

WEIGHT CHANGE SUBSTUDY

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WEIGHT CHANGE SUBSTUDY

1. Background and hypotheses

The Weight Change Substudy will describe the natural history, frequency and time course of weight loss and weight gain. Those with weight changes, identified at the Year 4 annual clinic visit, will be evaluated for further weight change, and the net changes in lean mass will be assessed at the clinic visit. While the annual exams in Health ABC will provide data to describe annual weight changes, the goal of the substudy is to describe the short term trajectory of weight change and associated short term outcomes in the year following the identification of the weight change. Weight changes may occur gradually or have a more steep trajectory. A proportion of those with weight changes may return to baseline weight, while others may show continued gain or loss.

Body weight peaks in late middle age, and generally declines in late life, but is likely to be a dynamic and heterogeneous process. Weight loss of 5% or more in older adults is associated with increased mortality. The proportion of individuals with weight loss who have reversible or preventable illness has not been well described. In Health ABC, the Acute Respiratory Infection Substudy (Flu Substudy) will evaluate weight changes in those with acute illness. However, weight changes may also occur in the absence of acute illness. In the Cardiovascular Health Study (CHS) cohort, about 20% of those with a 5% weight loss had a hospitalization or new diagnosis of cancer in the year preceding the weight loss. This suggests that the majority of those who have weight loss in Health ABC may not have an obvious serious illness to explain the weight loss. This substudy will provide the data to evaluate the importance and prevalence of various short-term patterns of weight change.

Hypotheses:

1. Participants characterized as having a weight change will be more likely to have had a recent health event than those who are weight stable, but the majority of participants with changes will have had no specific health event.
2. There will be a heterogeneous pattern of subsequent weight changes. A small proportion of participants will have continued weight change in the next 6 months.
3. Participants with continued weight loss will have higher markers of inflammation and lower markers of anabolic hormones than those who remain stable or regain. These participants will also have a greater increase in these markers in the 6 month follow-up period than those who are weight stable or those who regain weight.

4. Participants who are gaining weight will have a higher prevalence of mobility impairment and congestive heart failure or knee osteoarthritis, and may have an increased incidence of adverse health events.

2. Overview

Participants with a weight change of 5% or more will be classified as weight losers or weight gainers, and the remaining participants, if they have not gained or lost weight over the past 12 months, will be classified as weight stable. All participants who have a qualifying weight change ($\pm 5\%$), plus a random sample of those who have been weight stable will be enrolled in this substudy.

Participants who experienced a change in weight and a sample of those who are weight stable, will be tracked for 6 months to determine the natural history of the weight change. Follow-up will include a home visit (or, if the participant prefers, a clinic visit) in 6 months to reweigh the participant, and to draw a blood sample. New health events will be assessed using the standard Semi-Annual Telephone Contact form which will be completed for all Health ABC participants, including the participants enrolled in the Weight Change Substudy. Consent will be obtained prior to the additional visit. The annual DXA scan will be used to evaluate lean mass changes. During the 6-month follow-up visit, those evaluated for further weight change will be classified as having additional weight loss, as having re-gained their weight, or as remaining stable at the Year 4 weight.

3. Sample

The substudy will include all weight changers, defined as participants who experienced a $\geq 5\%$ weight gain or loss between the Year 3 and Year 4 annual clinic visits. Assuming that 2,751 participants will be enrolled as of the Year 4 clinic visit (90% of 3057), and that 7% will be “weight gainers” and 7% will be “weight losers,” a total of about 400 ($2,751 \times 14\%$) extra contacts will be needed, or 200 at each clinic. Each clinic will also evaluate 100 controls who are weight stable as a comparison group. This will result in six extra contacts per clinic per week (based on 50 weeks/year).

The Weight Change Substudy will be conducted over a one year period, starting with the Year 4 clinic visit. A participant enrolled in the Weight Change Substudy may also be enrolled in the Flu Substudy. The flu health event may be the primary explanation for the weight change.

4. Weight Change Substudy eligibility assessment

Cases and controls will be identified during the Year 4 clinic visit.

- A Weight Change Substudy Eligibility Assessment form will be filled out for every participant during their Year 4 clinic visit. Examiners will look at the participant's Data from Prior Visits Report to see what their weight was from their Year 3 clinic visit, and they will look at the participant's Year 4 Clinic Visit Workbook to find the participant's weight at the Year 4 clinic visit.
- Printed on the participant's Data from Prior Visits Report will be two numbers based upon their Year 3 weight:
 1. a number that represents a 5% weight increase, and
 2. a number that represents a 5% weight decrease.

The examiner should check the Data from Prior Visits Report to answer Question #3 on the Weight Substudy Eligibility Assessment form: "Did the participant's weight change (either a gain or loss) by 5% or more since their Year 3 clinic visit?" and base their answer on the numbers that have already been calculated and printed on this report.

For example, if the examiner reads on the Data from Prior Visits Report that the participant weighed 140 kg at their Year 3 clinic visit, 147 kg will be listed on the report as a 5% weight gain and 133 kg would be listed as a 5% weight loss. If the participant weighs 150 kg at their Year 4 clinic visit, you would answer "Yes" to Question #3 ("Did the participant's weight change [either a gain or loss] by 5% or more since their Year 3 clinic visit?") and choose the "Gained weight" response option. You will then be instructed to go to the Weight Change Substudy Workbook because this participant is eligible to be part of the Weight Change Substudy.

- If the participant did not gain or lose 5% of their weight since their Year 3 visit, you would ask the participant Question #4 on the Weight Change Substudy Eligibility Assessment form: "Did you gain or lose five or more pounds at any one time over the past 12 months. If they answer "Yes," they are not eligible to be a weight-stable control for the Weight Change Substudy. If they did not gain or lose five or more pounds at any one time over the past 12 months, and if their weight has not gone up or down 5% or more since Year 3, they are eligible to be a weight-stable control. Refer to the Weight Change Substudy Control Selection Log to see if they should be selected to be a weight-stable control.

5. Administration of Weight Change Substudy Workbook

The Weight Change Substudy Workbook will be administered during the Year 4 clinic visit to participants classified as weight changers and to the controls. Included in this

workbook are several questions about appetite, diet, weight, physical function, and physical activity.

Because questions about intent to change weight and attributable causes of weight change are very important, participants identified as weight changers will be asked about whether or not they were trying to lose or gain weight, and whether they know the cause of their weight gain or loss. Participants who have lost weight and say that they have been trying to lose weight will be asked about the methods they used to lose the weight. Participants who have lost weight and were not trying to lose weight will be asked what they think caused the weight loss. This information will be used by investigators to adjudicate “explained vs. unexplained” weight change and to help determine the major cause of the weight change.

6. Six-month follow-up visit

Participants who have been classified as weight changers and the control group will be seen again for a follow-up visit 6 months after their Year 4 clinic visit. This will be a brief visit, either in the participant’s home, or if they prefer, in the clinic, and will include a weight measurement, blood draw and the administration of a follow-up questionnaire.

After the weight is obtained, the weight change will be classified as further gain, further loss, or as stable since the Year 4 clinic visit.

For those with further weight change at 6 months, questions similar to those on the Weight Change Substudy Workbook will be asked again. Participants previously defined as stable may have a weight change at this visit.

The usual Semi-annual Telephone Contact will assess interim health events and can be asked at the 6-month weight change substudy follow-up visit or on the phone at the time of scheduling this visit.

6.1 Lab instructions for weight change substudy 6-month follow-up visit

One 5 mL serum tube should be drawn from the participant at their weight change substudy 6-month follow-up visit. The serum sample should be allowed to clot, and should be centrifuged, and aliquoted into four 0.5 mL aliquots that will be frozen and sent to LCBR. Special barcode labels with a distinct series of barcode numbers (100-xx and up for Memphis and 200-xx and up for Pittsburgh) have been sent to each field center. Make absolutely sure that the Phlebotomy and Laboratory Processing Forms in the Weight change Substudy Follow-up Workbook (pages 8-11) accompany the cryovials to LCBR. Please put the weight change substudy samples in a separate

freezer box from the regular Year 4 samples. These boxes may be shipped in the same weekly dry ice shipment as the other samples, however. Do not make blind duplicate aliquots with these samples.

7. Determination of the cause of the weight change

The Year 4 Weight Change Substudy Workbook includes several questions regarding whether or not the weight change was intentional and assesses potential reasons for the weight change. This information will be reviewed by the investigator. In addition, ask the participant whether or not there is an explanation for this weight change. This should be recorded as a simple narrative in the participant's chart for the investigator to review. Because not all possible reasons for weight change are included in the Year 4 Weight Change Substudy Workbook, this narrative may be very helpful in determining whether additional action is warranted. All of the cases of significant weight change will be reviewed by an investigator or designee to determine whether additional action, such as sending a letter (Appendix 1) to the participant's health care provider, is warranted.

8. Alert values

Participants with steep trajectories present a concern for occult disease (such as cancer or heart failure). Those with weight change (gain or loss) of $\geq 10\%$ at the Year 4 clinic visit or a total of $\geq 10\%$ at the subsequent 6 month follow-up visit will have their study chart reviewed by an investigator at the field center. Participants with weight change of $\geq 10\%$ that appears to be unexplained, or a weight gain that is thought to be due to undiagnosed fluid retention (renal, hepatic or heart failure) will have the weight change brought to the attention of their physician with the participant's permission. The number of such cases would be a small proportion of the weight changers.

To determine whether or not a participant has gained or lost $\geq 10\%$ of their weight, check the Data from Prior Visits Report to see what their weight was at their last visit. Move the decimal point to the left one digit. Subtract that number from their previous weight to see what a $\geq 10\%$ loss would be and add that number to their Year 3 weight to see what a $\geq 10\%$ gain would be. For example, if a participant weighed 150.0 kgs at their Year 3 clinic visit, you would subtract 15 from 150.0. If the participant weighs 135 kg or less at their Year 4 clinic visit, this would represent a $\geq 10\%$ weight loss.

9. Quality assurance

9.1 Training requirements

The examiner requires no special qualifications or prior experience to perform this assessment. Training should include.

- Read and study operations manual chapter on the Weight Change Substudy
- Discuss protocol and data collection forms with local expert or QC Coordinator

9.2 Certification requirements

- Complete training requirements
- Recite eligibility criteria for cases
- Recite eligibility criteria for controls
- Observation and evaluation of two to three *mock* Weight Change Substudy eligibility assessments and interviews (at least one mock interview should be observed by the QC Coordinator or their designate).
- Observation and evaluation of one *actual* Weight Change Substudy eligibility assessment and interview by the QC Coordinator or their designate.
- Complete two Weight Change Substudy Eligibility Assessment forms and two Weight Change Substudy Workbooks and have reviewed by QC Coordinator:

9.3 Quality assurance checklist

- Records correct Year 3 weight on the Weight Change Substudy Eligibility Assessment form (same as the weight that is printed on the Data from Prior Visits Report).
- Records correct Year 4 weight on the Weight Change Substudy Eligibility Assessment form (same as the weight recorded on page 2 of the Year 4 Clinic Visit Workbook).
- Correctly determines whether the participant should or should not be included in the Weight Change Substudy as a case.
- Correctly determines whether the participant should or should not be included in the Weight Change Substudy as a weight-stable control.
- Asks the correct first question to begin the Weight Change Substudy Workbook depending upon whether the participant is a weight gainer, weight loser, or weight-stable control.
- Reads questions exactly as written on the Weight Change Substudy Workbook (same order, same wording).

- Response options read/not read when appropriate
- Follows skip pattern in Weight Change Substudy Workbook.
- Accurately records participant's responses on Weight Change Substudy Workbook.
- Follows the guidelines for recording data on scannable forms.
- At the end of interview, reviews Weight Change Substudy Workbook for completeness.
- Correctly completes form

Interviewing techniques

- Reads slowly, speaks clearly and uses appropriate inflection when speaking
- Reduces the chance of bias by maintaining a neutral attitude towards the participant
- Able to elicit accurate and complete information using non-directive probes
- Keeps interview on track by presenting questions at a regular pace.
- Focus participant's attention on questions while always being polite.
- Treats participant with respect
- Maintains a professional and friendly manner

APPENDIX 1

Weight Change Alert Letter for Physician

September 13, 2000

Charles Cutler, M.D.
512 Hamilton Road
Marion, PA 19066

Dear Dr. Cutler:

On September 1, 2000, _____ was seen at the Health ABC Research Clinic.

At the last clinic visit one year ago, his/her weight was _____ lbs (kgs)
The weight today was _____ lbs (kgs)

This weight is $\geq 10\%$ (more) (less) than one year ago.

All tests done for Health ABC were performed for research purposes only and will be used to describe the health status of men and women in their seventies and eighties who are taking part in this study. These tests are not intended to replace any tests that might be ordered for a specific clinical indication. Although we do not suggest a specific diagnosis or treatment, we hope this information is useful to you and your patient.

If you have any questions, please feel free to contact us at _____.
Thanks you for your support.

Sincerely,

Anne Newman, M.D., MPH
Health ABC Principal Investigator

Piera Kost