Restoring Insulin Secretion

STUDY POLICIES

Manual of Procedures
Volume 1: General Procedures

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Chapter 13. Study Policies

13.1 Dualities of Interest (DOI)

13.1.1 Purpose of the Policy

A key element in monitoring relevant dualities of interest and in avoiding potential conflicts of interest is a system in which those serving the RISE Study provide disclosure of their interests. By disclosing such interests, we can determine if a duality of interest is relevant and can determine the steps that should be taken to minimize the likelihood that a conflict would arise. It is not the intent of this policy to prohibit or discourage anyone from participation in RISE but perceived or actual conflicts must be avoided in order to preserve the integrity of the studies being conducted in RISE.

13.1.2 Scope of the Policy

The following categories of staff are required to disclose any dualities of interest that may be relevant to RISE:

1. Members of the Board of Directors or other senior advisory roles with diabetes drug and other biomedical companies

2. Senior staff (including PIs, other senior scientific staff, NIDDK senior staff)

4. All speakers/presenters in continuing medical education events, including presenters of original scientific research at local or national scientific meetings;

5. Other members of committees and task forces whose work focuses on continuing medical education or focuses on scientific/medical issues that are of interest to the biomedical industry.

Reviewers of manuscripts need not make a formal disclosure of their relevant dualities of interest to RISE. They must follow the disclosure requirements of the respective journal. However, reviewers are encouraged to disqualify themselves from reviewing any manuscript that deals with a matter in which they or an immediate family member has a direct interest.

13.1.3 Types of Dual Interests that Should be Reported

The following relationships must be disclosed:

1. Employment. The name and nature of all employers must be disclosed.

2. Membership on the board of directors or any fiduciary relationship with another organization.

3. Membership on a scientific advisory panel or other standing scientific/medical committees of another organization.

4. Any other relationship that the individual sees as a potential or actual conflict.

4. Stock ownership. Shares of stock directly owned or controlled, including those owned or controlled by an immediate family member.

5. All consultative or advisory arrangements for which monetary compensation is received.

6. Grants/research support. Grants or research support from a company/organization whose products or services are directly related to RISE.

7. If relevant dualities exist for immediate family members they, too, should be disclosed. It is obvious that all categories, conditions, or circumstances that should be disclosed cannot be listed. A test to guide decisions about what to disclose is to ask whether any particular affiliation or interest could lead to questions about an individual's motives, if such an affiliation or interest was made known.

13.1.4 Reporting Process

Those individuals affected by this policy must complete a Duality of Interest Disclosure Statement at the time they become officially associated with RISE (see Scope of the Policy). Thereafter, a new Statement must be completed annually. Members of the staff required to complete the form will do so annually. Additionally, those completing a Statement are expected to notify RISE in writing if there are any material changes since the last form was completed. The individual also should notify RISE investigators of any new COI at a meeting where he/she would be in conflict with an issue that is to be discussed and/or voted upon and take action to avoid any COI (see below). All completed statements are stored at the CoC and are kept strictly confidential.

13.1.5 If a Relevant Duality of Interest Arises

In any matter coming before the committees in which an individual has a relevant duality of interest or a real conflict occurs, the individual affected shall leave the room in which the meeting is being held and refrain from any discussions or actions on that subject. In most situations, no further action will be required. However, in some instances, the nature of the situation may require other actions be taken. The minutes of the meeting will reflect abstentions from voting due to these circumstances.

In the case of scientific/medical presentations or publications, those individuals with a relevant duality of interest will be identified in the program or publication.

13.2 Presentations and Publications (March 15, 2013)

13.2.1 Introduction

The Publications and Presentations Subcommittee (PPS) will coordinate, monitor, review, and assume responsibility for all scientific communications (press releases, interviews, presentations, and publications) using RISE data. These policies apply to data derived from the adult, pediatric or gastric banding components of the RISE Consortium, which, in this chapter, will be jointly referred to as RISE. These policies apply to data directly involving RISE identified outcomes, as well as data developed using funding from the RISE consortium not directly related to pre-identified outcomes of RISE, and concepts and data derived from discussions within the RISE Consortium. This policy covers communications from all RISE participating centers, including the Coordinating Center and the NIDDK. When the Research Group is identified in communications, it will be referred to as the "RISE Consortium." During the course of these studies, there will be no publications or presentations of study plans or results *that have not been reviewed and approved by a majority of the PPS,* and for most types of communications, a majority of the Steering Committee.

The RISE Consortium consists of three component studies – an adult medication study, a pediatric medication study, and a gastric banding/medication study. Each study has its individual objectives and design. The three studies also share aspects of design and conduct that will allow comparisons of some outcomes between and among studies. This format allows for data analysis, presentation and publication of results from the individual studies, as well as multi-study analyses and publications. Policies and Procedures specific to publications and presentations from single component studies, multiple component studies, and the full RISE consortium are provided. These policies and procedures promote the rights of single component investigators to develop and submit presentations and publications independently of the full RISE Consortium. *However, all publication types will be subject to review and approval by PPS prior to presentation or publication in order to coordinate data release, avoid overlap and damage to other planned RISE publications, ensure appropriate acknowledgement, and maintain the quality of RISE publications.*

The PPS will be appointed by the RISE Executive Committee and have representation from all participating clinical centers. The goals of the PPS are to:

- Promote accurate, uniform, timely, and high quality reporting of RISE activities and results;
- Preserve the scientific integrity of the study;
- Safeguard the rights and confidentiality of participants; and
- Ensure that the timing of publications and presentations serves the right of the public to know the results of the program without jeopardizing its conduct.

The PPS will solicit and approve a writing group for each publication or presentation proposed by the members of the RISE Consortium. The PPS will coordinate the efforts of the writing

groups, establish priorities for data analysis by the Coordinating Center, and help edit the manuscripts produced by the writing groups.

13.2.1.1 Duties of the Publications and Presentations Subcommittee

- Develop and maintain policy guidelines for authorship of RISE publications.
- Recommend policy and procedures for review and approval of all scientific communications regarding the RISE outcomes to outside groups.
- Work with investigators to identify publications to be written, abstracts to be submitted, and presentations to be made during the course of the study, and collaborate with the authors to establish target dates for each.
- Review proposals for RISE-related publications or presentations.
- Work with writing groups to monitor the progress of each paper to ensure publication in a timely fashion.
- Work with writing groups to identify appropriate journals for RISE publications and monitor the process of publication.
- Perform other writing, reviewing, or editing tasks assigned by the Steering Committee.
- Assist writing groups in publishing papers of the highest quality and clarity.
- Review all RISE publications and presentations prior to submission, enlisting the special assistance of other members of RISE Consortium and subcommittees whenever appropriate.
- Review and approve slides that will be part of the official RISE slide set.
- The PPS will also review and suggest necessary revisions for any publications arising from approved ancillary studies prior to their submission for publication. In addition to the issues cited in the editorial policy above, proposed publications of ancillary studies will be scrutinized to ensure that the content and timing of their reporting will not threaten the viability of main RISE reports.

13.2.1.2 Definition of communications

Types of communications

Any communication from RISE will be classified as a press release, interview, presentation, or publication.

Press Releases and Interviews. A press release is defined as a document given to radio, television, newspapers, popular periodicals, or scientific journals (including publications of pharmaceutical companies or professional organizations) not indexed in Index Medicus. An interview is any discussion with a member of the press, a science writer, or a radio or television commentator, who in turn provides information for public dissemination.

Presentations. A presentation is the delivery of information to scientific, professional, or public groups. A presentation may include an abstract to be published by the group to which the presentation is made.

Publications. A publication is any document (other than an abstract) submitted to a professional journal listed in the Index Medicus or any popular periodical with wide circulation.

13.2.1.3 Classification of communications

Old or new information. A communication will be classified as containing old information if the content is limited to review of background material, substantive information available either in the final Protocol, the Manual of Operations, previously published RISE results or other published data, with no added interpretations or inferences.

A communication will be classified as containing new information if it contains RISE material neither previously published nor presented. A communication containing both old and new material is considered new.

If an abstract is submitted to a national meeting, the abstract may be published before the meeting, and the presentation at the meeting is likely to occur before the full article on the same topic is published in a journal. This gives rise to the question of when the information changes from being "new" to "old". For example, data in a published abstract are, to some extent, public, and could be discussed or cited by anyone, including members of the RISE Consortium. However, further presentation of these data by RISE Consortium members is discouraged prior to print publication so as not to jeopardize such publication. Furthermore, no background data or interpretations which are still new and were not included in the abstract can be discussed or otherwise considered “old” information. Similarly, if new information not included in the abstract are presented at a national meeting, this information could be cited or discussed to the extent that it was actually presented. However, again, such further public use of presented data is discouraged until print publication. Any other details that will appear in a full article cannot be cited or discussed until that article is published.

Copies of slides or other presentation materials (e.g. poster figures) used in meetings will be made available to other members of the RISE Consortium through placement on the RISE website. However, such material should not be used in additional public presentations without the approval of PPS until print publication of data or determination that data will not be published. PPS will review copies of presentations to determine which slides are available for public use by RISE investigators. Once slides are approved by PPS for public use, they will be placed in the official slide set on the RISE website and may be used without specific permission of the PPS. Such use should be for legitimate academic purposes but not for commercial activities.

Invited or submitted communications. A communication is invited if it is made in response to an invitation from an entity outside RISE, whether the invitation is to an individual member of the RISE Consortium or RISE as a group. A communication is submitted if it is initiated by the RISE Consortium, which chooses the meeting (for a presentation) or journal (for a publication).

13.2.2 Categories of communications and authorship of publications

The following categories of communications apply to all types of communications, i.e. press releases, interviews, presentations, and publications. Presentations without published abstracts, press releases and interviews are not considered to have authors. When presentations are accompanied by published abstracts, the authorship rules for the abstracts are the same as for other types of publications, as described in this section. Responsibility for the category assignment for all publications and presentations rests with the PPS.

There will be several categories of publications and presentations, with different rules for authorship, ranging from publications of the main results of the study (with authorship by a group writing on behalf of the entire research group) to other types of publications with named authors. The authorship rules balance the need to recognize the contributions of all members of the RISE Consortium and staff with the need to recognize individuals for specific contributions to certain types of publications and presentations.

Writing groups may be comprised of two types of authors:

Regular members of the RISE Consortium are those who have been members (staff, investigators, and co-investigators) of a RISE clinic, coordinating center, or collaborating unit, independent of a paper in question.

Outside collaborators are those who collaborate in the primary RISE study or a particular RISE ancillary and/or substudy or paper(s) but are not regular members of the Research Group. Outside collaborators may work at institutions that are RISE centers or at other institutions. For example, they may represent laboratories performing special tests for a RISE project, but that have no other role in RISE. They will propose their manuscripts through a regular member of the RISE consortium or will be recruited by such a member.

Regular members and collaborators are considered members of the RISE Consortium for that particular manuscript whether it is from the primary study or an ancillary or substudy. When authors' names are listed individually (for papers of any category), they will be those of the members of the writing group. Authors must also meet the qualifications for authorship of the target journal.

13.2.3 Categories of communications and authorship of publications

13.2.3.1 Type of communications by extent of study involvement

13.2.3.1.1 Single-study communications.

Results from each study may be published independently of the other studies. Such communications report on outcome measurements that are unique to a single component study. In this circumstance, authorship and analysis will be from the center or centers involved in that particular study, with other RISE investigators added to the writing group as deemed appropriate by the investigators of that study. The proposed writing group will be submitted to PPS for review and for tracking and monitoring purposes.

13.2.3.1.2 Full-RISE study group communications.

These communications will describe common primary and secondary outcomes of all RISE studies, as well as comparative analyses of outcomes among studies. Data resulting from measurements common to all three protocols and pertaining to secondary endpoints is also predictably scientifically stronger if published from all groups simultaneously. Writing groups for these papers will be recruited from all RISE investigators, as well outside collaborators and experts as needed.

13.2.3.1.3 Less-than-full RISE Study Group Communications

Some communications will present results from more than one, but not all, studies. These may be ancillary studies or studies funded entirely by the main budgets in which a subset of centers adopts common measures they would like to report together. Such communications may report on outcome measurements that are unique to two component studies. For this type of paper, the writing group will be drawn only from the participating centers and/or studies, with other RISE investigators and outside experts added as deemed appropriate by the PPS.

13.2.4 Categories of Communications by Data Reported

Publications and presentations will also be categorized by the nature of the data they address, from primary study outcomes and analyses through a spectrum to papers addressing study methodology. In RISE, proposed publications and presentations will, in addition to being categorized by the studies and centers involved, be classified by the following:

13.2.4.1 Primary RISE Communications – Category A:

These communications address the principal goals and objectives of the study. Category A papers may use consortium-wide data, or may include data from one or more studies independently. Examples of topics are: baseline participant demographic and metabolic data, study design, and primary and secondary outcomes, either at baseline or in response to treatment. The PPS will work with the Consortium members to identify Type A papers before and during the study and propose these for approval to the Steering Committee. The writing group will almost always be comprised entirely of regular members of the RISE Consortium.

Examples

Full RISE Study group communications: The RISE Consortium, prepared by John Doe (Chairperson), John Doe #2, and Jane Doe.

Single study communications: The RISE Consortium Pediatric Study Group, prepared by John Doe (chairperson), Jane Doe, Jesse Doe et al.

Multiple study communications: The RISE Consortium Adult and Pediatric Study Groups, prepared by John Doe (chairperson), Jane Doe, Jesse Doe et al.

There may be some variation of the format of this listing of authors according to the journal requirements, e.g., the writing group members may be listed on the authors' line, in a footnote

on the title page or in an appendix. Whenever possible, the complete list of members of the RISE Consortium will appear at the end of the paper or, if the journal requires, in an online appendix. A standard study support paragraph is included in all publications. Additional support is also included if applicable.

13.2.4.2 Secondary Communications – Category B:

These communications use the data from one or more RISE studies and centers, but address issues that are peripheral to the major objectives of the study or involve measurements or analyses that were not specified in detail in the RISE protocols or manuals of operation. Examples of topics are: previously unanticipated relationships between variables, measures of substances in blood or urine samples that had not been previously planned (such as new diabetes or cardiovascular risk factors), or genomic studies. The writing group will usually include regular members of the study (for individual study publications) or the RISE Consortium (for multi-study publications), but may also include outside collaborators.

Examples

Authors – John Doe, John Doe #2, and Jane Doe and the RISE Consortium

There may be some variation of the format of this listing of authors according to the journal requirements, e.g., the writing group members may be listed on the authors' line, in a footnote on the title page or in an appendix. Whenever possible, the complete list of members of the RISE Consortium will appear at the end of the paper or, if the journal requires, in an online appendix. A standard study support paragraph is included in all publications. Additional support is also included if applicable.

13.2.4.3 Ancillary or Substudy Communications – Category C:

These communications use only limited subgroups of RISE participants and/or a significant amount of non-RISE data. RISE data may arise from a subgroup of clinics or from one clinic. Protocols for obtaining additional non-RISE data using RISE participants would require approval by the RISE Steering Committee before activation. The writing group may include regular RISE Consortium members plus outside collaborators.

Examples

Authors – John Doe, John Doe #2, and Jane Doe with the RISE Consortium +

+ Acknowledge RISE: a complete list of the members of the RISE Consortium can be found in (appropriate journal citation) or an online appendix. A standard study support paragraph is included in all publications, along with ancillary study support.

13.2.4.4 Miscellaneous Communications – Category D:

Some communications, mostly concerned with methodological issues, will not deal with the RISE population or the RISE Consortium directly but will be prompted by discussions during the development of the RISE consortium study designs or utilization of specific methodology during

RISE. Such a communication, prepared by a member or members of RISE, must include an acknowledgment of its NIDDK/RISE support.

Examples

Authors – John Doe, John Doe #2, and Jane Doe *

* This study was partially supported by the RISE Consortium, NIDDK. A standard study support paragraph is included in all publications.

13.2.4.5 Reviews or Commentaries – Category E:

Review or commentary presentations (papers or lectures) summarize and discuss RISE methods or results that have already been published or publicly presented elsewhere. They are typically written as book chapters or review articles in journals, and require PPS review. This category will apply to presentations dealing primarily with RISE, although reference to other studies of diabetes prevention or early treatment will usually be included.

Review papers covering a broader field of diabetes prevention, treatment or risk factors in which information from one or more RISE study is discussed but is not the major topic will not be considered RISE presentations and will not be reviewed by the PPS. Similarly, presentations made by non-RISE investigators are of necessity outside the purview of this policy.

Examples

Authors – John Doe, John Doe #2, and Jane Doe for RISE Consortium *

* Acknowledge RISE: a complete list of the members of the RISE Consortium can be found in (appropriate journal citation).

13.2.5 RISE Consortium Authorship

All professional members of the RISE Consortium who have the approval of the Principal Investigators and have served at least two years in a significant capacity with the study will be listed at the end of category A and B papers and will be considered as authors. In addition, a Principal Investigator may provide justification in writing to the PPS to include individuals who have been with RISE for less than two years for inclusion. PPS will maintain an updated listing of RISE investigators and staff for the purposes of authorship listing.

Whenever appropriate, a list of all participating centers will appear in the category A and B publications. Under each center, a roster of names, as described above, will appear, each followed by the academic degree(s), when allowed by the journal. For the purposes of this listing, the Coordinating Center, the central units and core facilities, and the NIDDK will be considered as special units and be listed as participating centers. A standard study support paragraph is included in all publications which includes NIDDK and other organizations providing scientific input and funding, as well as scientific, government, or commercial organizations only providing funding or supplies. If the roster of credits is deemed too lengthy by a journal, the PPS may approve the payment of a reasonable amount towards page costs to

permit such a roster to be printed intact. If the list does not appear in the publication, reference will be made in that to publication to the most recent published article with the full list included.

The categories and authorship rules for abstracts accompanying presentations are as above except that a full list of members of the RISE Consortium will not be included.

13.2.6 Policies and Procedures

Proposals for presentations and publications will come from the members of the RISE Consortium at large. An outside collaborator may submit a proposal but it must include a member of the RISE Consortium who will be responsible for compliance with policies and procedures. The PPS, through the Coordinating Center, will keep the Steering Committee informed of the status of all communications, from their proposal, through writing, review, submission, and the final presentation or publication.

The review of a proposed presentation by the PPS considers scientific, programmatic, and stylistic aspects of the presentation or abstract, but does not consider the costs of making the presentation. Approval of an abstract or presentation by the PPS implies no commitment of RISE funds to support the presentation. The head of the writing group proposing an abstract or agreeing to the committee's request to head a writing group is responsible for obtaining necessary funds for travel, meeting registration, and other costs of making the presentation.

All communications from RISE, including those of ancillary studies, require review of the PPS. Approval for publications or presentations from RISE ancillary studies may be withheld until it is deemed appropriate by the PPS if they utilize primary RISE Study data and thus may jeopardize outcome manuscripts from the primary study.

13.2.6.1 Press releases and interviews

Except for the purposes of recruitment, press releases and interviews will not be initiated by individual clinical centers or RISE Consortium component studies. Press releases or interviews concerning old or new information may not be made without the prior approval of the PPS. When needed, centrally prepared press releases will be reviewed by the PPS and distributed to the centers. Prepared releases should be given to the media when interviews are requested. This procedure will help ensure uniformity and accuracy of the information disseminated through the media. The clinical centers should refer the soliciting party to the Chairperson of the PPS if information other than what is available in the press release is requested.

A press release or interview providing new information may be appropriate simultaneously with a presentation or publication announcing a study result. Such a press release or interview needs to be approved in advance by the PPS and the Steering Committee (by majority vote of each), and the simultaneous presentation or publication must be approved as specified below. A presentation of old information to a regional or local meeting may be given without prior review and approval by the PPS using previously approved slides. Any change to the old information, will need prior approval by the PPS. "Regional or local" refer to the scope of

influence of the meeting, not to the location relative to the workplace of the presenter; i.e. a local meeting can take place at a great distance from the workplace of the presenter.

The following process applies to any RISE presentation involving new data and any presentation to a national or international meeting, regardless of content:

13.2.7 Presentations

A presentation of old information to a regional or local meeting may be given without prior review and approval by the PPS using previously approved slides. Any change to the old information, will need prior approval by the PPS. "Regional or local" refer to the scope of influence of the meeting, not to the location relative to the workplace of the presenter; i.e. a local meeting can take place at a great distance from the workplace of the presenter.

The following process applies to any RISE presentation involving new data and any presentation to a national or international meeting, regardless of content:

13.2.7.1 Invited presentations (of old information)

If a member of RISE is personally invited to present old RISE information or represent RISE at a national or international meeting, and only PPS approved slides about RISE will be used, the invitation must be forwarded to the PPS as soon as possible for information purposes. The PPS reserves the right to suggest a presenter other than the invited RISE member in order to distribute the opportunities for presentation among the members of the RISE Consortium. If an abstract is required, this needs to be approved by PPS prior to submission.

13.2.7.2 Submitted presentations (of old or new information) or invited presentations of new information

The PPS will work with investigators and RISE component studies to identify scientific and professional meetings where RISE presentations should be made on behalf of the group. Suggestions for such meetings and topics for presentation will be made by both the PPS and individual members of the RISE Consortium. The PPS will work with proposers and other investigators to identify one or more members of the RISE Consortium to prepare and present the material. These persons will be referred to as the presentation group, and the person designated to make the presentation as its chairperson. In the case of presentations arising from data from a single RISE component study, the component study investigators will be expected to identify the members of the presentation group and chairperson. If several proposals for similar presentations are made, the PPS will request the involved persons to resolve their differences, and if appropriate, join in a common presentation group.

13.2.7.3 Preparation and review of submitted presentations or invited presentations of new information

For any proposed presentation, a member of the PPS who is not a member of the presentation group will be designated by the PPS Chairperson to serve as the PPS primary reviewer. The PPS primary reviewer will assist the presentation group Chair in coordinating the efforts of the

presentation group. For presentations including new data, the PPS will establish priorities for data analysis by the Coordinating Center. The Principal Investigator of the Coordinating Center will designate one of his/her staff to work with each presentation group in order to provide liaison, analyses and resource material for the presentation.

13.2.7.3.1 Abstracts of Category A or B

The presentation group must write an abstract of the proposed presentation. This will be the abstract submitted to the organization sponsoring the meeting, if one is required. If new data are to be presented and no abstract is required by the meeting organization, an abstract or description of the presentation must be prepared for RISE review. The presentation group will submit the abstract to the entire PPS (through the Coordinating Center) for review and approval. The PPS will appoint a primary reviewer(s) to review the abstract, who may recommend changes to the abstract prior to its approval.

After approval by the PPS, the final abstract will be distributed to the Steering Committee. The abstract must be delivered to the Steering Committee at least 14 days prior to the deadline for submission to the organization holding the meeting. At least 7 days prior to the submission deadline, the Coordinating Center will conduct a vote of the Steering Committee for approval of the abstract of a category A or B presentation. In addition to voting, Steering Committee members may give suggestions for revision to the presentation group and the PPS primary reviewer(s). If the writing group chooses to revise the abstract in response, the revised abstract must again be approved by the PPS. If the revision alters the substance of the abstract (rather than merely improving style and clarity), it must be distributed to the Steering Committee for another vote. If a majority of the Steering Committee approves the abstract, it can be submitted. If it is not approved, the presentation group can revise and resubmit to the PPS only if sufficient time for review remains, or they can resubmit it to the PPS for consideration for a different meeting with a later submission deadline. Non-votes by steering committee members will be considered as YES votes.

13.2.7.3.2 Abstracts of Category C-E

Presentations will be distributed as above mentioned, and members of the Steering Committee may comment to the Chairperson of the presentation group and to the PPS, but a vote of the Steering Committee will not be taken. Submission of an abstract or agreement to a category C-E presentation requires approval of a majority of the PPS, but not of the Steering Committee. *Slides, posters, tables, and/or a presentation script must be sent to the PPS primary reviewer(s) at least two weeks prior to the scheduled presentation.*

13.2.7.4 Publication associated with a presentation

Ordinarily, a manuscript or other written material except for an abstract should not accompany a RISE Consortium presentation. If a manuscript is requested in conjunction with a presentation (e.g., a "proceedings" paper), such manuscript must be prepared and approved according to the rules and procedures for publications, and approval of the presentation does not constitute approval of the publication. A member of the RISE Consortium accepting an

invitation to present RISE material must make the inviting organization aware of these requirements.

A complete list of RISE publications will be posted on the RISE website, which will be updated when new publications are available.

13.2.8 Publications

The following procedures apply to all publications (of any category), whether the publication is pre-identified by the RISE Consortium as type A and B papers or proposed by RISE investigators, and whether they consist of old or new information.

13.2.8.1 Writing group

The PPS will select a writing group of up to 12 individuals for each publication. For publications pre-identified as Type A or B papers, the PPS will work with investigators to identify the writing group chair and writing group. For publications arising from single RISE component studies, the component study investigators will select the writing group[and have primary responsibility for manuscript identification and production, with the oversight and collaboration of PPS. For publications arising from more than one RISE component studies, members of writing groups will be solicited from the members of the RISE Consortium at large. In the case of publications that are not pre-identified by the Research Group, members of the RISE Consortium who initially propose and formulate topics for publication will be included to the extent practical. The individuals proposing a new manuscript may also propose a writing group and identify its members. A writing group may also include non-RISE individuals such as outside experts if he/she makes a significant contribution and adds expertise not available within the RISE study group. For papers involving analysis of data generated by RISE, at least one member of the writing group will be from the Coordinating Center. The PPS will designate one individual as Chairperson of the writing group, who will be responsible for ensuring that the first draft of the publication is written.

The PPS will review and approve the manuscript topic as well as the members, including Chairperson, of the newly formed writing group. It will then determine a category and assign priority to the manuscript. Potential conflict with other proposals for publication will be evaluated. If several proposals for similar papers or data analyses are made, the PPS will request that the involved persons resolve their differences, and if appropriate, join in a common writing group. Any disagreements between a member of the RISE Consortium and the PPS may be appealed as discussed in Section 13.2.7 (Grievances). Finally, the Coordinating Center will post the approved proposal, category, and priority on the website.

13.2.8.2 Manuscript proposal

In some instances, an individual member of the research group may volunteer to develop a manuscript and submit a short concept proposal with suggested writing group membership to the PPS. In other instances, such as pre-identified type A and B papers, the PPS develops the idea and description of the paper as well as nominates members of the writing group for a proposed paper. Once an investigator accepts responsibility as writing group leader, he/she

will complete the PPS proposal form posted to the internal study website. This form is submitted to the chair of PPS and the coordinating center. The PPS circulates the short concept proposal and proposed writing group membership to the RISE Consortium. Members of the study group may request to join the writing team with permission of the site PI and are included to the extent practical. PPS will monitor distribution of writing group membership to encourage widespread participation.

13.2.8.3 Journal identification

The writing group will identify an appropriate journal for the submission of each proposed publication so that the manuscript can be prepared according to the guidelines of a specific journal and be directed towards its known readership. PPS will endorse the recommendation of the writing group or propose alternatives for consideration.

13.2.8.4 Preparation and Review

For each proposed publication, at least two members of the PPS who are not members of the writing group will be designated by the PPS Chairperson to serve as the PPS primary reviewers. The PPS primary reviewers will assist the writing group Chairperson in coordinating the efforts of the writing group. For publications including new data, the PPS will establish priorities for data analysis by the Coordinating Center. The Principal Investigator of the Coordinating Center will designate one of his/her staff to work with each writing group in order to provide liaison and resource material for the publication. The writing group chairperson and Coordinating Center statistician will formulate a working analysis plan for the manuscript. Additional PPS review may be needed if the analysis plan is changed dramatically from the original proposal. Upon the completion of analyses, tables, and results by the Coordinating Center, the chairperson of the writing group will prepare a manuscript draft to be submitted to the Coordinating Center. When submitted to the PPS, the Coordinating Center will post the manuscript draft for review by the PPS primary reviewers.

If revisions are requested, the writing group must obtain approval of the revised manuscript from the PPS primary reviewers. Upon receipt of such approval, the final manuscript will be reviewed by the PPS. If approved by a majority of the PPS, the manuscript will be distributed to the Steering Committee by the Coordinating Center.

After distribution of the final draft to the Steering Committee, the Coordinating Center will conduct a vote (by fax or e-mail, or in person if the Steering Committee is in session) for approval of a category A or B paper. Non-votes (i.e., abstention or non-response) by a Steering Committee member will be counted as a “yes” vote. Any member of the RISE Steering Committee who wishes to comment on the paper must communicate his/her concerns directly to the writing group Chairperson and the PPS primary reviewers by the time the vote is taken. If the writing group Chairperson and the PPS primary reviewers agree that the comments warrant a further revision of the paper, the writing group will make such a revision, and the revised paper must again be approved by the PPS primary reviewers. If the revision alters the substance of the paper (rather than merely improving style and clarity), it must be distributed to the Steering Committee for another vote.

Category C-E manuscript will be distributed as above, and members of the Steering Committee may comment to the Chairperson of the writing group and to the PPS, but a vote of the Steering Committee will not be taken. Submission to a journal of a category C-E publication requires approval of a majority of the PPS, but not of the Steering Committee.

The PPS monitors progress of the writing group toward publication. If timely progress toward publication is not made, the responsibility for writing group leadership may be reassigned by the PPS. Some papers are followed as "urgent" if publication is essential for the success of the study or for the publication of subsequent papers. The PPS has the responsibility to rank the priority of papers for data analysis by the coordinating center.

13.2.8.5 Submission of manuscript

If the Category A or B manuscript is approved by a majority of the Steering Committee, it will be submitted to the journal. The Chairperson of the writing group will serve as corresponding author. Papers of categories C-E will be submitted by the chairperson of the writing group who will also serve as the corresponding author.

The RISE coordinating center covers costs or charges involved in preparing or submitting Type A or B publications and presentations. This typically includes submission charges and graphics and poster preparation. Reprints are not funded by RISE. Any charges incurred for publications arising from category C, D & E manuscripts must be funded separately.

If the manuscript is rejected, the writing group will target another journal. For rejected manuscripts, or those where a journal offers a resubmission, PPS and Steering Committee review is required if substantial changes have been made. For minor revisions, review of the PPS primary reviewer is sufficient.

13.2.8.6 Standards of excellence

In addition to the review system established for the critique of publications and presentations as described in the previous section, the following guidelines are suggested for maintaining the highest standards of excellence for RISE publications and presentations.

For manuscript reviews: If, in the opinion of the members of the PPS, no member of the RISE Consortium has sufficient scientific background to review the pertinent material, then outside (of RISE) expert consultants will be selected by the PPS and asked to critique the material.

For the major publications and presentations, the completeness and adequacy of the reports will be assured by consideration of the 32 steps described in "A Proposal for Structured Reporting of Randomized Controlled Trials", JAMA 272: 1926-1931, 1994. While these considerations should govern the design and conduct of any of the reports, not all points need to be mentioned in each publication or presentation.

13.2.9 Grievances

A member of the RISE Consortium may formally appeal in case of disagreement with the PPS concerning the following:

- Classification of a communication,
- Membership or chair of a writing or presentation group,
- Handling or approval of a communication,
- Authorship inclusion and order,
- Suitability of a presentation or publication, or
- Any other action taken by the PPS.

To initiate an appeal, the claimant should initially discuss the issue with the Chairperson of the PPS to clarify why the disputed judgment was made. If this does not satisfactorily resolve the matter, the claimant should send a letter of appeal (supported by appropriate documentation) to the Coordinating Center for distribution to the entire PPS. The PPS will review the grievance and respond in writing within four weeks of receipt of the appeal. If the claimant still feels that the issue has not been satisfactorily resolved, copies of the letter of appeal and the response of the PPS will be sent to the Coordinating Center within two weeks for distribution to the entire Steering Committee for review and decision. The decision of the Steering Committee regarding a grievance will be binding.

13.2.10 Ownership of Data

For purposes of publication and presentation policies, study data are defined as all data specified in the Manual of Operations pertaining to participants in the studies of the RISE Consortium. Participants evaluated for eligibility but not randomized (for whatever reason) can be used by the individual Clinical Centers for other studies. Any RISE data obtained during the screening and eligibility process, however, can be presented or published only according to these policies and must cite relevant support for RISE from NIH, and, when appropriate, other groups.

Common study data from the adult and pediatric medication studies and the adult bariatric/medication study will be owned jointly by the individual Clinical Centers and the Coordinating Center, but will be kept at the Coordinating Center. The Coordinating Center and Clinical Centers will make no use of study data nor disclose them to any other parties except as specified in the Protocol or Manual of Operations, unless such use or disclosure is approved by a majority of the Steering Committee

13.2.11 Public availability of RISE data

Approximately two years after RISE participant visits end, the Coordinating Center will make the appropriately anonymized data available to the scientific community through the NIDDK data repository. The repository will require all future recipients of the data to sign a data use

agreement. The Coordinating Center will release a fully documented copy of all RISE data to each Clinical Center no more than two years after RISE participant visits end.

Decisions regarding disclosure of data to other parties, such as pharmaceutical companies or the FDA (beyond the required adverse events reports), shall be determined by the Steering Committee according to terms of relevant Clinical Trial Agreements in collaboration with the NIDDK. Confidentiality of individual participants will be maintained with all releases of data.

13.2.12 Presentations of study results to volunteer participants

Presentation of all key results (e.g. effects of treatments on the primary outcome) will be offered to the volunteer participants in conjunction with presentation to the public and professional communities.

13.3 Ancillary Studies

13.3.1 Overall Principles

Ancillary studies offer opportunity for maximizing the scientific impact and research benefits that can be derived from resources developed during the course of RISE. Investigators within and outside the RISE Study Group are encouraged to submit proposals for ancillary studies. Ancillary studies will be evaluated with careful consideration of their potential impact on the objectives and performance of RISE. Ancillary studies that complement the objectives and thereby enhance the value of RISE are encouraged. Such studies should augment and promote the continued interest of both participants and investigators. To protect the integrity of the primary RISE study, a proposal to conduct an ancillary study must be reviewed and approved by the RISE Steering Committee and funding must be secured before study initiation. RISE clinical sites can choose to participate or not participate in an ancillary study.

13.3.2 Definition of an Ancillary Study

An ancillary study is defined as research or data collection involving study sites, participants or specimens, using any technique, medication, procedure, questionnaire or observation other than those set forth in the Protocol or using information collected under the Protocol for purposes not included in the Protocol.

The investigator responsible for the conduct of an ancillary study may or may not be a member of the RISE Consortium. If an ancillary study is proposed by an individual who is not a member of the RISE Consortium, a member of the Consortium must be a co-investigator. A member of the RISE Consortium who serves as a co-investigator must be scientifically involved in the design, execution, and interpretation of the ancillary study. In addition, he/she shall be responsible for ensuring that RISE policies and procedures are followed during the conduct of the ancillary study.

13.3.3 Obtaining Approval for Ancillary Studies

The Steering Committee welcomes preliminary concept proposals (maximum length 3 pages) for ancillary studies before the submission of a full proposal. The proposal must be submitted using the format provided in the RISE Ancillary Study Proposal Form (available from the RISE Coordinating Center or RISE website) as detailed below.

After initial approval of an ancillary study by the Steering Committee and the NIDDK, final study approval is contingent upon receipt by the Steering Committee of a letter signed by the principal and all collaborating investigators. The letter must state that the investigators agree to abide by the policies for ancillary studies described herein, including those regarding publication and presentation of results. The Data, Safety, and Monitoring Board (DSMB) must also review ancillary studies that involve participant contact or data collection.

13.3.3.1 Reasons for Requirement of Approval

Investigators and participants are entitled to prior assurance that all ancillary studies are of high scientific merit and that no ancillary study will:

- Cause a deviation from the primary RISE protocol.
- Confound interpretation of the RISE Study results.
- Adversely affect participant cooperation.
- Adversely affect participant safety.
- Jeopardize the public image of RISE.
- Create a significant diversion of RISE resources at the clinical sites, the Coordinating Center (CoC) or any other RISE entity.
- Negatively influence the cooperative spirit of the collaborating investigators in any way.
- Otherwise compromise the scientific integrity of RISE.

13.3.4 Submitting an Ancillary Study

Submission of a completed application using the RISE Ancillary Studies Proposal Form is required. This form is available from the RISE Coordinating Center or on the RISE website. Completed forms should be forwarded to the RISE Coordinating Center. If an external investigator is proposing an ancillary study, he/she can obtain the form through the RISE Consortium member who will be the Co-Investigator for the study.

The request for approval of an ancillary study should be in narrative form. It should contain a brief description of the objectives, methods, study significance, power calculations, plans for analysis and publications, and information regarding funding level and source. The proposal should be written with sufficient detail to allow the Steering Committee to assess the study's scientific merit and potential impact on RISE. If a proposal is being submitted elsewhere for funding (e.g., a grant application), the source of funding should be identified. Full details should be provided concerning any procedures or tests to be carried out on a study participant including: any ophthalmologic, renal, cardiovascular, neurologic, psychological or other evaluation to be performed; any substances to be injected or otherwise administered to the participants; any observations to be made or procedures to be conducted on participants outside of the clinic; any extra clinic visits required of the participant or any prolongation of the participant's usual clinic visits; any additional specimens (blood, urine, etc.) to be obtained or additional procedures to be performed on specimens collected according to the RISE Protocol. The proposal should discuss the measures to be taken to ensure participant safety and confidentiality and an assessment by the investigator(s) of the potential impact of the ancillary study on RISE.

Prior commitment by clinical sites and approval by the appropriate Human Subjects Review Committee should be demonstrated.

Once complete, the investigators should send their ancillary study proposal to the Coordinating Center, which will distribute it to all members of the Steering Committee.

13.3.5 Review of Ancillary Studies

The Steering Committee will perform a comprehensive review of each ancillary study proposal. To ensure a thorough scientific review, the Chair of the Steering Committee may elect to seek outside expert opinions in advance of the Committee meeting. In general, ancillary study proposals will be reviewed by two RISE investigators assigned by the Study Chair. A statistical review by the Coordinating Center will also be performed. Upon completion of the scientific and statistical reviews, the Steering Committee will discuss these reviews and vote on the merits of the proposal under review. Approval or disapproval is based on a simple majority of the Steering Committee. A copy of the consensus statement generated from the Steering Committee review will be sent to the submitting investigator(s).

If the Steering Committee approves the proposal, the consensus statement and approval will be forwarded to the RISE Data Safety and Monitoring Board. Following their review, the investigator may proceed with the ancillary study if funding is available.

If the Steering Committee does not approve the ancillary study, the proposed study will not move forward.

The Steering Committee will maintain documentation of the final study design and any modifications approved by the Steering Committee, including any RISE data or specimens that are approved to be released.

13.3.6 Funding of Ancillary Studies

The RISE Study will not provide funds for ancillary studies. No funds will be provided for Central Biochemistry Laboratory or Coordinating Center activities or services in support of ancillary studies. If funds are needed, the investigator must explore other avenues such as: 1) submission of a research grant application; or 2) use of other sources of funds (i.e., a foundation, drug company, etc.). The anticipated source of funds must always be identified. If the funding agency requires substantial changes to the original ancillary study, the Steering Committee and the DSMB must approve the revised ancillary study.

Ancillary studies that require data and/or specimen retrieval or related services by the Coordinating Center must make adequate provision for defraying the cost of personnel time and effort. The exact FTE shall be determined in consultation with the RISE Coordinating Center.

13.3.7 Publication of Ancillary Study Results

All manuscripts, abstracts and presentations generated by ancillary studies for scientific meetings must follow the policies of the RISE Publications and Presentations (P&P) Committee.

Ancillary Study investigators are required to inform the P&P Committee of all planned publications once the proposal has been approved and funding is available.

13.3.8 Protocol Changes

If the ancillary study requires a change in protocol, the proposed modification must be submitted to the Steering Committee for consideration and approval.

13.3.9 Timeline

The Steering Committee will meet monthly or as needed to consider ancillary study applications and will work expeditiously to minimize delay in approving meritorious proposals. However, prospective investigators should understand that the approval process by the Steering Committee may take 60 days. Therefore, early submission is strongly recommended, especially if approval of an ancillary study proposal is deemed necessary in order to secure funding for the proposed research.

In general, studies requiring review by all parties, i.e. the Steering Committee and the RISE Data Safety and Monitoring Board, require receipt of the proposal by the Coordinating Center ten to twelve weeks prior to the funding agency's submission deadline.

To facilitate planning for ancillary study reviews and to prepare for a speedy response, it is recommended that investigators notify the Coordinating Center in advance of their plan to submit an ancillary study proposal. This letter of intent is not required but highly recommended, and should include an outline of the study aims, the proposed use of the parent study data, and the anticipated date of submission to the funding agency. Without advance notification, it may be difficult to convene the Steering Committee for a timely review.

13.3.10 Determination of Priority

Proposals for ancillary studies will be reviewed and adjudicated on a first-come, first served basis. Proposals with identical or closely related scientific objectives, submitted contemporaneously or within the same review period, will be reviewed and adjudicated on their scientific merits. For efficient use of available resources and to maximize their scientific value, investigators with similar interests are encouraged to submit broad collaborative applications.

13.3.11 Procedures for Requests of RISE Data

A list of required items, such as variables and participant samples, should be submitted with the original ancillary study proposal. Once an ancillary study has been approved, a Coordinating Center statistician will contact the Principal Investigator to confirm and review the materials requested.

The Principal Investigator will also be required to send an annual report containing an account of data collected by the Ancillary Study, and specimens or data requested and obtained from the CBL or the CoC.

13.3.12 IRB Requirements

For studies collecting new data on participants, the following documents should be submitted to the Coordinating Center for each clinic that is going to be involved in an Ancillary Study:

- Letter of agreement,
- IRB approval letter,
- Approved consent (any future consents and yearly stamped approved consents should also be sent to the Coordinating Center) and
- HIPAA data use agreement.

Should the ancillary study require IRB renewal, a copy of the IRB approval letter needs to be provided to the Coordinating Center as a requisite for work to continue.

13.3.13 Initiation and Progress Report

The Principal Investigator of an approved ancillary study shall provide a brief (approximately 2-page length) status report on the progress of the study to the Steering Committee annually. The progress report should include the following information, in table format wherever possible.

- Date of initiation of ancillary study,
- Current or pending sources of funding,
- Number of subjects enrolled,
- Completion of ancillary data collection instruments, by visit,
- Completion of ancillary outcomes, by visit,
- Receipt of specimens from CBL by date of receipt and visit, and
- Summary of results obtained during the project period, (means of notable variables).

13.3.14 Quality Surveillance for Ancillary Studies

Data, biological samples and other materials collected by ancillary studies through mechanisms distinct from those of the main RISE study will have quality oversight performed by the investigators sponsoring the ancillary study. However, it is in the interest of the overall study that data and samples collected during the conduct of RISE be of high quality to ensure the success of the ancillary study. Thus, the goal is to provide timely and effective troubleshooting for data or sample quality problems arising with ancillary studies being undertaken as part of RISE. Therefore, on a quarterly basis, the ancillary study principal investigator will be invited to join the standing Procedures & Quality Committee calls to provide a summary report of the data or sample quality, and to report any problems that have arisen. This is not intended to be

the only opportunity for discussion of problems; ancillary study teams are encouraged to communicate directly with the chair of the Procedures & Quality Committee as needed between quarterly reviews to notify the study of potential problems and cooperatively work toward a solution.

13.3.15 Future goals and expected Completion of Ancillary Study.

Approval shall lapse if the study has not been initiated within one year of the date of RISE Consortium endorsement (absent extenuating circumstances). Significant deviation from the research plan or scientific, ethical or procedural infringements will be grounds for termination of an ancillary study.

13.3.16 The role of the RISE CoC with Respect to Ancillary Studies

The Coordinating Center's funded role for ancillary studies is limited to coordinating Steering Committee reviews, participating as a voting member of that committee, presenting studies to the Steering Committee for voting, and, for studies approved by the Steering Committee, transferring data and/or samples as approved by the Steering Committee. The funds budgeted for the Coordinating Center by proposals in response to RFAs will provide resources for delivering the approved data and samples to these studies or for data analysis, to be determined jointly by the Coordinating Center Principal Investigator and the Ancillary Study investigator. The Coordinating Center Principal Investigator has the same right as other RISE Principal Investigators to decline participation in any ancillary study beyond distribution of approved data and specimens.

13.3.16.1 Activities Excluded from the Funded Work Scope

The Coordinating Center cannot divert its RISE staff or other resources to assist ancillary studies beyond what is covered in the funded work scope. The following activities are generally not included in the Coordinating Center's funded work scope, and are the responsibility of the ancillary study investigator: study design, sample size and power estimation, sample selection, training, coordinating study conduct, arranging or participating in conference calls, managing additional data or specimens collected especially for the ancillary study, conducting statistical analyses, and submitting ancillary study papers for publication.

13.3.16.2 Mechanism for CoC Direct Participation in Ancillary Studies

The Coordinating Center Principal Investigator or Co-Investigators may join an ancillary study's consortium as an investigator with an expanded role by being part of the consortium's application for funding. In this case, the resources budgeted will be separate from the Coordinating Center's RISE award. The Coordinating Center Principal Investigator has the right, as do other RISE Principal Investigators, to decline participation in an ancillary study consortium.

Chapter 14. Appendices

14.1 Exclusion Criteria Lists

14.1.1 Exclusionary Medications List

Exclusionary Medications

- Medications that affect glucose metabolism:
  - Adults:
    - Aminophylline or Theophylline, if used daily
    - Steroid inhaler or requiring daily oral glucocorticoid therapy
    - Inhaled beta-agonists, if used daily
    - Inhaled glucocorticoids
  - Pediatrics:
    - Exclude if >1000 mcg daily Flovent (or equivalent)
    - Oral steroid use within the last 60 days and/or greater than 30 days in the last year.
  - Use of oxygen at home
- Lipid-lowering agents
  - Niacin and bile acid sequestrants
  - Statins and gemfibrozil *are not exclusionary*
- Antibiotics/Immune modulators
  - HIV-related agents
  - AZT
  - DDI
  - HAART therapy
  - Pentamadine
- Antituberculous agents
  - INH (*except INH alone as prophylaxis*)
  - Ethambutol
- Antineoplastic agents
- Psychotropic agents
  - Valproic acid, also called divalproex sodium (Depakote)
  - Lithium
  - Carbamazepine (Tegretol)
  - Lamotrigine (Lamictal)
  - Oxcarbazepine (Trileptal)
  - SSRI antidepressants *are not exclusionary*
- Atypical antipsychotics
  - Olanzapine (Zyprexa)
  - Aripiprazole (Abilify)
  - Risperidone (Risperdal)
  - Ziprasidone (Geodon)
  - Clozarine (Clozaril)
- Other medications
  - Phenytoin
  - Amphetamines
  - Any weight-loss drugs (including Phentermine, Topamax and over the counter)
  - Orlistat
  - Transplant related medications
  - Metoclopramide (Reglan)

14.1.2 Exclusionary Medical Conditions List

Exclusionary Medical Conditions

- Underlying disease likely to limit life span and/or increase risk of interventions:
    - Cancer requiring treatment in the past 5 years, with the exception of cancers that have been cured or, in the opinion of the investigator, carries a good prognosis. (e.g. non-melanoma skin cancer, papillary thyroid carcinoma, and cervical carcinoma in situ)
    - Disease associated with disordered glucose metabolism
        - Cushing's Syndrome
        - Acromegaly
        - Pheochromocytoma currently under treatment (i.e. not surgically cured)
        - ANY episode of pancreatitis of any etiology
        - Known growth hormone deficiency
        - Hemochromatosis
        - Exclude other kinds of diabetes – e.g. CFRD, MODY, neonatal, genetic syndrome, T1D, Pediatrics only: IA-2 or GAD65 positive
    - Cystic fibrosis
    - Adults: Chronic obstructive airways disease or asthma requiring regular therapy.
    - Seizure disorders requiring regular treatment
- Active infectious disease
    - Self-reported HIV positivity
    - Active tuberculosis
- Renal disease (eGFR <45 mL/minute/1.73 m)
- Anemia or known coagulopathy (hemoglobin <11 g/dl in females, <12 g/dl in males)
- Cardiovascular disease, including uncontrolled hypertension.
    - Hospitalization for treatment of heart disease in the past 6 months
    - Uncontrolled hypertension:
        - Adults: SBP >160 mmHg or DBP >100 mmHg on treatment
        - Pediatrics: SBP >130 mmHg or DBP >80 mmHg on treatment
    - *Milder degrees of hypertension would prompt referral to primary care provider for treatment but would not exclude participation.*
- History of conditions that may be exacerbated by or associated with a study drug:
    - Self-reported chronic hepatitis or cirrhosis
    - Thyroid disease, suboptimally treated
    - Medullary thyroid carcinoma or MEN2 will be excluded (in participant or a positive family history)
    - Hypertriglyceridemia (>400 mg/dl despite treatment)
- Other chronic disease or condition likely to limit participation
    - Inflammatory bowel disease requiring treatment in the past year
    - Recent or significant abdominal surgery (e.g. gastrectomy)
    - History of gastroparesis or any disorder that results in altered GI motility
    - History of major psychiatric disorder that, in the opinion of clinic staff, would impede the conduct of RISE.

14.1.3 Exclusionary Behaviors List

Exclusionary Behaviors

- Participant is unable or unwilling to:
  - give informed consent
  - adequately communicate with clinic staff
  - accept treatment assignment by randomization
  - complete RISE run-in tasks
- Another household member is a participant or staff member in RISE
- Current or anticipated participation in another intervention research project
- Likely to move away from participating clinics in next 2 years
- Pregnancy and childbearing (temporary)
  - Currently pregnant or less than 3 months post-partum
  - Currently nursing or within 6 weeks of having completed nursing
  - Pregnancy anticipated during study.
  - Unwilling to undergo pregnancy testing or to report possible or confirmed pregnancies promptly during the course of RISE
  - Unwilling to take adequate contraceptive measures, if potentially fertile
- Weight loss of >5% in past 3 months for any reason other than post-partum weight loss.
- Excessive alcohol intake, either acute or chronic. Defined as any one of the following:
  - average consumption of 3 or more alcohol containing beverages daily
  - consumption of 7 or more alcoholic beverages within a 24 hr period in the past 12 months
  - clinical assessment of alcohol dependence

14.2 Certification Procedures for Staff

Procedure	***Staff Performing the Procedure***	**Certification Requirements**	***Tracking Procedures***
Height	Any staff member	The technician will measure the volunteer's height two times. The average of the two measurements will be compared to the average of the trainer's two measurements. The technician will be considered certified to measure height if the comparison between the technician and trainer is within .5 cm.	At least one staff member at each site will be certified at study training. The certified staff member can then train and certify other staff members at the site, submitting completed certification forms to the Coordinating Center.
Weight	Any staff member	The technician will measure the volunteer's weight two times with the volunteer stepping off the scale between measurements. The average of the two measurements will be compared to the average of the trainer's two measurements. The technician will be considered certified to measure weight if the comparison between the technician and trainer is within .2 kg.	At least one staff member at each site will be certified at study training. The certified staff member can then train and certify other staff members at the site, submitting completed certification forms to the Coordinating Center.
Waist circ.	Any staff member	The technician will measure the volunteer's waist circumference two times with the tape repositioned between measurements. The average of the two measurements will be compared to the average of the trainer's two measurements. The technician will be considered certified to measure waist circumference if the comparison between the technician and trainer is within .5 cm.	At least one staff member at each site will be certified at study training. The certified staff member can then train and certify other staff members at the site, submitting completed certification forms to the Coordinating Center.
Hip circ.	Any staff member	The technician will measure the volunteer's hip circumference two times with the tape repositioned between measurements. The average of the two measurements will be compared to the average of the trainer's two measurements. The technician will be considered certified to measure hip circumference if the comparison between the technician and trainer is within .5 cm.	At least one staff member at each site will be certified at study training. The certified staff member can then train and certify other staff members at the site, submitting completed certification forms to the Coordinating Center.
Blood pressure	Any staff member	The technician will take two blood pressure measurements on a volunteer using an electric monitor, allowing one full minute between each measurement. The average of the two systolic and two diastolic blood pressure measurements will be compared to the average of the trainer's measurements. The technician will be considered certified to measure	At least one staff member at each site will be certified at study training. The certified staff member can then train and certify other staff members at the site, submitting completed certification forms to the Coordinating Center.

		blood pressure if the comparison between the technician and trainer is within 10 mm/Hg.	
Data entry	Any staff member	At least one person at each site will attend the virtual training session at the CoC. The certification process involves data entry of "dummy" forms with acceptable accuracy.	Each staff member must independently complete the data entry certification process.
General protocol knowledge	Required for all staff except investigators	Attend the RISE training and participate in Jeopardy. OR Review the protocol and MOP, and complete a short quiz.	Attended RISE training OR Completed quiz is submitted to the CoC.