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Supplementary appendix

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Authors: Edward W. Gregg, PhD; John M. Jakicic, PhD; George Blackburn, MD, PhD; Paul Bloomquist, MD; George A. Bray, MD; Jeanne M. Clark, MD, MPH; Mace Coday, PhD; Jeffrey M. Curtis, MD, MPH; Caitlin Egan, MS; Mary Evans, PhD; John P. Foreyt, PhD; Gary Foster, PhD; Helen P. Hazuda, PhD; James O. Hill, PhD; Edward S. Horton, MD; Van S. Hubbard, MD; Robert W. Jeffery, PhD; Karen C. Johnson, MD, MPH; Abbas E. Kitabchi, PhD, MD; William C. Knowler, MD; Andrea Kriska, PhD; Wei Lang, PhD; Cora E. Lewis, MD, MSPH; Maria G. Montez, RN, MSHP, CDE; David M. Nathan, MD; Rebecca H. Neiberg, MS; Jennifer Patricio, MS; Anne Peters, MD; Xavier Pi-Sunyer, MD; Henry Pownall, PhD; Bruce Redmon, MD; Judith Regensteiner, PhD; Jack Rejeski, PhD; Paul M. Ribisl, PhD; Monika Safford, MD; Kerry Stewart, EdD; Dace Trence, MD; Thomas A. Wadden, PhD; Rena R. Wing, PhD; Susan Z. Yanovski, MD.

Writing Group: Edward W. Gregg, Cora E. Lewis, Judy Regensteiner, Xavier Pi-Sunyer, John Jakicic, Rena Wing, Jeff Curtis, Sue Z. Yanovski, Mary Evans, Wei Lang, Rebecca H. Neiberg, Paul M. Ribisl.

Contributions: All authors conceived and designed the study and critically revised the manuscript. JMJ, GB, PB, GAB, JMC, MC, JMC, CE, JPF, GF, HPH, JOH, ESH, VSH, RWJ, KCJ, AEK, WCK, AK, CEL, MGM, DMN, JP, AP, X, HP, BR, RF, JR, PMR, MS, KW, DT, TAW, RRW acquired data. EWG, CEL, JR, XP-S, JK, RRW, JC, SY, ME, WL, RN, PR analysed and interpreted data and wrote the manuscript. WL and RHN did the statistical analysis.

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Appendix: Look AHEAD Research Group at End of Intervention

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Clinical Sites

The Johns Hopkins University Frederick L. Brancati, MD, MHS¹; Jeanne M. Clark, MD, MPH¹ (Co-Principal Investigators); Lee Swartz²; Jeanne Charleston, RN³; Lawrence Cheskin, MD³; Kerry Stewart, EdD³; Richard Rubin, PhD³; Jean Arceci, RN; Susanne Danus; David Bolen; Danielle Diggins; Sara Evans; Mia Johnson; Joyce Lambert; Sarah Longenecker; Kathy Michalski, RD; Dawn Jiggetts; Chanchai Sapun; Maria Sowers; Kathy Tyler

Pennington Biomedical Research Center George A. Bray, MD¹; Allison Strate, RN²; Frank L. Greenway, MD³; Donna H. Ryan, MD³; Donald Williamson, PhD³; Timothy Church, MD³; Catherine Champagne, PhD, RD; Valerie Myers, PhD; Jennifer Arceneaux, RN; Kristi Rau; Michelle Begnaud, LDN, RD, CDE; Barbara Cerniauskas, LDN, RD, CDE; Crystal Duncan, LPN; Helen Guay, LDN, LPC, RD; Carolyn Johnson, LPN, Lisa Jones; Kim Landry; Missy Lingle; Jennifer Perault; Cindy Puckett; Marisa Smith; Lauren Cox; Monica Lockett, LPN

The University of Alabama at Birmingham Cora E. Lewis, MD, MSPH¹; Sheikilya Thomas, MPH²; Monika Safford, MD³; Stephen Glasser, MD³; Vicki DiLillo, PhD³; Charlotte Bragg, MS, RD, LD; Amy Dobelstein; Sara Hannum, MA; Anne Hubbell, MS; Jane King, MLT; DeLavallade Lee; Andre Morgan; L. Christie Oden; Janet Wallace, MS; Cathy Roche, PhD, RN, BSN; Jackie Roche; Janet Turman

Harvard Center

Massachusetts General Hospital. David M. Nathan, MD¹; Enrico Cagliero, MD³; Kathryn Hayward, MD³; Heather Turgeon, RN, BS, CDE²; Valerie Goldman, MS, RD²; Linda Delahanty, MS, RD³; Ellen Anderson, MS, RD³; Laurie Bissett, MS, RD; Virginia Harlan, MSW; Theresa Michel, DPT, DSc, CCS; Mary Larkin, RN; Christine Stevens, RN

Joslin Diabetes Center: Edward S. Horton, MD¹; Sharon D. Jackson, MS, RD, CDE²; Osama Hamdy, MD, PhD³; A. Enrique Caballero, MD³; Sarah Bain, BS; Elizabeth Bovaird, BSN, RN; Barbara Fagnoli, MS, RD; Jeanne Spellman, BS, RD; Kari Galuski, RN; Ann Goebel-Fabbri, PhD; Lori Lambert, MS, RD; Sarah Ledbury, MEd, RD; Maureen Malloy, BS; Kerry Ovalle, MS, RCEP, CDE

Beth Israel Deaconess Medical Center: George Blackburn, MD, PhD¹; Christos Mantzoros, MD, DSc³; Ann McNamara, RN; Kristina Spellman, RD

University of Colorado Anschutz Medical Campus James O. Hill, PhD¹; Marsha Miller, MS RD²; Holly Wyatt, MD³, Brent Van Dorsten, PhD³; Judith Regensteiner, PhD³; Debbie Bochert; Ligia Coelho, BS; Paulette Cohrs, RN, BSN; Susan Green; April Hamilton, BS, CCRC; Jere Hamilton, BA; Eugene Leshchinskiy; Loretta Rome, TRS; Terra Thompson, BA; Kirstie Craul, RD, CDE; Cecilia Wang, MD

Baylor College of Medicine John P. Foreyt, PhD¹; Rebecca S. Reeves, DrPH, RD²; Molly Gee, MEd, RD²; Henry Pownall, PhD³; Ashok Balasubramanyam, MBBS³; Chu-Huang Chen, MD, PhD³; Peter Jones, MD³; Michele Burrington, RD, RN; Allyson Clark Gardner, MS, RD; Sharon Griggs; Michelle Hamilton; Veronica Holley; Sarah Lee; Sarah Lane Liscum, RN, MPH; Susan Cantu-Lumbreras; Julieta Palencia, RN; Jennifer Schmidt; Jayne Thomas, RD; Carolyn White

The University of Tennessee Health Science Center

University of Tennessee East. Karen C. Johnson, MD, MPH¹; Carolyn Gresham, RN²; Mace Coday, PhD; Lisa Jones, RN; Lynne Lichtermann, RN, BSN; J. Lee Taylor, MEd, MBA; Beate Griffin, RN; Donna Valenski

University of Tennessee Downtown. Abbas E. Kitabchi, PhD, MD¹; Ebenezer Nyenwe, MD³; Helen Lambeth, RN, BSN²; Moana Mosby, RN; Amy Brewer, MS, RD, LDN; Debra Clark, LPN; Andrea Crisler, MT; Gracie Cunningham; Debra Force, MS, RD, LDN; Donna Green, RN; Robert Kores, PhD; Renate Rosenthal, PhD; Elizabeth Smith, MS, RD, LDN

University of Minnesota Robert W. Jeffery, PhD¹; Tricia Skarphol, MA²; Carolyn Thorson, CCRP²; John P. Bantle, MD³; J. Bruce Redmon, MD³; Richard S. Crow, MD³; Kerrin Brelje, MPH, RD; Carolyn Campbell; Lisa Hoelscher, MPH, RD, CHES; Melanie Jaeb, MPH, RD; LaDonna James; Patti Laqua, BS, RD; Vicki A. Maddy, BS, RD; Therese Ockenden, RN; Birgitta I. Rice, MS, RPh, CHES; Ann D. Tucker, BA; Mary Susan Voeller, BA; Cara Walcheck, BS, RD

St. Luke's Roosevelt Hospital Center Xavier Pi-Sunyer, MD¹; Jennifer Patricio, MS²; Carmen Pal, MD³; Lynn Allen, MD; Janet Crane, MA, RD, CDN; Lolline Chong, BS, RD; Diane Hirsch, RNC, MS, CDE; Mary Anne Holowaty, MS, CN; Michelle Horowitz, MS, RD

University of Pennsylvania Thomas A. Wadden, PhD¹; Barbara J. Maschak-Carey, MSN, CDE²; Robert I. Berkowitz, MD³; Seth Braunstein, MD, PhD³; Gary Foster, PhD³; Henry Glick, PhD³; Shiriki Kumanyika, PhD, RD, MPH³; Stanley S. Schwartz, MD³; Yuliis Bell, BA; Raymond Carvajal, PsyD; Helen Chomentowski; Renee Davenport; Anthony Fabricatore, PhD; Lucy Faulconbridge, PhD; Louise Hesson, MSN, CRNP; Nayyar Iqbal, MD; Robert Kuehnel, PhD; Patricia Lipschutz, MSN; Monica Mullen, RD, MPH

University of Pittsburgh John M. Jakicic, PhD¹; David E. Kelley, MD¹; Jacqueline Wesche-Thobaben, RN, BSN, CDE²; Lewis H. Kuller, MD, DrPH³; Andrea Kriska, PhD³; Amy D. Rickman, PhD, RD, LDN³; Lin Ewing, PhD, RN³; Mary Korytkowski, MD³; Daniel Edmundowicz, MD³; Rose Salata, MD³; Rebecca Danchenko, BS; Tammy DeBruce; Barbara Elnyczky; David O. Garcia, MS; Patricia H. Harper, MS, RD, LDN; Susan Harrier, BS; Dianne Heidingsfelder, MS, RD, CDE, LDN; Diane Ives, MPH; Juliet Mancino, MS, RD, CDE, LDN; Lisa Martich, MS, RD; Tracey Y. Murray, BS; Karen Quirin; Joan R. Ritchea; Susan Copelli, BS, CTR

The Miriam Hospital/Brown Medical School Rena R. Wing, PhD¹; Renee Bright, MS²; Vincent Pera, MD³; John Jakicic, PhD³; Deborah Tate, PhD³; Amy Gorin, PhD³; Kara Gallagher, PhD³; Amy Bach, PhD; Barbara Bancroft, RN, MS; Anna Bertorelli, MBA, RD; Richard Carey, BS; Tatum Charron, BS; Heather Chenot, MS; Kimberley Chula-Maguire, MS; Pamela Coward, MS, RD; Lisa Cronkite, BS; Julie Currin, MD; Maureen Daly, RN; Caitlin Egan, MS; Erica Ferguson, BS, RD; Linda Foss, MPH; Jennifer Gauvin, BS; Don Kieffer, PhD; Lauren Lessard, BS; Deborah Maier, MS; JP Massaro, BS; Tammy Monk, MS; Rob Nicholson, PhD; Erin Patterson, BS; Suzanne Phelan, PhD; Hollie Raynor, PhD, RD; Douglas Raynor, PhD; Natalie Robinson, MS, RD; Deborah Robles; Jane Tavares, BS

The University of Texas Health Science Center at San Antonio Steven M. Haffner, MD¹; Helen P. Hazuda, PhD¹; Maria G. Montez, RN, MSHP, CDE²; Carlos Lorenzo, MD³; Charles F. Coleman, MS, RD; Domingo Granado, RN; Kathy Hathaway, MS, RD; Juan Carlos Isaac, RC, BSN; Nora Ramirez, RN, BSN

VA Puget Sound Health Care System / University of Washington Steven E. Kahn, MB, ChB¹; Anne Murillo, BS²; Robert Knopp, MD³; Edward Lipkin, MD, PhD³; Dace Trence, MD³; Elaine Tsai, MD³; Basma Fattaleh, BA; Diane Greenberg, PhD; Brenda Montgomery, RN, MS, CDE; Ivy Morgan-Taggart; Betty Ann Richmond, MEd; Jolanta Socha, BS; April Thomas, MPH, RD; Alan Wesley, BA; Diane Wheeler, RD, CDE

Southwestern American Indian Center, Phoenix, Arizona and Shiprock, New Mexico William C. Knowler, MD, DrPH¹; Paula Bolin, RN, MC²; Tina Killean, BS²; Cathy Manus, LPN³; Jonathan Krakoff, MD³; Jeffrey M. Curtis, MD, MPH³; Sara Michaels, MD³; Paul Bloomquist, MD³; Peter H. Bennett, MB, FRCP³; Bernadita Fallis RN, RHIT, CCS; Diane F. Hollowbreast; Ruby Johnson; Maria Meacham, BSN, RN, CDE; Christina Morris, BA; Julie Nelson, RD; Carol Percy, RN; Patricia Poorthunder; Sandra Sangster; Leigh A. Shovestull, RD, CDE; Miranda Smart; Janelia Smiley; Teddy Thomas, BS; Katie Toledo, MS, LPC

University of Southern California Anne Peters, MD¹; Siran Ghazarian, MD²; Elizabeth Beale, MD³; Kati Konersman, RD, CDE; Brenda Quintero-Varela; Edgar Ramirez; Gabriela Rios, RD; Gabriela Rodriguez, MA; Valerie Ruelas MSW, LCSW; Sara Serafin-Dokhan; Martha Walker, RD

Coordinating Center

Wake Forest University Mark A. Espeland, PhD¹; Judy L. Bahnson, BA, CCRP³; Lynne E. Wagenknecht, DrPH³; David Reboussin, PhD³; W. Jack Rejeski, PhD³; Alain G. Bertoni, MD, MPH³; Wei Lang, PhD³; Michael S. Lawlor, PhD³; David Lefkowitz, MD³; Gary D. Miller, PhD³; Patrick S. Reynolds, MD³; Paul M. Ribisl, PhD³; Mara Vitolins, DrPH³; Daniel Beavers, PhD³; Haiying Chen, PhD, MM³; Dalane Kitzman, MD³; Delia S. West, PhD³; Lawrence M. Friedman, MD³; Ron Prineas, MD³; Tandaw Samdarshi, MD³; Kathy M. Dotson, BA²; Amelia Hodges, BS, CCRP²; Dominique Limprevil-Divers, MA, MEd²; Karen Wall²; Carrie C. Williams, MA, CCRP²; Andrea Anderson, MS; Jerry M. Barnes, MA; Mary Barr; Tara D. Beckner; Cralen Davis, MS; Thania Del Valle-Fagan, MD; Tamika Earl, Melanie Franks, BBA; Candace Goode; Jason Griffin, BS; Lea Harvin, BS; Mary A. Hontz, BA; Sarah A. Gaussoin, MS; Don G. Hire, BS; Patricia Hogan, MS; Mark King, BS; Kathy Lane, BS; Rebecca H. Neiberg, MS; Julia T. Rushing, MS; Valery S. Effeo, MD,MS; Michael P. Walkup, MS; Terri Windham

Central Resources Centers

DXA Reading Center, University of California at San Francisco Michael Nevitt, PhD¹; Ann Schwartz, PhD²; John Shepherd, PhD³; Michaela Rahorst; Lisa Palermo, MS, MA; Susan Ewing, MS; Cynthia Hayashi; Jason Maeda, MPH

Central Laboratory, Northwest Lipid Metabolism and Diabetes Research

Laboratories Santica M. Marcovina, PhD, ScD¹; Jessica Hurting²; John J. Albers, PhD³; Vinod Gaur, PhD⁴

ECG Reading Center, EPICARE, Wake Forest University School of Medicine

Elsayed Z. Soliman MD, MSc, MS¹; Charles Campbell²; Zhu-Ming Zhang, MD³; Mary Barr; Susan Hensley; Julie Hu; Lisa Keasler; Yabing Li, MD

Diet Assessment Center, University of South Carolina, Arnold School of Public Health, Center for Research in Nutrition and Health Disparities

Elizabeth J Mayer-Davis, PhD¹; Robert Moran, PhD¹

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Richard Foushee, PhD; Nancy J. Hall, MA

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National Institute of Diabetes and Digestive and Kidney Diseases Mary Evans, PhD; Barbara Harrison, MS; Van S. Hubbard, MD, PhD; Susan Z. Yanovski, MD

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Centers for Disease Control and Prevention Edward W. Gregg, PhD; Ping Zhang, PhD

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¹ Principal Investigator

² Program Coordinator

³ Co-Investigator

All other Look AHEAD staffs are listed alphabetically by site.

Supplemental Analyses Table 1. Association of weight change and fitness change with additional Look AHEAD Pre-specified Secondary Outcomes.

	Weight Change Groups (percent weight loss in first year)				
	Gain /Stable (<2% loss)	Small Loss (2 to 5%)	Medium Loss (5 to 10%)	Large Loss (≥10%)	Test for Trend
Secondary Outcome 2					
Events / person years	198 / 17563	87 / 8139	113 / 8785	76 / 9171	
Crude rate/100 person years	1.13	1.07	1.29	0.83	
Unadjusted HR (95% C.I.)	1.0	0.96 (0.75 – 1.24)	1.16 (0.92 – 1.46)	0.71 (0.55 – 0.93)*	0.1162
Adjusted HR [‡] (95% C.I.)	1.0	0.94 (0.73 – 1.22)	1.24 (0.97 – 1.57)	0.69 (0.53 – 0.91)*	0.1178
Secondary Outcome 3					
Events / person years	369 / 17076	175 / 7870	179 / 8570	167 / 8941	
Crude rate/100 person years	2.16	2.22	2.09	1.87	
Unadjusted HR (95% C.I.)	1.0	1.04 (0.87 – 1.25)	0.98 (0.82 – 1.17)	0.85 (0.71 – 1.02)	0.1119
Adjusted HR [‡] (95% C.I.)	1.0	1.03 (0.86 – 1.24)	1.03 (0.86 – 1.24)	0.80 (0.66 – 0.97)*	0.0598
	Fitness Change Groups (METs change in first-year)				
	Loss/Stable (<0.5)	Small Gain (0.5 to 1.0)	Medium Gain (1.0 to 2.0)	Large Gain (≥2.0)	Test for Trend
Secondary Outcome 2					
Events / person years	239 / 20579	65 / 6240	69 / 7335	37 / 5461	
Crude rate/100 person years	1.16	1.04	0.94	0.68	
Unadjusted HR (95% C.I.)	1.0	0.88 (0.67 – 1.15)	0.80 (0.61 – 1.04)	0.56 (0.40 – 0.80)*	0.0008
Adjusted HR [‡] (95% C.I.)	1.0	0.86 (0.64 – 1.14)	0.85 (0.64 – 1.12)	0.59 (0.41 – 0.85)*	0.0051
Secondary Outcome 3					
Events / person years	778 / 19997	119 / 6091	123 / 7184	85 / 5312	
Crude rate/100 person years	2.23	1.95	1.71	1.60	
Unadjusted HR (95% C.I.)	1.0	0.86 (0.70 – 1.05)	0.75 (0.62 – 0.92)*	0.70 (0.55 – 0.88)*	0.0002
Adjusted HR [‡] (95% C.I.)	1.0	0.85 (0.69 – 1.05)	0.77 (0.62 – 0.94)*	0.73 (0.57 – 0.93)*	0.0013

[‡]adjusted for sex, age, baseline weight(weight change models), baseline fitness (fitness change models),CVD history, insulin use, diabetes duration, smoking status, LDL, SBP, DBP. *P< 0.05;Secondary Outcome 2: (MI, stroke, CVD Death); Secondary Outcome 3: (non-fatal MI, stroke, hospitalized angina, CVD death , total mortality)

Supplemental Analyses Table 2. Primary and Secondary Outcomes Associated with Percent Weight Change, Stratified by Randomization Group

	Weight Change Groups (percent weight loss in first year)				
ILI Group	Gain /Stable (<2% loss)	Small Loss (2 to 5%)	Medium Loss (5 to 10%)	Large Loss (≥10%)	Test for Trend
Primary Outcome					
Events / person years	58 / 3096	69 / 3766	114 / 6446	120 / 8257	
Crude rate/100 person years	1.87	1.83	1.77	1.45	
Unadjusted HR (95% C.I.)	REF	0.94 (0.66 – 1.33)	0.91 (0.66 – 1.25)	0.72 (0.52 – 0.99)*	0.0268
Adjusted HR [†] (95% C.I.)	REF	0.78(0.54 – 1.13)	0.89 (0.63 – 1.25)	0.61 (0.44 – 0.86)*	0.0066
Secondary Outcome					
Events / person years	82 / 3018	108 / 3643	151 / 6335	173 / 8127	
Crude rate/100 person years	2.72	2.96	2.38	2.13	
Unadjusted HR (95% C.I.)	REF	1.04 (0.78 – 1.39)	0.84 (0.64 – 1.10)	0.73 (0.56 – 0.96)*	0.0028
Adjusted HR [†] (95% C.I.)	REF	0.90 (0.67 – 1.22)	0.79 (0.59 – 1.05)	0.61 (0.45 – 0.80)*	<0.0001
	Weight Change Groups (percent weight loss in first year)				
DSE Group	Gain /Stable (<2% loss)	Small Loss (2 to 5%)	Medium Loss (5 to 10%)	Large Loss (≥10%)	Test for Trend
Primary Outcome					
Events / person years	231 / 13978	72 / 4104	40 / 2124	8 / 685	
Crude rate/100 person years	1.65	1.75	1.88	1.17	
Unadjusted HR (95% C.I.)	REF	1.10 (0.84 – 1.43)	1.16 (0.82 – 1.62)	0.72 (0.35 – 1.45)	0.8227
Adjusted HR [†] (95% C.I.)	REF	1.17 (0.89 – 1.54)	1.26 (0.88 – 1.79)	0.71 (0.33 – 1.51)	0.5111
Secondary Outcome					
Events / person years	340 / 13681	98 / 4014	52 / 2076	13 / 665	
Crude rate/100 person years	2.49	2.44	2.50	1.95	
Unadjusted HR (95% C.I.)	REF	1.02 (0.81 – 1.27)	1.03 (0.77 – 1.38)	0.80 (0.46 – 1.40)	0.7626
Adjusted HR [†] (95% C.I.)	REF	1.01 (0.79 – 1.27)	0.99 (0.73 – 1.35)	0.77 (0.42 – 1.42)	0.6669

[†]adjusted for sex, age, baseline weight(percent weight loss models), baseline fitness (fitness change models),CVD history, insulin use, diabetes duration, smoking status, LDL, SBP, DBP. Primary Outcome: (non-fatal MI, stroke, hospitalized angina, CVD death); Secondary Outcome: (non-fatal MI, stroke, hospitalized angina, CABG/PTCA, hospitalized CHF, carotid endarterectomy, PVD, total mortality)

Appendix Table 3. Primary and Secondary Outcomes Associated with Fitness Change, Stratified by Randomization Group.

	Fitness Change Groups (METs change in first-year)				
ILI Group	Loss/Stable (<0.5)	Small Gain (0.5 to 1.0)	Medium Gain (1.0 to 2.0)	Large Gain (≥2.0)	Test for Trend
Primary Outcome					
Events / person years	139 / 7731	53 / 3082	64 / 4744	59 / 4190	
Crude rate/100 person years	1.80	1.72	1.35	1.41	
Unadjusted HR (95% C.I.)	REF	0.93 (0.68 – 1.28)	0.74 (0.55 – 0.99)*	0.78 (0.57 – 1.07)	0.0415
Adjusted HR [†] (95% C.I.)	REF	0.91 (0.65 – 1.27)	0.74 (0.54 – 1.01)	0.80 (0.58 – 1.12)	0.0753
Secondary Outcome					
Events / person years	197 / 7564	78 / 3041	92 / 4663	86 / 4111	
Crude rate/100 person years	2.60	2.57	1.97	2.09	
Unadjusted HR (95% C.I.)	REF	0.95 (0.73 – 1.24)	0.74 (0.58 – 0.95)*	0.79 (0.61 – 1.03)	0.0180
Adjusted HR [†] (95% C.I.)	REF	0.95 (0.72 – 1.25)	0.70 (0.54 – 0.91)*	0.80 (0.61 – 1.06)	0.0214
	Fitness Change Groups (METs change in first-year)				
DSE Group	Loss/Stable (<0.5)	Small Gain (0.5 to 1.0)	Medium Gain (1.0 to 2.0)	Large Gain (≥2.0)	Test for Trend
Primary Outcome					
Events / person years	208 / 12266	42 / 3009	38 / 2439	13 / 1122	
Crude rate/100 person years	1.70	1.40	1.56	1.16	
Unadjusted HR (95% C.I.)	REF	0.80 (0.57 – 1.12)	0.89 (0.63 – 1.26)	0.65 (0.37 – 1.13)	0.0898
Adjusted HR [†] (95% C.I.)	REF	0.77 (0.54 – 1.10)	0.98 (0.68 – 1.40)	0.66 (0.37 – 1.17)	0.1909
Secondary Outcome					
Events / person years	307 / 12032	53 / 2955	307 / 12032	14 / 1109	
Crude rate/100 person years	2.55	1.79	2.22	1.26	
Unadjusted HR (95% C.I.)	REF	0.68 (0.51 – 0.91)*	0.86 (0.64 – 1.16)	0.49 (0.28 – 0.83)*	0.0032
Adjusted HR [†] (95% C.I.)	REF	0.69 (0.51 – 0.93)*	0.90 (0.66 – 1.23)	0.54 (0.31 – 0.94)*	0.0183

[†]adjusted for sex, age, baseline weight(percent weight loss models), baseline fitness (fitness change models),CVD history, insulin use, diabetes duration, baseline fitness smoking status, LDL, SBP, DBP. Primary Outcome: (non-fatal MI, stroke, hospitalized angina, CVD death); Secondary Outcome: (non-fatal MI, stroke, hospitalized angina, CABG/PTCA, hospitalized CHF, carotid endarterectomy, PVD, total mortality

Appendix Table 4. Association of weight change and fitness change with additional Look AHEAD Pre-specified Secondary Outcomes. Comparison of DSE Condition (Referent Group) with ILI weight loss and fitness change groups.

	Overall DSE	ILI Weight Change Groups (percent weight loss in first year)				HR per SD weight change	P value
		Gain /Stable (<2% loss)	Small Loss (2 to 5%)	Medium Loss (5 to 10%)	Large Loss (≥10%)		
Secondary Outcome 2							
Events / person years	239 / 21478	38 / 3203	46 / 3872	81 / 6617	70 / 8488		
Crude rate/100 person years	1.11	1.19	1.19	1.22	0.82		
Unadjusted HR (95% C.I.)	1.0	1.08 (0.76 – 1.53)	1.08 (0.79 – 1.48)	1.18 (0.87 – 1.44)	0.72 (0.55 – 0.94)*	0.87 (0.76 – 0.99)	0.0318
Adjusted HR [‡] (95% C.I.)	1.0	1.15 (0.80 – 1.65)	1.06 (0.77 – 1.46)	1.22 (0.94 – 1.59)	0.70 (0.54 – 0.92)*	0.85 (0.74 – 0.98)	0.0264
Secondary Outcome 3							
Events / person years	449 / 20892	69 / 3088	86 / 3766	132 / 6447	154 / 8266		
Crude rate/100 person years	2.15	2.23	2.28	2.05	1.86		
Unadjusted HR (95% C.I.)	1.0	1.07 (0.83 – 1.38)	1.07 (0.85 – 1.35)	0.96 (0.79 – 1.17)	0.85 (0.71 – 1.02)	0.90 (0.81 – 0.99)	0.0231
Adjusted HR [‡] (95% C.I.)	1.0	1.22 (0.93 – 1.58)	1.04 (0.82 – 1.32)	1.02 (0.84 – 1.25)	0.80 (0.66 – 0.97)*	0.86 (0.78 – 0.95)	0.0033
	Overall DSE	ILI Fitness Change Groups (METs change in first-year)				HR per SD fitness change	P value
		Loss/Stable (<0.5)	Small Gain (0.5 to 1.0)	Medium Gain (1.0 to 2.0)	Large Gain (≥2.0)		
Secondary Outcome 2							
Events / person years	208 / 19521	104 / 8257	35 / 3172	39 / 4856	31 / 4312		
Crude rate/100 person years	1.07	1.26	1.10	0.80	0.72		
Unadjusted HR (95% C.I.)	1.0	1.20 (0.95 – 1.52)	1.03 (0.72 – 1.47)	0.75 (0.53 – 1.05)	0.66 (0.45 – 0.96)*	0.83 (0.72 – 0.97)	0.0162
Adjusted HR [‡] (95% C.I.)	1.0	1.22 (0.96 – 1.56)	1.04 (0.72 – 1.51)	0.79 (0.55 – 1.12)	0.69 (0.47 – 1.03)	0.82 (0.70 – 0.97)	0.0171
Secondary Outcome 3							
Events / person years	385 / 19026	183 / 8025	69 / 3081	77 / 4744	72 / 4190		
Crude rate/100 person years	2.02	2.28	2.24	1.62	1.72		
Unadjusted HR (95% C.I.)	1.0	1.15 (0.97 – 1.37)	1.09 (0.85 – 1.41)	0.80 (0.62 – 1.02)	0.84 (0.65 – 1.08)	0.90 (0.81 – 0.99)	0.0469
Adjusted HR [‡] (95% C.I.)	1.0	1.16 (0.97 – 1.39)	1.11 (0.85 – 1.44)	0.79 (0.62 – 1.02)	0.87 (0.67 – 1.14)	0.90 (0.80 – 1.01)	0.0751

[‡]adjusted for sex, age, baseline weight(weight change models), baseline fitness (fitness change models), CVD history, insulin use, diabetes duration, smoking status, LDL, SBP, DBP. Secondary Outcome 2: (MI, stroke, CVD Death); Secondary Outcome 3: (non-fatal MI, stroke, hospitalized angina, CVD death , total mortality)