Fundamental Principles of Writing a Successful Grant Proposal

Kevin C. Chung, MD, Melissa J. Shauver, MPH

It is important for the field of hand surgery to develop a new generation of surgeon-scientists who can produce high-impact studies to raise the profile of this specialty. To this end, organizations such as the American Society for Surgery of the Hand have initiated programs to promote multicenter clinical research that can be competitive for fiscal support from the National Institutes of Health and other funding agencies. Crafting a well-structured grant proposal is critical to securing adequate funding to investigate the many clinical and basic science questions in hand surgery. In this article, we present the key elements of a successful grant proposal to help potential applicants to navigate the complex pathways in the grant application process. (J Hand Surg 2008;33A:566–572. Copyright © 2008 by the American Society for Surgery of the Hand.)

Key words: Grant writing, guide, principles, research, NIH.

To the majority of hand surgeons and to many in the research field, grant writing is a stressful and arduous process. It has been stated that writing a grant is much harder than actually doing the proposed research.1 But today, with funding becoming increasingly difficult to obtain, grant-writing skills are more important than ever. The National Institutes of Health (NIH) projected that it will fund only 21% of the more than 35,000 proposals submitted in 2007, down from 32% in 2001.2 Although fewer proposals are being funded, more proposals are being submitted. In the past 10 years, applications to the NIH have increased by more than 40%.2 With increasing numbers of proposals to review, minute differences among proposals matter more than ever before.3 This means that the grant application process has become extremely detail oriented. Gone are the days when good science could make up for less than stellar grant-writing abilities. Today’s applicants have to excel in every one of the 5 NIH Review Criteria: significance, approach, innovation, investigators, and environment4 (Table 1).

GETTING STARTED

If one is considering writing a grant proposal, including grant submissions to specialty foundations, he or she will most likely already have an idea of the study question. But this idea may not be fully articulated into a formal research question. The research question is central to the entire grant by providing a strong platform on which to build the rest of the proposal. The research question should lend itself to a testable hypothesis and have the potential to provide results that have an impact. This is also the point when an extensive literature review should be conducted. A comprehensive understanding of the background of a field will avoid conducting a study that has already been published. Furthermore, knowledge of the literature will allow one to frame the significance and innovation of the research question. These two factors play an important role in achieving funding.

After a solid research question has been formulated, it is important to select the appropriate funding agency for the proposal. It is critical that the subject of the investigation is consistent with the mission of the agency and the guidelines presented in the Request for Proposals. This may seem self-evident, but a study of proposals submitted to the National Kidney Foundation found that 7% of proposals were ineligible to be reviewed because the nature of the research did not match the priority goals specified by the Request for Proposals.5 If one is unclear about whether the research question falls within the scope of the particular funding agency, investigators should not hesitate to contact the grant administrator at that agency. It is preferred to determine the suitability of the proposal prior to writing the grant rather than wasting time and effort only to have the grant returned as inappropriate.
The best way to organize these items is to make a checklist of support to be written by consultants and collaborators. These materials include forms to be filled out by the sponsored research office in one’s institution or letters information. These materials include forms to be filled out by the sponsored research office in one’s institution or letters of support to be written by consultants and collaborators. The best way to organize these items is to make a checklist (Fig. 1). This will allow one to easily see, at a glance, what is completed and what is missing.

When organizing the checklist, authors should take a moment to decide what the course of action will be if any of the items are unobtainable. Finding alternative solutions will be easier in the planning stage than near the deadline. Having alternative plans is especially important when proposing a multicenter trial. For example, our team planned an 8-center clinical trial when, approximately 3 weeks before the proposal was due, 1 of the centers dropped out because of administrative issues. Fortunately, we had planned ahead and made a list of all items that would need to be changed if this were to happen. Within hours, we were able to alter the proposal and all supporting documents and submit our now 7-center trial proposal to the NIH on time.

The time for writing a proposal ranges from 3 months to 1 year, although the time period for the grant planning

<table>
<thead>
<tr>
<th>Item</th>
<th>Responsible Party</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proposal Approval Form (ePAF)</td>
<td>Sponsored Research Office</td>
</tr>
<tr>
<td>Abstract page</td>
<td>Investigator</td>
</tr>
<tr>
<td>Project Narrative</td>
<td>Investigator</td>
</tr>
<tr>
<td>Budget</td>
<td>Sponsored Research Office</td>
</tr>
<tr>
<td>Budget Justification</td>
<td>Investigator</td>
</tr>
<tr>
<td>Biosketches</td>
<td>Investigator/Consultants</td>
</tr>
<tr>
<td>Resources Page</td>
<td>Investigator</td>
</tr>
</tbody>
</table>

**TABLE 1: NIH Review Criteria**

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significance</td>
<td>0</td>
</tr>
<tr>
<td>Approach</td>
<td>0</td>
</tr>
<tr>
<td>Innovation</td>
<td>0</td>
</tr>
<tr>
<td>Environment</td>
<td>0</td>
</tr>
</tbody>
</table>

The first step in writing an outstanding grant, before a single word of the proposal is written, is to read the instructions—all of them. With instruction booklets for NIH grants numbering 200-plus pages, it is tempting to skim through the instructions, particularly when the information contained is often quite bland. But the information, which includes page limits, font sizes, and the like, is very important, no matter how unimportant the details may seem. For example, a NIH grant will be returned if the margin justification is incorrect. In one study of grants submitted to the NIH, 20% of proposals had formatting errors for which the instructions were clearly spelled out.6

Although completing everything the instructions ask for is critical, it is just as important not to include things that are not requested. Padding the proposal with irrelevant information will not impress the reviewers; quite to the contrary, it will annoy them. Each reviewer has many grants to read; they are not sympathetic to applications that are unfocused and loquacious. Information that is not requested in the application instructions but that the author feels is absolutely necessary to the proposal should be included in the appendix.

Finally, the instructions will provide information on how to submit the proposal. It may need to be submitted electronically or via mail; it may need to include copies of the entire application or just portions of it. It is important to know all of these details well in advance of the deadline. Of course, the most critical piece of information included in the instructions is the application due date. Circle it on your calendar and memorize it. This date is rarely negotiable. Finally, be sure to know where the application components should be sent.

**START EARLY**

Crafting a winning grant proposal takes time, often lots of time. Plenty of time should be left for the actual proposal writing, but there are other portions of the process that can take just as much time. While reading the instructions, make a list of everything that will need to be submitted and who will be involved in or responsible for gathering this information. These materials include forms to be filled out by the sponsored research office in one’s institution or letters of support to be written by consultants and collaborators. The best way to organize these items is to make a checklist (Fig. 1). This will allow one to easily see, at a glance, what is completed and what is missing.

When organizing the checklist, authors should take a moment to decide what the course of action will be if any of the items are unobtainable. Finding alternative solutions will be easier in the planning stage than near the deadline. Having alternative plans is especially important when proposing a multicenter trial. For example, our team planned an 8-center clinical trial when, approximately 3 weeks before the proposal was due, 1 of the centers dropped out because of administrative issues. Fortunately, we had planned ahead and made a list of all items that would need to be changed if this were to happen. Within hours, we were able to alter the proposal and all supporting documents and submit our now 7-center trial proposal to the NIH on time.

The time for writing a proposal ranges from 3 months to 1 year, although the time period for the grant planning
process will vary. If much of the preliminary work is already done, 3 months may be sufficient; if the preliminary work has not been started, it may take more than a year. Similarly, if one has previously written a proposal on the same topic, some sections can be incorporated into the new grant, thereby reducing the writing time. In our experience, we have found that, regardless of writing time, at least 1 month should be allowed between the completion of grant writing and the grant-submission deadline. This gives time to focus on collecting all the remaining unchecked items from the checklist. This will also allow the proposal to be set aside for at least a week and revisited for later review with “fresh eyes.”

One final note on timing of submission: with annual or biannual funding cycles for most agencies, missing a deadline can seem disastrous. But one’s time will be much better spent, and sanity preserved, by perfecting the proposal for the next funding cycle rather than rushing to submit a less than perfect proposal.4,6 In addition to providing a much better chance of being funded, an unhurried-appearing grant will reflect more positively on one’s professional reputation and will enhance the prospect of grant funding when the study section reviews the proposal.

MAKE FRIENDS WITH THE SPONSORED RESEARCH OFFICE
Confusing even to seasoned veterans, the grant-submission process can seem especially daunting to young investigators. Anticipating these difficulties, every institution has an office that handles sponsored research. The personnel in this office are well versed in the administrative end of the grant-submission process, in addition to other aspects of receiving and administering grant funds. They will be able to help fill out forms, double-check that the proposal includes all the necessary components, obtain the required signatures, and often even perform the actual grant submission. This is particularly helpful when submitting a multisite project; the sponsored research office can help negotiate other institutions’ internal requirements.

Contact someone in the research office early in the application process to determine specifically what components they will be able to complete. Expect to provide necessary documentation, such as an approved budget and budget justification, as early as 6 weeks prior to the grant due date. Be mindful of their deadlines. Whereas the funding agency has its deadline, the sponsored research office will likely need the completed application and all supporting documents 7 to 10 days prior to the grant deadline in order to obtain institutional approval and for timely submission of the application. Although it may be tempting to request a later deadline, bear in mind that the research office handles numerous applications. Such requests can result in substantially more work. These individuals in the research office have a wealth of knowledge and are a tremendous source of support. It is definitely in one’s best interest to stay in their good graces.

WRITE CLEARLY AND PERSUASIVELY
Although we have been giving a lot of attention to the exterior details of the grant-writing process, the most important part of any grant application is the written proposal itself. No matter how innovative one’s ideas are, sloppy or unfocused writing can completely obscure these ideas. In addition to basic writing skills, such as sentence structure and grammar, one’s writing needs to flow clearly from one idea to the next.

As noted above, sections taken from previous grants and placed into the new proposal can be a substantial time-saver. But this practice can also be treacherous if one is not extremely detail oriented. The integrated paragraphs may not be harmonious with the rest of the grant, and the overall grant structure may appear “choppy.” Accuracy of information is paramount. A literature search will supply updated information for the background section with addition of new data. There is no need to completely re-create work, but one must be careful to not appear lazy. The grant proposal should be scholarly and reflect the most current information.

Grants have basically the same structure. Below we provide detailed information about these basic sections.

Specific Aims
Generally, the first section of the body of the grant will begin with a statement of the specific aims and hypotheses of the project. This research question is considered the most important section of the grant.6,7 It is the cornerstone of the entire proposal. This provides context for the hypotheses by focusing on the significance (1 of the 5 NIH Review Criteria) of the chosen problem. In this 1-page summary, the purpose and methods of the proposed project are explicitly stated. The specific aims of the project will follow this statement. For each aim, state the specific ways the hypothesis will be tested by using words such as to measure, to compare, to develop, or to perform. Each aim should be followed by the rationale for performing the aim and conclude with the hypothesis for the aim (Table 2).

Limit the aims to 4 or fewer. Overly ambitious aims constitute the most frequent problem identified in this section for proposals submitted to the NIH.6 The aims should be focused, measurable, and be able to be accomplished within the time and budget proposed by the grant. Because all aims proceed from the same research question, they will be interrelated, but they should not be dependent upon one another. If the conduct of aim 2 depends on data derived from aim 1 and performing the study associated with aim 1 is not successful, aim 2 cannot be completed. Reviewers will not recommend support for a proposal that cannot be completed with null results in 1 of the aims. Finally, because the specific aims section is such an important component of the proposal, investigators should continually remind the reviewers of the aims by making frequent and explicit references to the specific aims throughout the subsequent sections.8
**Background and Significance**

If a literature search was performed during the research question development stage, the major portion of the work for this section will have been already accomplished. The first portion will be a more detailed version of the context portion of the specific aims. This section must demonstrate to the reviewers an in-depth knowledge of the important history and current state of knowledge of the field. It should flow from presentation of existing knowledge to informational

---

**TABLE 2: Example of Specific Aims**

The purpose of this proposal is to perform an outcome study that incorporates the MHQ, functional assessments, and an arthritis-specific questionnaire (the Arthritis Impact Measurement Scales 2) to evaluate the effectiveness of SMPA in improving health-related quality of life (HRQL) for patients whose hands are impaired by RA.

The specific aims for this project and their rationales are as follows:

**Aim 1:** To longitudinally evaluate a prospective cohort of RA patients with MCP joint subluxation who will or will not have SMPA. The primary outcome will be evaluated using a hand-specific instrument, the MHQ.

**Rationale:** Outcome assessments in previous studies of SMPA were based mainly on biomechanical criteria (e.g., grip strength, pinch strength) or subjective evaluations by the authors. No study applied validated HRQL questionnaires in the outcome evaluations. Follow-up time varied widely within each study and among studies, ranging from a short follow-up time of a few months to as long as 16 years. The wide range of follow-up time made meaningful comparisons among studies difficult, as short-term surgical outcomes are often markedly different from long-term outcomes. This project will be the first of its kind to recruit a unique cohort of RA patients with defined MCP joint deformities who will enter either a surgery plus medical therapy group or a medical therapy alone group.

**Hypothesis:** RA patients who have SMPA will have clinically and statistically significant improvements in all of the MHQ domains (hand function, activities of daily living, pain, work performance, aesthetics, and satisfaction) compared with non-SMPA patients. These improvements will be maintained at long-term follow-up.

**Aim 2:** To longitudinally evaluate a prospective cohort of RA patients with MCP joint subluxation who will or will not have SMPA. The secondary outcome is biomechanical measurements, which will be evaluated using a panel of objective hand function tests (grip strength, pinch strength, and Jebsen–Taylor test).

**Rationale:** Prior studies have shown that biomechanical parameters do not improve significantly after SMPA, but no control groups were used in these studies. In our study, patients who have SMPA will be compared with a control group of non-SMPA patients to determine whether SMPA will halt the progressive deterioration of hand function in RA patients.

**Hypothesis:** In long-term follow-up, the non-SMPA group will have statistically significant deterioration of hand strength and simulated ADL tests compared with the SMPA group.

**Aim 3:** To compare the global functioning of the SMPA and non-SMPA groups by using an arthritis specific instrument, the Arthritis Impact Measurement Scales (AIMS2).

**Rationale:** Although hand-specific outcomes are important, it is also important to assess whether improvements in hand function and appearance lead to an overall improvement in quality of life. Previous studies on SMPA have not assessed quality of life outcomes using a validated questionnaire.

**Hypothesis:** RA patients who have SMPA will have significant improvements in global functioning compared with patients who do not have SMPA, and the improvements will be maintained at long-term follow-up.

**Aim 4:** To identify clinical factors and patient demographic characteristics that are associated with favorable or unfavorable outcomes after SMPA.

**Rationale:** Clinical and demographic factors are important predictors of patient function after joint replacement surgery, but these factors have not been evaluated in any previous SMPA studies. We plan to identify variables that are associated with favorable or unfavorable outcomes after SMPA to assist surgeons in the patient selection process for this procedure.

**Hypothesis:** RA patients with stage 3 MCP joint disease will have statistically significant greater improvement in hand function after SMPA compared with RA patients with more severe, later stage 4 MCP joint disease.

MHQ, Michigan Hand Outcomes Questionnaire; SMPA, Swanson Metacarpophalangeal Joint Arthroplasty; RA, rheumatoid arthritis; MCP, metacarpophalangeal; ADL, activities of daily living.
deficiencies and controversies in the literature; finally, authors must state how the proposed project will fill these informational gaps.

As the title of this section indicates, this is also an opportunity to show the reviewers the importance of the project. Because this is one of the NIH Review Criteria, consider adding a “significance” or “potential impact” subheading to draw the reviewers’ attention to this criterion. Frame the impact of the project to the mission of the funding agency. For instance, a proposal that had been previously submitted to the National Institute for Arthritis, Skin and Musculoskeletal Diseases was redirected for submission to the National Institute on Aging (NIA).

Although the protocol was nearly identical, we changed the focus, and the project’s impact on the elderly population was enhanced, both in the significance section and throughout the proposal, to match the mission of the NIA. Finally, despite its importance, take care not to overstate the importance of the project. Implying that the study will have worldwide impact is certainly impressive, but only if it is true.

**Preliminary Studies**

This section is focused on the principal investigator and the environment. It provides an opportunity to demonstrate to the reviewers an expertise with the field of research. It also shows that the project is feasible and there is sufficient institutional support to bring the project to completion. This is not the time to be modest. In this section, “more is more.” But one must also be selective. Only previous work that is directly related to the population, methods, or setting of the proposed project should be included.

This section should use pilot data to support the more ambitious study under funding consideration. The pilot data should show that the hypotheses have merit. It is helpful to use charts, graphs, or tables to enhance this section. Irrelevant and redundant paragraphs will diminish the interest of the reviewers and decrease the luster of the proposal. One must avoid including so much pilot data that the project will appear to have already been conducted. Reviewers do not want to support funding for a project that has already been done.

**Research Design and Methods**

This section should constitute the major portion of the grant proposal both in page number (approximately 50% of the page allowance) and in content. Because it is the largest section, the majority of errors appear here. In a study of proposals submitted to the NIH, every grant had at least 1 problem identified in the methods section, and 72% of all identified errors were located in this section. Frequently, problems were found within study sample (example: sample is flawed, sample poorly described), outcomes (example: concerns about blinding, outcome measures not adequately described), and data analysis (example: inadequate control for confounders, insufficient description of analytical approach).

The purpose of the research design and methods section is to describe the proposed project in detail. Attention to the most minute details of the study protocol indicates the investigators’ proficiency in performing the study, which gives the reviewers assurance that the investigators are thoughtful in anticipating pitfalls and limitations associated with the project. The reviewers understand that no study protocol is perfect and unforeseen problems may arise that will affect the conduct of the project, such as inadequate number of subjects recruited or subjects dropping out of the study. Addressing these concerns in this section demonstrates the competency of the research team.

The organization of this section should flow from the general study design to participant recruitment, to data collection, to data analysis. Headings can be used to subdivide the sections. General study design should explicitly state the study design (clinical trial, cohort study, and so forth) and should include a timeline of events over the course of grant support. A visual representation of this will add clarity to the flow of the study (Fig. 2).

It should be clearly stated from where participants will be recruited and what methods will be used to recruit them. List the inclusion and exclusion criteria to be used and adequately justify each exclusion criterion. Take care to note where the exclusion criteria may create biases and how the biases will be prevented or controlled. If participants will be randomized, state the randomization method. Include information on participant incentives, if applicable, including why incentives were chosen and if this may present a bias. Finally, it is useful to present a visual algorithm of how the participants will progress through the study (Fig. 3).

Describe the data collection methods explicitly. This should include what instruments will be used (include copies of questionnaires in the appendix) and how the outcome measurements will be standardized among sites. Indicate with appropriate supporting citations that the instruments are valid and reliable. List the variables that will be collected and at which time points in the study these data will be collected and who will be collecting the data. If blinding will be used, describe the procedures. Reviewers will want...
to see evidence of experience using these instruments or the research team’s experience collecting these types of data. It is helpful to indicate competency through previous publications or pilot data. If one is not well versed in a method being used, consider recruiting a colleague to act as a consultant. The reviewers understand that the principal investigator cannot be an expert in every phase of the project and engaging experienced consultants in the grant is often helpful. However, adding consultants with a national reputation who will not contribute substantially to the grant will be apparent to the reviewers. “Padding” of the grant with an impressive biosketch that serves as “window dressing” will reflect poorly on the principal investigator and hamper the grant’s funding prospects.

Limitations and Conclusion

The limitations subsection often is limited to one-half page but is an important component of a grant proposal. In this section, the investigators will demonstrate an understanding of potential problems and how they can be resolved, as well as address possible confounders and biases and their solutions. Investigators should assume the point of view of potential problems and how they can be resolved, as well as address possible confounders and biases and their solutions. Investigators should understand that the principal investigator cannot be an expert in every phase of the project and engaging experienced consultants in the grant is often helpful. However, adding consultants with a national reputation who will not contribute substantially to the grant will be apparent to the reviewers. “Padding” of the grant with an impressive biosketch that serves as “window dressing” will reflect poorly on the principal investigator and hamper the grant’s funding prospects.

Abstract

This is the investigators’ opportunity to make a good first impression in the proposal, and sufficient time should be spent writing it. The abstract should be a comprehensive summation of the entire proposal. This section is often overlooked, but first impressions are always important. If the abstract is similar or even identical to the introduction, the reviewers may become so irritated that the grant will receive a failing score at the outset. Crafting the abstract can be difficult, and it is usually written after the content of the proposal is finalized. By then, the whole scope of the study can be summarized into the abstract.

Typically, only 2 or 3 reviewers will read the full proposal. The remainder of the reviewers will rely on the abstract. Therefore, the abstract must be an extremely well-polished document that can stand alone from the rest of the proposal. It should emphasize the importance of the project. As there is not much space to explain technical details, use lay-language instead of jargon. Finally, if the proposal will be submitted to the NIH, the abstract will be used to assign the application to a study section. Include key words that will make it easy to identify the appropriate study section for the proposal.

FIGURE 3: Sample of study flowchart.

THINK LIKE A REVIEWER

Writing with the reviewers in mind can be summarized to one simple concept: Do not make the reviewers work harder than they have to. Reviewers are busy people, with lives and careers outside of reviewing grants; they are asked to read multiple grant applications in a short period of time. Reviewers’ time is of the essence, and the majority of reviewers will make up their minds very quickly.

As noted above, the abstract is very important. It allows the reviewers to know immediately what problem will be addressed and how the investigators plan to study it. Likewise, the reviewers want to know the main ideas at the beginning of each section. The first paragraph should serve as the “abstract” for the section. Similarly, the last paragraph of each section should review pertinent information and restate the main ideas, in the event that the reviewers’ attention is lost in the midst of the grant. The artistry of writing the grant, or “grantsmanship,” is a skill that is acquired by a seasoned grant writer. In most cases, a reviewer may be assigned a topic with which he or she is not familiar. Without writing too simplistically for an expert in the field, an experienced grant writer can introduce a complex concept in understandable terms to a reviewer who is not familiar with the topic. The ability to craft a grant that moves effortlessly between highly technical ideas and elegant language structure is the height of grantsmanship.

There are other things one can do to make reviewers’ lives easier and thus make one’s proposal more appealing. First, a grant proposal is not the time to be overly creative. A proposal that deviates from the expected normal format will only confuse the reviewers. Follow the format recommended by the grant application and make the proposal aesthetically pleasing on the page. This can be done by using figures, charts, and diagrams wherever possible. This saves space by conveying large amounts of information in a condensed form and also simplifies complex concepts.
for reviewers who are not experts in the field. Items like timelines, study flow charts, randomization schemes, and preliminary data lend themselves well to graphic presentation. Use headings and subheadings to break up long paragraphs and bullet points to simplify long lists. Use of “white spaces” will provide reviewers a chance to rest their eyes. A proposal that overwhelms reviewers with endless blocks of text is not one they will find appealing.

**PROOFREAD, PROOFREAD, PROOFREAD**

Once the proposal is clearly written, flows well, demonstrates each of the 5 NIH Review Criteria, and has been edited until it seems “perfect,” set it aside for at least a week. Sometimes, once one has read something multiple times, he or she begins to read on autopilot and will miss key errors. After it has been set aside, proofread 2 more times, once for content and once for grammar and punctuation.

It can also be helpful to have a trusted colleague or two read the proposal. Ideally, one of them is someone outside the field but who is an experienced grant writer and can review the proposal for excessive jargon usage, as well as grammar, spelling, and syntax. An expert in the field can comment on the accuracy of content. However, it is important to use good judgment when revising the proposal based on the colleague’s advice. If something is correct in the original document or deviates from the intent of the proposal, do not feel pressured to change it. Finally, when the proposal has been completely edited, print it to check the formatting (especially important for online submissions). Headings should be on the same page as their paragraphs; figures and charts should be numbered correctly and appropriately inserted into the text.

These tips are, of course, just the fundamentals. There are many exhaustive sources that go into much more detail about the grant-application process. One that is especially useful is the “All About Grants” tutorial from the National Institute of Allergy and Infectious Diseases (http://www.niaid.nih.gov/ncn/grants/default.htm). It contains more than 40 pages of information, tips, checklists, and suggestions on all facets of NIH grant submission.

Finally, perseverance is an important trait for any grant writer. At some point, everyone will have a proposal rejected. Only 8% of grant proposals are funded by the NIH on the first submission, but determination, along with revisions that pay attention to reviewers’ critiques, can lead to future success. The percentage of grant proposals funded jumps to 28% for second submissions and 47% for third submissions.

The grant-writing process is long and detailed. It is a facet of the academic environment that competes for the highest level of academic success. With persistence, this process will become more intuitive, and the task will seem far less daunting. All the efforts will be worthwhile when one receives an award that will provide support to conduct a project to address an important question in medicine.

**REFERENCES**