Dataset Integrity Check for the Look Ahead End-of-Intervention Data Files

Prepared by Allyson Mateja
IMS Inc.
3901 Calverton Blvd, Suite 200 Calverton MD 20705
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Contents

1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

The Look AHEAD study is a multicenter randomized clinical trial in overweight and obese individuals with type 2 diabetes to evaluate the long-term effects of an intensive weight loss intervention (diet and exercise) on major cardiovascular events. Subjects were randomized to either intensive lifestyle intervention or diabetes support and education (control group). A total of 5,145 participants from 16 clinical centers were randomized between 2001 and 2004. The published manuscript by the Look AHEAD Research Group provides baseline and follow-up characteristics of this randomized cohort. Follow-up data is available until the end of the intervention period, when the study was stopped for futility, resulting in an average of 9.6 years of follow-up. Although intensive lifestyle intervention did result in a greater reduction in glycated hemoglobin levels and improvements in fitness and cardiovascular risk factors, it did not decrease the rate of cardiovascular events in overweight and obese individuals with type 2 diabetes.

Users of the Look AHEAD data should note that data on participants that did not consent to data sharing, including those from American Indian clinical sites, were not included in the data transferred to the NIDDK repository. Data on a total on 4,901 subjects is included.

3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the Look AHEAD data package. For this replication, variables were taken from the "la_key", "la2_baselinevariables", "laboratorymeasures", "physicalmeasures_abi_waist", "physicalmeasures_bp_bmi", "stresstest_maximalgxt", "healthoutcomes_meduse", and "la4_outcomes1" datasets.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by the Look AHEAD Research Group [1] in the New England Journal of Medicine in July 2013.

To verify the integrity of the datasets, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Characteristics of the Patients at Baseline, Table A lists the variables that were used in the replication and Table B compares the results calculated from the archived data file to the results published in Table 1. The results of the replication are within expected results considering the removal of Native American records.

For Figure 1 in the publication [1], Changes in Weight, Physical Fitness, Waist Circumference, and Glycated Hemoglobin Levels during 10 Years of Follow-up, Table C lists the variables that were used in the replication and Figure A compares the results calculated from the archived data file to the results published in Figure 1. The results of the replication are within expected results considering the removal of Native American records.

For Supplementary Table 1 in the publication [1], Comparison of Diabetes Support and Education (DSE) and Intensive Lifestyle Intervention (ILI) groups and baseline and end of study, Table D lists the variables that were used in the replication and Table E compares the results calculated from the archived data file to the results published in Supplementary Table 1. The results of the replication are within expected results considering the removal of Native American records.

For Table 2 in the publication [1], Primary and Secondary Outcomes and Other Cardiovascular Outcomes, Table F lists the variables that were used in the replication and Table G compares the results calculated from the archived data file to the results published in Table 2. The results of the replication are within expected results considering the removal of Native American records.

For Figure 2 in the publication [1], Cumulative Hazard Curves for the Primary Composite End Point, Table H lists the variables that were used in the replication and Figure B compares the results calculated from the archived data file to the results published in Figure 2. The results of the replication are within expected results considering the removal of Native American records.

For Figure 3 in the publication [1], Primary Outcomes in Prespecified Subgroups, Table I lists the variables that were used in the replication and Table J compares the results calculated from the archived data file to the results published in Figure 3. The results of the replication are within expected results considering the removal of Native American records.

The data for Supplementary Table 2 in the publication [1], Serious adverse events plausibly related to ILI: number of events reported over follow-up and rates per 100 person-years, were not included in the data package and so could not be verified.

6 Conclusions

The NIDDK repository is confident that the Look AHEAD data files to be distributed are within expected results considering the removal of Native American records.

7 References

[1] The Look AHEAD Research Group. Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes. N Engl J Med. 2013; 369; 2: 145-154.

Table A: Variables used to replicate Table 1: Characteristics of the Patients at Baseline

Table Variable	dataset.variable
Treatment Arm	la_key.treatment
Age – yr	la2_baselinevariables.baseline_age
Female sex	la2_baselinevariables.female
Race or ethnic group	la2_baselinevariables.racevar
History of Cardiovascular Disease	la2_baselinevariables.CVDhis
Use of insulin	healthoutcomes_meduse.insulins
Current smoking	la2_baselinevariables.smoking
Duration of Diabetes	la2_baselinevariables.diab_dur
Weight	physicalmeasures_bp_bmi.bswgt1
Body-mass index	la2_baselinevariables.bmi
Waist circumference	la2_baselinevariables.waistcm_mean
Glycated hemoglobin	laboratorymeasures.hba1cpct
Systolic Blood Pressure	physicalmeasures_bp_bmi.bssbp2
Diastolic Blood Pressure	physicalmeasures_bp_bmi.bsdbp2
High density lipoprotein	laboratorymeasures.hdlchlmgdl
Low-density lipoprotein	laboratorymeasures.ldlchlmgdl
Triglycerides	laboratorymeasures.trigmgdl

Table B: Comparison of values computed in integrity check to reference article Table 1 values

Variable	Control Group Manuscript (N=2575)	Control Group DSIC (N=2453)	Difference (N=122)	Intervention Group Manuscript (N=2570)	Intervention Group DSIC (N=2448)	Difference (N=122)
Age - yr	58.9 ± 6.9	59.8 ± 6.8	0.9 ± 0.1	58.6 ± 6.8	59.4 ± 6.7	0.8 ± 0.1
Female sex - no. (%)	1537 (59.7)	1437 (58.6)	100 (1.1)	1526 (59.4)	1434 (58.6)	92 (0.8)
Race or ethnic group - no. (%)						
Black	404 (15.7)	404 (16.5)	0 (0.8)	400 (15.6)	400 (16.3)	0 (0.7)
Native American	128 (5.0)	N/A	N/A	130 (5.1)	N/A	N/A
Asian or Pacific Islander	21 (0.8)	N/A	N/A	29 (1.1)	N/A	N/A
White	1631 (63.3)	1629 (66.4)	2 (3.1)	1621 (63.1)	1618 (66.1)	3 (3.0)
Hispanic	340 (13.2)	338 (13.8)	2 (0.6)	340 (13.2)	338 (13.8)	2 (0.6)
Other	51 (2.0)	82 (3.3)	31 (1.3)	50 (1.9)	92 (3.8)	42 (1.9)
History of Cardiovascular Disease - no. (%)	348 (13.5)	334 (13.6)	14 (0.1)	366 (14.2)	354 (14.5)	12 (0.3)
Use of insulin - no. (%)	410 (16.5)	385 (16.3)	25 (0.2)	382 (15.4)	363 (15.3)	19 (0.1)

Variable	Control Group Manuscript (N=2575)	Control Group DSIC (N=2453)	Difference (N=122)	Intervention Group Manuscript (N=2570)	Intervention Group DSIC (N=2448)	Difference (N=122)
Current Smoking - no. (%)	110 (4.3)	100 (4.1)	10 (0.2)	117 (4.6)	108 (4.4)	9 (0.2)
Median duration of diabetes (interquartile range) - yr	5.0 (2.0-10)	5.0 (2.0-10)	0 (0)	5.0 (2.0-10)	5.0 (2.0-10)	0 (0)
Weight - kg	101 ± 19	101.2 ± 18.8	0.2 ± 0.2	101 ± 20	100.9 ± 19.6	0.1 ± 0.4
Body-mass index	36.0 ± 5.8	36 ± 5.7	0 ± 0.1	35.9 ± 6.0	35.9 ± 6	0 ± 0
Waist circumference - cm	114 ± 14	114.1 ± 13.6	0.1 ± 0.4	114 ± 14	113.8 ± 14.4	0.2 ± 0.4
Glycated hemoglobin - %	7.3 ± 1.2	7.3 ± 1.2	0 ± 0	7.2 ± 1.1	7.2 ± 1.1	0 ± 0
Blood Pressure - mm Hg						
Systolic	129 ± 17	129 ± 17.6	0 ± 0.6	128 ± 17	127.9 ± 17.8	0.1 ± 0.8
Diastolic	70.4 ± 9.6	70.2 ± 9.7	0.2 ± 0.1	69.9 ± 9.5	69.8 ± 9.6	0.1 ± 0.1
Cholesterol - mg/dl						
High-density lipoprotein	43.5 ± 12	43.5 ± 11.9	0 ± 0.1	43.4 ± 12	43.5 ± 11.8	0.1 ± 0.2
Low-density lipoprotein	112 ± 32	112.7 ± 32.2	0.7 ± 0.2	112 ± 32	112.5 ± 32.3	0.5 ± 0.3
Median triglycerides (interquartile range) - mg/dl	152 (107-218)	152 (107-218)	0 (0)	155 (110-221)	155 (109-221)	0 (0)

Table C: Variables used to replicate Figure 1: Changes in Weight, Physical Fitness, Waist Circumference, and Glycated Hemoglobin Levels during 10 Years of Follow-up.

Table Variable	dataset.variable
Weight	physicalmeasures_bp_bmi.bswgt1
METS	stresstest_maximalgxt.metsbase1 (baseline) stresstest_submaxgxt.pctchgmets_1, stresstest_submaxgxt.pctchgmets_4
Waist Circumference	physicalmeasures_abi_waist.waistcm1, physicalmeasures_bp_bmi.waistcm1
A1c	laboratorymeasures.hba1cpct

Figure A: Comparison of values computed in integrity check to reference article Figure 1 values

Manuscript:
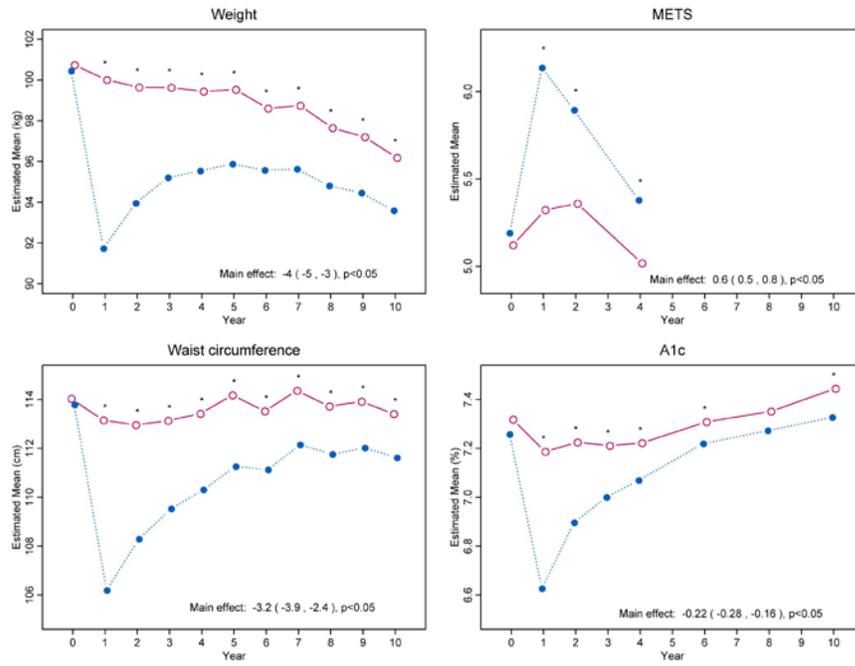
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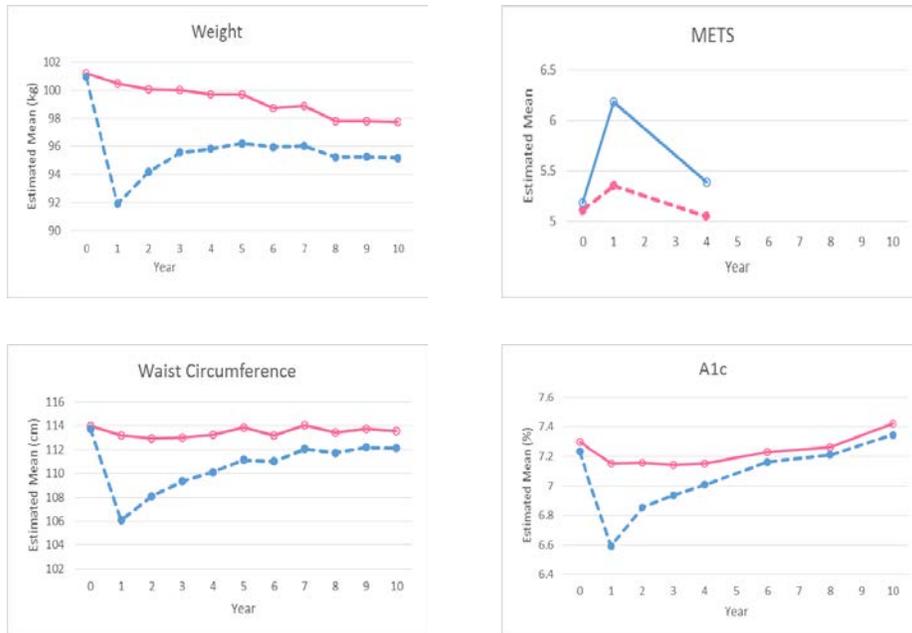
Table D: Variables used to replicate Supplementary Table 1. Comparison of Diabetes Support and Education (DSE) and Intensive Lifestyle Intervention (ILI) groups and baseline and end of study

Table Variable	dataset.variable
Treatment Arm	la_key.treatment
Weight	physicalmeasures_bp_bmi.bswgt1
Waist Circumference	physicalmeasures_abi_waist.waistcm1 (baseline), physicalmeasures_bp_bmi.waistcm1 (end-of-study)
A1c	laboratorymeasures.hba1cpct
Systolic Blood Pressure	physicalmeasures_bp_bmi.bssbp2
Diastolic Blood Pressure	physicalmeasures_bp_bmi.bsdbp2
HDL Cholesterol	laboratorymeasures.hdlchlmgdl
Triglycerides	laboratorymeasures.trigmgdl*
LDL Cholesterol	laboratorymeasures.ldlchlmgdl
METS	stresstest_maximalgxt.metsbase1 (baseline) stresstest_submaxgxt.pctchgmets_1, stresstest_submaxgxt.pctchgmets_4
Hypertension medications	healthoutcomes_meduse.htndrug
Statins	healthoutcomes_meduse.statins
Insulin	healthoutcomes_meduse.insulins
Angiotensin Converting Enzymes	healthoutcomes_meduse.ace
Angiotensin Receptor Blockers	healthoutcomes_meduse.arb
Beta Blockers	healthoutcomes_meduse.bb
Calcium Channel Blockers	healthoutcomes_meduse.ccblock
Biguanides	healthoutcomes_meduse.biguanides

*Note: Mean is taken of the log-transformed values, then a back-transformation is done to restore the original units

Table E: Comparison of values computed in integrity check to reference article Supplementary Table 1 values

	Baseline DSE Manuscript	Baseline DSE DSIC	Difference	Baseline ILI Manuscript	Baseline ILI DSIC	Difference
Weight (kg)	101	101.2	0.2	100	100.9	0.9
Waist Circumference (cm)	114	114.1	0.1	114	113.8	0.2
A1c (%)	7.32	7.3	0.02	7.26	7.23	0.03
Systolic blood pressure (mmHg)	129	129	0	128	127.9	0.1
Diastolic blood pressure (mmHg)	70.4	70.2	0.2	70	69.8	0.2
HDL Cholesterol	43.5	43.5	0	43.5	43.5	0

	Baseline DSE Manuscript	Baseline DSE DSIC	Difference	Baseline ILI Manuscript	Baseline ILI DSIC	Difference
Triglycerides	154	153.7	0.3	157	156.5	0.5
LDL Cholesterol	112	112.7	0.7	112	112.5	0.5
METS	5.12	5.11	0.01	5.19	5.19	0
Use of specific medications (%)						
Hypertension medications	0.72	0.73	0.01	0.73	0.73	0
Statins	0.44	0.46	0.02	0.44	0.46	0.02
Insulin	0.16	0.16	0	0.15	0.15	0
Angiotensin Converting Enzymes	0.45	0.45	0	0.43	0.43	0
Angiotensin Receptor Blockers	0.15	0.16	0.01	0.16	0.17	0.01
Beta Blockers	0.2	0.21	0.01	0.22	0.24	0.02
Calcium Chanel Blockers	0.2	0.22	0.02	0.18	0.19	0.01
Biguanides	0.61	0.61	0	0.62	0.62	0

	End of Study DSE Manuscript	End of study DSE DSIC	Difference	End of Study ILI Manuscript	End of Study ILI DSIC	Difference
Weight (kg)	96.2	97.8	1.6	93.6	95.3	1.7
Waist Circumference (cm)	113	113.4	0.4	112	111.7	0.3
A1c (%)	7.44	7.26	0.18	7.33	7.21	0.12
Systolic blood pressure (mmHg)	127	126.6	0.4	126	124.5	1.5
Diastolic blood pressure (mmHg)	65.9	65.9	0	66.3	65.5	0.8
HDL Cholesterol	47.8	47.9	0.1	48.7	48.8	0.1
Triglycerides	124	126.5	2.5	126	127.2	1.2
LDL Cholesterol	88.3	89.8	1.5	89.5	90.2	0.7
METS	5.02	5.05	0.03	5.38	5.39	0.01
Use of specific medications (%)						
Hypertension medications	0.88	0.9	0.02	0.87	0.86	0.01
Statins	0.74	0.75	0.01	0.71	0.74	0.03
Insulin	0.41	0.37	0.04	0.36	0.32	0.04
Angiotensin Converting Enzymes	0.5	0.55	0.05	0.5	0.51	0.01
Angiotensin Receptor Blockers	0.32	0.33	0.01	0.31	0.3	0.01

	End of Study DSE Manuscript	End of study DSE DSIC	Difference	End of Study ILI Manuscript	End of Study ILI DSIC	Difference
Beta Blockers	0.38	0.39	0.01	0.35	0.35	0
Calcium Chanel Blockers	0.26	0.29	0.03	0.23	0.26	0.03
Biguanides	0.67	0.73	0.06	0.67	0.72	0.05

Table F: Variables used to replicate Table 2: Primary and Secondary Outcomes and Other Cardiovascular Outcomes

Table Variable	dataset.variable
Treatment Arm	la_key.treatment
Primary outcome	la4_outcomes1.primary
Secondary outcome - Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke	la4_outcomes1.secondary_1
Secondary outcome - Death from any cause, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	la4_outcomes1.secondary_2
Secondary outcome - Death from any cause, nonfatal myocardial infarction, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization for heart failure, carotid endarterectomy, or peripheral vascular disease	la4_outcomes1.secondary_3
Death, any cause	la4_outcomes1.death
Death, cardiovascular cause	la4_outcomes1.cvd_death
Myocardial infarction, fatal or nonfatal	la4_outcomes1.allmi
Myocardial infarction, fatal	la4_outcomes1.cvd_death_mi
Myocardial infarction, nonfatal	la4_outcomes1.mi
Hospitalization for angina	la4_outcomes1.angina
Stroke	la4_outcomes1.allstroke
Heart failure	la4_outcomes1.chf
CABG	la4_outcomes1.cabg
Carotid endarterectomy	la4_outcomes1.carotid

Table G: Comparison of values computed in integrity check to reference article Table 2 values

Outcome	Patients with Event Manuscript *no.*	Patients with Event DSIC *no.*	Diff.	Control Group Manuscript *no. of events (rate/100 person-yr)*	Control Group DSIC *no. of events (rate/100 person-yr)*	Diff.
Primary outcome						
Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	821	799	22	418 (1.92)	406 (1.96)	12 (0.04)
Secondary outcomes						
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke	550	532	18	283 (1.25)	273 (1.27)	10 (0.02)
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	1025	994	31	529 (2.43)	511 (2.47)	18 (0.04)
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization for heart failure, carotid endarterectomy, or peripheral vascular disease	1177	1139	38	600 (2.81)	578 (2.85)	22 (0.04)
Other cardiovascular outcomes						
Death						
Any cause	376	363	13	202 (0.86)	195 (0.87)	7 (0.01)
Cardiovascular cause	109	107	2	57 (0.24)	56 (0.25)	1 (0.01)
Myocardial infarction						
Fatal or nonfatal	354	344	10	191 (0.84)	187 (0.86)	4 (0.02)
Fatal	16	16	0	11 (0.05)	11 (0.05)	0 (0)
Nonfatal	342	332	10	183 (0.80)	179 (0.82)	4 (0.02)
Hospitalization for angina	390	383	7	196 (0.87)	193 (0.90)	3 (0.03)
Stroke	165	158	7	80 (0.34)	75 (0.34)	5 (0)
Heart failure	218	211	7	119 (0.51)	116 (0.53)	3 (0.02)
CABG	525	518	7	269 (1.21)	267 (1.26)	2 (0.05)
Carotid endarterectomy	54	54	0	25 (0.11)	25 (0.11)	0 (0)

Outcome	Intervention Group Manuscript *no. of events (rate/100 person-yr)*	Intervention Group DSIC *no. of events (rate/100 person-yr)*	Diff.	Hazard Ratio (95% CI) Manuscript	Hazard Ratio (95% CI) DSIC	Diff.
Primary outcome						
Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	403 (1.83)	393 (1.87)	10 (0.04)	0.95 (0.83-1.09)	0.96 (0.83-1.10)	0.01 (0-0.01)
Secondary outcomes						
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke	267 (1.17)	259 (1.20)	8 (0.03)	0.93 (0.79-1.10)	0.94 (0.79-1.11)	0.01 (0-0.01)
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	496 (2.25)	483 (2.30)	13 (0.05)	0.93 (0.82-1.05)	0.93 (0.82-1.06)	0 (0-0.01)
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization for heart failure, carotid endarterectomy, or peripheral vascular disease	577 (2.67)	561 (2.73)	16 (0.06)	0.94 (0.84-1.05)	0.96 (0.85-1.08)	0.02 (0.01-0.03)
Other cardiovascular outcomes						
Death						
Any cause	174 (0.73)	168 (0.74)	6 (0.01)	0.85 (0.69-1.04)	0.86 (0.70-1.05)	0.01 (0.01-0.01)
Cardiovascular cause	52 (0.22)	51 (0.23)	1 (0.01)	0.88 (0.61-1.29)	0.90 (0.62-1.32)	0.02 (0.01-0.03)
Myocardial infarction						
Fatal or nonfatal	163 (0.71)	157 (0.72)	6 (0.01)	0.84 (0.68-1.04)	0.83 (0.67-1.03)	0.01 (0.01-0.01)

Outcome	Intervention Group Manuscript *no. of events (rate/100 person-yr)*	Intervention Group DSIC *no. of events (rate/100 person-yr)*	Diff.	Hazard Ratio (95% CI) Manuscript	Hazard Ratio (95% CI) DSIC	Diff.
Fatal	5 (<0.02)	5 (0.02)	0 (0)	0.44 (0.15-1.26)	0.45 (0.16-1.30)	0.01 (0.01-0.04)
Nonfatal	159 (0.69)	153 (0.70)	6 (0.01)	0.86 (0.69-1.06)	0.85 (0.68-1.05)	0.01 (0.01-0.01)
Hospitalization for angina	194 (0.85)	190 (0.88)	4 (0.03)	0.97 (0.80-1.19)	0.98 (0.80-1.19)	0.01 (0-0)
Stroke	85 (0.36)	83 (0.37)	2 (0.01)	1.05 (0.77-1.42)	1.10 (0.80-1.50)	0.05 (0.03-0.08)
Heart failure	99 (0.42)	95 (0.43)	4 (0.01)	0.80 (0.61-1.04)	0.81 (0.62-1.06)	0.01 (0.01-0.02)
CABG	256 (1.14)	251 (1.18)	5 (0.04)	0.93 (0.78-1.10)	0.93 (0.79-1.11)	0 (0.01-0.01)
Carotid endarterectomy	29 (0.12)	29 (0.13)	0 (0.01)	1.10 (0.64-1.87)	1.15 (0.68-1.97)	0.05 (0.04-0.1)

Table H: Variables used to replicate Figure 2: Cumulative Hazard Curves for the Primary Composite Endpoint

Table Variable	dataset.variable
Treatment Arm	la_key.treatment
Primary outcome	la4_outcomes1.primary
Years	la4_outcomes1.t_primary

Figure B: Comparison of values computed in integrity check to reference article Figure 2 values

Manuscript:
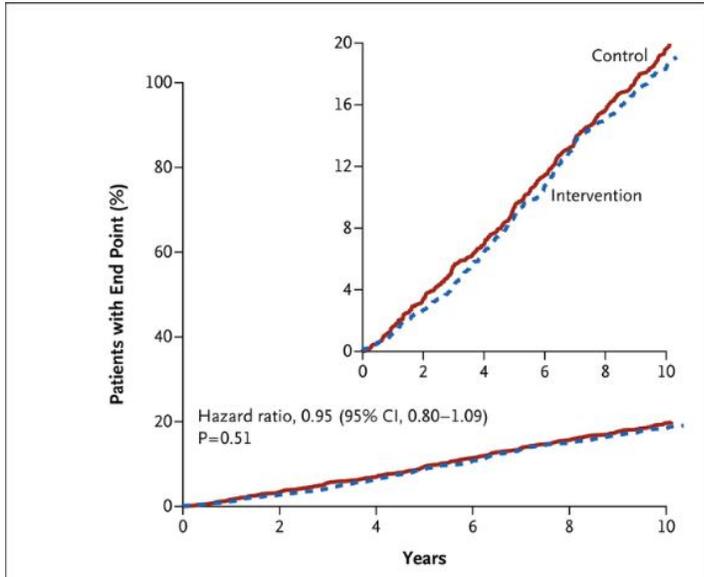
Shown are Kaplan–Meier estimates of the cumulative proportion of patients with a primary event. The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina. The numbers below the graph are the numbers of patients at risk in each study group at years 2, 4, 6, and 8 and at 10.4 years, when the last observed event occurred. The inset shows the same data on an expanded y axis.

DSIC:
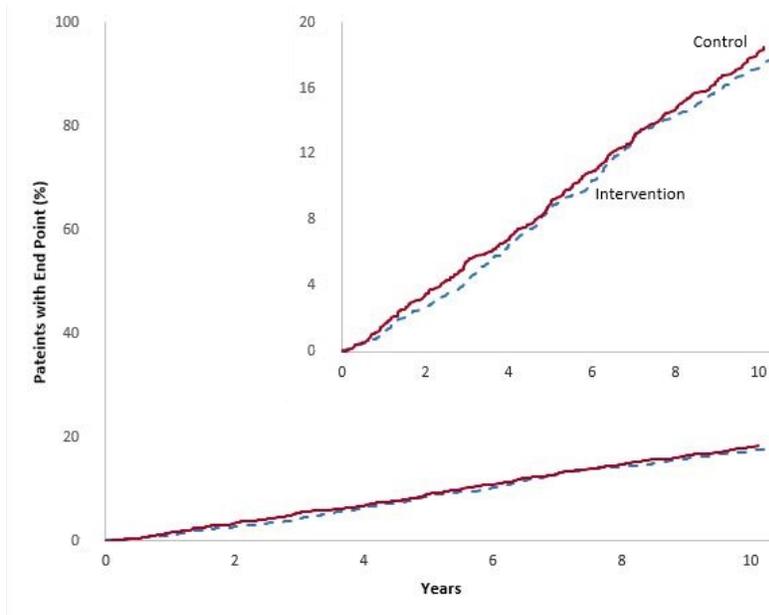
No. at Risk	Year 0 Manuscript	Year 0 DSIC	Diff.	Year 2 Manuscript	Year 2 DSIC	Diff.	Year 4 Manuscript	Year 4 DSIC	Diff.
Control	2575	2543	32	2425	2303	122	2296	2183	113
Intervention	2570	2448	122	2447	2327	120	2326	2206	120

No. at Risk	Year 6 Manuscript	Year 6 DSIC	Diff.	Year 8 Manuscript	Year 8 DSIC	Diff.	Year 10 Manuscript*	Year 10 DSIC	Diff.
Control	2156	2048	108	2019	1912	107	688	664	24
Intervention	2192	2081	111	2049	1943	106	505	489	16

*Note that Year 10 represents the timing of the last observed event. 10.4 years is the last reported event for the intervention group, and 10.1 years is the last reported event for the control group.

	Manuscript	DSIC	Diff.
Hazard ratio	0.95 (95% CI, 0.80-1.09)	0.96 (95% CI, 0.83-1.10)	0.01 (0.03-0.01)

Table I: Variables used to replicate Figure 3: Primary Outcome in Prespecified Subgroups

Table Variable	dataset.variable
Treatment Arm	la_key.treatment
Primary outcome	la4_outcomes1.primary
Cardiovascular disease at baseline	la2_baselinevariables.CVDhis
Sex	la2_baselinevariables.female
Race or ethnic group	la2_baselinevariables.racevar

Table J: Comparison of values computed in integrity check to reference article Figure 3 values

Subgroup	Control Manuscript *no. of events (rate/100 person-yr)*	Control DSIC *no. of events (rate/100 person-yr)*	Diff.	Intervention Manuscript *no. of events (rate/100 person-yr)*	Intervention DSIC *no. of events (rate/100 person-yr)*	Diff.
Overall	418 (1.92)	406 (1.96)	12 (0.04)	403 (1.83)	393 (1.87)	10 (0.04)
Cardiovascular disease at baseline						
No	274 (1.42)	266 (1.44)	8 (0.02)	240 (1.23)	234 (1.26)	6 (0.03)
Yes	144 (5.92)	140 (6.02)	4 (0.1)	163 (6.56)	159 (6.62)	4 (0.06)
Sex						
Male	245 (2.94)	243 (2.98)	2 (0.04)	232 (2.72)	229 (2.77)	3 (0.05)

Subgroup	Control Manuscript *no. of events (rate/100 person-yr)*	Control DSIC *no. of events (rate/100 person-yr)*	Diff.	Intervention Manuscript *no. of events (rate/100 person-yr)*	Intervention DSIC *no. of events (rate/100 person-yr)*	Diff.
Female	173 (1.29)	163 (1.30)	10 (0.01)	171 (1.26)	164 (1.29)	7 (0.03)
Race or ethnic group						
Black	46 (1.32)	46 (1.32)	0 (0)	63 (1.82)	63 (1.82)	0 (0)
Native American	13 (1.18)	N/A	N/A	10 (0.86)	N/A	N/A
Asian or Pacific Islander	3 (1.67)	N/A	N/A	1 (0.38)	N/A	N/A
White	303 (2.19)	302 (2.19)	1 (0)	286 (2.06)	285 (2.06)	1 (0.01)
Other	10 (2.35)	15 (2.20)	5 (0.15)	12 (2.96)	14 (1.78)	2 (1.18)
Hispanic	43 (1.54)	43 (1.55)	0 (0.01)	31 (1.06)	31 (1.07)	0 (0.01)

Subgroup	Hazard Ratio (95% CI) Manuscript	Hazard Ratio (95% CI) DSIC	Diff.
Overall	0.95 (0.83-1.09)	0.96 (0.83-1.10)	0.01 (0-0.01)
Cardiovascular disease at baseline			
No	0.86 (0.72-1.02)	0.87 (0.73-1.04)	0.01 (0.01-0.02)
Yes	1.13 (0.90-1.42)	1.10 (0.88-1.38)	0.03 (0.02-0.04)
Sex			
Male	0.93 (0.78-1.11)	0.93 (0.78-1.11)	0 (0-0)
Female	0.97 (0.79-1.20)	0.99 (0.80-1.24)	0.02 (0.01-0.04)
Race or ethnic group			
Black	1.34 (0.91-1.96)	1.38 (0.94-2.02)	0.04 (0.03-0.06)
Native American	0.74 (0.31-1.76)	N/A	N/A
Asian or Pacific Islander	0.71 (0.06-8.28)	N/A	N/A
White	0.94 (0.80-1.11)	0.94 (0.80-1.11)	0 (0-0)
Other	1.15 (0.45-2.89)	0.81 (0.39-1.67)	0.34 (0.06-1.22)
Hispanic	0.66 (0.41-1.05)	0.69 (0.44-1.10)	0.03 (0.03-0.05)

Appendix A: SAS Code

```
*** Look AHEAD end of intervention study data DSIC;

*** Replicate Table 1 from paper - baseline characteristics;

***NOTE: Those from Native American sites were excluded (resulting in cohort of 4901 per Overview document), thus the overall population differences and
differences in statistics;

proc format;
        value $smokingf 'Missing' = 'No'
                        'Past'    = 'No'
                        'Never'   = 'No'
                        'Present' = 'Yes';


libname key '/prj/niddk/ims_analysis/Look_AHEAD/private_orig_data/LA.INTERVENTION/INTERVENTION/3-Key Data/3a-Key Data/';

libname meas '/prj/niddk/ims_analysis/Look_AHEAD/private_orig_data/LA.INTERVENTION/INTERVENTION/4-Measures/4a-Measurement Data Sets/';

libname ques '/prj/niddk/ims_analysis/Look_AHEAD/private_orig_data/LA.INTERVENTION/INTERVENTION/5-Questionnaires/5a-Questionnaire Data Sets';

data baseline;
        set key.la2_baselinevariables;

data treatments;
        set key.la_key;

proc contents data=baseline;

proc contents data=treatments;

data labmeasures;
        set meas.laboratorymeasures;

data labmeasures_bl;
        set labmeasures;
        if visit='Baseline' then output labmeasures_bl;

proc contents data=labmeasures;

data bp;
        set meas.physicalmeasures_bp_bmi;

data bp_bl;
        set bp;
        if visit='Baseline' then output bp_bl;

proc contents data=bp;

data meds;
        set ques.healthoutcomes_meduse;
```

```
data meds_bl;
      set meds;
      if visit='Baseline' then output meds_bl;

data stresstest;
      set meas.stresstest_maximalgxt;

data stresstest_bl;
      set stresstest;
      if visit='Baseline' then output stresstest_bl;

data mets;
      set meas.stresstest_submaxgxt;

proc freq data=treatments;
      tables randarm treatment;

proc sort data=treatments;
      by maskid;

proc sort data=baseline;
      by maskid;

data baseline_table;
      merge treatments (in=val1)
            baseline   (in=val2);
      by maskid;
      if val1 and val2 then output baseline_table;

proc sort data=labmeasures;
      by maskid;

proc sort data=bp;
      by maskid;

proc sort data=meds;
      by maskid;

data baseline_table;
      merge baseline_table  (in=val1)
            labmeasures_bl  (in=val2)
            bp_bl           (in=val3)
            meds_bl         (in=val4)
            stresstest_bl   (in=val5);
      by maskid;
      trans_trig = log10(trigmgdl);
      if val1 then output baseline_table;

proc freq data=baseline_table;
      tables treatment;
      title3 'Treatment Group';

proc means data=baseline_table mean std;
      var baseline_age;
      class treatment;
      title3 'Table 1 - Baseline Age';
```

18

```
proc sort data=baseline_table;
      by treatment;

proc freq data=baseline_table;
      tables female;
      by treatment;
      title3 'Table 1 - Baseline Gender';

proc freq data=baseline_table;
      tables racevar ;
      by treatment;
      title3 'Table 1 - Baseline Race or Ethnic Group';

proc freq data=baseline_table;
      tables CVDhis ;
      by treatment;
      title3 'Table 1 - Baseline CVD History';

proc freq data=baseline_table;
      tables insulins;
      by treatment;
      title3 'Table 1 - Baseline Use of Insulin';

proc freq data=baseline_table;
      tables smoking;
      by treatment;
      title3 'Table 1 - Baseline Current Smoking';
      format smoking $smokingf.;

proc means data=baseline_table median p25 p75;
      var diab_dur;
      class treatment;
      title3 'Table 1 - Baseline Duration of Diabetes';

proc means data=baseline_table mean std;
      var bswgt1;
      class treatment;
      title3 'Table 1 - Baseline Weight';

proc means data=baseline_table mean std;
      var bmi ;
      class treatment;
      title3 'Table 1 - Baseline BMI';

proc means data=baseline_table mean std;
      var waistcm_mean;
      class treatment;
      title3 'Table 1 - Baseline Waist Circumference';

proc means data=baseline_table mean std;
      var hba1cpct;
      class treatment;
      title3 'Table 1 - Baseline Glycated Hemoglobin';

proc means data=baseline_table mean std;
```

```
        var bssbp2;
        class treatment;
        title3 'Table 1 - Baseline Systolic Blood Pressure';

proc means data=baseline_table mean std;
        var bsdbp2;
        class treatment;
        title3 'Table 1 - Baseline Diastolic Blood Pressure';

proc means data=baseline_table mean std;
        var hdlchlmgdl;
        class treatment;
        title3 'Table 1 - Baseline High-density lipoprotein';

proc means data=baseline_table mean std;
        var ldlchlmgdl;
        class treatment;
        title3 'Table 1 - Baseline Low-density lipoprotein';

proc means data=baseline_table median p25 p75;
        var trigmgdl;
        class treatment;
        title3 'Table 1 - Baseline Triglycerides';

*** Supplementary Table 1;

*** Baseline;

proc means data=baseline_table mean;
        var bswgt1;
        class treatment;
        title3 'Supplementary Table 1 - Baseline Weight';

proc means data=baseline_table mean;
        var waistcm_mean;
        class treatment;
        title3 'Supplementary Table 1 - Baseline Wasit circumference';

proc means data=baseline_table mean;
        var hba1cpct;
        class treatment;
        title3 'Supplementary Table 1 - Baseline HBA1C';

proc means data=baseline_table mean;
        var bssbp2;
        class treatment;
        title3 'Supplementary Table 1 - Baseline Systolic BP';

proc means data=baseline_table mean;
        var bsdbp2;
        class treatment;
        title3 'Supplementary Table 1 - Baseline Diastolic BP';

proc means data=baseline_table mean;
        var hdlchlmgdl;
        class treatment;
```

```
        title3 'Supplementary Table 1 - Baseline HDL Cholesterol';

proc means data=baseline_table mean;
        var trans_trig;
        class treatment;
        output out = trig_mean mean = mean;
        title3 'Supplementary Table 1 - Baseline Trigglycerides';

data trig_mean;
        set trig_mean;
        mean=10**mean;

proc print data=trig_mean;

proc means data=baseline_table mean;
        var ldlchlmgdl;
        class treatment;
        title3 'Supplementary Table 1 - Baseline LDL Cholesterol';

proc means data=baseline_table mean;
        var metsbase1;
        class treatment;
        title3 'Supplementary Table 1 - Baseline METS';

proc freq data=baseline_table;
        tables htndrug statins insulins ace arb bb ccblock biguanides;
        by treatment;
        title3 'Supplementary Table 1 - Baseline Use of Specific Medications';

*** End of Study;

proc freq data=labmeasures;
        tables visit;
        title3 'Lab measures visits';

proc freq data=bp;
        tables visit;
        title3 'BP visits';

proc freq data=stresstest;
        tables visit;
        title3 'Stress Test visits';

proc freq data=meds;
        tables visit;
        title3 'Medications visits';

data labmeasures_end;
        set labmeasures;
        if visit = 'FV96' then output labmeasures_end;

data bp_end;
        set bp;
        if visit = 'FV96' then output bp_end;

data meds_end;
```

21

```
        set meds;
        if visit = 'FV96' then output meds_end;

proc sort data=baseline_table;
        by maskid;

data end_of_study_table;
        merge baseline_table   (in=val1 keep=maskid treatment)
                labmeasures_end
                bp_end
                meds_end;
        by maskid;
        trans_trig = log10(trigmgdl);
        if val1 then output end_of_study_table;

proc sort data=end_of_study_table;
        by treatment;

proc means data=end_of_study_table mean;
        var bswgt1;
        class treatment;
        title3 'Supplementary Table 1 - End of Study Weight';

proc means data=end_of_study_table mean;
        var waistcm1;
        class treatment;
        title3 'Supplementary Table 1 - End of Study Wasit circumference';

proc means data=end_of_study_table mean;
        var hba1cpct;
        class treatment;
        title3 'Supplementary Table 1 - End of Study HBA1C';

proc means data=end_of_study_table mean;
        var bssbp2;
        class treatment;
        title3 'Supplementary Table 1 - End of Study Systolic BP';

proc means data=end_of_study_table mean;
        var bsdbp2;
        class treatment;
        title3 'Supplementary Table 1 - End of Study Diastolic BP';

proc means data=end_of_study_table mean;
        var hdlchlmgdl;
        class treatment;
        title3 'Supplementary Table 1 - End of Study HDL Cholesterol';

proc means data=end_of_study_table mean;
        var trans_trig;
        class treatment;
        output out=trig_mean mean=mean;
        title3 'Supplementary Table 1 - End of Study Trigglycerides';

data trig_mean;
        set trig_mean;
```

22

```
       mean=10**mean;

proc print data=trig_mean;

proc means data=end_of_study_table mean;
       var ldlchlmgdl;
       class treatment;
       title3 'Supplementary Table 1 - End of Study LDL Cholesterol';

data mets;
       merge mets            (in=val1)
             baseline_table (in=val2 keep=maskid metsbase1 treatment);
       by maskid;
       if visit = 'FV12' then mets_val = metsbase1 + (.01*pctchgmets_1*metsbase1);
       if visit = 'FV48' then mets_val = metsbase1 + (.01*pctchgmets_4*metsbase1);
       if val1 and val2 then output mets;

proc means data=mets mean;
       var mets_val;
       class treatment;
       where visit = 'FV48';
       title3 'Supplementary Table 1 - End of Study METS';

proc freq data=end_of_study_table;
       tables htndrug statins insulins ace arb bb ccblock biguanides;
       by treatment;
       title3 'Supplementary Table 1 - End of Study Use of Specific Medications';

data labmeasures;
               merge labmeasures
                     treatments (in=val1);
               by maskid;
               if visit = 'Baseline' then year=0;
               else if visit = 'FV12' then year=1;
               else if visit = 'FV24' then year=2;
               else if visit = 'FV36' then year=3;
               else if visit = 'FV48' then year=4;
               else if visit = 'FV60' then year=5;
               else if visit = 'FV72' then year=6;
               else if visit = 'FV84' then year=7;
               else if visit = 'FV96' then year=8;
               else if visit = 'FV108' then year=9;
               else if visit = 'FV120' then year=10;
               if val1 then output labmeasures;

proc sort data=labmeasures;
       by treatment;

ods graphics on;
proc glm data=labmeasures plots=meanplot(connect);
       class year;
       model hba1cpct=year;
       means year;
       by treatment;
       run;
ods graphics off;
```

```
data bp;
                merge bp
                        treatments (in=val1);
                by maskid;
                if visit = 'Baseline' then year=0;
                else if visit = 'FV12' then year=1;
                else if visit = 'FV24' then year=2;
                else if visit = 'FV36' then year=3;
                else if visit = 'FV48' then year=4;
                else if visit = 'FV60' then year=5;
                else if visit = 'FV72' then year=6;
                else if visit = 'FV84' then year=7;
                else if visit = 'FV96' then year=8;
                else if visit = 'FV108' then year=9;
                else if visit = 'FV120' then year=10;
                if val1 then output bp;

proc sort data=bp;
        by treatment;

ods graphics on;
proc glm data=bp plots=meanplot(connect);
        class year;
        model bswgt1=year;
        means year;
        by treatment;
        run;
ods graphics off;

data waist;
        set meas.physicalmeasures_abi_waist;

proc sort data=bp;
        by maskid;

data waist;
                merge waist      (rename = (waistcm1 = waistcmbeg))
                        bp        (rename = (waistcm1 = waistcmend))
                        treatments (in=val1);
                by maskid;
                if visit = 'Baseline' then do;
                        year=0;
                        waistcm = waistcmbeg;
                end;
                else if visit = 'FV12' then do;
                        year=1;
                        waistcm = waistcmbeg;
                end;
                else if visit = 'FV24' then do;
                        year=2;
                        waistcm = waistcmbeg;
                end;
                else if visit = 'FV36' then do;
                        year=3;
                        waistcm = waistcmbeg;
```

24

```
                    end;
                    else if visit = 'FV48' then do;
                            year=4;
                            waistcm = waistcmbeg;
                    end;
                    else if visit = 'FV60' then do;
                            year=5;
                            waistcm = waistcmend;
                    end;
                    else if visit = 'FV72' then do;
                            year=6;
                            waistcm = waistcmend;
                    end;
                    else if visit = 'FV84' then do;
                            year=7;
                            waistcm = waistcmend;
                    end;
                    else if visit = 'FV96' then do;
                            year=8;
                            waistcm = waistcmend;
                    end;
                    else if visit = 'FV108' then do;
                       year=9;
                            waistcm = waistcmend;
                    end;
                    else if visit = 'FV120' then do;
                            year=10;
                            waistcm = waistcmend;
                    end;
                    if val1 then output waist;

proc sort data=waist;
        by treatment;

ods graphics on;
proc glm data=waist plots=meanplot(connect);
        class year;
        model waistcm=year;
        means year;
        by treatment;
        run;
ods graphics off;

data mets;
        set mets
            baseline_table (keep = maskid metsbase1 treatment visit);
        by maskid;
        if visit = 'Baseline' then do;
                year = 0;
                mets_val = metsbase1;
        end;
        if visit = 'FV12' then year = 1;
        if visit = 'FV48' then year = 4;

proc sort data=mets;
        by treatment;
```

25

```
ods graphics on;
proc glm data=mets plots=meanplot(connect);
        class year;
        model mets_val=year;
        means year;
        by treatment;
        run;
ods graphics off;

*** Look AHEAD End of Intervention DSIC Outcomes Data;
*** Programmer: Allyson Mateja;
*** Date: 12/14/16;

title 'Look AHEAD End-of-Intervention Outcomes DSIC';
title2 ' ';

proc format;
        value sexf 0 = 'Male'
                   1 = 'Female';

libname ladata '/prj/niddk/ims_analysis/Look_AHEAD/private_orig_data/LA.INTERVENTION_v2/3-Key Data/3a-Key Data/';
libname keydata '/prj/niddk/public_orig_data/Look_AHEAD_V3/Data/End_of_Intervention/Key_Data/';

data outcomes;
        set ladata.la4_outcomes1;

data key;
        set keydata.la_key;

data baseline;
        set keydata.la2_baselinevariables;

proc contents data = outcomes;
proc contents data = key;
proc contents data = baseline;

proc sort data = baseline;
        by maskid;

proc sort data = outcomes;
        by maskid;

proc sort data = key;
        by maskid;

data outcomes;
        merge outcomes (in=val1)
              key      (in=val2 keep=maskid treatment randarm)
              baseline (in=val3 keep=maskid cvdhis female racevar);
        by maskid;
        primary_years = t_primary/365.25;
        if val1 and val2 and val3 then output outcomes;

proc sort data = outcomes;
        by treatment;
```

26

```
proc freq data = outcomes;
      tables primary;
      title3 'Table 2 - Primary outcome';

proc freq data = outcomes;
      tables primary /out=freq_data;
      by treatment;
      title3 'Table 2 - Primary outcome by treatment group';

proc means data = outcomes sum noprint;
      var t_primary;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if primary=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Table 2 - Primary outcome no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_primary*primary(0) = treatment /risklimits;
      title3 'Table 2 - Primary outcome hazard ratio';

proc freq data = outcomes;
      tables secondary_1;
      title3 'Table 2 - Secondary outcome 1 - Death from cardiovascular causes, nonfatal MI, or nonfatal stroke';

proc freq data = outcomes;
      tables secondary_1 /out=freq_data;
      by treatment;
      title3 'Table 2 - Secondary outcome 1 - Death from cardiovascular causes, nonfatal MI, or nonfatal stroke by treatment group';

proc means data = outcomes sum noprint;
      var t_secondary_1;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if secondary_1=1;

data person_years;
      merge total
            freq_data;
```

```
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Secondary outcome 1 no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_secondary_1*secondary_1(0) = treatment /risklimits;
        title3 'Table 2 - Secondary outcome 1 hazard ratio';

proc freq data = outcomes;
        tables secondary_2;
        title3 'Table 2 - Secondary outcome 2 - Death from any cause, nonfatal MI, nonfatal stroke, or hospitalization for angina';

proc freq data = outcomes;
        tables secondary_2 /out=freq_data;
        by treatment;
        title3 'Table 2 - Secondary outcome 2 - Death from any cause, nonfatal MI, nonfatal stroke, or hospitalization for angina by treatment group';

proc means data = outcomes sum noprint;
        var t_secondary_2;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if secondary_2=1;

data person_years;
        merge total
              freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Secondary outcome 2 no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_secondary_2*secondary_2(0) = treatment /risklimits;
        title3 'Table 2 - Secondary outcome 2 hazard ratio';

proc freq data = outcomes;
        tables secondary_3;
        title3 'Table 2 - Secondary outcome 3 - Death from any cause, nonfatal MI, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization';
        title4 'for heart failure, carotid endarterectomy, or peripheral vascular disease';

proc freq data = outcomes;
        tables secondary_3 /out=freq_data;
        by treatment;
        title3 'Table 2 - Secondary outcome 3 - Death from any cause, nonfatal MI, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization';
```

28

```
                    title4 'for heart failure, carotid endarterectomy, or peripheral vascular disease by treatment group';

proc means data = outcomes sum noprint;
        var t_secondary_3;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if secondary_3=1;

data person_years;
        merge total
                freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Secondary outcome 3 no. of events (rate/100 person-yr)';
        title4 ' ';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_secondary_3*secondary_3(0) = treatment /risklimits;
        title3 'Table 2 - Secondary outcome 3 hazard ratio';

proc freq data = outcomes;
        tables death;
        title3 'Table 2 - Death any cause';

proc freq data = outcomes;
        tables death /out=freq_data;
        by treatment;
        title3 'Table 2 - Death any cause by treatment group';

proc means data = outcomes sum noprint;
        var t_death;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if death=1;

data person_years;
        merge total
                freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Death any cause no. of events (rate/100 person-yr)';
```

29

```
proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_death*death(0) = treatment /risklimits;
      title3 'Table 2 - Death any cause hazard ratio';

proc freq data = outcomes;
      tables cvd_death;
      title3 'Table 2 - Death cardiovascular cause';

proc freq data = outcomes;
      tables cvd_death /out=freq_data;
      by treatment;
      title3 'Table 2 - Death cardiovascular cause by treatment group';

proc means data = outcomes sum noprint;
      var t_cvd_death;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if cvd_death=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Table 2 - Death cardiovascular cause no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_cvd_death*cvd_death(0) = treatment /risklimits;
      title3 'Table 2 - Death cardiovascular cause hazard ratio';

proc freq data = outcomes;
      tables allmi;
      title3 'Table 2 - Myocardial infarction fatal or nonfatal';

proc freq data = outcomes;
      tables allmi /out=freq_data;
      by treatment;
      title3 'Table 2 - Myocardial infarction fatal or nonfatal by treatment group';

proc means data = outcomes sum noprint;
      var t_allmi;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
```

```
        if allmi=1;

data person_years;
        merge total
                freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Myocardial infarction fatal or nonfatal no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_allmi*allmi(0) = treatment /risklimits;
        title3 'Table 2 - Myocardial infarction fatal or nonfatal hazard ratio';

proc freq data = outcomes;
        tables cvd_death_mi;
        title3 'Table 2 - Myocardial infarction fatal';

proc freq data = outcomes;
        tables cvd_death_mi /out=freq_data;
        by treatment;
        title3 'Table 2 - Myocardial infarction fatal by treatment group';

proc means data = outcomes sum noprint;
        var t_cvd_death_mi;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if cvd_death_mi=1;

data person_years;
        merge total
                freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Myocardial infarction fatal no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_cvd_death_mi*cvd_death_mi(0) = treatment /risklimits;
        title3 'Table 2 - Myocardial infarction fatal hazard ratio';

proc freq data = outcomes;
        tables mi;
        title3 'Table 2 - Myocardial infarction nonfatal';
```

31

```
proc freq data = outcomes;
      tables mi /out=freq_data;
      by treatment;
      title3 'Table 2 - Myocardial infarction nonfatal by treatment group';

proc means data = outcomes sum noprint;
      var t_mi;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if mi=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Table 2 - Myocardial infarction nonfatal no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_mi*mi(0) = treatment /risklimits;
      title3 'Table 2 - Myocardial infarction nonfatal hazard ratio';

proc freq data = outcomes;
      tables angina;
      title3 'Table 2 - Hospitalization for angina';

proc freq data = outcomes;
      tables angina /out=freq_data;
      by treatment;
      title3 'Table 2 - Hospitalization for angina by treatment group';

proc means data = outcomes sum noprint;
      var t_angina;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if angina=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
```

```
        var treatment no_of_events;
        title3 'Table 2 - Hospitalization for angina no. of events (rate/100 person-yr)';


proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_angina*angina(0) = treatment /risklimits;
        title3 'Table 2 - Hospitalization for angina hazard ratio';


proc freq data = outcomes;
        tables allstroke;
        title3 'Table 2 - Stroke';


proc freq data = outcomes;
        tables allstroke /out=freq_data;
        by treatment;
        title3 'Table 2 - Stroke by treatment group';


proc means data = outcomes sum noprint;
        var t_allstroke;
        class treatment;
        output out=total sum=sum;


data freq_data;
        set freq_data;
        if allstroke=1;


data person_years;
        merge total
              freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;


proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Stroke no. of events (rate/100 person-yr)';


proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_allstroke*allstroke(0) = treatment /risklimits;
        title3 'Table 2 - Stroke hazard ratio';


proc freq data = outcomes;
        tables chf;
        title3 'Table 2 - Heart failure';


proc freq data = outcomes;
        tables chf /out=freq_data;
        by treatment;
        title3 'Table 2 - Heart failure by treatment group';


proc means data = outcomes sum noprint;
        var t_chf;
        class treatment;
        output out=total sum=sum;
```

33

```
data freq_data;
      set freq_data;
      if chf=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Table 2 - Heart failure no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_chf*chf(0) = treatment /risklimits;
      title3 'Table 2 - Heart failure hazard ratio';

proc freq data = outcomes;
      tables cabg;
      title3 'Table 2 - CABG';

proc freq data = outcomes;
      tables cabg /out=freq_data;
      by treatment;
      title3 'Table 2 - CABG by treatment group';

proc means data = outcomes sum noprint;
      var t_cabg;
      class treatment;
      output out=total sum=sum;

data freq_data;
      set freq_data;
      if cabg=1;

data person_years;
      merge total
            freq_data;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Table 2 - CABG no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_cabg*cabg(0) = treatment /risklimits;
      title3 'Table 2 - CABG hazard ratio';

proc freq data = outcomes;
      tables carotid;
```

34

```
        title3 'Table 2 - Carotid endarterectomy';

proc freq data = outcomes;
        tables carotid /out=freq_data;
        by treatment;
        title3 'Table 2 - Carotid endarterectomy by treatment group';

proc means data = outcomes sum noprint;
        var t_carotid;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if carotid=1;

data person_years;
        merge total
              freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Table 2 - Carotid endarterectomy no. of events (rate/100 person-yr)';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_carotid*carotid(0) = treatment /risklimits;
        title3 'Table 2 - Carotid endarterectomy hazard ratio';

proc freq data = outcomes;
        tables primary /out=freq_data;
        by treatment;
        title3 'Figure 3 - Primary outcome by treatment group';

proc means data = outcomes sum noprint;
        var t_primary;
        class treatment;
        output out=total sum=sum;

data freq_data;
        set freq_data;
        if primary=1;

data person_years;
        merge total
              freq_data;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr)';
```

35

```
proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_primary*primary(0) = treatment /risklimits;
      title3 'Figure 3 - Primary outcome hazard ratio';

proc freq data = outcomes;
      tables cvdhis /out=freq_data;
      by treatment;
      where primary = 1;
      title3 'Figure 3 - Primary outcome*Cardiovascular disease at baseline by treatment group';

proc means data = outcomes sum noprint;
      var t_primary;
      class treatment;
      where cvdhis = 'No';
      output out=total sum=sum;

data freq_data_no;
      set freq_data;
      if cvdhis = 'No';

data person_years;
      merge total
            freq_data_no;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where CVD history = No';

proc means data = outcomes sum noprint;
      var t_primary;
      class treatment;
      where cvdhis = 'Yes';
      output out=total sum=sum;

data freq_data_yes;
      set freq_data;
      if cvdhis = 'Yes';

data person_years;
      merge total
            freq_data_yes;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where CVD history = Yes';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
```

36

```
        model t_primary*primary(0) = treatment /risklimits;
        where cvdhis='No';
        title3 'Figure 3 - Primary outcome hazard ratio where CVD history = No';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where cvdhis='Yes';
        title3 'Figure 3 - Primary outcome hazard ratio where CVD history = Yes';

proc freq data = outcomes;
        tables female /out=freq_data;
        format female sexf.;
        by treatment;
        where primary = 1;
        title3 'Figure 3 - Primary outcome*Sex by treatment group';

proc means data = outcomes sum noprint;
        var t_primary;
        class treatment;
        where female = 0;
        output out=total sum=sum;

data freq_data_no;
        set freq_data;
        if female=0;

data person_years;
        merge total
              freq_data_no;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
        var treatment no_of_events;
        title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Sex=Male';

proc means data = outcomes sum noprint;
        var t_primary;
        class treatment;
        where female=1;
        output out=total sum=sum;

data freq_data_yes;
        set freq_data;
        if female=1;

data person_years;
        merge total
              freq_data_yes;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;

proc print data = person_years;
```

37

```
        var treatment no_of_events;
        title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Sex=Female';


proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where female=0;
        title3 'Figure 3 - Primary outcome hazard ratio where Sex=Male';


proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where female=1;
        title3 'Figure 3 - Primary outcome hazard ratio where Sex=Female';


proc freq data = outcomes;
        tables racevar /out=freq_data;
        by treatment;
        where primary = 1;
        title3 'Figure 3 - Primary outcome*Race by treatment group';


proc means data = outcomes sum noprint;
        var t_primary;
        class treatment;
        where racevar = 'African American / Black (not Hispanic)';
        output out=total sum=sum;


data freq_data_black;
        set freq_data;
        if racevar = 'African American / Black (not Hispanic)';


data person_years;
        merge total
              freq_data_black;
        by treatment;
        no_of_events = count/(sum/365.25/100);
        if _type_ = 1;


proc print data = person_years;
        var treatment no_of_events;
        title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Race=Black';


proc means data = outcomes sum noprint;
        var t_primary;
        class treatment;
        where racevar = 'Hispanic';
        output out=total sum=sum;


data freq_data_hispanic;
        set freq_data;
        if racevar = 'Hispanic';


data person_years;
        merge total
              freq_data_hispanic;
        by treatment;
```

```
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Race=Hispanic';

proc means data = outcomes sum noprint;
      var t_primary;
      class treatment;
      where racevar = 'Other/Mixed';
      output out=total sum=sum;

data freq_data_other;
      set freq_data;
      if racevar = 'Other/Mixed';

data person_years;
      merge total
            freq_data_other;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Race=Other';

proc means data = outcomes sum noprint;
      var t_primary;
      class treatment;
      where racevar = 'White';
      output out=total sum=sum;

data freq_data_white;
      set freq_data;
      if racevar = 'White';

data person_years;
      merge total
            freq_data_white;
      by treatment;
      no_of_events = count/(sum/365.25/100);
      if _type_ = 1;

proc print data = person_years;
      var treatment no_of_events;
      title3 'Figure 3 - Primary outcome no. of events (rate/100 person-yr) where Race=White';

proc phreg data=outcomes;
      class treatment (ref='Diabetes Support and Education');
      model t_primary*primary(0) = treatment /risklimits;
      where racevar = 'African American / Black (not Hispanic)';
      title3 'Figure 3 - Primary outcome hazard ratio where Race = Black';

proc phreg data=outcomes;
```

```
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where racevar = 'Hispanic';
        title3 'Figure 3 - Primary outcome hazard ratio where Race=Hispanic';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where racevar = 'Other/Mixed';
        title3 'Figure 3 - Primary outcome hazard ratio where Race = Other';

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        where racevar = 'White';
        title3 'Figure 3 - Primary outcome hazard ratio where Race=White';


title3 'Figure 2a';
ods graphics on;

ods csv file = '/prj/niddk/ims_analysis/Look_AHEAD/private_created_data/outcomes_dsic.csv';
PROC LIFETEST DATA=outcomes plots=survival(atrisk=0 to 10.4 by 2 nocensor failure);
TIME  primary_years * primary (0);
strata randarm;

RUN;
ods csv close;

proc import datafile = '/prj/niddk/ims_analysis/Look_AHEAD/private_created_data/outcomes_dsic.xls'
        dbms = xls
        out = outcomes_control;
        sheet = 'Control';
        getnames = yes;
run;

proc import datafile = '/prj/niddk/ims_analysis/Look_AHEAD/private_created_data/outcomes_dsic.xls'
        dbms = xls
        out = outcomes_intervention;
        sheet = 'Intervention';
        getnames = yes;
run;

proc contents data = outcomes_control;
proc contents data = outcomes_intervention;

proc sort data = outcomes_control nodupkey;
        by primary_years failure_control;

proc sort data = outcomes_intervention nodupkey;
        by primary_years failure_intervention;

data outcomes_both;
        merge outcomes_control (in=val1)
              outcomes_intervention (in=val2);
        by primary_years;
```

40

```
        if val1 or val2 and (failure_control ne . or failure_intervention ne .) then output;

ods csv file = '/prj/niddk/ims_analysis/Look_AHEAD/private_created_data/outcomes_dsic_v2.csv';
        proc print data = outcomes_both noobs;
run;
ods csv close;

proc phreg data=outcomes;
        class treatment (ref='Diabetes Support and Education');
        model t_primary*primary(0) = treatment /risklimits;
        title3 'Figure 2 - Hazard Ratio';
```

41