

Look AHEAD Continuation and Extension Protocol Issue and Revision Dates

21st Revision – August, 13, 2019

20th Revision – May 02, 2018

19th Revision – March, 2018

18th Revision – November 13, 2017

17th Revision – May 04, 2017

16th Revision – November, 2016

15th Revision – January 19, 2016

14th Revision – July 27, 2015

13th Revision – August 18, 2014

12th Revision – June 6, 2014

11th Revision – Look AHEAD Continuation Trial - June 27, 2013

Summary of Changes to Protocol 21, August 2019

Changed headers to reflect Version 21 and date

Changes Footers to reflect version 21 and date

Page 3 added twenty-first revision

Page 40 removed fasting from the statistical analysis plan participants have the option for doing a non- fasting visit. We are not currently collecting samples that require a fasting visit. Our participants are getting older and some who are on insulin have an increased risk for hypoglycemia. The unknown benefit of saving fasting blood samples is not worth the very small, but potentially devastating, risk of hypoglycemia associated with fasting for a visit. So the study voted to do away with the fasting requirement for visits. This would also facilitate clinic scheduling.

Summary of Changes for Look AHEAD Protocol 20, May 2018

Page 1- 57 Header and Footer changed to reflect the Twentieth Revision

Page 3 Twentieth Revision May 2018 added

Page 13 sub studies spelling corrected.

Page 15 Waist girth is now included in Table 1 Study Measures and Time Points and will be done at the 2nd clinic visit.

Page 16 Shipley Vocabulary Test Removed

Page 26 Waist Circumference added to Physical measures and ankle reflexes were deleted. It was taken out in Protocol 19 but was missed on this page.

Page 27 Font changed to be consistent with the rest of the document.

Page 28 Risks of Cognitive Tests underlined to be consistent with the rest of the document.

Summary of changes to Protocol 19, March 2018

Changes to the Protocol reflect additional funding to repeat the cognitive testing which was done in the Look AHEAD study Cohort (protocol Revision 11, 2013). In addition, funding is being provided to analyze samples that were previously stored.

Header and footer changed March 2018

Page 3 Nineteenth Revision March 2018 3. Page 4 Back ground including adding including Alzheimer's and related diseases.

Page 5 spelled out National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Page 6 Tertiary aims Assess the legacy of behavioral intervention on the prevalence of cognitive impairment and rates of cognitive decline and Identify factors related to cognitive resilience.

Page 10 two changed to co-primary outcomes

Page 12 ankle reflexes were removed from the test as confirmation of was difficult with reduced staff. Self-report amputation was added as it had been deleted by mistake. These were part of the last amendment for the Coordinating Center but not were not updated by the clinical centers.

Page 13 cognitive function was added back to the protocol and the Lab sub-study using stored samples was added.

Page 15- 16 all the cognitive assessments were added back to the study as they were in the past.

Page 19 cognitive training and certification for staff added back.

Page 21 Dexa deleted and DXA used for consistency.

Page 22 Wording added in the event that participants has concerns about cognitive abilities clinical centers will provide an IRB approved list of resources available in their community and encouraged to contact their PCP. New reference added.

Page 23 New references added.

Page 25 - 34 Informed consent updated to reflect cognitive tests added back in to the study visit, the risks and agreement check boxes and that they will be paid an additional \$25.00 for the study visit.

Look AHEAD Extension Study Protocol 18, November 2017

Summary of Changes

Header and footers changed to reflect Protocol 18 November 2017

Page 1-14 Pittsburgh Fatigability, Loneliness, and Resilience forms will be removed for the 2 year exam.

Memo:

To: Look AHEAD Clinical Centers

From: Judy Bahnson Look AHEAD Coordinating Center

Subject Corrections to Protocol Numbering on the Look AHEAD Protocol

It came to my attention that the Look AHEAD sites were showing the most recent protocol amendment as Protocol 16 instead of protocol 17. In review of the Look AHEAD protocols and discussion with Brian Moore, chairman of the Wake Forest IRB, we found that two mistakes had occurred; the first was in the timing from protocol 15 and 16 which were approximately one month, and that the November 20th 2015 protocol had been miss-numbered as 15 instead of Protocol 16.

We have reviewed the protocols and ask you to include this memo to your IRB as a note to file.

The Look AHEAD Protocol 15 was approved November 20, 2015 and miss-numbered as Protocol 15 it should have been numbered as Protocol 16.

The Look AHEAD Protocol 17 was approved by the Wake Forest IRB on 5/5/17 I am attaching the editorial changes that were made below to the past 3 protocols.

Summary of Changes to Protocol 15, January 2016

Page 1

Formatting changed so that "Approved by the Look AHEAD Protocol Review Committee" changed to be all on 1 line instead of 2 lines.

Page 5

Correction to BMI to read as the original eligibility criteria of BMI ≥ 25 kg/m² (≥ 27 kg/m² if currently taking insulin) the 27 was a typo 27 was only for insulin users.

Page 10 and 12

Spelling of Fatigability corrected

Page 13

Sentence changed to say that meeting will occur in person/ by phone, webinar, or other means according to available technology.

Summary of Changes to Protocol 16, November 2016

Editorial changes not affecting protocol, re wording for clarity and correcting typos.

Pages 6, 7, 9, 10, 13, 37

Page 14 whole blood added to the stored sample list. We are not doing any additional collection but we are saving and storing the blood leftover from the HbA1c test.

Page 16 Safety Committee added under study organization. The Safety Committee reviews safety events as needed and any clinic related serious adverse event.

Summary of Changes to Protocol 17, May 2017

Changed header and footer to correct dates and protocol number

P.3: Seventeenth Revision May 4, 2017

Section 9 corrected to be 1.9

P. 19 -20 Safety Management Alert table replaced to increase alert monitoring and clinic actions for blood pressure, eGFR, Cumulative BMD decreases, PHQ-9

Questionnaire for alerts and the emergency action plan.

Protocol 14(LA-C) to Protocol 15 (LA-E) Summary of Changes for IRB

Formatting, grammatical corrections and header/footers updated throughout the document

Page 1- Removed text “Approved by the Look AHEAD Protocol Review Committee”;

Added timelines to list of revisions for Look AHEAD, Look AHEAD C and Look AHEAD E

Page 1 and page 3- title changed Continuation replaced with Extension Study

Page 2- added “Fifteenth Revision November 10, 2015

Page 3- In 1st paragraph 3rd line corrected “end point” into a compound word endpoint; Added “The timeline for Look AHEAD through Look AHEAD-C is shown in Figure 1.” To bottom of 3rd paragraph; Added Acronym for Look AHEAD Extension in the last paragraph

Page 3 thru page 6- Section 1 title and text updated to reflect the Background information pertaining to the Look AHEAD-Continuation

Page 6- Second paragraph, the last sentence to clarify the timeline for Look AHEAD-C was added. And Section 2 updated to list Look AHEAD Extension Study objectives

Page 7 thru page 18- Section 3 updated to describe the Study Population

Page 8- Section 3a last sentence in the first paragraph text was removed “ by their study number”

Page 9- Section 3c Clarification for the percentage of enrollment; Section3d removed reference to 69% of the Look AHEAD cohort

Page 16- returned text to original state removed “BRC” set back to “coordinating center”; last sentence in paragraph 1 text clarified surrogate consenting.

Page 18- first paragraph removed text “Biostatistics Research Center”; last sentence “Confidentiality” as added to the last sentence and coordinating center reference removed;

Section 3g text removed in first sentence, “the Look AHEAD trial” is now “Look AHEAD”

Page 18 thru page 24- Section 4 updated to describe the Look AHEAD E Study

Outcomes and Scheduling of ascertainment of outcomes

Page 19- first paragraph last sentence revised to drop “three” description of adjudication committee; second paragraph “attempt to” was removed from the second sentence; last paragraph “Short Physical Performance Battery” removed.

Page 20- first paragraph third and fourth sentences removed (PMMD reference); fourth paragraph first sentence divided into two sentences, added “Supporting analysis will also include;” MOS” spelled out in fifth paragraph;

Page 21- Clarified sample size for accelerometry in paragraph two; Bone mineral content added to the fifth paragraph

Page 24- table 1 Accelerometry clarified to be only selected sites

Page 24 and page 25- Section 5 updated statistical considerations for Look AHEAD E Study

Page 25 second paragraph “three” removed from description of adjudication committee Page

25 and page 26- Section 6 updated to describe the Look AHEAD E study organization

Page 26 first paragraph revised schedule for committee meetings “up to twice a month” to

“regularly”; second paragraph text “three” removed and text for “NIDDK Project Scientist” replaced with “NIDDK representative(s)”

Page 26 thru page 27- Section 7 updated to describe the Quality Control process of the Look AHEAD E study

Page 27- third paragraph “committee” removed from the last sentence for DSMB; fourth paragraph clarifications to sentences 1 thru 3

Page 28 thru page 31- Section 8 updated to describe the Centralized Data Management System for the Look AHEAD E study

Page 31 and page 32- Section 9 updated to describe the Confidentiality of the Look AHEAD E study process

Page 32- section 10- first sentence clarified trial is Look AHEAD

Page 32 thru page 34- Section 10 - Education/Retention activities removed and Section for Safety Management updated to describe the process for the Look AHEAD E Study

Page 34 thru 39- Section 11 References have been updated for the Look AHEAD E study

Page 40 thru page 52- Appendix 1: Informed Consent updated for the Look AHEAD E study

Page 41-last paragraph text corrected in the third sentence replaced “ask” with “answer” Page

42- Social Event, modified last sentence to “fellow participants” to clarify who attends the social events; removed text “other event (such as heart attack)” from the telephone call section, discharge summaries are no longer collected for other events.

Page 44- Section for “What About My Health Information?” removed “audiotapes” from the examples of PHI in the last sentence and made all health information references match “protected health information”

Page 45- 5th bullet and Page 51 third bullet- list of sponsors, removed NHLBI and NIH Office of Women’s Health and added National Institute of Aging (NIA); moved paragraph type of disclosure to the paragraph after bullets: “Some of these people, agencies, and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study.”

Page 50- first sentence revised text for Look AHEAD-E and corrected fourth sentence to clarify when medical records will be collected

Page 51- Verbal Consent section for confidentiality, corrected the spelling of safety. Page 53 thru 97- Appendix 2: Statistical Analysis Plan updated for the Look AHEAD E study

Page.....53 Statistical Analysis Plan Version date updated to December 14,2015;

Page 54- second sentence clarified goals for LA-E are distinct from LA or LA-C Page 55- section Study schedule text removed in first sentence. Table 1 removed from statistical analysis plan.

Page 56- Exhibit 1 the frequency for the health events was added

Page 57- First paragraph clarified the approximate time for exam; last paragraph was edited for clarity

Page 59- first paragraph after bullets revised to add clarity for statistical power

Page 61- section for Power- clarified 509 deaths

Page 62 and 63- last paragraph for SPPB- first sentence 4 meters changed to 8-feet. Year for Guralnik paper corrected to 1993. Second sentence was removed; third sentence text changed to clarify which value will be used for grip strength. Page 72- Supporting analyses, last sentence removed

Page 74- Weight Change – Physical activity assessment clarified and wrist actigraph identified as device to be used.

Page 75-last paragraph, Body composition and bone density time points clarified

Page 76- Supporting analyses: text changed to clarify and provide an example of events.

Page 81 References-

Removed: Guralnick - A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission.

Removed: Simonsick EM, Newman AB, Nevitt MC, et al. Measuring higher level physical function in well-functioning older adults: expanding familiar approaches in the Health ABC study Jeopardy

14th Revision – July 27, 2015

Summary of IRB Changes Page 6 and Page 22 the dates for data collection have been changed to reflect the date of the No Cost Extension of 1/31/2016

Summary of Changes to Look AHEAD Protocol 13th Amendment

Page 1

1. Header Changed to reflect August 18, 2014^h date
2. Thirteenth Revision added

Page 2

1. And mortality added to study outcomes

Page 7

1. Paragraph added on mortality under secondary aims.

Page 8

1. Dates corrected for closeout and analysis corrected

Page 10

1. Of reflexes added to sentence.

Page 22

1. Dates corrected for closeout and analysis corrected

Page 31 – 38

1. ADDENDUM TO ANALYSIS PLAN: Action for Health in Diabetes Continuation (Look AHEAD-C)

Protocol changes

P. 1 Twelfth Revision June 6, 2014

P.7 Dates changed to reflect the additional funding with No-cost extension to November 30, 2015.

P. 9 Measuring waist and height were left out of this section but are part of the original protocol.

P. 11 Spacing between words corrected

P.10 Neuropathy tests include mono-filament, reflex testing, and vibration test using a tuning fork which was left out of this section.

P.13 Correction to grammar: word and added

P.14 Correction to grammar: comma added

P.20 Correction to grammar: comma added

P.22 Correction to grammar: comma added dates changed to reflect the additional No-cost extension funding to November 30, 2015. Sentence re-worded for clarity, as depending when the participant was randomized they could have 2 or 3 phone calls.

11th Summary of Protocol Revision 7/23/13.

1. In September 2012, the NIDDK, acting on the recommendation of the data and safety monitoring board (DSMB), discontinued the lifestyle intervention arm of Look AHEAD and recommended that the study should proceed as an observational cohort study. This was because there was a very low likelihood of finding a difference in the primary outcome of cardiovascular disease morbidity and mortality between the lifestyle and diabetes support and education groups even with further intervention. Both groups had a low incidence of cardiovascular disease and death compared to previous cohorts with diabetes. The intervention was not stopped as a result of safety concerns. We submitted our Protocol 10th Revision dated 11/7/12 and received IRB approval on 01/02/13.
2. We submitted our Continuation Review and received IRB approval July 16, 2013.
3. The Look AHEAD Principal Investigators submitted a proposal “Action For Health In Diabetes Continuation” to the NIDDK December 20, 2012. The DSMB met June 19, 2013 to review the continuation protocol and gave authorization to the NIDDK to approve the protocol based on identified contingencies being met. The NIDDK gave written notice of approval to the Look AHEAD investigators on June 28, 2013.
4. The documents identified in #3 above (DSMB report dated 6/19/13 and NIDDK letter of approval dated 6/28/13) are attached to the addendum to support the current request for approval for the continuation. In addition, the description of changes (2.a) and justification of changes (2.b) were previously submitted on 7/19/13.
5. As a result of the extensive revisions and newly added measures found in the protocol addendum in the “Specific Aims”, both primary and secondary, it would extremely complicated and confusing to provide a redlined copy of the changes that comprise the addendum. Therefore, with the recommendation of the IRB reviewer, the above summary of activity is being submitted to support the addendum to the protocol.