.002)	0.218 (0.002)
Current	0.241 (0.005)	0.244 (0.005)
	$p < .001$	$p < .001$

Note: BMI = body mass index. [a]Means and inference are from analyses of covariance with adjustment for age, sex, and race/ethnicity.

After the initial year of intervention, FIs in the DSE group increased by about 0.03 units over the subsequent 7 years, that is, about 0.0043 units per year. For comparison, the FI used in the Longitudinal Aging Study Amsterdam representative sample of adults aged 65 (mean 76) years and older at baseline, increased at a rate of 0.013 units per year across 17 years of follow-up (20), that is, about three times the rate of DSE participants who were 20 years younger.

Diabetes and obesity have been described as accelerating biological aging, resulting in lost muscle mass and strength (21), vascular diseases such as atherosclerosis and microvascular dysfunction (22–24), telomere shortening (25,26), accrual of age-related chronic diseases (27), changes in brain structure and function (28), cognitive decline (29), cell senescence (30), and age-related changes in immunological function (31). To capture broadly these interdependent processes, an index cutting across many potential underlying health

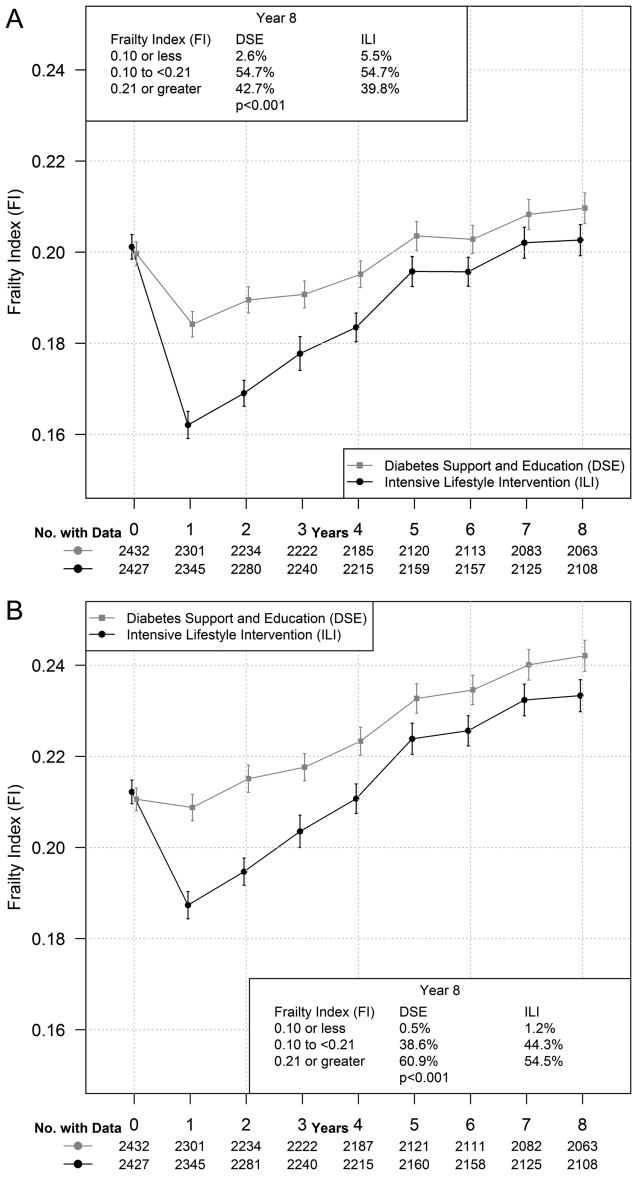

Figure 2. Trajectory of mean FI_{SPR} (A) and FI_{AUG} (B) with bars from 95% confidence intervals over follow-up by intervention assignment.

domains may be more informative than measures focused on individual pathways. An advantage of the deficit accumulation approach is that indices can be assembled from data collected in many contexts, as long as there is a sufficiently rich panel of age-related deficits (32). Multidomain lifestyle interventions have the potential to slow many of the processes listed above. Complex mediation analyses would be required to identify the most influential mechanisms toward benefit, and the relative importance of individual components for predicting outcomes may vary across clinical subgroups, for example, by sex (33).

It is unclear the extent that FIs reflect biological aging. Further work is necessary for validation by examining the associations of FIs with other indices of aging, including health span. Importantly, the ability of any index to serve as a surrogate for an outcome such as biological aging in a clinical trial can only be established in the context of an effective intervention (34,35). Demonstrating that the Look AHEAD multidomain lifestyle intervention conveyed benefits on the FIs, and also on the other accepted measures of disability-free

Table 3. Estimated Mean Differences Between Intervention Groups in the Area Under the Curve (*SE*) Traced by Mean Values of Frailty Indices Over Time: Over Time and Among Subgroups

		AUC (*SE*) Difference Between Intervention Groups Over Time	
Subgroup	*N*	FI_{SPR}	FI_{AUG}
Overall	4,859	0.0912 (0.002)	0.0976 (0.002)
		$p < .001$	$p < .001$
Sex			
Female	2,847	0.0999 (0.002)	0.0949 (0.003)
Male	2,012	0.0789 (0.003)	0.1019 (0.003)
		$p = .263$	$p = .409$
Age group			
44–59	2,716	0.0621 (0.002)	0.0688 (0.003)
60–76	2,142	0.1265 (0.003)	0.1324 (0.003)
		$p = .023$	$p = .031$
Diabetes duration, y			
0–4	2,217	0.0896 (0.003)	0.0879 (0.003)
≥5	2,612	0.0924 (0.003)	0.1048 (0.003)
		$p = .453$	$p = .297$
Body mass index, kg/m²			
25–29	716	0.1377 (0.003)	0.1326 (0.003)
≥30	4,140	0.0786 (0.002)	0.0869 (0.003)
		$p = .023$	$p = .080$
CVD history			
No	2,179	0.1045 (0.003)	0.1123 (0.003)
Yes	680	0.0420 (0.003)	0.0387 (0.003)
		$p = .020$	$p = .016$

Notes: AUC = area under curve; CVD = cardiovascular disease. Inference is based on re-randomization tests. Parenthesis represents *SE*. Positive values reflect relative benefit for intensive lifestyle intervention.

life years and multimorbidity (18,19), indicates the potential value of the trial as a resource to validate surrogate makers of health span and aging-related health status.

Relative benefits from ILI on FI appeared to accrue within the first few years. It is during this time that ILI was most intense and the greatest weight loss was achieved (10). Of some potential concern however, following the initial decline in FI scores from baseline to year 1, scores in the ILI group thereafter appeared to increase at a slightly greater rate in the ILI compared with DSE cohort, although never closing the gap between cohorts completely. This convergence may correspond to a mean regain of weight (primarily adipose tissue) in the ILI group following the initial year (36). Increased adipose tissue is associated with greater cellular senescence and inflammation, biological mechanisms thought to lead to functional and metabolic decline (3), which may account for these findings. In the ILI cohort, weight cycling, compared with maintained weight loss, was associated with poorer physical function (37).

ILI appeared to be equally beneficial toward buffering against increases in the FIs over time for women and men and for individuals with diabetes durations of less than 5 years versus longer durations. Importantly, there is evidence that the ILI effect on the FIs was stronger for older individuals, nonobese individuals, and those without history of cardiovascular disease. In Look AHEAD, older individuals achieved greater weight loss and comparable increases in physical activity than younger individuals (38). Although obese participants in ILI were successful in losing weight (39), they predominantly remained obese, which may have counteracted any potential benefits from ILI. Prevalent cardiovascular disease may identify individuals who have passed a window of opportunity for ILI benefits.

In Look AHEAD, ILI appeared to benefit a number of individual age-related conditions more strongly among these subgroups: physical function among older participants (39); several metabolic risk factors (10,41), cognitive function (42), nephropathy (43), and cognitive impairment (44) among those with lower BMI; and health care costs (19), physical function (45), and cognitive function (46) for those without cardiovascular disease history.

The model of deficit accumulation is very different from the frailty phenotype of Fried (47) and should not be conflated. The phenotypic conception of frailty reflects clinicians' impressions of highly vulnerable patients and focuses on measures in domains identified by geriatricians. Conversely, the model of deficit accumulation derives from engineering, where frailty refers to the likelihood of a material or system failure. These approaches are related: the five factors included in the phenotype could be included within an FI. However, the phenotype is problematic in trials of caloric restriction as weight loss is one of its criteria: unless intent is somehow considered, a caloric restriction intervention may appear to exacerbate frailty simply by inducing weight loss. Changes in the phenotype also depend on an individual crossing measurement thresholds for gait speed and grip strength. Given the number of deficits typically included (≥30), FIs tend to have a more dynamic range, likely improving sensitivity to change and providing greater statistical power.

Limitations

The Look AHEAD cohort consists of eligible volunteers for a randomized weight-loss trial and may not reflect more general clinical populations. The components we have included in the two FIs are based on data collected by Look AHEAD; other sets of components may yield different results. We have relied on self-reported clinical events rather than adjudication, consistent with other FIs. We did not address mortality in our analyses, although the mortality rate was similar between the groups (11). FI_{AUG} includes nine additional deficits that have not been previously used in other studies: future studies should validate this index. The additional deficits included in FI_{AUG} mostly reflect disease-specific severity: it is possible that improvements in diabetes-specific complications or glucose levels contribute to observed improvements in FI_{AUG}.

Summary

Based on a deficit accumulation approach, our results provide further evidence that multidomain lifestyle interventions may buffer against declines in individuals' age-related health status.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None reported.

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