Chapter 6

Alerts

INTRODUCTION

This chapter addresses management of clinical concerns that may arise during the visit or related to the results of tests that are obtained.

Alerts: An "alert" is identified as a situation in which specific responses to questions, signs, or symptoms exist that should result in medical oversight by the principal investigator or designee.

Alerts may appear during the following six parts of the exam:

- Heart rate
- Blood Pressure
- CES-D
- Laboratory Analysis
- Living Conditions
- Carotid Ultrasound

Definitions and procedures:

Each field center may have differing procedures based on local standard operating procedures and institutional board requirements. However, the guiding principle for alerts is that any POTENTIALLY CLINICALLY SIGNIFICANT finding in the above six parts of the exam that is NOT KNOWN to the participant should be reported to them, and should also be reported to their physician if the participant has consented to the release of information to the MD). (NOTE that for this chapter, any reference to "participant" is understood to also, alternatively, refer to participant's legally authorized representative, as applicable.)

Immediate referral – Discuss with the field center-designated supervisory clinician and/or PI ("clinician") within 24 hours. The clinician will decide whether the finding warrants a phone call to the participant, and also whether a letter should be sent to the participant's physician (provided the participant has consented to release of the information to MD). Actions taken with regard to the alert will be documented in the participant's research chart.

Urgent referral – Discuss with clinician within 2 weeks of receipt of the information. The clinician will decide whether the finding warrants a phone call to the participant, and also whether a letter should be sent to the participant's physician (provided the participant has consented to release of the information to MD). Actions taken with regard to the alert will be documented in the participant's research chart.

Elective reporting – Normal or borderline results can be provided to the participant and/or reported to the participant's physician (with signed participant's consent) at the discretion of the field center PI.

Heart Rates Alerts:
Heart rate will be measured by Omron HBP-1300 Professional Blood Pressure Monitor or manufacturer equivalent. Because some irregular heartbeats are not transmitted to the monitor, pulse rate can be inaccurate compared to direct measurement of heart rate by electrocardiogram or direct auscultation of the

heart. Heart rates can be low in older adults because of medications or heart disease. Very low heart rates assessed by automated machine may require further clinical assessment to determine significance.

IMMEDIATE referral levels within 24 hours:

Rate > 150
Rate < 40

URGENT referral alert levels requiring referral (within two weeks) are:

Rate > 130
Rate < 50

Blood Pressure Alerts:

The blood pressure values below and urgency for clinical follow-up are based on the recommendations of the Joint National Commission on Blood Pressure, 8th guidelines published in 2013 and further guidelines from AHA that distinguish between older and younger adults.

IMMEDIATE referral alert levels (within 24 hrs) are:

Diastolic BP ≥ 120
Systolic BP ≥ 210

Systolic BP < 80 with symptoms of lightheadedness, severe weakness or fatigue.

URGENT referral alert levels (within two weeks) are:

Diastolic BP = 110-119
Systolic BP = 180-209

ELECTIVE REPORTING alert levels are:

Age 65 and older: SBP ≥ 150
DBP ≥ 100
Under age 65: Systolic BP > 140
Diastolic BP > 90

CES-D Alerts: A CES-D alert is identified as a score of greater than or equal to 14 on the modified 30 point CES-D (Depression) scale. In addition, any mention or indication during the clinic exam of suicidal tendencies is also to be considered an alert. If this occurs, the interviewer should let the participant know that it is possible to obtain help in dealing with such feelings. If the interviewer is uncomfortable with doing this, a supervisor may discuss this with the participant. The participant should be asked if he/she has a physician that could be consulted regarding depression. All staff concerns regarding depression must be reported to the study supervisor and the PI. Confidentiality is of utmost importance. Staff should not engage in discussion with family without the express permission of the participant. If the participant indicates he/she has no outside resource, the interviewer may provide a professional referral which has been selected by the site's Principal Investigator.

Laboratory Alerts:

Field centers may have differing procedures, based on local operating procedures and institutional board requirements for assessment of laboratory results reported as being "outside of normal range". However, upon receipt of the below listed lab values, the field center staff must consult the clinician on immediate or urgent basis as specified below:

IMMEDIATE:

WBC >18 x 10^9/L
WBC <2 x 10^9/L
Glucose >350 mg/dL
Glucose <50 mg/dL
Hemoglobin < 7 mg/dL

URGENT:

Cholesterol >360 mg/dL

LDL-cholesterol >260 mg/dL
Triglycerides >1000 mg/dL

Creatinine >2.0 mg/dL

Glucose >200 mg/dL
Glucose <60 mg/dL

Hemoglobin >17 g/dL
Hemoglobin <8 g/dL

Platelets >600 x 10^9/L
Platelets <60 x 10^9/L

Living Condition Alerts: During a home visit staff may encounter living conditions that are unsafe or unhealthy. Clinics should develop a local resource list of social services that may be able to address problems of cleanliness or lack of basic services such as heat or water. Any unsafe or unhealthy conditions including suspected abuse should be discussed with the clinic coordinator and principle investigator for follow-up based on local statutes.

Carotid Ultrasound Alerts:

Carotid Ultrasound images will be obtained in the field at the home visits to assess vascular health. The images will be screened at the reading center for clinically important findings. Management of potentially clinically significant findings will require communication between the reading center and the field center. The procedure for reviewing the scans will be as follows:

If the site personnel, at time of examination, believes there is a finding of potential clinical significance, he or she should alert the URL by indicating it on the log sheet and contacting the URL by email or phone. This should be done **within 48 hours**. The site personnel should not notify the study participant of any potential findings

at any time during the study visit. Details of reading potentially clinically significant ultrasounds can be found in the LLFS MOP, Chapter 15.

Ultrasound Alert Criteria

Immediate Alerts: Criteria for URL coordinating sonographer to notify URL Physician immediately:

1) An aneurysm or dissection which is currently leaking.
2) A moving structure within the carotid artery, i.e.: loose plaque, thrombus or intimal tear (recent trauma must have occurred).

Urgent Alerts: Criteria for URL Coordinating sonographer to notify URL physician within 48 hours

1) Any grade 3* plaque (> 50% diameter reduction, long view)
2) Any other reason for the sonographer to be concerned

Plaque Grade:** ***Plaque grade is an estimate of the extent of focal plaque in the carotid artery segments visualized. Each carotid segment (CCA, Bulb, ICA and ECA) is assessed and scored individually using the criteria that follows:

Estimated percentage of stenosis	Grade
1-29% (one small plaque)	1
30-50% (1 medium plaque or several small plaques)	2
50-100% (1 large. plaque or several plaques w/ at least 1 medium plaque)	3

Procedure for Reporting Alerts to Steering Committee and OSMB

All sites will report **IMMEDIATE** alerts during the Field Operations and Steering Committee conference calls.

These alerts will be documented in the LLFS Observational Study Monitoring Board (OSMB) report.

Study Documents Referred to in this Chapter:

- BP, Weight, Height and Waist Circumference Data Collection Form
- Mood and Personality Data Collection Form
- Spirometry Data Collection Form
- Ultrasound Log Sheet

Samples of possible letters follow. Each field center may have its own language and exact detailed notification procedures based on local medical practices, standard operating procedures, and institutional review board requirements.

Sample – MD Alert Letter

[DATE]

[PHYSICIAN NAME]
[ADDRESS]
[CITY, STATE, ZIP CODE]

Dear Dr. [INSERT NAME]:

Your patient is participating in the LONG LIFE Family Study, an observational study of exceptional survival in families. As part of this research study several tests were performed on [Insert Date]. [Because of unanticipated and/or clinically significant findings, a copy of the results is attached for your review.]

[PI may insert narrative here, if needed.]

All tests were performed for research purposes only and will be used to describe the health status of men and women 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 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 [Insert name, phone number of site-specific study clinical coordinator here].

Thank you for your support.

Sincerely,

[Insert site-specific PI Name Here]
Principal Investigator
LONG LIFE Family Study

Sample – Participant Alert Letter

[DATE]

[PARTICIPANT'S NAME]
[ADDRESS]
[CITY, STATE, ZIP CODE]

Dear [INSERT PARTICIPANT'S NAME]:

On [Insert Date] we performed a research interview and examination as part of your participation in the LONG LIFE Family Study, an observational study of exceptional survival in families. As part of this research study several tests were performed. [Enclosed are results from your visit.] As we discussed on the telephone, several of the results are unanticipated and/or of clinical importance. .

[PI may insert narrative here, if needed.]

All tests were performed for research purposes only and will be used to describe the health status of families who are taking part in this study.

These tests are not intended to replace any tests that your doctor may order for a specific reason, but do provide information about your health. Although we do not suggest specific diagnosis or treatment, we hope this information is useful to you and your physician. If you have any questions, please feel free to contact us at [Insert name, phone number of site-specific study clinical coordinator here].

Thank you for your support.

Sincerely,

[Insert site-specific PI Name Here]
Principal Investigator
LONG LIFE Family Study

Sample – MD Alert Letter, Ultrasound

[DATE]

[PHYSICIAN NAME]
[ADDRESS]
[CITY, STATE, ZIP CODE]

Dear Dr. [INSERT NAME]:

Your patient is participating in the LONG LIFE Family Study, an observational study of exceptional survival in families. As part of this research study an assessment of the prevalence of vascular disease using noninvasive measures to determine the degree of atherosclerosis and its associated risk factors was performed on [Insert Date]. [Because of unanticipated and/or clinical significant findings, a copy of the results is attached for your review.]

[PI may insert narrative here, if needed.]

We performed a carotid duplex scan on your patient which revealed evidence of atherosclerotic plaque(s) in the <left/right bulb/internal carotid artery/external carotid artery>. There is evidence of greater than ____% stenosis in the <left/right bulb/internal carotid artery/external carotid artery>. The ICA/CCA ratio is _____. These results should be interpreted within the context of your patient's overall health and cardiovascular risk factor profile.

The carotid duplex scan was performed for research purposes only and will be used to describe the health status of men and women who are taking part in this study. *This scan was limited in scope and did not include all the views and measurements usually made in a clinical vascular laboratory*. A standard noninvasive examination, performed in a clinical vascular laboratory, may be helpful in determining the clinical significance of this finding. Although clinical decisions cannot be made based upon the carotid duplex scan results, we hope this information is useful to you and your patient.

If you have any questions, or require any additional information, please do not hesitate to contact us [Insert name, phone number of site-specific study clinical coordinator here].

Thank you for your support.

Sincerely,

[Insert site-specific PI Name Here]
Principal Investigator
LONG LIFE Family Study

Sample – Participant Alert Letter, Ultrasound

[DATE]

[PARTICIPANT'S NAME]
[ADDRESS]
[CITY, STATE, ZIP CODE]

Dear [INSERT PARTICIPANT'S NAME]:

On [Insert Date] we performed a research interview and examination as part of your participation in the LONG LIFE Family Study, an observational study of exceptional survival in families. As part of this research study we performed a carotid duplex scan (ultrasound) to evaluate the degree of plaque build-up in the carotid arteries in your neck. [Enclosed are results from your visit.] Many people in the general population have some plaque in their arteries. As we have discussed with you over the phone, you do have a potentially clinically significant plaque(s) in the <left/right bulb/internal carotid artery/external carotid artery> and we have notified your designated physician(s) as well.

The carotid duplex scan is for research purposes only. *Therefore it is not the same as the carotid duplex scan used in a clinical vascular laboratory that your doctor might order*. A standard noninvasive examination, performed in a clinical vascular laboratory, may be helpful in determining the clinical significance of this finding. Although clinical decisions cannot be made based upon the carotid duplex scan results, we hope this information is useful to you and your physician.

[PI may insert narrative here, if needed.]

These tests are not intended to replace any tests that your doctor may order for a specific reason, but do provide information about your health. Although we do not suggest specific diagnosis or treatment, we hope this information is useful to you and your physician. If you have any questions, please feel free to contact us at [Insert name, phone number of sitespecific study clinical coordinator here].

Thank you for your support.

Sincerely,

[Insert site-specific PI Name Here]
Principal Investigator
LONG LIFE Family Study