

NOTE: Still open, last updated 7/12/01.

October 25, 1998

**OFFICE OF RESEARCH AND DEVELOPMENT
HEALTH SERVICES RESEARCH AND DEVELOPMENT SERVICE (HSR&D)**

PROGRAM ANNOUNCEMENT: DIABETES



Investigator-Initiated Research Priorities in Diabetes

1. Purpose. The Veterans Health Administration (VHA) is focusing major resources and energy to improve the quality of the health care it provides and to create improvements that are measurable, rapid and sustainable. With the inauguration of the Quality Enhancement Research Initiative (QUERI) in early 1998, special emphasis has been placed on improving the quality of care in ten clinical areas that are prevalent in VA: chronic heart failure, ischemic heart disease, diabetes, prostate disease, stroke, substance abuse, mental health depression, schizophrenia), spinal cord injuries, HIV/AIDS, and cancer. For each of these areas, QUERI will identify gaps in science, practice, and information systems, and develop and evaluate methods for translating evidence of clinical effectiveness into practice. Additional information about QUERI is available on the VA web page at <http://www.va.gov/resdev>.

2. Synopsis. This announcement invites research proposals to enhance the quality of care for veterans with diabetes. Proposals must focus on: 1) evaluating the effectiveness of specific approaches for enhancing adherence to aspects of diabetes care that are highlighted in diabetes guidelines used in VHA, with special emphasis on glycemic control and modifiable cardiovascular risk factors; and, 2) examining the effects of guideline adherence on health outcomes, including patient quality of life. Proposed projects are expected to evaluate potentially efficient ways for promoting diabetes care best practices throughout the VA health care system, document that best practices improve outcomes, and provide information that guides future quality improvement efforts. Projects may request up to four years and total costs of \$750,000. However, HSR&D is especially interested in projects that can demonstrate results in a shorter timeframe. For the initial round of review, a brief planning letter (see Attachment A) must be received by December 10, 1998. Full proposals must be received by February 5, 1999. The first opportunity for proposal review will be March 1999, with the earliest possible funding date of April 1999. Thereafter, projects will require a Letter of Intent consistent with regular Investigator-Initiated research (IIR) policy, and proposal due dates are May 1 and November 1, annually until further notice.

These investigator-initiated research projects are part of a comprehensive and merit-approved strategic plan that also includes two research solicitations for service-directed research projects to develop and validate quality measures in diabetes (see "Service Directed Research on the Development of Diabetes Quality Measures not Available through VISTA and Validation of Quality Profiles Using VISTA," and "Implementation and Evaluation of Amputation Prevention Measures" both available this month on the VA web page at <http://www.va.gov/resdev/hsr-sols.htm>). Investigators interested in diabetes quality of care also should consider two solicitations for

research that cuts across the conditions identified in paragraph one above. Specifically, HSR&D is issuing announcements entitled “QUERI:

Common Issues in Implementation of Clinical Practice Guidelines” and “QUERI: Patient-Centered Outcomes,” also available this month on the VA web page at <http://www.va.gov/resdev/hsr-sols.htm>.

3. Research Priorities. Experts advising the VA have identified three high priority areas of research related to best practices of care in diabetes. These are: glycemic control, hypertension and hyperlipidemia, and self-management education.

a. Improving Glycemic Control.

Over the past decade, efficacy studies have demonstrated that improved processes of care can substantially delay or prevent both microvascular and macrovascular complications of diabetes (National Diabetes Data Group, 1995; Vijan et al., 1997). Microvascular disease, which affects small blood vessels in the eye, kidney and nerves, is predominantly influenced by level of glycemic control (i.e., blood sugar control). The Diabetes Complications and Control Trial and the United Kingdom Prospective Diabetes Study demonstrated that reductions in microvascular disease can be achieved by improving glycemic control for individuals with type 1 and type 2 diabetes respectively (Diabetes Control and Complications Trial Research Group, 1993; UKPDS33, 1998; UKPDS34, 1998).

Unfortunately, the potential benefits related to adequate glycemic control and/or early detection and treatment of complications are often not achieved; substantial deficiencies in the care delivered to patients with diabetes have been documented in almost every sector of the health care system (Hiss, 1996; Hayward et al, 1997). These deficiencies lead to preventable complications of diabetes including blindness, renal failure, amputation, strokes, heart attacks and premature death. A report by VA’s National Center for Cost Containment, using FY 1994 data from 18 VHA facilities, found that a substantial proportion of patients had poor glycemic control (National Center for Cost Containment, 1996). Baseline data from VA’s Office of Performance and Quality indicate that about 17 percent (range by VISN: 13% to 23%) of patients with a documented hemoglobin A1c level had a level greater than 10 percent, which is considered poor glycemic control. In general, the level of glycemic control found at the VA facilities appears similar to that reported in cohort studies and community practice and is better than the level of glycemic control reported for some indigent populations (Hayward et al, 1997).

In response to widespread deficiencies in diabetes care, guidelines and quality standards have been produced by a variety of organizations, including the VHA, health insurers, the American Diabetes Association, and individual provider groups. The glycemic control module of the VHA national diabetes guidelines recommends that HbA1c target goals be individualized, based primarily on life expectancy and the presence or absence of microvascular complications (Diabetes Mellitus Working Group, 1997). This approach is justified by analyses suggesting that the majority of preventable complications occur in the subset of persons with type 2 diabetes with early onset disease (age 50-55 or younger), and anyone with diabetes and poor glycemic control (HbA1c > 9.5%). Therefore, in VHA, this is the highest priority group in targeting for improved glycemic control. The guidelines also discuss various strategies for managing glycemic control including medication, nutrition therapy, home monitoring and physical activity.

Despite several efficacy studies demonstrating that moderate glycemic control can be achieved in virtually all diabetes patients using currently available medications and regimens (UKPDS33, 1998; National Diabetes Data Group, 1995), and clinical guidelines that highlight

various steps for achieving good glycemic control, the most efficient and effective ways to improve glycemic control at the population level are still not clear. Strategies discussed in the literature focus on patient education (Bloomgarden et al., 1987), provider education (Davis et al., 1992), and nurse-coordinated interventions (Weinbeger et al., 1995). However, which strategies are most likely to produce sustained improvements in glycemic control, are acceptable to patients and providers, and are cost effective has yet to be determined.

This program announcement invites large demonstration projects aimed at implementing strategies for improving glycemic control on a broad scale and evaluating both the costs and outcomes of the intervention. Higher priority will be given to projects that place emphasis on targeting patients with high microvascular risk.

Examples of suitable research areas include:

1. Develop or evaluate provider feedback mechanisms that educate and promote best practices, and evaluate their effects on diabetes care and patient outcomes.
2. Develop and/or evaluate patient education or training programs to increase patient knowledge of medication, nutrition therapy, home monitoring, and physical activities and their impact on health outcomes.
3. Create or assess patient and/or provider reminder systems to enhance adherence to best practices and improve health outcomes.
4. Introduce new technologies, pharmaceuticals or supplies to improve or replace existing glycemic control strategies and improve quality of life for patients with diabetes.

b. Improving Management of Hypertension and Hyperlipidemia

Although eye, kidney, and foot complications are the most publicized and feared diabetes complications, macrovascular complications are far more common and are the leading cause of preventable mortality in individuals with type 2 diabetes (National Diabetes Data Group, 1995; Mogensen, 1998). Whether macrovascular disease (i.e., cardiovascular, cerebrovascular and peripheral vascular disease) is delayed by improved glycemic control is somewhat controversial, but there are effective treatments for several cardiovascular risk factors (including hypertension control, serum cholesterol reduction, and aspirin therapy) and reason to believe that risk factor modification will provide even greater benefit for people with diabetes (Hansson et al., 1998; UKPDS38, 1998; UKPDS39, 1998). The results from a large randomized controlled trial of patients with type 2 diabetes show clear benefits, both clinical and economic, related to tight blood pressure control for patients with hypertension and type 2 diabetes (UKPDS38, 1998; UKPDS39, 1998; UKPDS40, 1998). In addition, other blood pressure studies suggest that people with diabetes often have twice the benefit of others (mainly due to their higher baseline risk) from having their blood pressure reduced (Hansson et al., 1998). A *post hoc* analysis of a diabetes cohort in a controlled secondary intervention trial of lipid-lowering agents (statins or HMG-CoA reductase inhibitors) also demonstrated that persons with diabetes had significantly fewer cardiovascular events when their LDL-C levels were lowered (Pyorala et al., 1997).

By providing focus on hyperglycemia, providers may not adequately address major macrovascular risk because of time constraints and the absence of adequate support systems. Studies of community practice have shown that poor control of blood pressure is common (Winickoff and Murphy, 1987). Moreover, even in an HMO that achieved levels of glycemic control that far exceed community norms, major problems were found with serum cholesterol management (Hayward et al., 1997).

Hypertension is defined in the VHA national diabetes guidelines as a blood pressure greater than 140/90; and, according to the guidelines, the goals of therapy (i.e., BP < 140/90 or < 130/85) should be individualized (Diabetes Mellitus Working Group, 1997). Recent experimental trials suggest that tighter diastolic goals (DBP < 80-85 mm Hg) may be even more beneficial for those with type 2 diabetes (Hansson et al., 1998; UKPDS38, 1998; UKPDS39, 1998). Management strategies include medication, nutrition and lifestyle counseling. It is recommended that a lipid profile be done annually (for patients whose life expectancy is \geq 5 years and who are not already being treated for hyperlipidemia) with a target LDL-C value of < 130 mg/dL for all persons with diabetes and < 100 mg/dL for persons with prior coronary artery bypass surgery (Diabetes Mellitus Working Group, 1997). However, effective strategies have not been identified for implementing the guidelines and improving the management of hypertension and/or hyperlipidemia in patients with diabetes.

This announcement invites large demonstration projects that implement strategies for improving control of hypertension and hyperlipidemia in type 2 diabetics on a broad scale and for evaluating both the costs and outcomes of the intervention. Higher priority will be given to projects that emphasize targeting of high-risk patients.

Examples of suitable research areas include:

1. Develop or evaluate provider feedback mechanisms to promote best practices in the areas of hypertension control, serum cholesterol reduction, and aspirin therapy for diabetics.
2. Develop and/or evaluate patient education or training programs to increase patient knowledge of risk factor modification (e.g., hypertension control, serum cholesterol reduction, and aspirin therapy) for diabetics.
3. Create or assess patient and/or provider reminder systems to enhance adherence to best practices and improve health outcomes for diabetics.
4. Introduce new technologies, pharmaceuticals or supplies to improve or replace current risk factor modification strategies for diabetics.

c. Improving Self-Management Education

Although patient education is one of the cornerstones of diabetes care, there is increasing evidence that many traditional approaches to patient education are not successful at optimizing important health outcomes (Bloomgarden et al., 1987; Anderson et al., 1994). Educational interventions that are designed to promote a more active role for patients in managing their diabetes and teach them about the practical aspects of care may be effective (Greenfield et al., 1988; Hiss, 1986), but there is little information about the large scale implementation of such strategies in a way that is cost effective. Consequently, the current

challenge is to identify and implement effective and efficient educational interventions that can be applied throughout the VA system and produce measurable improvements.

This announcement invites large demonstration projects aimed at implementing strategies for improving educational interventions on a broad scale and evaluating both the costs and outcomes of the intervention.

Examples of suitable research areas include:

1. Evaluate periodic versus ongoing contacts and the effects of those contacts on the level of patient self-care.
2. Develop and/or evaluate educational strategies for patients on insulin versus patients on oral agents.
3. Evaluate various educational interventions and investigate the most effective distribution channels for these interventions.

5. Research Methods. All HSR&D studies are expected to use research designs and methods that maximize the validity, reliability, generalizability, and usefulness of findings. While the research needs to be grounded in the realities of VA practice and address real world information needs, it also needs to have a clear theoretical framework, demonstrate familiarity with the pertinent literature, and employ a data collection and analysis strategy that will yield valid conclusions. The multidisciplinary nature of health services research needs to be evident in the formulation of the research questions, and the methodological approach may draw from any, or several, discipline(s). Study teams should generally include individuals with experience and expertise in clinical and non-clinical fields, including pertinent social scientists and research methodologists. The research needs to be designed to maximize the eventual application of findings and conclusions.

Studies responsive to this solicitation are expected to meet the above general criteria. They should add new knowledge based on an appropriate conceptual framework and appropriate research design and methods, including adequate controls and statistical power.

Investigators responding to this solicitation are asked to submit feasible, well-planned, large demonstration projects, not small studies, or randomized controlled trials. It is important to note that this solicitation is not requesting efficacy studies but evaluations that focus on large scale quality improvement efforts, with an evaluation component, that can help identify efficient ways of promoting diabetes care best practices. All projects should provide specific plans for documenting that best practices improve outcomes and that outcomes are associated with improved quality of life. Projects that are not able to address end-stage outcomes directly should include a plan for translating validated intermediate outcomes (e.g., glycemic control and blood pressure) into expected levels of patient benefit (e.g., risk of blindness or renal disease). This translation is important in examining whether the effect of the intervention is clinically significant and in communicating the significance of the intervention to veterans, clinicians and managers.

Demonstration projects submitted for this announcement must:

- focus on well-designed interventions with clear applicability to multiple VA sites,
- test explicit hypothesis(es) about the relationship between the intervention and specified outcomes, and
- include a well-designed plan for obtaining and analyzing the intervention's effects on cost and quality of care

Special review criteria include:

- The extent to which the project addresses diabetes quality of care issues that are prevalent in VA and where variations in care substantially affect health outcomes including microvascular complications (e.g., blindness, end-stage renal disease, and amputation) and macrovascular complications (e.g., coronary artery disease and stroke).
- The feasibility of the project having a national impact within a 2-4 year time period.
- The extent to which the project addresses the priorities of veterans with diabetes.
- The project includes evaluation of costs and effectiveness so as to determine whether the intervention is worth maintaining or extending to new sites.
- The likelihood that the proposed intervention would be acceptable to veterans, providers and managers and could be sustained in the long term.

6. Application Process.

a. Eligibility. Investigators who hold a VA appointment of at least 5/8 time are eligible to apply for research support. Co-investigators, consultants, and support staff may be non-VA employees. Refer questions about eligibility to Robert Small at 202/273-8256 or robert.small@mail.va.gov.

b. Planning Letter. A planning letter is the first step in preparing a proposal. It will be used only for administrative purposes (for format, see attachment A). The usual Letter of Intent (LOI) process required for Investigator-Initiated Research projects, whereby a detailed description of the project must be approved prior to submitting a full proposal, **does not apply** to this round of review. Planning letters are due at the address listed in paragraph 9 ("Inquiries"), by the close of business on December 10, 1998. Facsimile and electronic mail copies will be accepted; address these to John Francis, HSR&D Service, at FAX number 202/273-9007 or john.francis@mail.va.gov.

c. Proposal Preparation and Submission. For detailed instructions regarding preparation and submission of a full proposal, and general review criteria, applicants should refer to HSR&D's "Instructions for Submitting Investigator-Initiated Research Proposals" (available at all VA research offices and on the VA research home page at <http://www.va.gov/resdev>). Full proposals must be received by February 5, 1999 for review in March 1999.

d. Review. The first set of proposals based on this announcement will be reviewed at the Scientific Review and Evaluation Board subcommittee meeting in March 1999. Starting in June 1999, and until further notice, such proposals will be reviewed at regularly scheduled meetings of the Board, along with other IIR projects. Subsequently, and until further notice, proposals responsive to this announcement, based on an approved LOI, will be reviewed at regularly scheduled meetings of the Board, along with other IIR projects. Proposals received by May 1 are reviewed in June; proposals received by Nov. 1 are reviewed.

7. Review Criteria. The review is rigorous and standards very high; both scientific merit and expected contribution to improving VA health services are considered. Investigators are expected to develop and describe their research plan completely and in detail. Proposals recommended for approval will be considered for funding.

7. Funding. Studies submitted in response to this solicitation may not exceed four years or total costs of \$750,000. Both short-term and long-term projects may be proposed, but HSR&D is particularly interested in projects that can demonstrate results in the shortest possible time. For projects that require more than two years, investigators are *strongly encouraged* to identify major milestones or project components for which interim results can be reported and published. In planning project budgets, applicants are reminded to adhere to R&D guidelines regarding allowable use of research funds for specific items. HSR&D expects to fund the first projects under this program in April 1999.

8. Coordination with QUERI. Principal Investigators will submit regular annual progress reports and requested updates to the Director, HSR&D, who will provide these to the appropriate QUERI Coordinating Center, through the Associate Director for QUERI.

9. Inquiries. For further information about this solicitation, contact:

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10. References

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ATTACHMENT A

SAMPLE FORMAT FOR HSR&D PLANNING LETTERS

Provide a one-page letter addressed to the Review Program Manager (124F) that includes the following information:

1. Principal Investigator's name, affiliation, address, phone number, e-mail, and FAX number.
2. Name and affiliation of co-principal investigator, if applicable, and other key project participants.
3. Title and date of the solicitation to which you are responding.
4. Section of solicitation to which you are responding (e.g., paragraph number such as "3a").
5. Proposal title.
6. Specific focus of the proposed study.
7. Major methods to be used and type(s) of analyses to be performed.
8. (Optional) Name two or more scientists who are qualified to review the proposal; include name, degree, title, academic affiliation, complete address, telephone number, and e-mail address, if available.
9. Signature of the ACOS for R&D.

<<<END OF SOLICITATION>>>