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Award Number: W81XWH-11-2-0232

TITLE: Extension of a Computer Assisted Decision Support (CADS) Study to Improve Outcomes in Patients with Type 2 DM Treated by Primary Cary Providers (short title, CADS-X)

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Tacoma, WA 98402

REPORT DATE: October 2012

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



| 1. REPORT DATE | 2. REPORT TYPE | 3. DATES COVERED |
|---|---|---|
| October 2012 | Annual | 30September2011-29September2012 |

**4. TITLE AND SUBTITLE**
Extension of a Computer Assisted Decision Support (CADS) Study to Improve Outcomes in Patients with Type 2 DM Treated by Primary Cary Providers

**5a. CONTRACT NUMBER**

**5b. GRANT NUMBER**
W81XWH-11-2-0232

**5c. PROGRAM ELEMENT NUMBER**

**6. AUTHOR(S)**

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**5d. PROJECT NUMBER**

**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

The Geneva Foundation, Tacoma, WA 98402

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSOR/MONITOR'S ACRONYM(S)**

**11. SPONSOR/MONITOR'S REPORT NUMBER(S)**

**12. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for Public Release; Distribution Unlimited

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
The overall aim of this proposal is to test the long-term, clinical effects of a Computer Assisted Decision Support (CADS) System for the management of Type 2 DM (T2DM) by primary care providers (PCPs). Moreover, the aims are to compare longitudinal patterns of change within and between patients who are managed with the CADS system for differing durations. This comparison will help us to understand the clinical utility of using the CADS system continuously or up to a certain threshold of patient improvement. To achieve these aims, we request a second year of funding (first year funded through United States Army Medical Research Acquisition Activity [USAMRAA], contract number W81XWH-09-2-0196, and is currently ongoing) for a prospective, cluster, randomized controlled trial (RCT). The ongoing project is a multi-site study including the Army (Walter Reed Health Care System or WHCS), the Air Force (Wilford Hall Medical Center or WHMC), and the University of Hawaii (UH).

The proposal herein is not duplicative of any current study but rather an extension of the already funded one. A detailed, technical explanation of the software and hardware elements of this study are included in reports for the original CADS study and available upon request.

**15. SUBJECT TERMS** none provided

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | USAMRMC |
| U | U | U | UU | 74 | 19b. TELEPHONE NUMBER *(include area code)* |

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**INTRODUCTION**

Diabetes mellitus (DM) affects nearly 26 million people in the United States and is associated with devastating complications in both personal and financial terms. Diabetes is the leading cause of blindness, non-traumatic amputations, and renal failure in adults and reduces life expectancy by 5-10 years. The direct ($116 billion) and indirect ($68 billion) costs of DM care have dramatically increased along with the epidemic increase in the number of those with DM over the past 10 years. The cost of medical care per capita is approximately $10,000 per year compared with $2,700 per year for those without DM. The vast majority of these costs are related to hospitalizations resulting from the chronic complications of DM, with only about 15% of the costs attributable to professional visits and pharmaceuticals.

The Diabetes Control and Complications Trial (DCCT), the United Kingdom Prospective Diabetes Study (UKPDS), and the "Kumamoto" study conclusively proved that improved glycemic control is important in reducing microvascular complications (1-3). Together, these studies showed that for every 1% decrease in A1C, there is a 25% decrease in microvascular complications. Based on these studies, the American Diabetes Association (ADA) recommends that the goal for A1C should be below 7% (normal = 4 - 6.1%) (4), and the American Association of Clinical Endocrinologists (AACE) recommends that it should be below 6.5%, corresponding to average blood glucose (BG) values of 150 and 135 mg/dL, respectively, [normal = 70 - 126 mg/dl] (5). Furthermore, years of improved glycemic control appear to have a legacy effect and not only reduce the future rate of microvascular complications but also decrease the incidence of macrovascular complications in both Type 1 and Type 2 diabetes (6-7).

Hypertension is one of the most common co-morbidities associated with DM and substantially contributes to the macrovascular disease that occurs in up to 80% of patients with DM (14). Several large randomized clinical trials (RCTs), including the UKPDS, demonstrated that, independent of the effects of glycemic control, improving blood pressure (BP) control significantly reduced macrovascular complications and cardiovascular-related deaths (14-17). Similarly, the UKPDS showed a 13% reduction in microvascular complications for every 10 mmHg reduction in systolic pressure (18). This finding was confirmed and extended to DM patients who were "normotensive" (19). Gaede et al. showed the marked benefit of aggressive blood pressure, lipid, and blood glucose management achieved through multifactorial intervention (20). There also appears to be a legacy effect of blood pressure control in Type 2 diabetes as recently shown by Holman et al. (21).

Despite the well-documented benefits of glycemic and BP control, these are still sub-optimal in most patients. Although there is a trend toward improved glycemic control, the latest (2004) National Health and Nutrition Examination Survey (NHANES) data demonstrated that 42.3% of patients with DM have A1Cs over 7% (22). The military healthcare system (MHS) - where there is no cost to the patient for care and testing supplies - has similar results with hemoglobin A1C's over 7% in 42% of all patients with diabetes, and over 9% in 23.3% of all patients with diabetes. The data from the Walter Reed Health Care System (WRHCS) is similar, with 51% of all patients with diabetes having an A1C above 7% as of December, 2009. Furthermore, BP control in our patients is similar to the national average, with 62% of our patients having either systolic over 140 mmHg and/or diastolic over 90 mmHg under current treatment. Recommended levels to reduce the risk of cardiovascular mortality and morbidity are less than 130/80 mm/Hg.

***Reasons for Sub-optimal Achievement of Diabetes Control***

The reasons why more patients do not reach appropriate goals for glycemic control are multiple and complex. First, due to an insufficient number of Endocrinologists and Certified Diabetes Educators in both military and civilian health care settings (23), the vast majority of patients with DM are managed by primary care providers (PCPs), including family practitioners, nurse generalists, nurse practitioners, and physicians' assistants, who are not necessarily equipped with the latest information and tools to provide optimum care, nor have the time required to evaluate relevant data necessary to do so. The patient may bring his/her handwritten logbook and/or meter to the clinic where the data must be reviewed manually or the patient will bring his/her memory-equipped meter to the clinic, where it may be uploaded to the provider's computer and analyzed. Manual review of the records precludes any statistical and graphical analysis of the data and often limits the provider's ability to recognize patterns and trends. Moreover, this approach is a time-consuming and an inefficient use of both the provider's and patient's time. Uploading of the glucose data provides the requisite statistical and graphical analysis. However, all the major glucose meter manufacturers have their own proprietary software – none of which are integrated into the electronic medical record (EMR) - and each of the meters has its own unique connecting cable. Thus, the multiplicity of non-integrated programs and connecting cables prevent the provider from efficiently reviewing BG data and thus creates a significant barrier to using this technology.

Second, the introduction of new oral and parenteral agents has exponentially increased the complexity of the management of T2DM in the last 10-15 years. Prior to the introduction of metformin in 1995, the only available class of oral agents was sulfonylureas. Now there are thirteen classes of oral medications, insulins, and non-insulin injectables. Recombinant human insulin and analog insulins have come into common use and the long-acting insulin analogs (insulin glargine and Detemir) have been incorporated into many regimens for Type 2 diabetes, either alone or in combination with oral agents. The enormous number of possible combinations of therapeutic agents makes it difficult for physicians to be familiar with all available approaches. Making matters more complex is that for each class there may be several options, e.g. for insulin

secretagogues one can choose sulfonylureas like glipizide, glipizide-XL, or glyburide or a meglitinide such as nateglinide or repaglinide.

Third, self–monitoring of blood glucose (SMBG) on the part of the patient is an essential tool in achieving improved glycemic control. Several studies have shown that improved glycemic control is cost effective in both Type 1 and Type 2 DM (T1DM and T2DM) despite the increase in cost of supplies, a greater number of clinic visits, and more pharmaceuticals used. Yet, many patients do not monitor as recommended, in part because of the barriers noted above (e.g., they perceive that their providers cannot or do not review the SMBG results), a lack of understanding of how to use their glucose data to improve their glycemic control, as well as social and personal barriers.

***The Case for Systematic, Rigorous Examination of a Computer Assisted Decision Support System for Diabetes Management***

Although many studies have demonstrated the potential advantages of telemedicine, web-based, and/or web-assisted DM management, most have used the web for patient education, performance monitoring, risk stratification, and case management by nurses (24-26). Only a few studies have shown that using the web and/or e-mail improves glycemic control (27-29) or can reduce the number of clinic visits (30) while others have not been able to show such an effect (31-32).

Computer-assisted algorithms to provide decision support for interpretation of the glucose profile have been previously developed and published by the collaborators on this project as well as others (33-36). We and our colleague (Berger) have previously developed methods to automatically select regimens and doses of insulin for patients with T1DM (37). Lehmann has adopted and slightly modified the models of Rodbard and Bergman, and used it to develop "AIDA" – http://www.2aida.org – a program intended for education of health care providers and patients (38). This has not been employed therapeutically and no controlled trials have been performed.

There are only a few studies investigating decision support in the management of diabetes. Holman (36) and Chiarelli (39) reported that portable decision support devices used by patients with T1DM resulted in improved glycemic control. A web-based decision support system (DSS) improved compliance with generally recognized process measures of DM care (e.g. the number of A1C and low density lipoprotein [LDL] tests obtained) but did not improve the actual A1C level (40). Cleveringa et al. were unable to show that a DSS used by a practical nurse improved A1C in T2DM although it did improve cardiovascular risk factors (41). Recently, the IDEATel consortium study showed that a telemedicine application improved A1C, BP and lipids in an older, ethnically diverse and underserved population (42). Salzsieder and colleagues used their Diabetiva® program to apply continuous glucose monitoring (CGM) data to a DSS to improve A1C (43). Decision support systems that have been used in blood pressure management show conflicting results (44-45).

Building on our prior experience in developing methods to select regimens and doses of insulin for patients with T1DM, we developed a CADS system for management of T2DM by PCPs to overcome many of the aforementioned barriers to the appropriate management of T2DM. The key feature of CADS is that it simplifies the work of the PCP by automatically integrating the essential factors necessary to make a recommendation for management - the patient's SMBG data from their uploads, current and previous medication, and current relevant laboratory data – and then making a recommendation based on established consensus algorithms (47).

**BODY**

The use of a computer assisted decision support (CADS) system has been described in detail in the quarterly, annual, and final reports that have been submitted. The goal of the first study (Year 1 or Months 1-12) was to determine whether or not the use of CADS by PCPs, i.e. Internists, Family Practitioners, Nurse Practitioners, and Physician's Assistants, can improve glycemic and other outcomes in patients with poorly controlled T2DM over one year. The theoretic construct for establishing the hypotheses is that non-endocrinologist providers have neither the time nor expertise to address critical issues of management for patients with T2DM and that a CADS system will help them do so. Additionally, a CADS system will, because it saves time in the management of glycemic-related outcomes, permit providers to give more attention to management of the important co-morbidities of T2DM. Finally, a patient with improved glycemic control and comorbidities will be more satisfied with their overall treatment.

This study, entitled "Extension of a Computer Assisted Decision Support (CADS-X) Study to Improve Outcomes in Patients with Type 2 DM Treated by Primary Care Providers" (CADS-X), was designed with two primary aims: (1) to provide those providers who were not assigned to the CADS arm in the initial study an opportunity to "cross-over" to CADS in a subsequent year provided that: a) CADS is shown to produce statistically significant improvements in A1C or other response variables (fasting plasma glucose {FPG}, post-prandial plasma glucose {PPG}, post prandial excursions, rate of hypoglycemia) and b) funding is available for continuation of the trial; and (2) to determine the legacy effect of CADS by providing primary care providers (PCPs) and their patients who were initially randomized to CADS an opportunity to use CADS for an additional year for a total of 2 years.

Significant challenges in the approval and implementation of the original study, "The Use of a Computer-Assisted Decision Support (CADS) System to Improve Outcomes in Patients with Type 2 Diabetes Who Are Treated by Primary Care Providers" (the CADS study), have delayed our ability to implement the extension study. The following provides a brief overview of the original study and the challenges that have prevented us from completing the first study.

The purpose of the original study, CADS, was to test the safety and efficacy of a computer assisted decision support (CADS) system in a multi-site, ethnically and geographically diverse study in a 12-month, open, prospective, cluster-randomized, controlled clinical trial. Specific aims included: (1) monitor the impact of the intervention on a) measures of glycemic control, b) the number of diabetes–related hospitalizations and emergency room visits, c) the control of co-morbidities, hyperlipidemia and hypertension, d) the number of clinic visits, and e) the change in the patients' quality of life as a result of the intervention; and (2) evaluate the PCPs' and patients' satisfaction with the technology. The progress of the CADS study as well as the challenges to the achievement of our specific aims has been described in detail in quarterly and annual reports submitted for the original study.

The following summarizes the challenges and our solutions to date.

1. Institutional Review Board (IRB) approvals for the three participating institutions, Walter Reed Army Medical Center (WRAMC), Wilford Hall Medical Center (WHMC), and the University of Hawaii (UH) School of Medicine.
    a. The protocol was submitted to the WRAMC IRB in December 2009. It was approved in March 2011.
    b. The protocol was submitted to the WHMC in February 2010. The investigators received final approval to begin the study in October 2011.

2. The adverse impact of the Base Realignment and Closure (BRAC) in August 2011 and on several factors relating to IT and provider and patient re-assignment prior to August 2011:
    a. The Information Assurance, Management, and Technology Departments at both Walter Reed National Military Medical Center (WRNMMC), formerly WRAMC, and Wilford Hall Ambulatory Surgery Center (WHASC), formerly WHMC.
        i. The Comprehensive Diabetes Management Program (CDMP), a web-based chronic disease management program was designed to exchange relevant medical information with the Integrated Clinical Data Base (ICDB), the electronic medical record (EMR) for patients being treated at MTFs throughout the U.S. ICDB was disabled at WRAMC when AHLTA was introduced. Through much effort and two AAMTI grants, a bi-directional test link was developed between AHLTA and CDMP at WRAMC.
        ii. It was then determined that CDMP and CADS must complete the DoD Information Assurance Certification and Accreditation Process (DIACAP) before they could be operationalized.
        iii. WRNNMC began the DIACAP approximately 2 years ago. CDMP received DIACAP approval at WHMC, but the addition of CADS has required additional DIACAP certification.
        iv. Delay of DIACAP certification has impacted the study in two major ways:
            1. There is no exchange of relevant patient information between the existing EMRs at WRNMMC and WHASC.
            2. Providers randomized to CADS and working at WRNMMC and WHASC are unable to access the program from their work computers.

v. The following strategy will be utilized as a temporary strategy until CDMP/CADS has been DIACAP certified:
    1. The Project Officers (POs) at WRNMMC and WHASC will manually load into CDMP the information from the patient's EMR that is necessary to correctly run the CADS analysis. This information includes relevant laboratory values, current and past medications, and co-morbid or co-existing diagnoses.
    2. The PO and the provider will determine the patient's target A1C level which the PO will enter into the CADS program.
    3. Once the patients have uploaded their de-identified glucose data into a password-protected server, the Project Officers at WRNMMC and WHASC will run the data through the CADS analysis and provide recommendations via email to the subjects' providers.
    4. The providers will select one of the recommendations which the PO will then select in the program.
    5. If the provider does not choose to follow any of the recommendations the PO will ask him/her for a reason and document the reason given.

b. The re-allocation of both providers and patients originally at WRAMC to either Fort Belvoir Community Hospital (FBCH) or Walter Reed National Military Medical Center (WRNMMC) further complicated enrollment for three reasons:
    i. Providers did not necessarily retain their same panel of patients.
    ii. There was a significant delay in recruiting from WRNMMC, FBCH, and KACC as both providers and patients became accustomed to new locations and, often, new rules and policies.
    iii. We were advised in March 2012 that FBCH and KACC needed site specific addenda (SSAs) in order to participate in the study. Since we were submitting other addenda at the time, we were advised by the WRNNMC IRB to not submit the SSAs until the other addenda were submitted.
        1. SSAs for both sites were submitted in July 2012.
        2. Approval to begin recruitment at KACC in was received November 2012
        3. Approval to resume recruitment at FBCH is pending.

3. The most recent challenge to the research being conducted at WRNMMC and WHASC has to do with the method patients will use to upload their glucometers in order to run the CADS analysis.
    a. *i*Metrikus, the original device developed by Numera, has been upgraded and is now called MetriLink.
    b. The negotiation of the contract between Numera and the Geneva Foundation was conducted independent of the research staff.
    c. The research staff was not informed that, with few exceptions, the MetriLink requires analog, landline telephones in order to work.
    d. When the protocol was being developed, the only information given to the researchers was that the device required a landline telephone in order to work.
    e. This has presented a huge problem since most of the patients have carriers that combine internet, digital telephone, and cable TV as one package. Options:
        i. Use of MyGlucoHealth, the cell phone compatible meter being used in HI is not an option because it was not budgeted, it is not on the Core Formulary at either WRNMMC or WHASC, and it would involve additional personnel costs as it would be distributed by the research pharmacy.
        ii. There has been some success with clients using Comcast, but it is not guaranteed.
        iii. There is a web-based connection that can be used with the purchase of a cable. The instructions are somewhat complex and thus add another level of complexity, and may require the patients to purchase them.

4. Recruitment efforts at UH have been hampered by providers who withdrew interest or were no longer practicing once the study began, and by the need to find additional providers in the clinics that have been approved to participate.

5. Recruitment efforts at all sites have been hindered by the sample size and A1C eligibility range. Efforts to address these factors are described in Research Accomplishments.

**KEY RESEARCH ACCOMPLISHMENTS**

***Enrollment during Period of Performance:***

WRNMMC: 11/18 providers; 18/234 patients. Providers need 13 patients for randomization. One provider has 10 patients who have been consented with 2 pending consent. Per protocol, once 13 patients per provider, provider and patient will be randomized to the intervention (CADS) or usual care.

WHASC: 7/18 providers; 17/234 patients. WHASC IRB required new consent forms for both providers and patients as a result of a recent amendment that reduced number of A1Cs within target range for eligibility from 2 to 1, increased number of providers and reduced number of patients per provider. The Project Officer at WHASC was required to re-consent providers and patients who had been previously consented. This requirement prompted another delay in recruitment.

UH: 5/6 providers; 2/78 patients.

An amendment identifying 2 changes designed to reduce barriers to enrollment was submitted and approved by all institutions' IRBs during the PoP:

1. Change in A1C requirement: We have determined that requiring 2 A1Cs does not add any scientific value to the study and may be a deterrent to enrolling patients.
2. Change in sample size: Number of patients per provider was decreased from 19-13 at all three research sites and number of providers was increased from 12 to 18 at WRNMMC and WHASC. The number of providers at UH remained the same.

The new sample size estimate was generated as follows and is included in the revised protocol. First, we calculated the sample size that would be needed to test our primary hypothesis regarding glycemic control (defined as change in A1C) without yet accounting for the clustering effect. The sample size needed is based on achieving a decrease in A1C of 1.0% (between subject SD = 1.5%) in the CADS "Intervention" group and 0.5% (between subject SD = 1.7%) in the "Usual Care" group. These estimates, regarding the average amount of decline in A1C for the two groups and the standard deviation, are based on our prior research of intervention with continuous glucose monitoring in a group of patients with poorly controlled T2DM (presented at the Annual Meeting of the Endocrine Society, June 11, 2009 and separately at a meeting of the Diabetes Technology Society November 2009). (54, 55) Furthermore, we assumed an alpha of 0.05 and power of 0.80, with a 1:1 ratio in study groups. Given these parameters, we expect that one would need to recruit at least 324 patients (162 patients per group). The effect sizes were selected as the minimal changes likely to have clinical significance and therefore be able to warrant adoption by primary care providers.

Second, we 'corrected' the sample size estimate by taking into account the clustering effect. Based on previous research, we assumed that the intra-class correlation coefficient (ρ, rho) would be about 0.03. (54) For this 'correction', we further assumed that we would need a minimum of 10 patients per cluster, to allow each provider to have sufficient opportunity to work with CADS (n = 10 patients times 3 consultations with CADS [at 3, 6, and 9 months] = 30 consultations on average, with some getting more and some getting less). These assumptions generated an estimate for the number of clusters/providers we would need, which was 42. We will distribute the number of providers as follows to achieve 42: 18 clusters at the WRNMMC, 18 clusters at the WHMC, and 6 clusters at the UH.

Given these assumptions and constraints, we estimated that we need a minimum of 412 patients (206 per group) total, distributed among the providers, before taking attrition into account.

Third, we considered the effect of attrition over the course of 1 year. For this consideration, we assumed two types of attrition could occur – patient attrition and provider attrition. Provider attrition would result in the loss of both provider and his/her patients. For both types of attrition, we assumed rates of 15%. Thus, to adjust for the possibility of patient and provider attrition, we estimated that we need to recruit 546 patients across 42 clusters. On average, each provider will work with about 13 patients.

***Bi-monthly Conference Calls***

Bi-monthly conference calls are held to assess screening and recruitment activity, identify problems, and discuss solutions. Recruitment has been one of the most difficult aspects of this study. Our attempts to facilitate enrollment resulted in the amendment that reduced the number of A1C levels between 7 and 11% from 2 to 1 in the previous 6 months, and to change our sample size. Changing the sample size was predicated on our ability to enroll providers fairly easily. Thus, increasing the number of providers allowed us to decrease the number of patients required to test our primary hypothesis regarding glycemic control (defined as change in A1C). The elimination of one of the two A1C within the specified range required for study entry did not change the value of the study.

Other efforts to increase enrollment include face-to-face meetings between the research staff at each site and providers, email reminders to consented providers to inform site research staff of potential patients, and database searches.

***CDMP and CADS Maintenance and Enhancements***
Further delays in the DIACAP approval process at both WRNMMC and WHASC have been explained in the CADS 1st and 2nd quarterly reports and will not be repeated in this report. The DIACAP process is cited briefly in the section under Task 1.

Task 1
In support of the CADS research protocol, Estenda Solutions, Inc. will integrate CADS into each site's electronic medical record (EMR) as necessary, maintain the CADS/CDMP systems and the links with the site EMR, ensure that links with iMetrikus are continuously functional, provide secure storage of the data, and re-program and test the algorithms as deemed necessary by the PI. The CDMP, CADS and iMetrikus services are fully operating and available to research staff. Estenda continues to work with the JTF on renewed DIACAP certification so that the system can be reconnected to the central patient medical record via ICDB. Minor updates and maintenance was conducted on the CADS system as required.

Task 2
In support of continued DISA compliance over the project lifetime, Estenda will update all of the third-party infrastructure components required to versions that have documented support through 2012. These infrastructure components include Oracle Database Server, Weblogic Application Server, MIRTH Integration Engine, Struts Java Framework, etc. Estenda completed major infrastructure updates during this quarter; the completed solution is pending a final system test and then will be migrated to production in mid 2013.

Task 3
In support of the research team's clinical data capture and management Estenda has made significant upgrades to the platform's existing Survey and Study Management sub-modules. Specific improvements included (1) adding a user friendly tool for users to create their own subject data collection forms; (2) improving navigation features based on feedback from use on prior Diabetes Institute research studies; (3) adding native support for additional study randomization schemes; (4) improved ability to correct site data entry errors through a managed workflow; and (5) improving subject informed consent workflow. These important modifications will help support efficient, accurate and auditable data collection across the study's lifecycle. Improvement 1 is complete pending a final system test. Development items 2, 3, 4 and 5 are underway with a target completion date of 6/30/2013.

Task 4
The core diabetes data management platform of which CADS is a module requires modification in order to fully support its research mission. Core improvements include (1) adding functionality for authorized clinical staff to merge duplicate patients; (2) supporting for a broader range of Web Browsers; (3) allowing users to customize the patient information "snapshot" to best meet their individual mission; (4) improved graphing; and (5) adding new support to capture for patient reported use of alternative medications. These efforts will be initiated during the first quarter of the second year of this award, October 1, 2012 to December 31, 2012. Estenda has completed modifications to support a range of current, common web browsers. The remaining modifications will be addressed Jan 2013 - Jun 2013.

***CDMP and CADS Maintenance and Enhancements: Additional Accomplishments***
***Completion of CADS User Manual***
The CADS User Manual (Appendix A) was completed in June 2012. Its use was demonstrated in a webinar that was held in June 2012. Additional minor changes are being made as deemed necessary.

***Completion of Study Manager and the Study Manager User Manual***
Study Manager is a standalone component within the Comprehensive Diabetes Management Program (CDMP) that was designed to track subjects' progress through an entire study and has the capacity to be customized to every study. Study Manager includes alerts to remind the research coordinators/project officer of tasks and due dates. Study Manager has been nearly completed for use in CADS. The Study Manager User Manual (Appendix B) was completed in June. Study Manager is undergoing some additional changes and the user manual will be modified to reflect changes once they are complete.

The list of algorithms has been expanded to include the combination of GLP-1 receptor agonists together with insulin, specifically basal insulin. One can have oral agents progressing to GLP-1, to insulin, or to GLP-1 + insulin. GLP-1 can progress to GLP-1 + insulin, and insulin can progress to GLP-1 + insulin.

***Development of Questionnaires and Surveys, and Design of Focus Groups to Monitor the Response of Health Care Providers and Patients to the Use of the CADS System***
Dr. David Rodbard has developed two questionnaires to be used in focus groups of 5 for providers who are participating in the study at one site. In order to keep a finger on the pulse of the study, especially with the providers who are randomized to CADS, Dr. Rodbard recommends that the first focus groups be held after training or exposure to the program and again at 6 months, 1 year, 18 months, and 24 months. Duration of each focus group

would be 30 minutes to minimize disruption in work flow. A focus group leader would be an MD or NP who has experience with the CADS and has seen the recommendations made by CADS for at least 3 patients.

1. The primary objectives of the CADS focus groups (Appendix C) would be to:
    a. Identify any major problems either with operations or with the content of the system
    b. Reduce the likelihood of provider and patient attrition
        i. Empower the providers by soliciting and respecting their opinions.
        ii. Their involvement or empowerment may help to sustain participation and reduce the risk of attrition.
        iii. The interest and enthusiasm of the clinician may significantly affect the participation of the patients, and thus reduce the likelihood that the patients will withdraw from the study.
2. The primary objectives of the usual care focus group (Appendix 5) would be to:
    a. Minimize the risk of skewing the results of the study in terms of differences between the CADS and usual care group by offering a focus group with 5 providers randomized to the usual care group.
    b. Questions that would guide this focus group would include those that address more “generic” aspects of caring for people with diabetes, such as the use of professional guidelines or use of the current EMR

Essentially the same topics for discussion could be reviewed with the study participants (clinicians) after 6 months, 1 year, 18 months and 24 months.

**REPORTABLE OUTCOMES**
None to date.

**CONCLUSION**
Diabetes mellitus is a significant cause of morbidity and mortality in the United States, and the leading cause of new blindness, chronic kidney disease, and non-traumatic amputation in the working-aged American population. Although the financial costs to individuals, communities, and health care systems are measurable, the devastating costs in terms of quality of life personal costs are not easily measured. A computer assisted decision support system that makes available the knowledge and expertise of endocrinologists to primary care providers who care for the majority of people with Type 2 diabetes has the potential to significantly improve the level of care provided to people with T2 DM, thus preventing or delaying the onset of and/or reducing the severity of diabetes-related complications. Reducing the risk and/or severity of complications promises to improve the quality of life for people with T2 diabetes and decrease the financial impact on the individual as well as both the military and civilian health care systems.

CADS is a web-based interactive application that enables primary care providers to aggressively and systematically use available medications to help their patients move increasingly and safely toward a level of glycemic control that minimizes their risk of developing diabetes-related complications and/or the severity of these complications. The extensive delays in and challenges to the implementation of the original study have made it impossible to begin the extension study as planned. The research staff at all three sites are making a consistent and concerted effort to meet enrollment goals. It is our hope that, once fully executed, the successes and lessons learned from this study can be applied to an even larger population of people with Type 1 and Type 2 diabetes, thus further mitigating the devastating financial and personal costs of poorly controlled diabetes mellitus.

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# COMPUTER ASSISTED DECISION SUPPORT

For Management of Patients with Type 2 Diabetes

# CADS

Quick Reference User Guide

June 13, 2012

Version 1

## NOTE:

This software is being introduced as part of a research study that has been approved at the Walter Reed National Military Medical Center (WRNMMC), Wilford Hall Ambulatory Surgery Center (WHASC), and the University of Hawaii (UH).

In order to main the integrity of the study, only physicians and other providers who have been enrolled in the study, consented, and randomized to CADS (the intervention arm) are authorized to use this program.

Table of Contents

## Key Personnel

**Walter Reed National Military Medical Center (WRNMMC)**

- PI: Dr. Robert Vigersky COL MC USA
- RC: Dr. Mary Chellappa
- Program Manager: Dr. Susan Walker

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## INTRODUCTION TO CADS

**Primary Purpose of CADS:**

- To enhance primary care providers' (PCPs) ability to help their patients on basal insulin, oral hypoglycemic agents, non-insulin injections, or diet and exercise to achieve and maintain glycemic control.

**Reasons for failure to achieve glycemic goals:**

- Patients
    - Insufficient education and/or inability to use self monitoring of blood glucose (SMBG) effectively
    - Inability or lack of resources to download glucose data at home or in clinics
- Providers
    - Inadequate amount of time allowed for PCP to identify patterns and discuss with patients
    - Overwhelming number of single and combination agents available to treat hyperglycemia
    - Clinical inertia

**Difficulties in maintaining glycemic goals:**

- Patients
    - Patients do not understand how to use SMBG to make lifestyle changes, e.g. diet and physical activity
    - Infrequent use of SMBG
    - Inefficient use of SMBG efficiently (i.e., pre and post prandial, aka structured or paired testing)
    - Inability or unwillingness to download SMBG data
- Providers
    - Not feasible to download SMBG data in Clinic
      No time available to analyze SMBG data
    - Therapy not adjusted frequently enough
      Numerous medications and combinations are available, but most physicians use only a subset
    - Cannot access literature, guidelines, algorithms

***CADS is the result of the development of a comprehensive set of algorithms by two endocrinologists with combined experience of more than 50 years as diabetologists. CADS makes recommendations, but the provider determines treatment!***

## CADS: Key Elements

- Patients will
  - Perform SMBG 2-4X/day, 4X/day once a week, and 8X/day once a month.
  - Upload glucometer every 2 weeks using a device called *i*Metrikus and a landline telephone (WR & WH) or using a cell phone and a glucometer called MyGlucoHealth (UH).
- Research Coordinator (RC) at WRNMMC & WHASC[1] will
  - Upload into CADS the necessary information for CADS to work, e.g. current medications, current laboratory values, current A1C level, and after discussion with the PCP, target A1C level for each patient.
  - Send provider's patient's BG data to coincide with patient's quarterly visits &/or t-cons.
  - Send providers the recommendations made by CADS for that set of data.
- CADS will
  - Provide statistics and graphs that identify glucose values and patterns
  - Make recommendations for therapy
    - Note: If 10% or more of the patient's BG levels are < 60 mg/dL, CADS will provide recommendations that address the hypoglycemia.
    - **Addressing hypoglycemia is always CADS first consideration!**
  - Identify major types of clinical problems &/or co-morbid conditions that would be contraindications to certain medications

**Benefits of CADS**

- Data available for you – the clinician – at the time of clinic visits and telephone consultations
- Quick, easy
- Automated access to SMBG data
- Automated access to laboratory data
  - A1C, Liver function tests, Renal function tests, Lipid panels
- Automated access to diagnoses
  - Possible contraindications to various medications identified
- Record of previous medications
  - Record of previous adverse events and side effects
- Ability to export or print a file for inclusion in the patient's medical record

Features which may be added at a later date

- Automated generation of a clinic note
- Automated generation of an electronic prescription
- Ability for patient to view SMBG data, graphs and statistics

**IMPORTANT THINGS TO REMEMBER**

- Only applicable for *Type 2 Diabetes* patients who are using diet and exercise, oral meds, non-insulin injectables, and basal insulin
- Not for Type 1 Diabetes
- Not for acute therapy, e.g. DKA, hyperosmolarity, or hospitalized patients
- Not for use in children, adolescents, for diabetes during pregnancy or for gestational diabetes

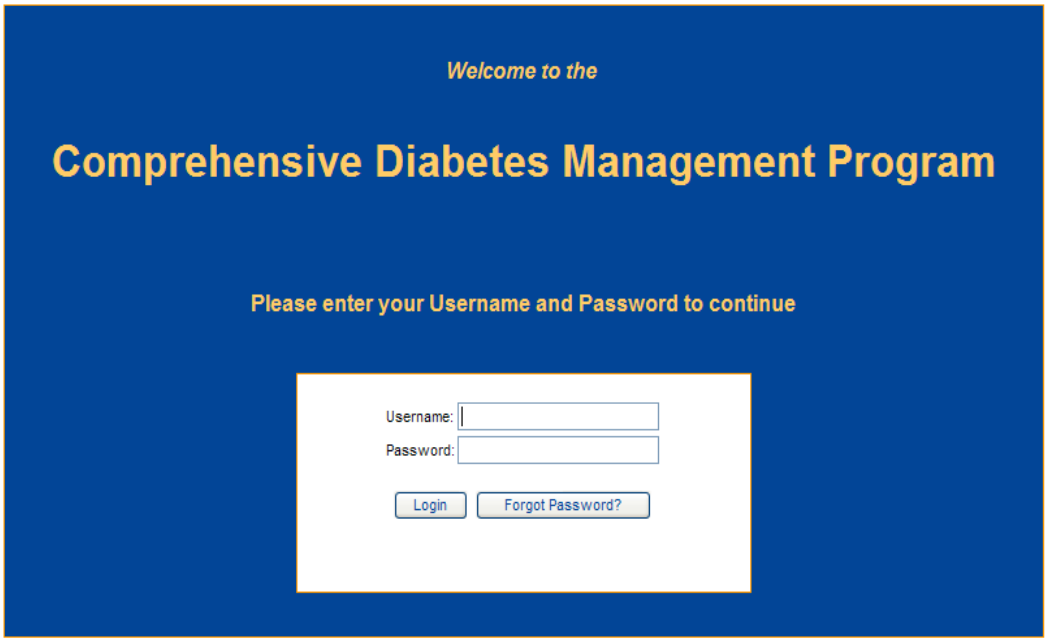
**Each physician/clinician must exercise their clinical judgment in view of the total clinical situation**.

**If in doubt, seek additional information and consult a colleague or a specialist!**

## USING CADS TO GET TREATMENT RECOMMENDATIONS

1. Login
2. Select Patient
3. Enter the CADS System
4. Run Analysis
5. Enter the target A1C
6. View Recommendations for Therapy
    - View multiple alternatives
    - Select preferred recommendation
    - Modify as desired
    - Record your comments re your decision
    - "Sign off" on recommendations
7. View other resources
    - Literature, Guidelines, Prescribing Information, Formulary, Costs of Medications

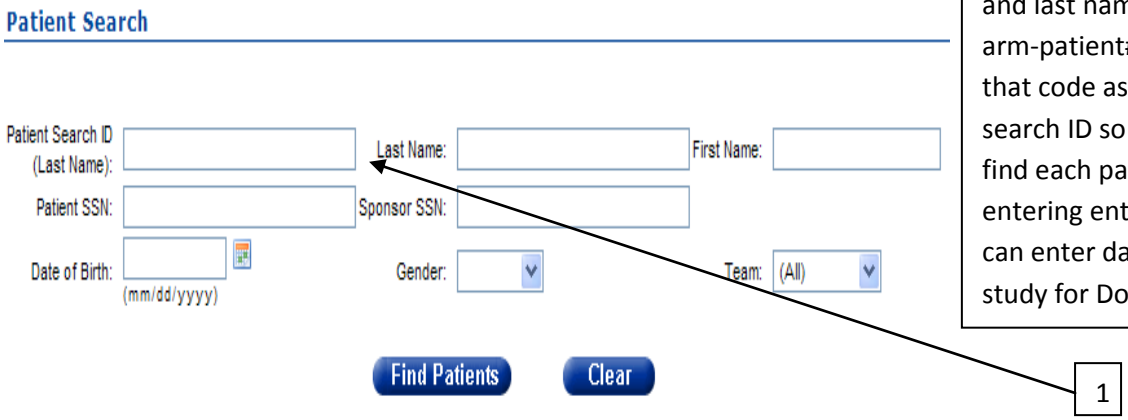
STEP 1: LOGIN



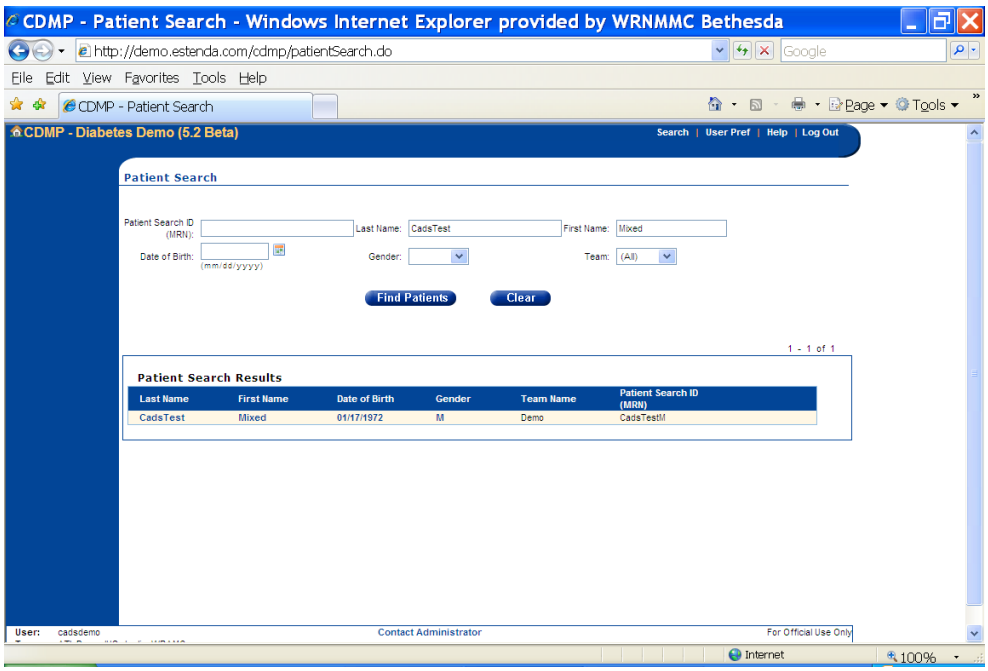

Each user will receive a Username and Password to log in to the system.

STEP 2: SELECT PATIENT

Split the patient's alphanumeric study ID code between the first (site-clinic) and last names (provider-arm-patient#). Use part of that code as the patient search ID so you can quickly find each patient without entering entire code. You can enter date of entry into study for DoB.




Select the patient by entering the Last Name or First Name (Arrow #1). Then select the [Find Patients] button.

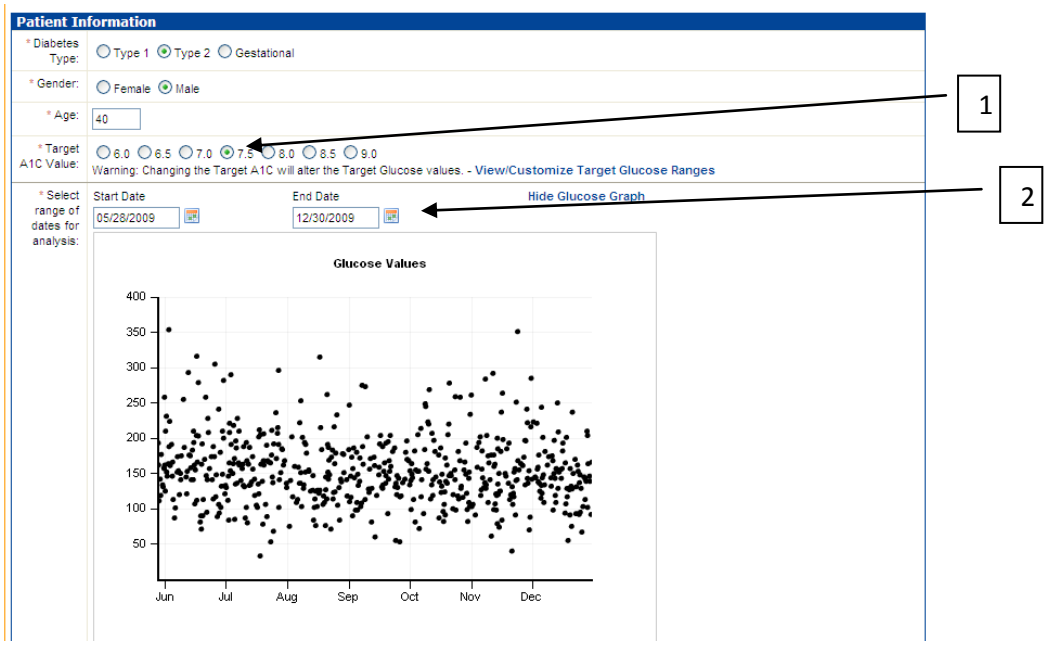



To select a specific patient, simply click on that patient's Last Name (CadsTest) or First Name (Mixed). For this example, the patient's name is Mixed CadsTest, for data entry purposes the patients name will be First name (site-clinic) and last name (provider-arm-patient#).

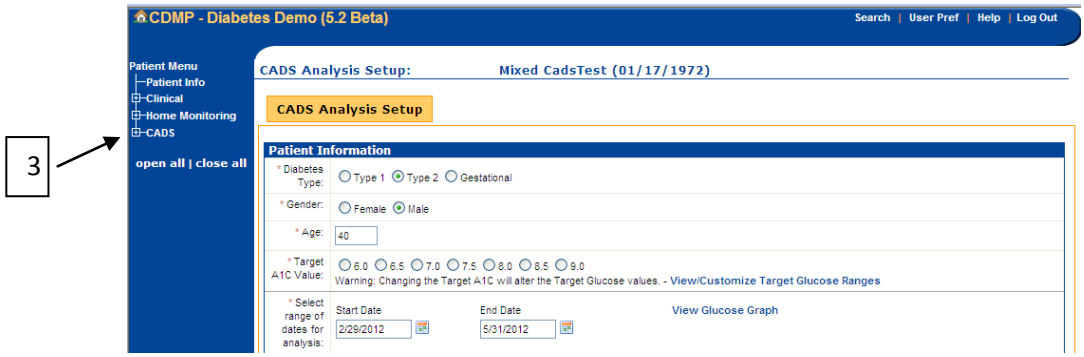
STEP 3: ENTER THE CADS SYSTEM

After selecting the Patient, you will be ready to enter the **CADS** System**.**

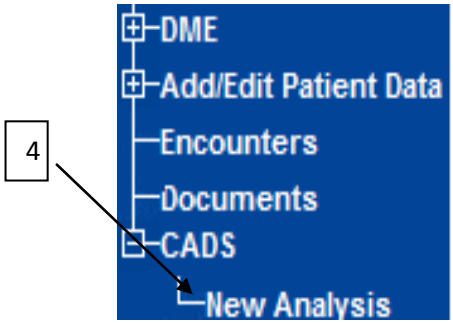
At this point, you will need to select the Target A1c value for this patient. Remember, this needs to be done every time you run a new CADS analysis (Arrow #1). You will also enter the Start Date and End Date for the range of glucose data that you are using for this CADS analysis (Arrow #2).



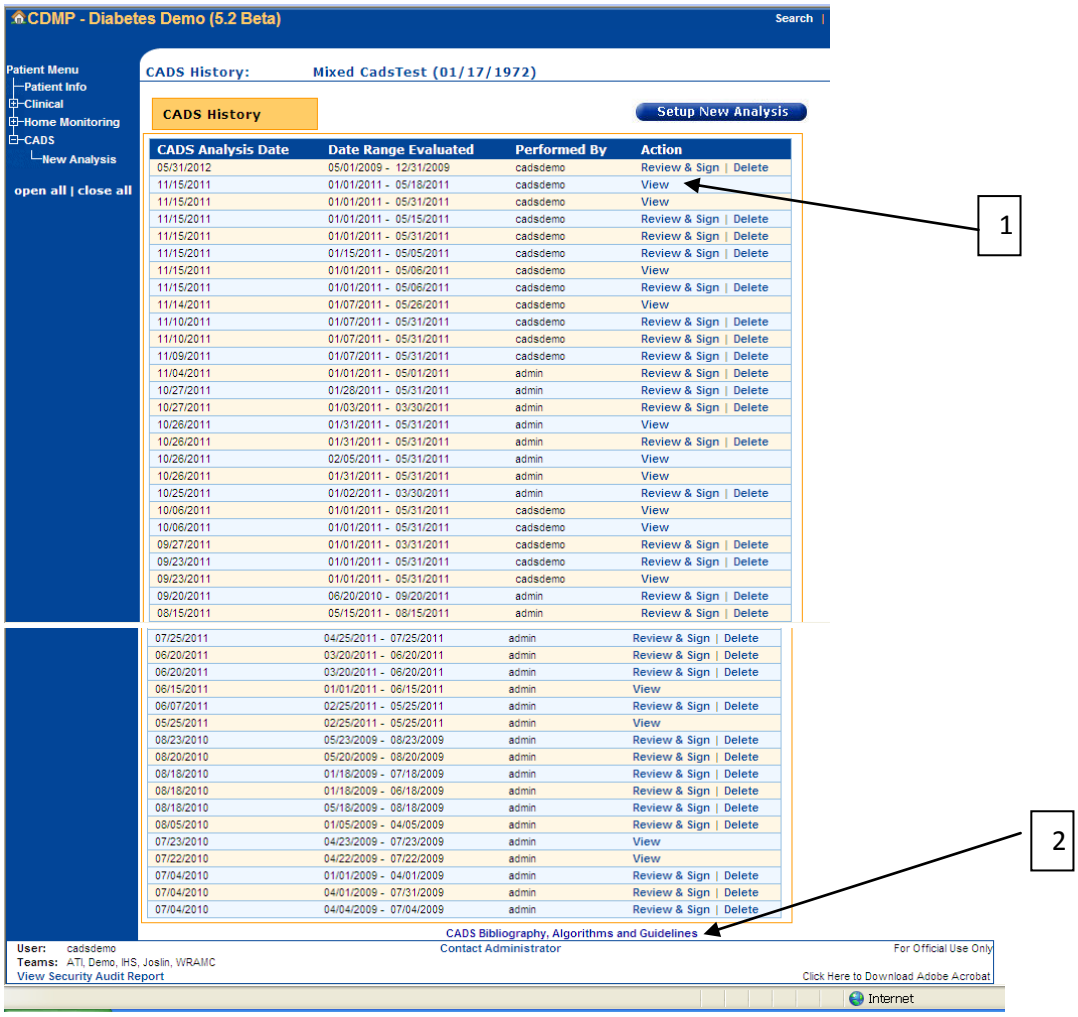
STEP 4: RUN ANALYSIS




Select **CADS** (Arrow #3) from the menu on the bottom of the navigation panel at the left of the screen.

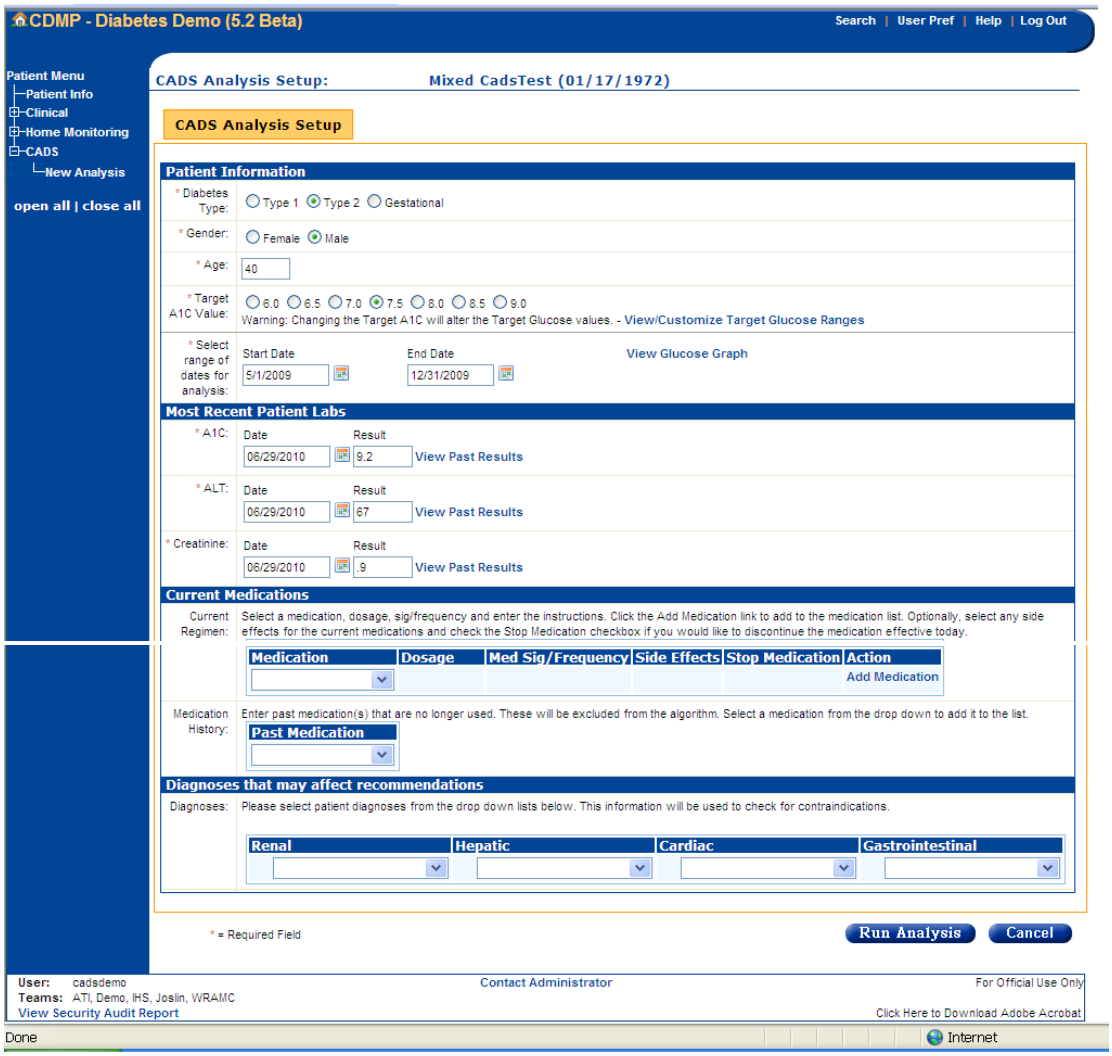



- After selecting CADS, the New Analysis choice will open. To perform a New Analysis of the available data, select New Analysis (Arrow # 4)
- You can also select run analysis at the bottom of the page.




To view a previously performed analysis, select **View** under **Action (**Arrow #1). You can also select background reading material is available (Arrow #2)

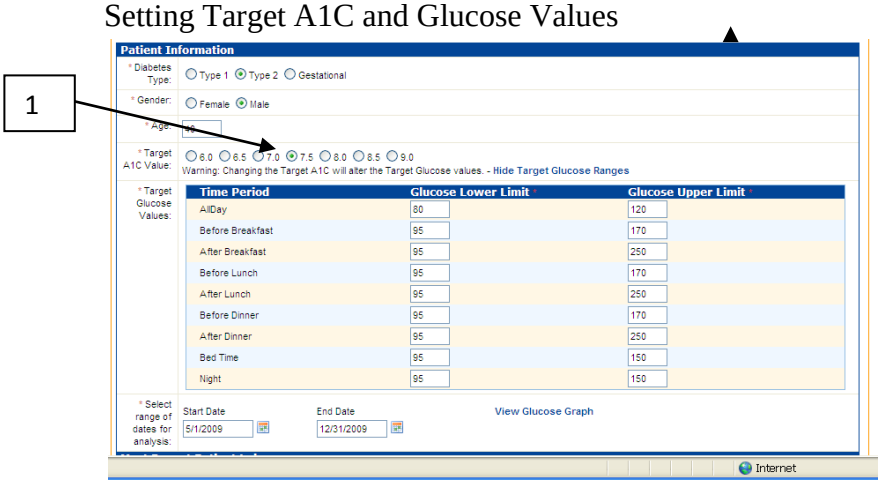
STEP 5: ENTER THE TARGET A1C




Factors considered for generation of recommendations:

- **Patient Information** (diabetes type, gender, age, target A1C, range of dates for analysis)
- **Glucose Data**
- **Laboratory Results** (A1C, ALT, creatinine)
- **Current and Past Medications** (drugs, dose, frequency, side effects)
- **Comorbid Conditions**

Setting Target A1C and Glucose Values

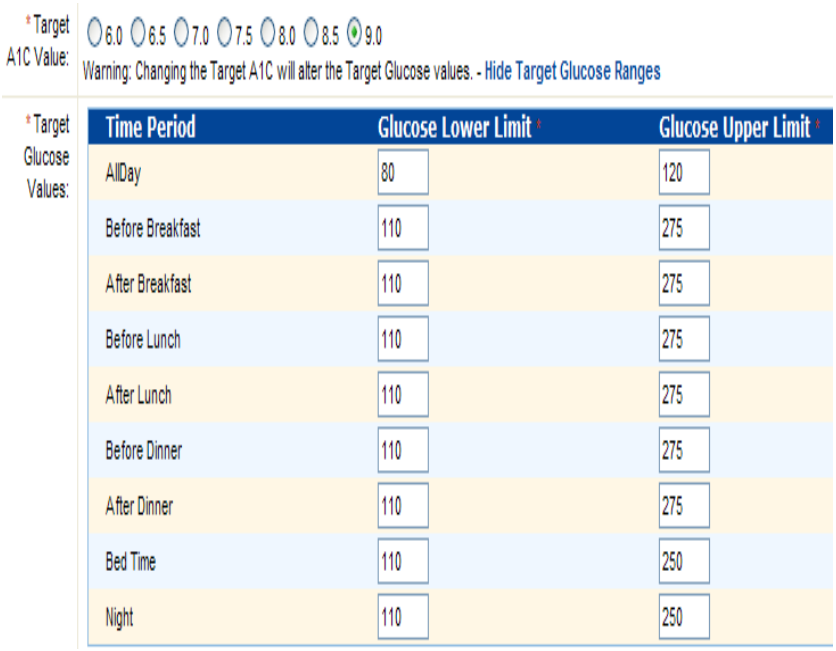



Setting the target A1C value (Arrow # 1) will automatically set the upper and lower limits of the target range for each of 8 separate times of day, and for the whole day ("AllDay").

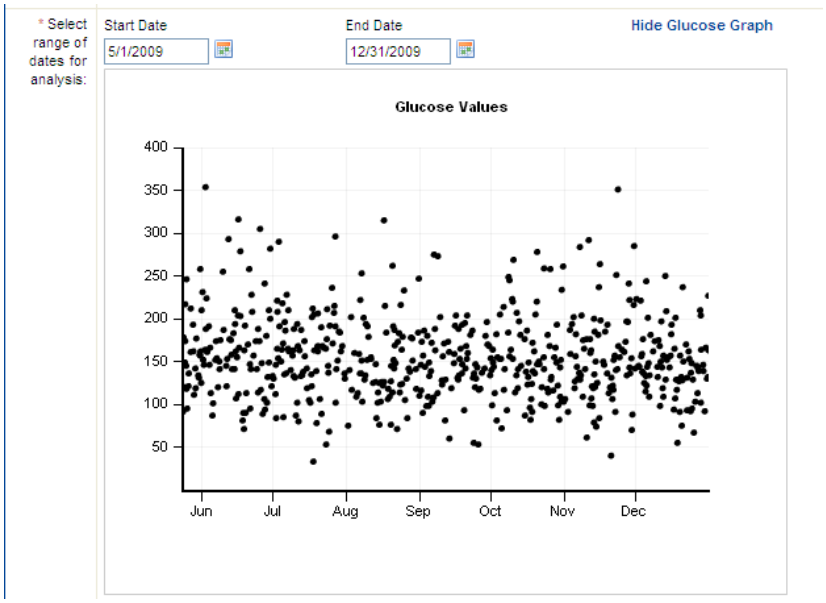
If you, the clinician, wish to modify any of these values, simply enter a value into the text box.

In general, the higher the target A1C is set, the higher the upper and lower limits of the target range will be in order to minimize risk of hypoglycemia.

For example, notice how the Glucose Lower Limit and Glucose Upper Limit change now that the Target A1c is set at 9.0 instead of 7.5.

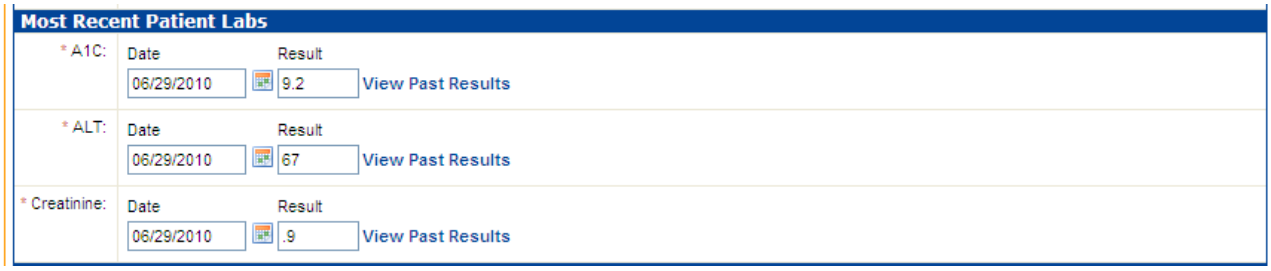


Select Date Range for Analysis

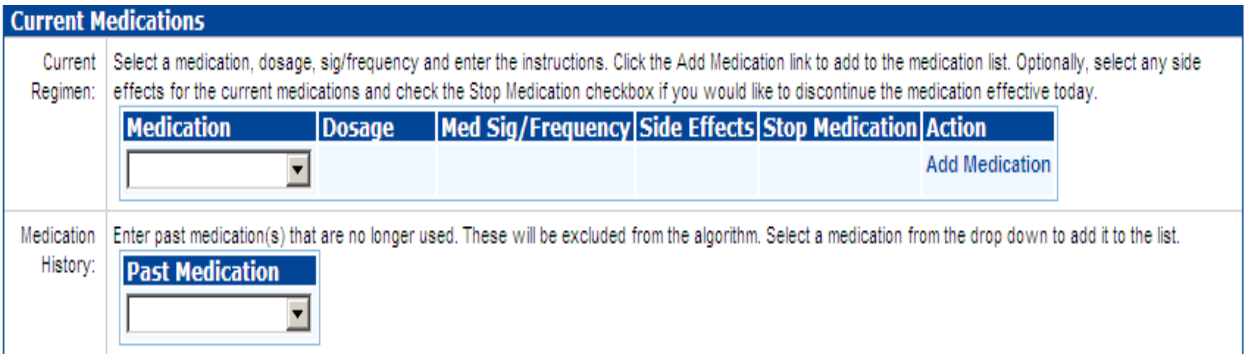



This Graph Glucose over time will be displayed automatically when you select a date range for glucose data analysis.

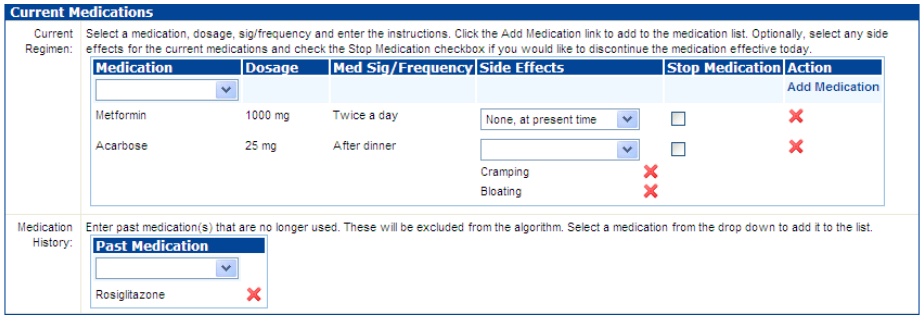
Enter/View Laboratory Results



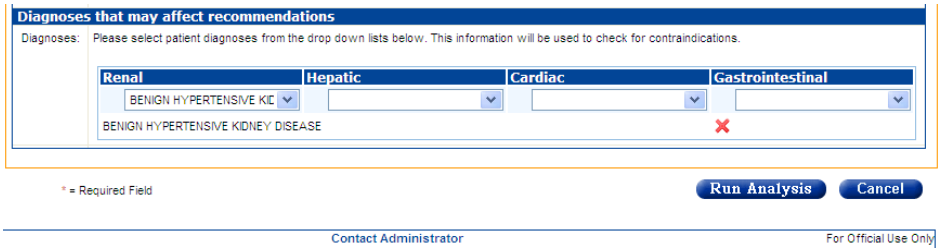

Enter/View Current Medications



This patient is taking two oral diabetes medications, Metformin and Acarbose. These were added by selecting the Medication in the dropdown menu, selecting the dosage, selecting the frequency and then clicking on the Add Medication button. If a mistake is made, you can remove the medication by clicking on the **X** next to the listing. The analysis also takes into account that this patient was previously on Rosiglitazone and will not include that medication in the recommendations.



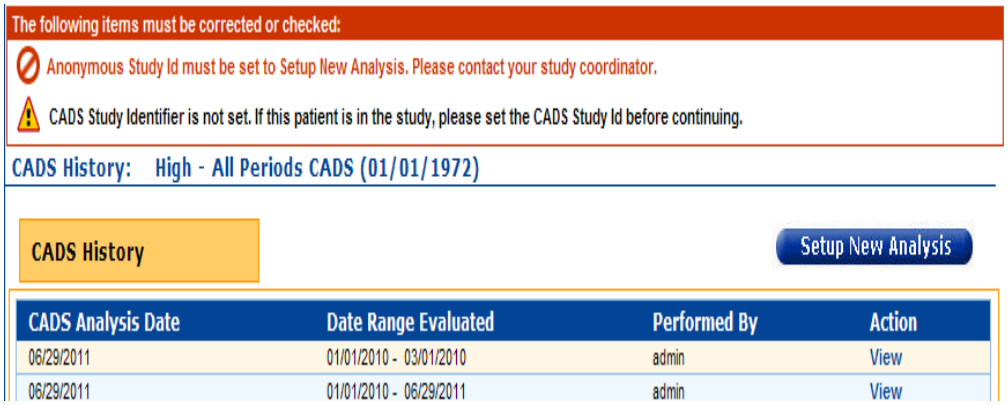

Diagnoses that May Affect Recommendations




For each drop menu (Renal, Hepatic, Cardiac, Gastrointestinal) select any pertinent diagnoses that this patient currently has to be factored into the CADS analysis.

After you have confirmed that the information is accurate, select Run Analysis.

POTENTIAL ISSUES




Two messages may be displayed at the top of the **CADS History** page. If the **Anonymous Study ID** has not been set, the message in red will be displayed. You will not be able to continue until it has been entered.

- If you see the **CADS Study Identifier** warning and the patient is part of the study, do not continue! Contact Sara Salkind or Susan Walker to make sure the patient's study identifier is properly configured

STEP 6: VIEW RECOMMENATIONS FOR THERAPY


Analysis of patient information, labs, medications, diagnoses, date range, and A1C (actual, predicted, and target) generates a ***Recommendation***. You can ***Accept Recommendation*** and ***Sign*** or select ***View Next (Recommendation)***.

The links below the recommendation (Formulary | Prescribing Information | Patient Information or Add Comments) provide more information for you or your patient and allow you to write comments.

**Items shown on the right hand side of the Recommendations screen identify the**

- Range of dates for SMBG data used in analysis
- Current A1C Lab value and date
- Predicted A1C based on SMBG Values
- Selected Target Value for A1C as specified by the clinician and entered into CADS Setup

**Date Range Analyzed**
05/01/2009 - 12/31/2009

**A1C Data**

| Type | Value | |
|---|---|---|
| Lab | 9.2 | 06/29/2010 |
| Predicted | 7.1 | |
| Target | 7.5 | |

**Problems**

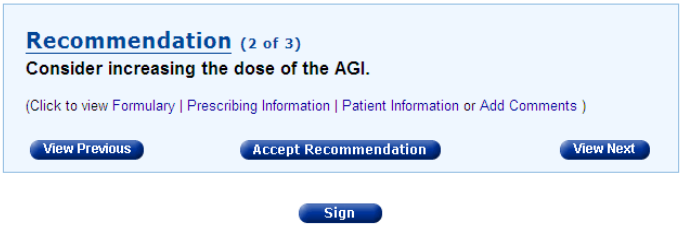
| Period | Problem |
|---|---|
| Before Breakfast | High |
| After Breakfast | |
| Before Lunch | Low |
| After Lunch | Low |
| Before Dinner * | |
| After Dinner | Low |
| Bed Time | High |
| Night | High |

* less than 20 results in period

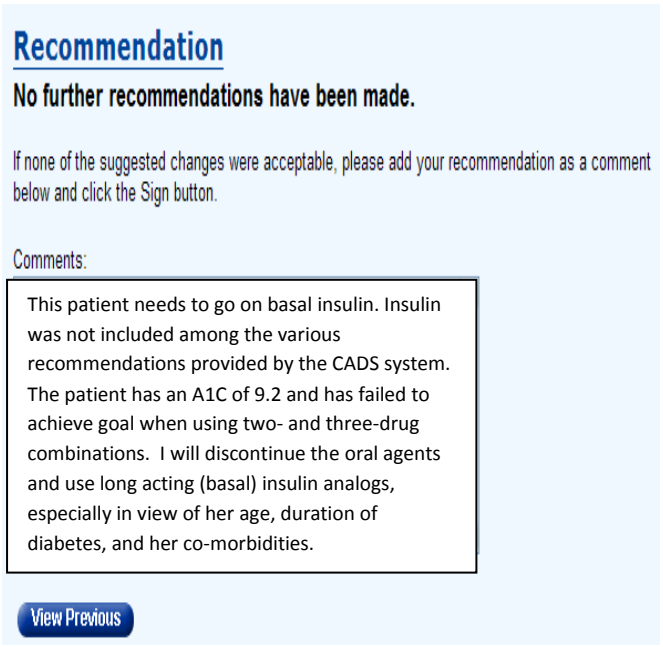
Problems shows a list of Problems identified at each of 8 time periods per day

- NOTE: If a time period has less than 20 values – this is flagged with an asterisk (*) because there are insufficient results to make a conclusive recommendation. A recommendation will still be made but with significantly less confidence.

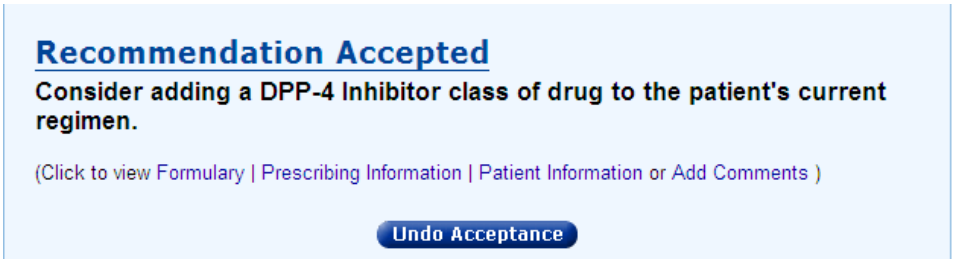
Second recommendation (2 of the 3 that CADS will provide)




The “View Previous” button means “View Recommendation # 1” (the prior recommendation)
The “View Next” button means “View Recommendation # 3” (the next recommendation)
After viewing all of the potential recommendations you will see this screen. The provider can enter their own recommendation at this point and click the “Sign” button.




ACCEPT AND SIGN

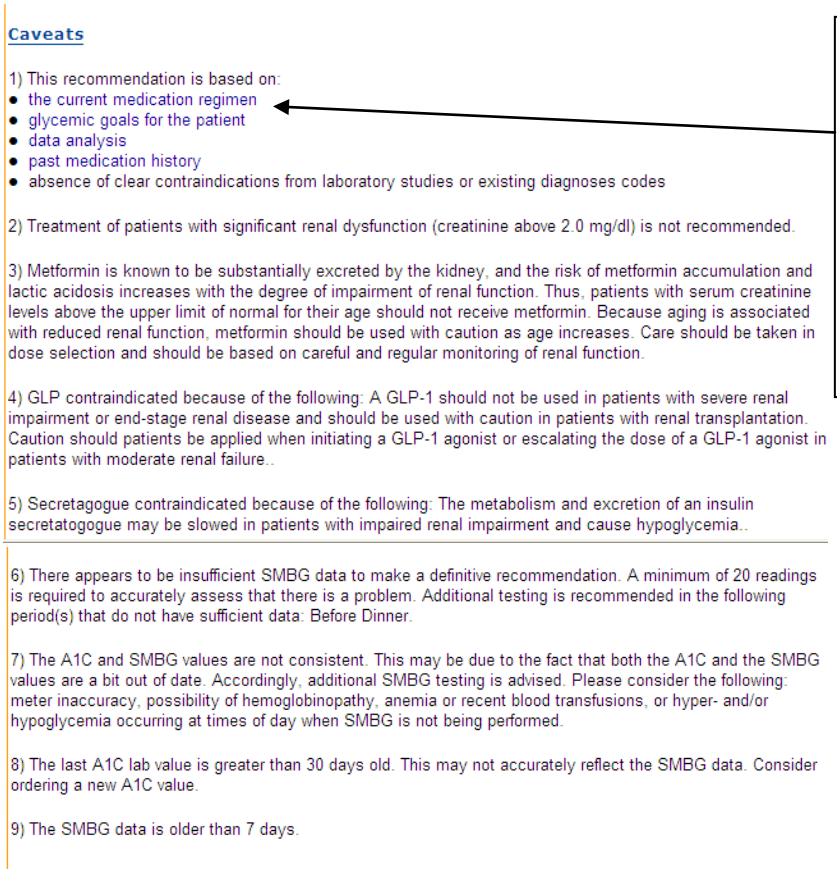



**Reviewing Signed CADS Analysis**

Once signed, a CADS Analysis **cannot be changed** – when viewing you can see the recommendation that has been accepted.

## STEP 7: CADS RESULTS: CAVEATS

Caveats include the rationale for the recommendation, as well as any contraindications or caution that needs to be addressed.



**Caveats**

1) This recommendation is based on:
- the current medication regimen
- glycemic goals for the patient
- data analysis
- past medication history
- absence of clear contraindications from laboratory studies or existing diagnoses codes

2) Treatment of patients with significant renal dysfunction (creatinine above 2.0 mg/dl) is not recommended.

3) Metformin is known to be substantially excreted by the kidney, and the risk of metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. Thus, patients with serum creatinine levels above the upper limit of normal for their age should not receive metformin. Because aging is associated with reduced renal function, metformin should be used with caution as age increases. Care should be taken in dose selection and should be based on careful and regular monitoring of renal function.

4) GLP contraindicated because of the following: A GLP-1 should not be used in patients with severe renal impairment or end-stage renal disease and should be used with caution in patients with renal transplantation. Caution should patients be applied when initiating a GLP-1 agonist or escalating the dose of a GLP-1 agonist in patients with moderate renal failure..

5) Secretagogue contraindicated because of the following: The metabolism and excretion of an insulin secretatogogue may be slowed in patients with impaired renal impairment and cause hypoglycemia..

6) There appears to be insufficient SMBG data to make a definitive recommendation. A minimum of 20 readings is required to accurately assess that there is a problem. Additional testing is recommended in the following period(s) that do not have sufficient data: Before Dinner.

7) The A1C and SMBG values are not consistent. This may be due to the fact that both the A1C and the SMBG values are a bit out of date. Accordingly, additional SMBG testing is advised. Please consider the following: meter inaccuracy, possibility of hemoglobinopathy, anemia or recent blood transfusions, or hyper- and/or hypoglycemia occurring at times of day when SMBG is not being performed.

8) The last A1C lab value is greater than 30 days old. This may not accurately reflect the SMBG data. Consider ordering a new A1C value.

9) The SMBG data is older than 7 days.

The blue type indicates that these are sections of the caveats that link to additional information within CADS. Click on the blue section to get more information about any of the caveats that are highlighted in blue.

STEP 8: PROBLEM SECTION

The problems section repeats the areas that were previously identified by showing the patterns and periods of hypoglycemia, hyperglycemia, and/or target glucose values.

**A1C Data**

| Type | Value | |
|---|---|---|
| Lab | 9.2 | 06/29/2010 |
| Predicted | 7.1 | |
| Target | 7.5 | |

**Problems**

| Period | Problem |
|---|---|
| Before Breakfast | High |
| After Breakfast | |
| Before Lunch | Low |
| After Lunch | Low |
| Before Dinner * | |
| After Dinner | Low |
| Bed Time | High |
| Night | High |

* less than 20 results in period

## STEP 8: VIEW GRAPHS AND INFORMATION PROVIDED BY THE GLUCOSE DATA

## CADS DISPLAYS

- Glucose log book
- Statistics: Mean, % Low, % High, by time of day
- Graphs:
  - Glucose by Date
  - Glucose by Time of Day
  - Glucose in Relationship to Meals
  - Glucose by Day of the Week
  - Pie Charts: % High, % Low, % in Target range
  - "Stacked bar charts": a more compact way to display data from Pie-charts
  - Two dimensional display vs. date and time of day

## SMBG DATA

- Glucose Summary
- Graphs
  - By Date
  - By Time of Day
  - By Day of the Week
  - Pie Charts
  - Stacked bar charts

Glucose Log Book

CADS Results for 05/31/2012: Mixed CadsTest (DOB 01/17/1972)

Recommendations | Glucose Summary | Glucose Log Book | Glucose Graphs | Input Data

| Date | Daily Average | Before Breakfast | After Breakfast | Before Lunch | After Lunch | Before Dinner | After Dinner | Bedtime | Night | Total Daily Readings |
|---|---|---|---|---|---|---|---|---|---|---|
| Time Period | | 07:00 AM - 09:00 AM | 09:00 AM - 11:30 AM | 11:30 AM - 12:30 PM | 12:30 PM - 03:00 PM | 03:00 PM - 06:00 PM | 06:00 PM - 09:00 PM | 09:00 PM - 11:00 PM | 11:00 PM - 07:00 AM | |
| Range | | 95 - 170 | 95 - 250 | 95 - 170 | 95 - 250 | 95 - 170 | 95 - 250 | 95 - 150 | 95 - 150 | |
| 05/24/2009 | 142 | 178 | | | 120 | | 149 | | 91 174 | 5 |
| 05/25/2009 | 164 | 145 | | | 118 246 | | 95 | | 217 | 5 |
| 05/26/2009 | 128 | | 121 | | 136 | | | | | 2 |
| 05/27/2009 | 186 | 161 212 | | | | | | | | 2 |
| 05/28/2009 | 155 | 193 | | 162 | | | 111 | | | 3 |
| 05/29/2009 | 146 | | | 119 | | | 177 | | 142 | 3 |
| 05/30/2009 | 132 | | | | 134 | | 131 | | | 2 |
| 05/31/2009 | 178 | 157 | 258 | | 162 | | 125 | | 158 210 | 6 |
| 06/01/2009 | 176 | 231 | | | 152 | | 146 | | | 3 |
| 06/02/2009 | 235 | | 164 | | 354 | | 188 | | | 3 |
| 06/03/2009 | 192 | | | | | | | | 224 161 191 | 3 |
| 06/04/2009 | 141 | 146 | | 166 | | | 113 | | | 3 |
| 06/05/2009 | 94 | | 87 | | | | 101 | | | 2 |
| 06/06/2009 | 163 | | | | | | 152 | | 174 | 2 |
| 06/07/2009 | 137 | 154 | | | | | 120 | | | 2 |
| 06/08/2009 | 155 | 150 | | | 141 | | 175 | | | 3 |
| 06/09/2009 | 255 | | | | | | | 255 | | 1 |
| 06/10/2009 | 187 | | | | | | | | 187 | 1 |
| 06/11/2009 | 139 | 145 | | 121 | | | 153 | | | 3 |
| 12/06/2009 | 150 | 201 | | | 148 | | 109 | | 144 | 4 |
| 12/07/2009 | 157 | 181 | | | | | | | 134 | 2 |
| 12/08/2009 | 162 | | | | 162 | | | | | 1 |
| 12/09/2009 | 174 | | | | | | | | 174 | 1 |
| 12/10/2009 | 150 | 144 | | 132 | | | 175 | | | 3 |
| 12/11/2009 | 153 | | 98 | | | 150 | | | 168 197 | 4 |
| 12/12/2009 | 132 | | | 119 | | | 109 157 | | 143 | 4 |
| 12/13/2009 | 178 | | | | 250 | | 129 | | 155 | 3 |
| 12/14/2009 | 180 | 152 | | | | | | | 209 | 2 |
| 12/15/2009 | 152 | | 143 | | 156 | | 157 | | | 3 |
| 12/16/2009 | 187 | 193 | | | | | | | 182 | 2 |
| 12/17/2009 | 141 | 94 | | 165 | | | 107 | | 201 | 4 |
| 12/18/2009 | 100 | | | 117 | | | 55 | | 129 | 3 |
| 12/19/2009 | 125 | | | | 127 | | 91 | 157 | | 3 |
| 12/20/2009 | 111 | 132 | | | 75 | | 128 | | | 3 |
| 12/21/2009 | 193 | 150 | | | | | | | 237 | 2 |
| 12/22/2009 | 131 | | 170 | | | | 93 131 | | | 3 |
| 12/23/2009 | 157 | | | | 162 | | 153 | | | 2 |
| 12/24/2009 | 118 | 92 | | 137 | | | 148 | 95 | | 4 |
| 12/25/2009 | 98 | | | | | | 67 | | 129 | 2 |
| 12/26/2009 | 124 | 103 | | | | | 145 | | | 2 |
| 12/27/2009 | 131 | 113 | | | 142 | | 139 | | | 3 |
| 12/28/2009 | 170 | 210 | | | 102 204 | | 164 | | | 4 |
| 12/29/2009 | 142 | | | | 146 | | 139 | | | 2 |
| 12/30/2009 | 129 | | | | | 166 | | | 92 | 2 |
| 12/31/2009 | 163 | 130 | | 132 | | | 227 | 163 | | 4 |
| # Readings | 2 | 117 | 37 | 53 | 80 | 7 | 156 | 26 | 119 | 595 |
| Average | 154 | 161 | 168 | 130 | 162 | 150 | 135 | 180 | 166 | 2 |

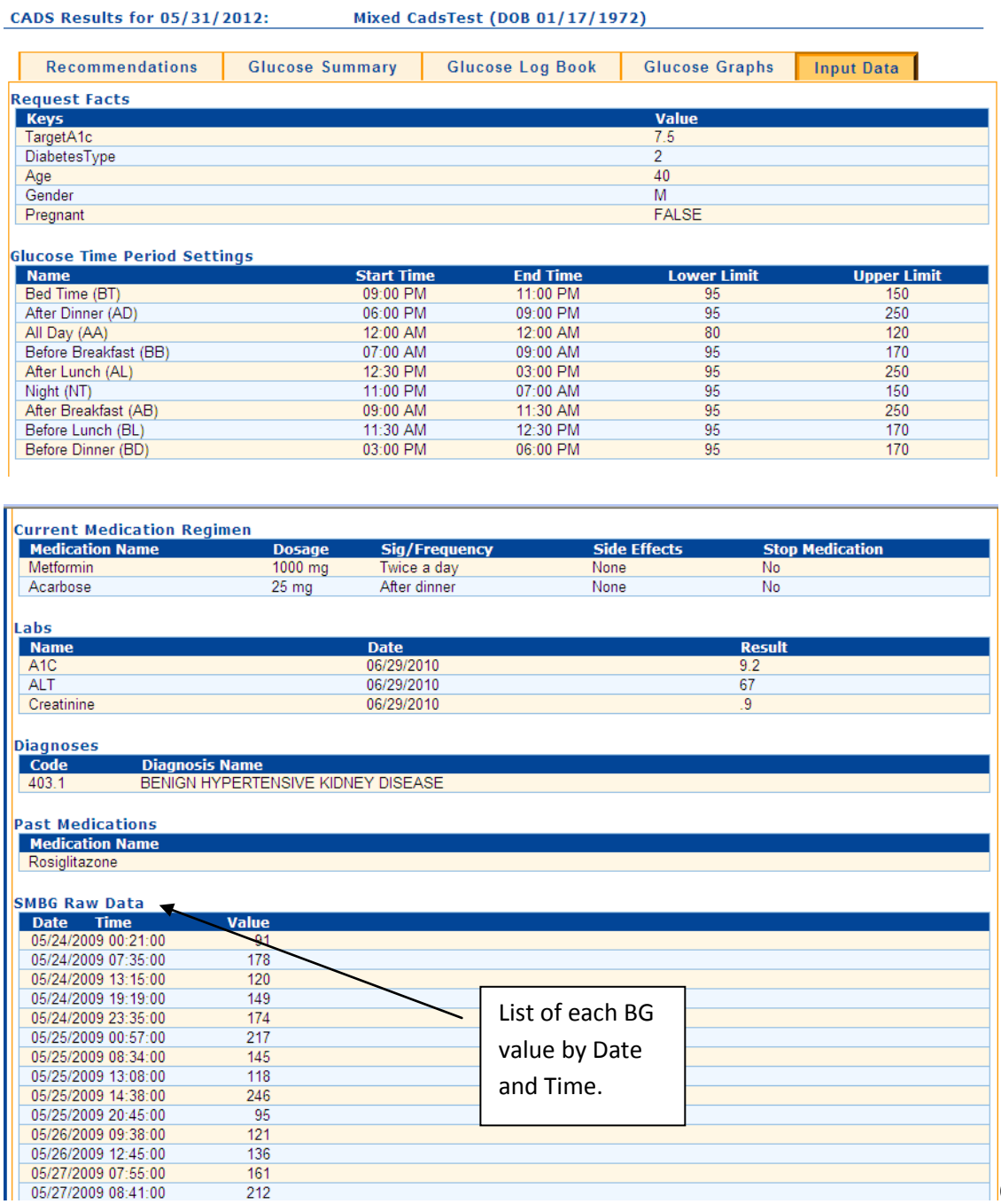
**# of Readings/time period** and **Average Reading** are the bottom values in Glucose Log Book

Red = High  Blue = Low  Black = In Target

VIEW GLUCOSE GRAPHS AND DATA FROM GLUCOMETER

This page provides a summary of

- Target A1C
- Target glucose range by time of day and in relationship to meals
- Demographic variables (i.e., type of diabetes, age, gender, pregnant)



CADS Results for 05/31/2012: Mixed CadsTest (DOB 01/17/1972)

Recommendations | Glucose Summary | Glucose Log Book | Glucose Graphs | Input Data

**Request Facts**

| Keys | Value |
|---|---|
| TargetA1c | 7.5 |
| DiabetesType | 2 |
| Age | 40 |
| Gender | M |
| Pregnant | FALSE |

**Glucose Time Period Settings**

| Name | Start Time | End Time | Lower Limit | Upper Limit |
|---|---|---|---|---|
| Bed Time (BT) | 09:00 PM | 11:00 PM | 95 | 150 |
| After Dinner (AD) | 06:00 PM | 09:00 PM | 95 | 250 |
| All Day (AA) | 12:00 AM | 12:00 AM | 80 | 120 |
| Before Breakfast (BB) | 07:00 AM | 09:00 AM | 95 | 170 |
| After Lunch (AL) | 12:30 PM | 03:00 PM | 95 | 250 |
| Night (NT) | 11:00 PM | 07:00 AM | 95 | 150 |
| After Breakfast (AB) | 09:00 AM | 11:30 AM | 95 | 250 |
| Before Lunch (BL) | 11:30 AM | 12:30 PM | 95 | 170 |
| Before Dinner (BD) | 03:00 PM | 06:00 PM | 95 | 170 |

**Current Medication Regimen**

| Medication Name | Dosage | Sig/Frequency | Side Effects | Stop Medication |
|---|---|---|---|---|
| Metformin | 1000 mg | Twice a day | None | No |
| Acarbose | 25 mg | After dinner | None | No |

**Labs**

| Name | Date | Result |
|---|---|---|
| A1C | 06/29/2010 | 9.2 |
| ALT | 06/29/2010 | 67 |
| Creatinine | 06/29/2010 | .9 |

**Diagnoses**

| Code | Diagnosis Name |
|---|---|
| 403.1 | BENIGN HYPERTENSIVE KIDNEY DISEASE |

**Past Medications**

| Medication Name |
|---|
| Rosiglitazone |

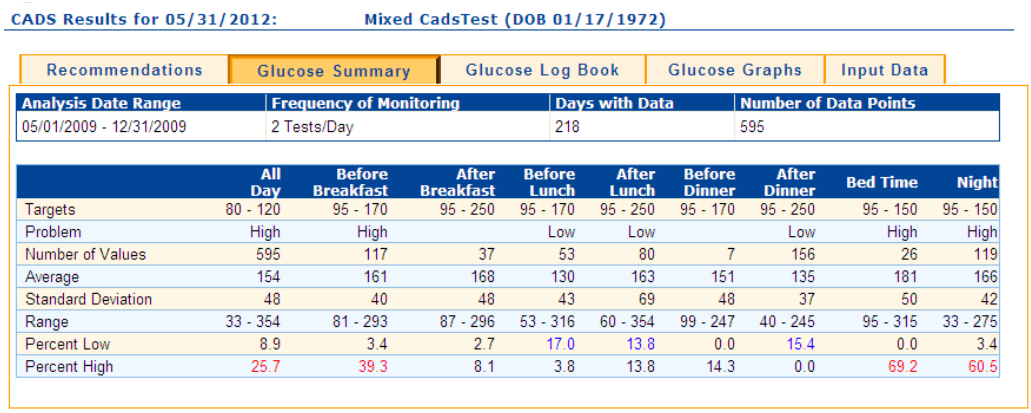
**SMBG Raw Data**

| Date Time | Value |
|---|---|
| 05/24/2009 00:21:00 | 91 |
| 05/24/2009 07:35:00 | 178 |
| 05/24/2009 13:15:00 | 120 |
| 05/24/2009 19:19:00 | 149 |
| 05/24/2009 23:35:00 | 174 |
| 05/25/2009 00:57:00 | 217 |
| 05/25/2009 08:34:00 | 145 |
| 05/25/2009 13:08:00 | 118 |
| 05/25/2009 14:38:00 | 246 |
| 05/25/2009 20:45:00 | 95 |
| 05/26/2009 09:38:00 | 121 |
| 05/26/2009 12:45:00 | 136 |
| 05/27/2009 07:55:00 | 161 |
| 05/27/2009 08:41:00 | 212 |



Glucose

Summary Tab



CADS Results for 05/31/2012: Mixed CadsTest (DOB 01/17/1972)

Recommendations | Glucose Summary | Glucose Log Book | Glucose Graphs | Input Data

| Analysis Date Range | Frequency of Monitoring | Days with Data | Number of Data Points |
|---|---|---|---|
| 05/01/2009 - 12/31/2009 | 2 Tests/Day | 218 | 595 |

| | All Day | Before Breakfast | After Breakfast | Before Lunch | After Lunch | Before Dinner | After Dinner | Bed Time | Night |
|---|---|---|---|---|---|---|---|---|---|
| Targets | 80 - 120 | 95 - 170 | 95 - 250 | 95 - 170 | 95 - 250 | 95 - 170 | 95 - 250 | 95 - 150 | 95 - 150 |
| Problem | High | High | | Low | Low | | Low | High | High |
| Number of Values | 595 | 117 | 37 | 53 | 80 | 7 | 156 | 26 | 119 |
| Average | 154 | 161 | 168 | 130 | 163 | 151 | 135 | 181 | 166 |
| Standard Deviation | 48 | 40 | 48 | 43 | 69 | 48 | 37 | 50 | 42 |
| Range | 33 - 354 | 81 - 293 | 87 - 296 | 53 - 316 | 60 - 354 | 99 - 247 | 40 - 245 | 95 - 315 | 33 - 275 |
| Percent Low | 8.9 | 3.4 | 2.7 | 17.0 | 13.8 | 0.0 | 15.4 | 0.0 | 3.4 |
| Percent High | 25.7 | 39.3 | 8.1 | 3.8 | 13.8 | 14.3 | 0.0 | 69.2 | 60.5 |

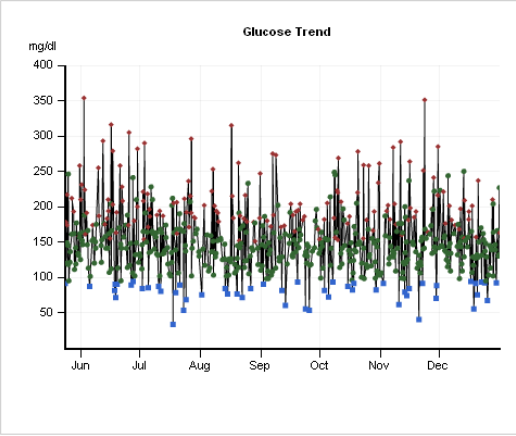
Glucose Summary identifies

- Analysis Date Range
- Frequency of Monitoring
- Days with Data
- Number of Data Points
- Target BG range for each time range
- Percentage of low BG values by time of day
- Percentage of target BG values by time of day
- Percentage of high BG values

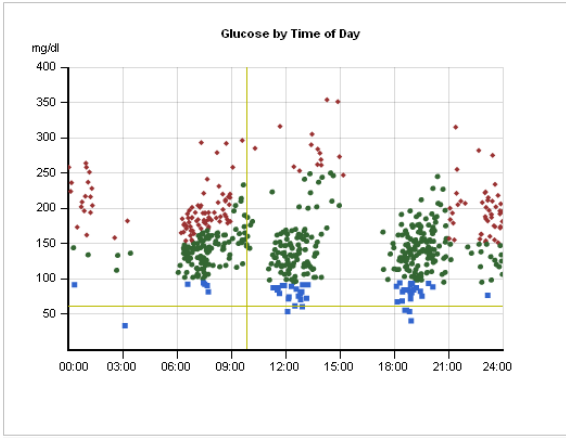
Problem areas are noted in “Percent low” and “Percent high” by the color change (red or blue). For example, this person has a high percentage of low BG readings before and after lunch, while bedtime and night readings run high.

Glucose Graphs

- To see the glucose graphs – click the "glucose graphs" tab on the screen above (between Glucose Log Book and Input Data)




Trends over Time

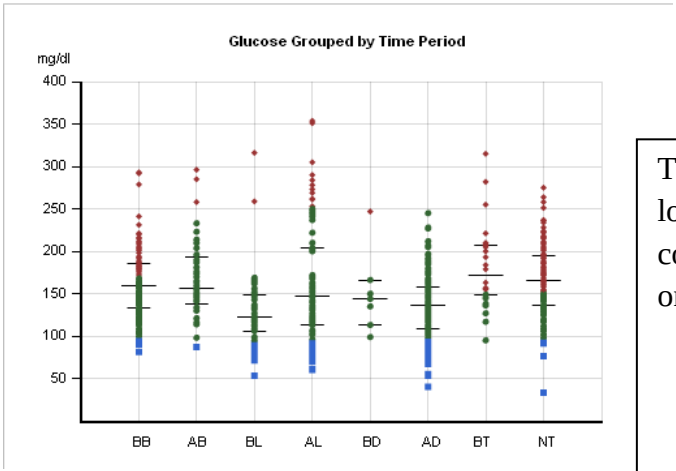


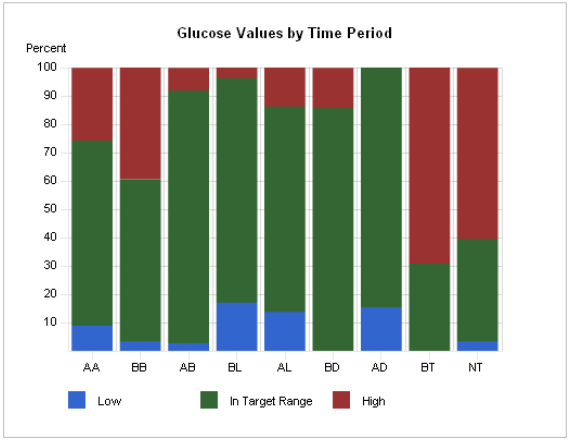

Trends by Time of Day

Remember: the colors mean the same things on these graphs that they did previously:

red = high
blue = low
green = target range

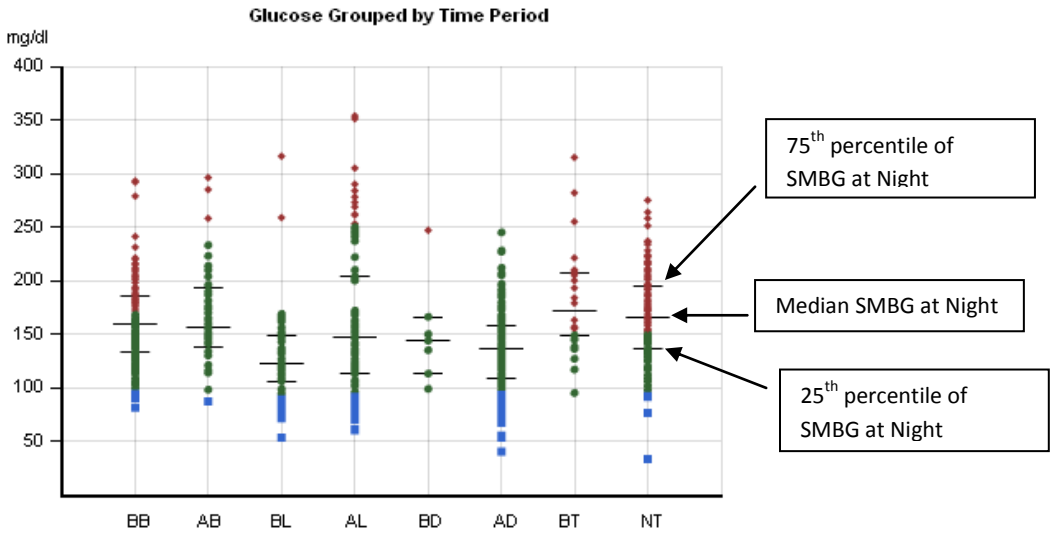
There are a lot of options for types of graphs that CADS can produce. Here are a few more examples:




The abbreviations on the lower axis of the graphs correpond to the time chunks on previous screens:

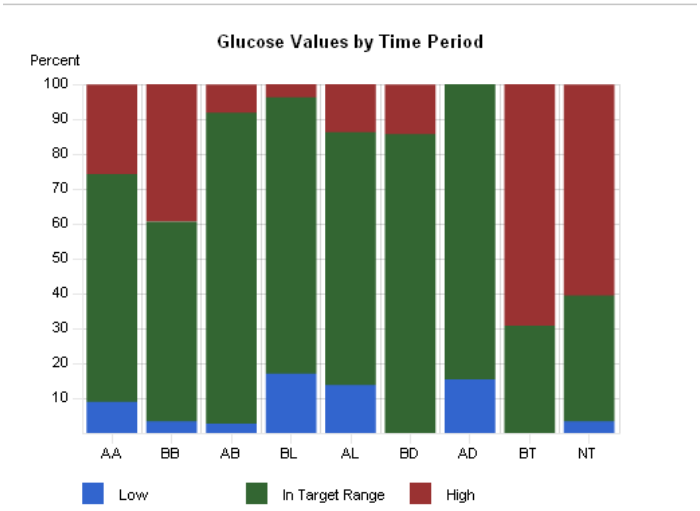
AA: All Day
BB: before breakfast
AB: after breakfast
BL: before lunch
AL: after lunch
BD: before dinner
AD: after dinner
BT: Bedtime
NT: Nighttime



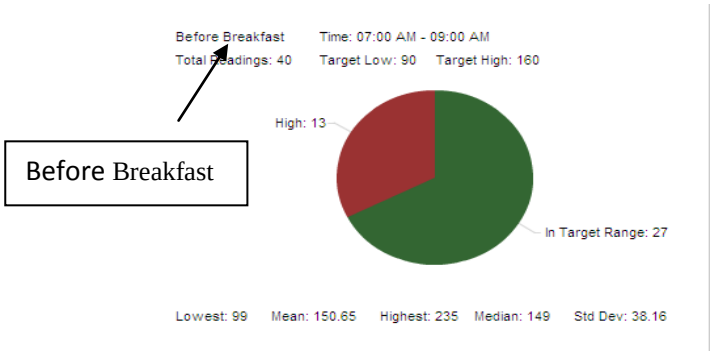

When the glucose data is grouped by Time Period, horizontal lines are shown for the median (50$^{th}$ percentile) (longer lines), and for the 25$^{th}$ and 75$^{th}$ percentiles (shorter lines). In the example shown, slightly more than 50% of the night-time glucoses are within target and slightly less than 50% are higher than target.

Data points are still color coded red (high), green (target) and blue (low) with the ranges that were set in CADS during setup and identification of the ideal A1c for this specific patient.

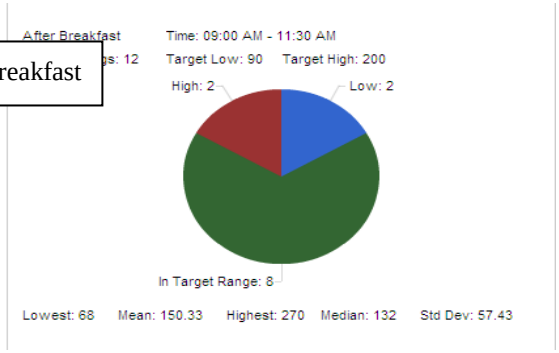
Remember that all these ranges can be set by the provider, so that the ranges are specific to the individual circumstances of each of the patients. These values can be adjusted in Analysis Setup at any point while using the program.



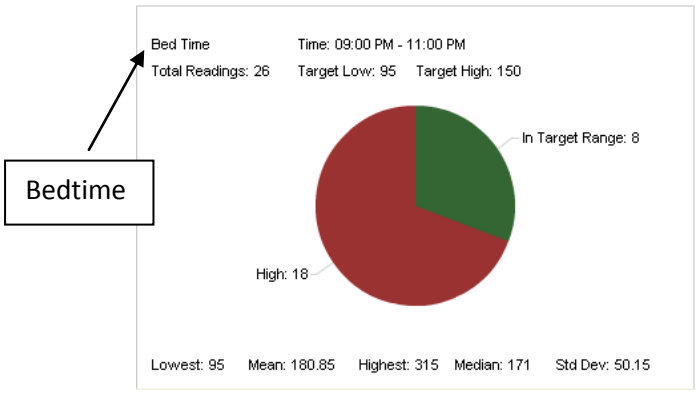
Pie Charts can be created as another way to display the patterns of BG over time and by meals.




Before Breakfast




After Breakfast


Bedtime
Bed Time
Time: 09:00 PM - 11:00 PM
Total Readings: 26
Target Low: 95
Target High: 150
In Target Range: 8
High: 18
Lowest: 95
Mean: 180.85
Highest: 315
Median: 171
Std Dev: 50.15

## BIBLIOGRAPHY

Algorithms and Guidelines
- AACE/ACE
- ADA
- VA/DOD

CADS system

Analysis of SMBG data


1. **AACE Algorithm**

https://www.aace.com/sites/default/files/GlycemicControlAlgorithm.pdf

https://www.aace.com/sites/default/files/GlycemicControlAlgorithmPPT.pdf

https://www.aace.com/sites/default/files/Diabetes_Algorithm_120909_PC_final_animated.ptt

2. **ADA/EASD**
http://care.diabetesjournals.org/content/29/8/1963.full.pdf+html

**3. VA/DOD guideline** short version:

http://www.healthquality.va.gov/diabetes/DM2010_SUM-v4.pdf

**4. VA/DOD guideline** long version**:**

http://www.healthquality.va.gov/diabetes/DM2010_FUL-v4e.pdf

5. **AACE guideline 2011**

https://www.aace.com/sites/default/files/DMGuidelinesCCP.pdf

**CADS**:

Rodbard D, Vigersky RA. Design of a Decision Support System to Help Clinicians Manage Glycemia in Patients with Type 2 Diabetes Mellitus. J Diab Sci Tech. 2011 (Mar); 5 (2): 402-411 and on-line Appendix.

**Analysis and Interpretation of SMBG Data:**

Rodbard, D. Optimizing Display, Analysis, Interpretation and Utility of Self-Monitoring of Blood Glucose (SMBG) Data for Management of Patients with Diabetes. Journal of Diabetes Science and Technology, 1 (1): 62 - 71, 2007.

**CURRENT ISSUES WITH TZDs**

GSK re Rosiglitazone (Avandia), with Risk elimination program:

http://www.gsk.com/media/pressreleases/2011/2011_pressrelease_10024.htm

FDA re withdrawal of Pioglitazone (Actos) in France and Germany:

http://www.fda.gov/Drugs/DrugSafety/ucm259150.htm

http://care.diabetesjournals.org/content/34/4/916.long

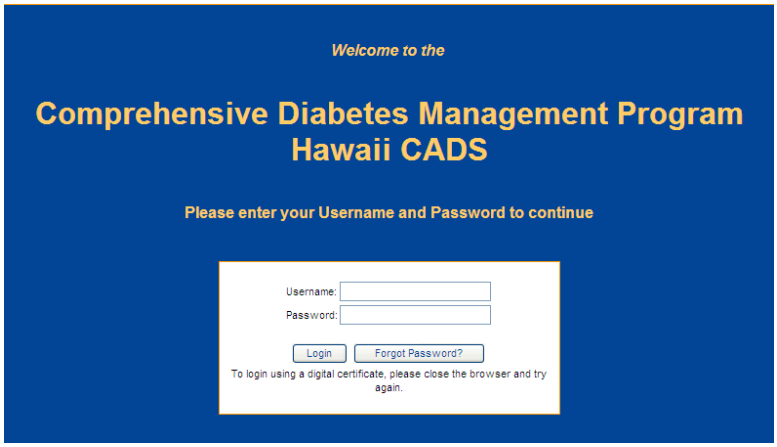
# Trouble Report

**Note: This form can be submitted anonymously without the name of the provider, or patient, or both.**

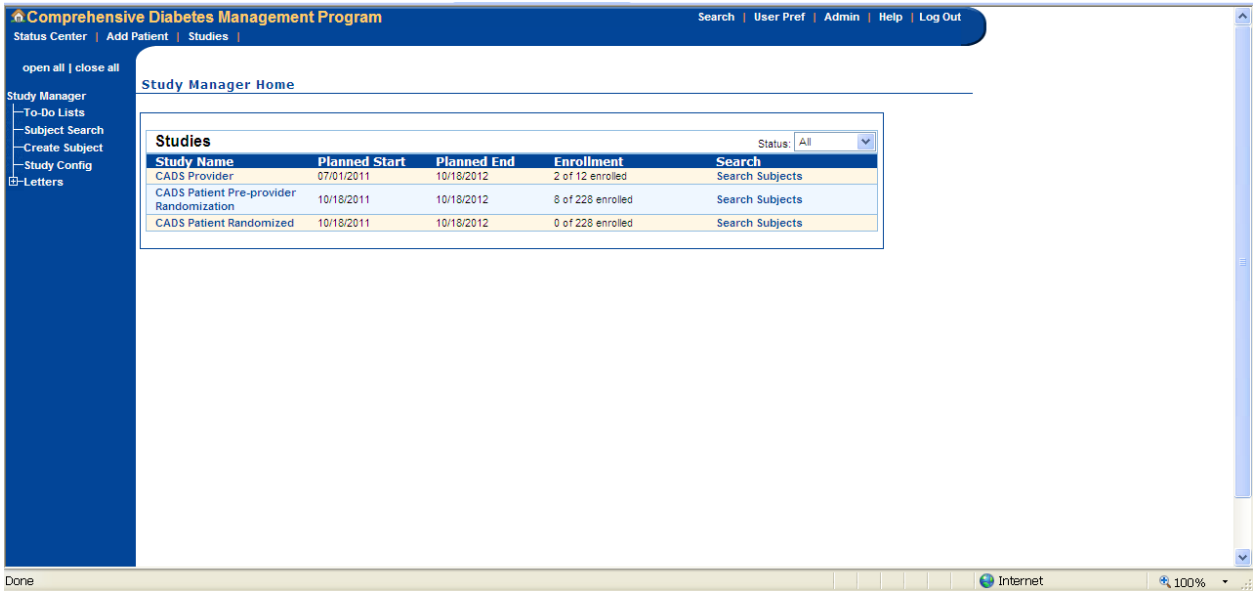
1. Name of Clinician: (optional)
2. Date:
3. Facility: WRNMMC, WHASC, UH
4. Patient Identifier: (optional)
5. Nature of the Problem
6. Severity of the Problem
7. Is there any risk to the patient, or likely to be any risk to any other patient as a result of this problem?

# Directions for using CDMP for Hawaii for the CADS Study

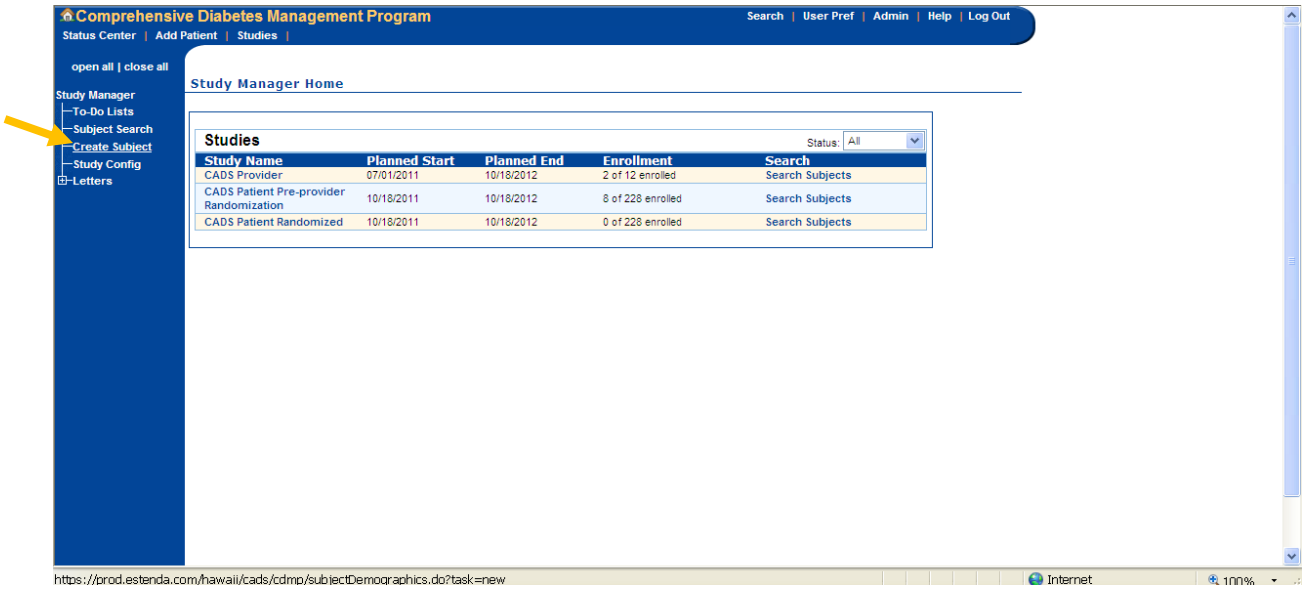
**TO BEGIN**



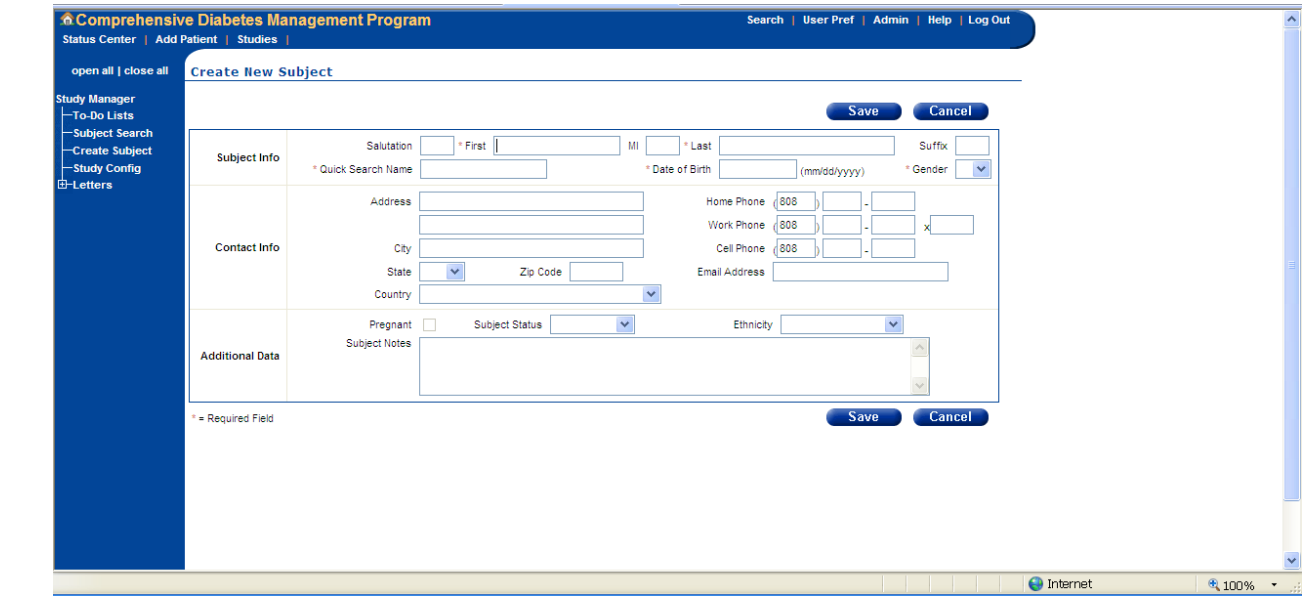

Enter the Username and Password you have been assigned to login to the Comprehensive Diabetes Management Program Hawaii CADS Website. The link for the website is https://prod.estenda.com/hawaii/cads/cdmp/



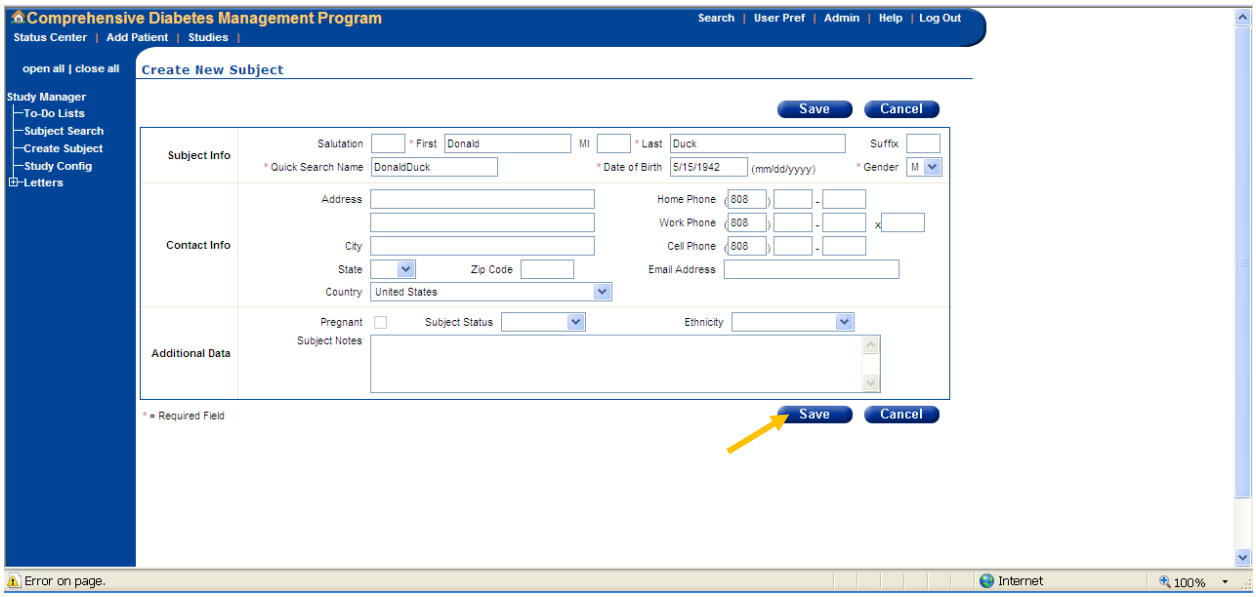

In order to begin entering data, you will need to create a subject.



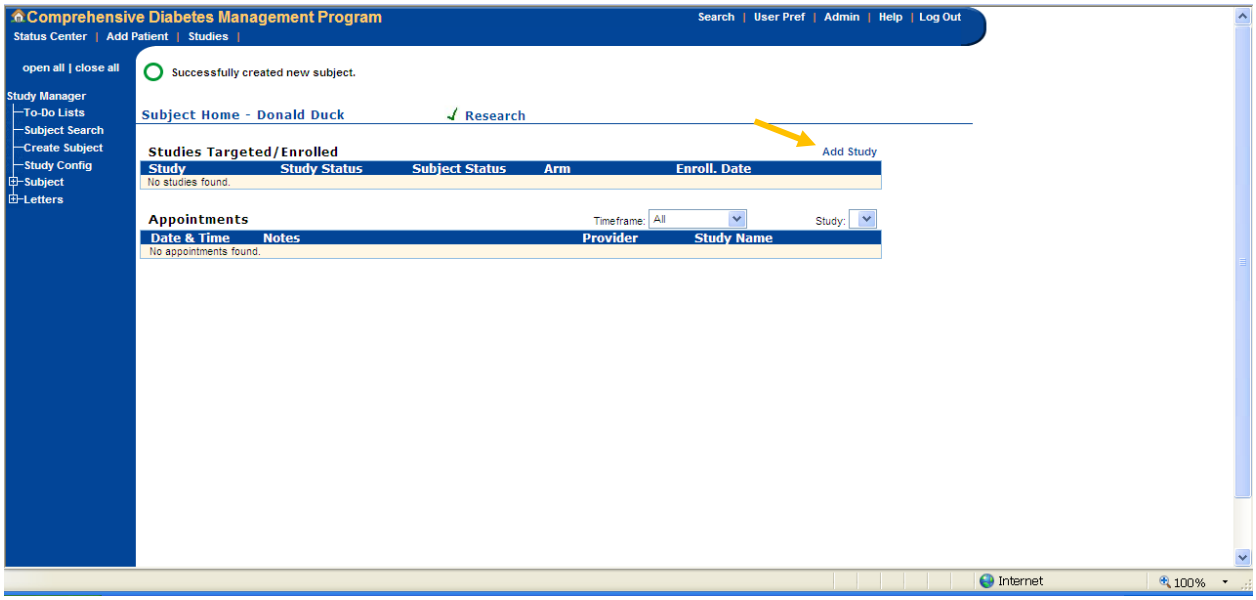

Click the “Create Subject” button on the right hand side of the screen.



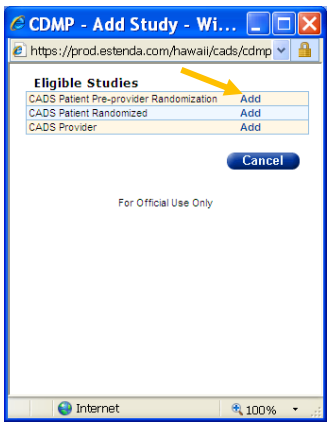

Now type in the information you want entered into CDMP for your subject. For now (when testing) make a “fake” patient – for this example I have used Donald Duck.



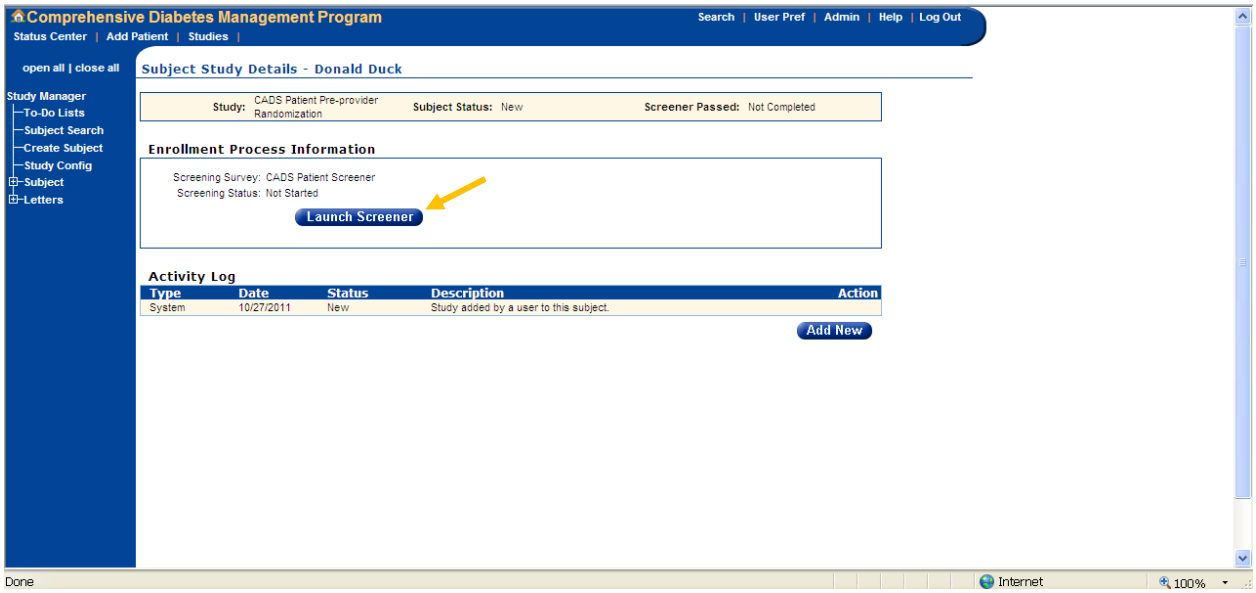

Click Save.



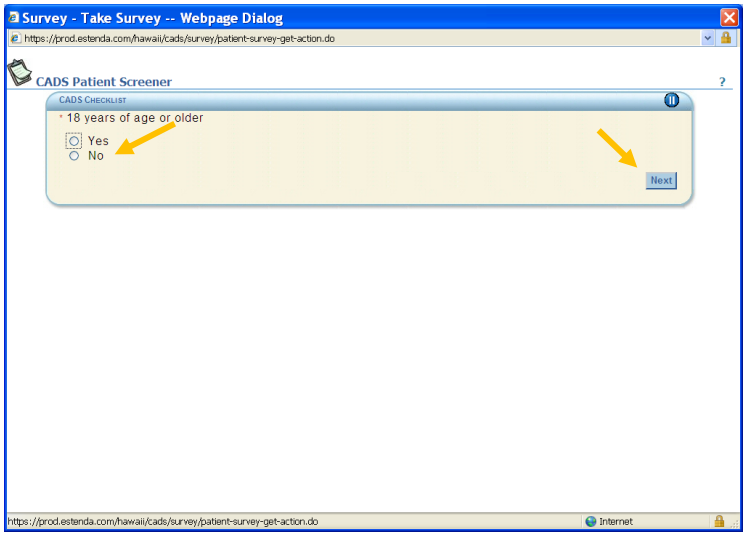

Now you want to add Donald Duck to the study. Click “Add Study.”



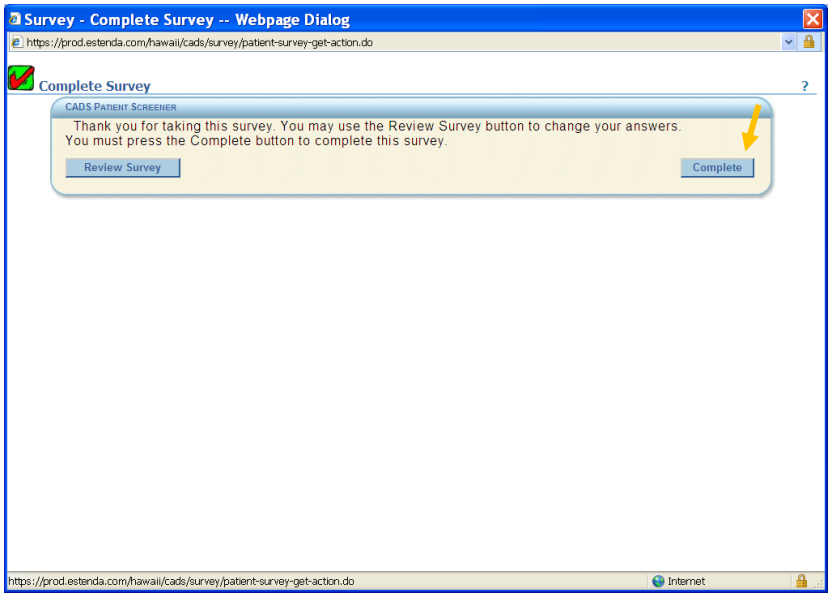

There are three studies available. If Donald Duck were a provider, you would Add the CADS Provider study. For this example, we are assuming Donald Duck is a patient, so we are adding him to the CADS Patient Pre-provider Randomization study. All patients will start with this study. After 19 patients have been recruited for a specific provider and all patients have completed the CADS Patient Pre-provider Randomization study, the patients will be enrolled in the CADS Patient Randomized study.



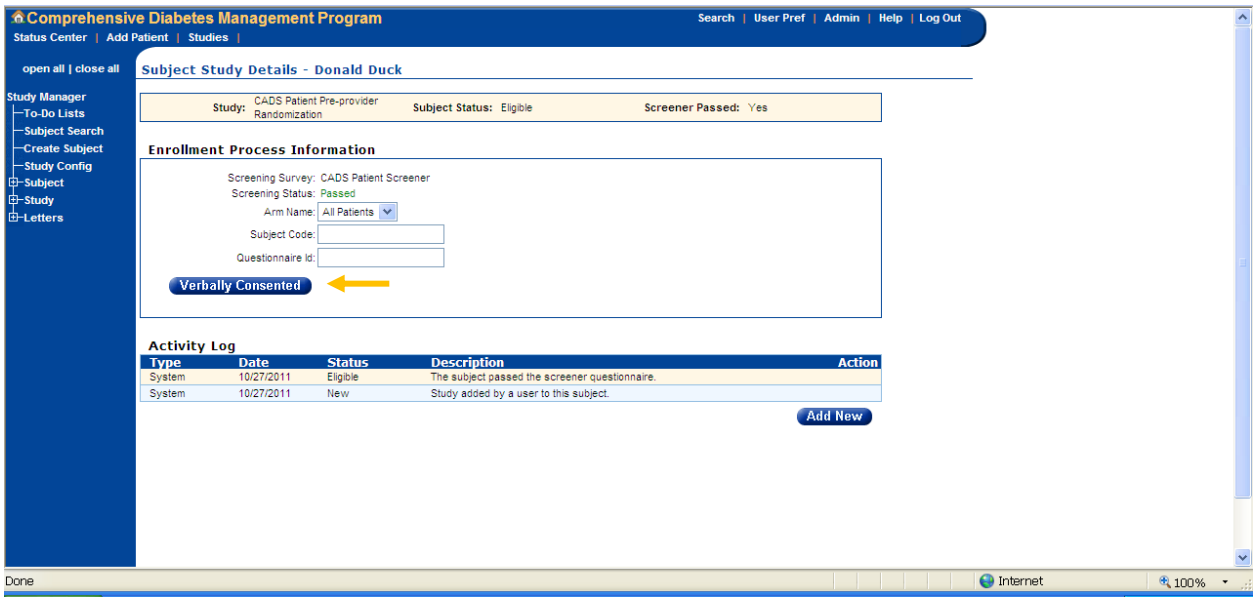

You need to screen the patient to make sure they are eligible for the study. For test purposes, all the answers on the Screener must be yes for CDMP to allow you to continue to enroll your fake patient in the study.



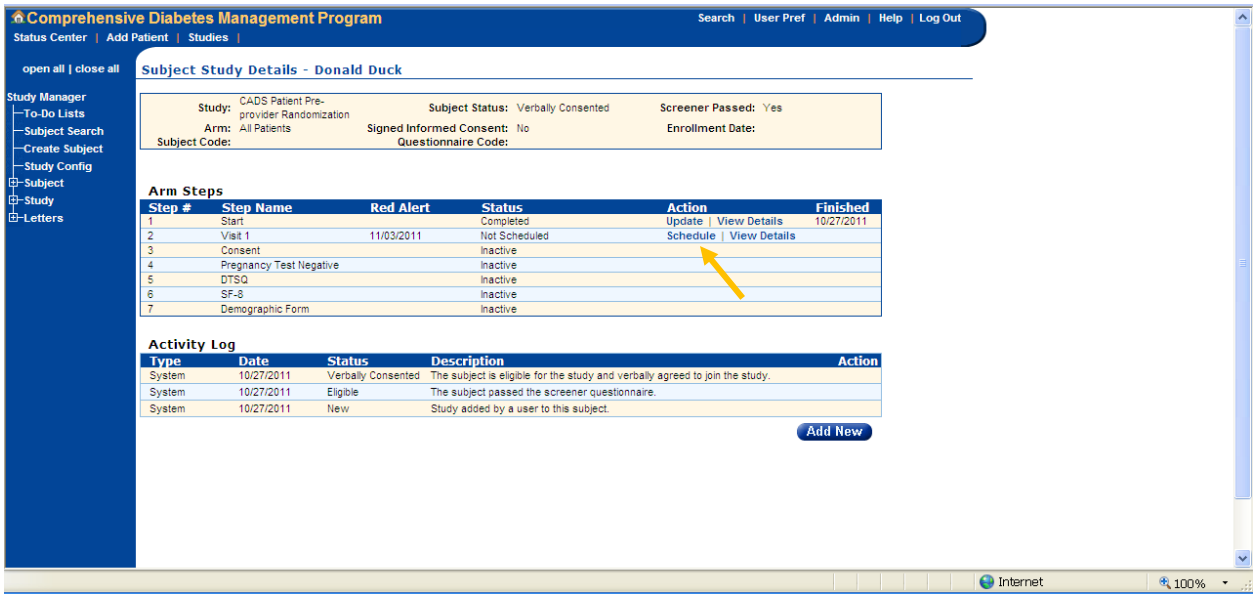

In every survey question, you will enter an aswer and either push the “enter” key on your keyboard or click on the “next” box.



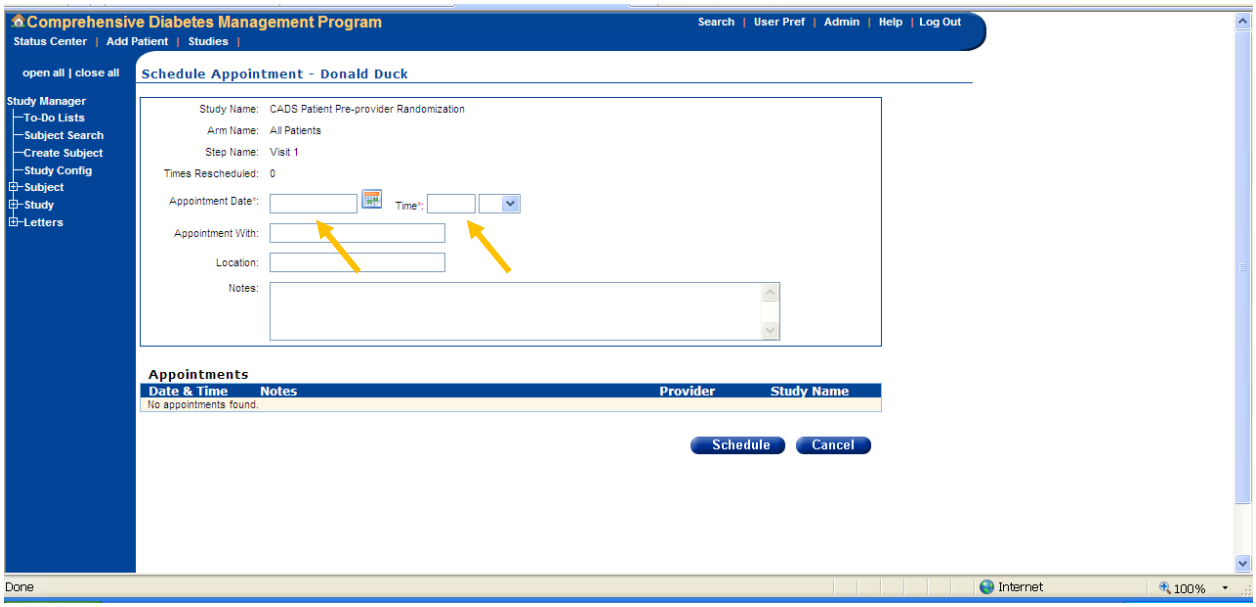

When you are finished with the survey you can either click on “Review Survey” to check yoru answers or click on “Complete” to finish and save the data.



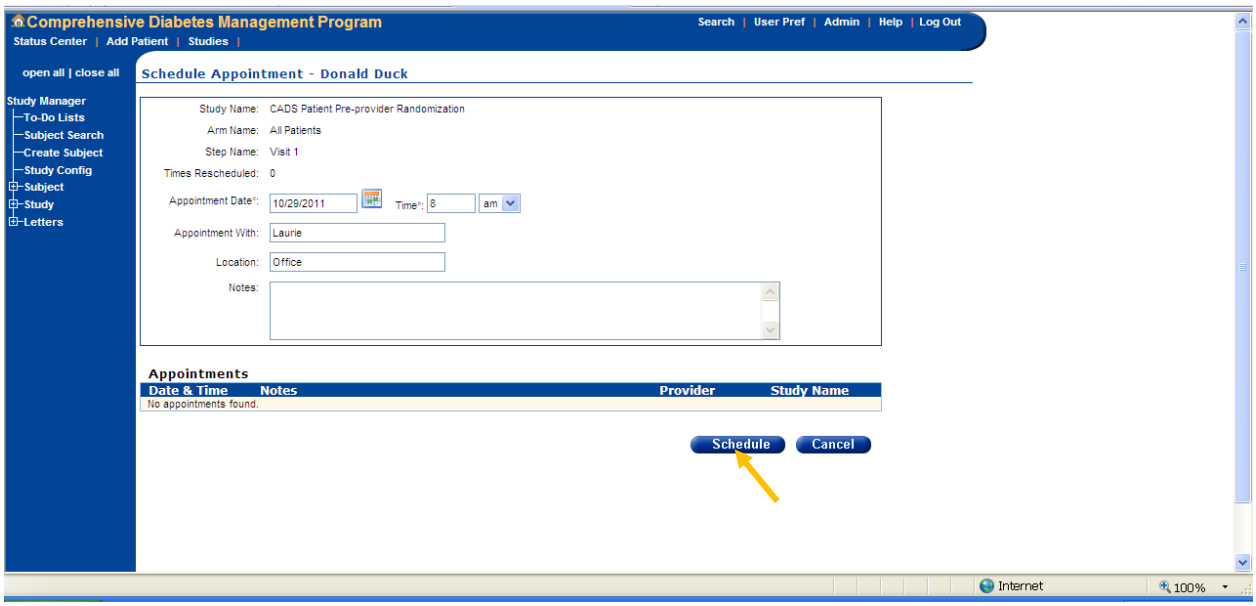

Donald Duck has passed the screener so you can consent him to participate in the study. You will have him sign the consent, enter his Subject Code and Questionnaire id based on yoru assigned values and then click on the button that says “verbally consented.” Later in the process you will be uploading the signed consent form (during study visit 1).



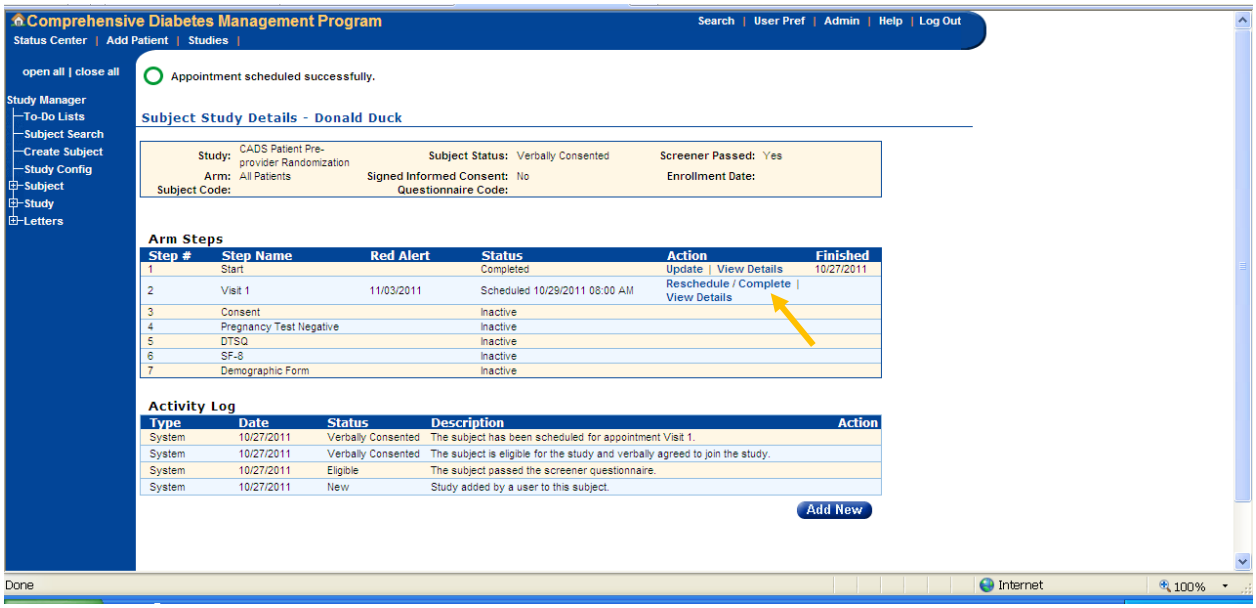

Schedule visit 1 for Donald Duck by clicking on the area that says “Schedule.”



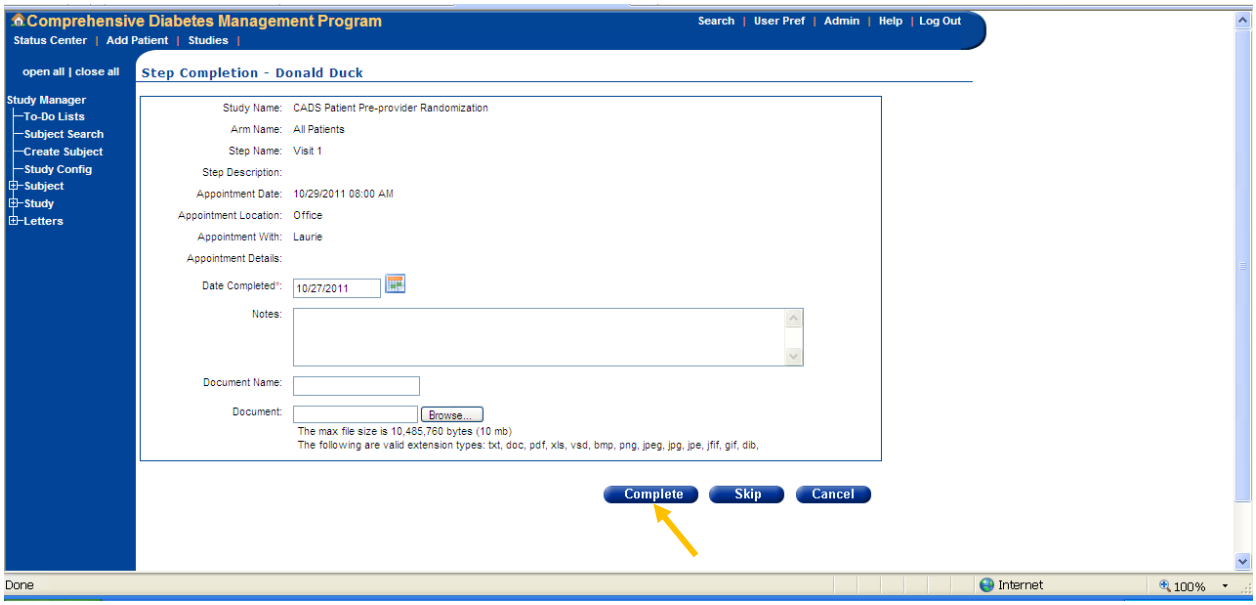

Enter the Appointmnet Date and Time for Visit 1.



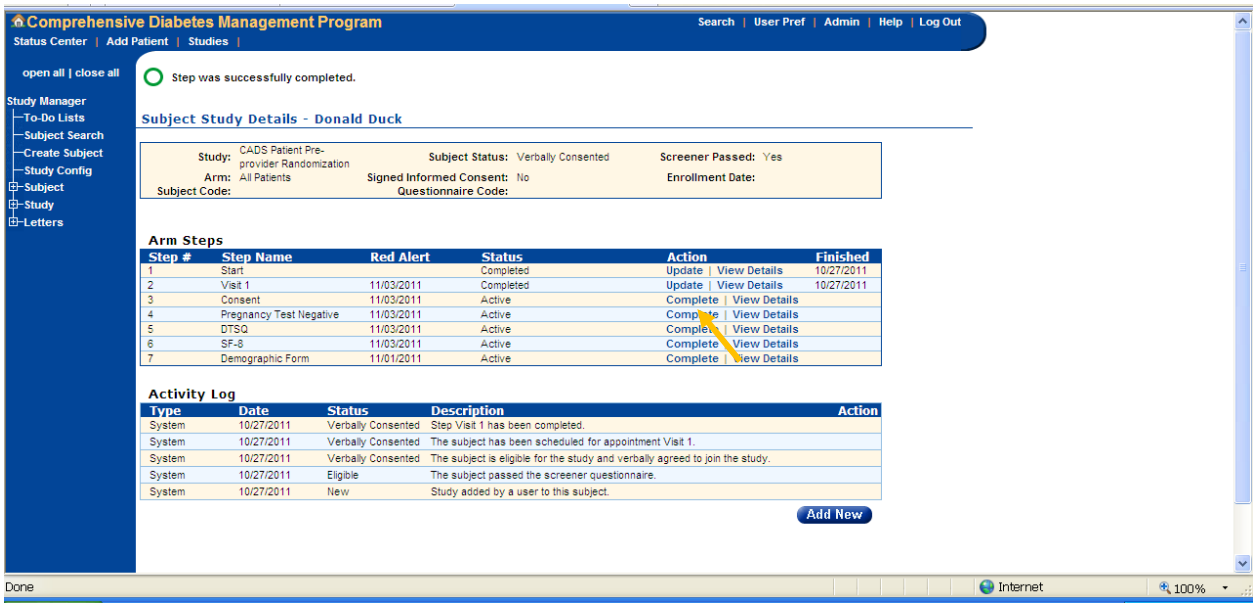

Press Schedule to enter the appointment into the system.



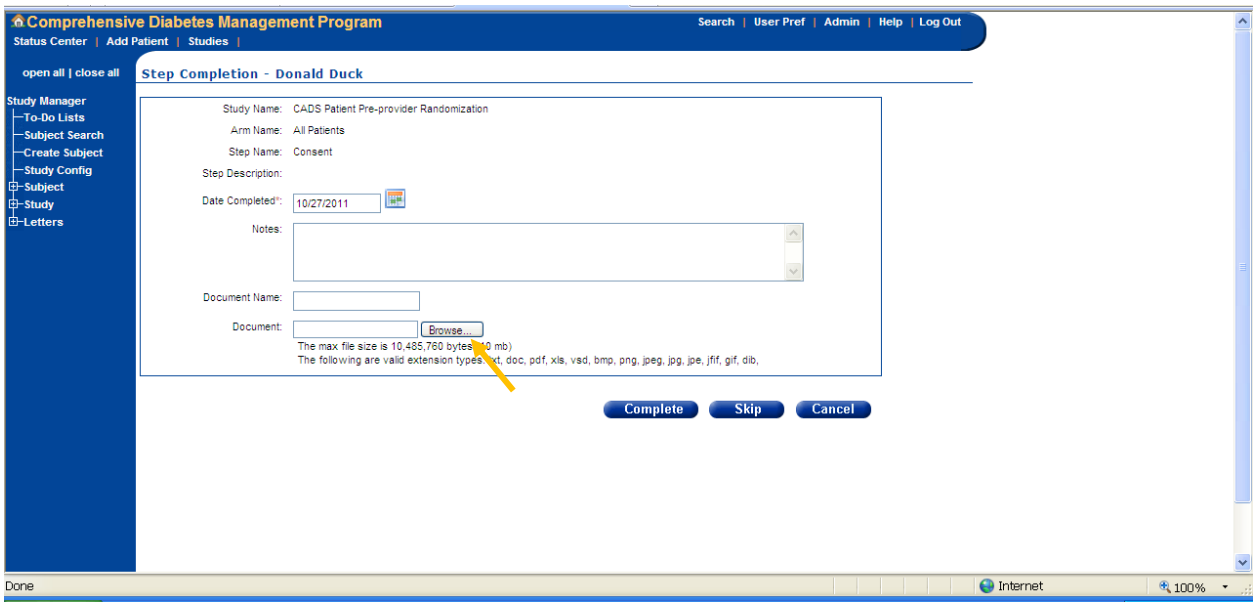

You can now continue the steps in Visit 1. Do this by pressing “Complete” and the other steps will open up and allow you to complete them.



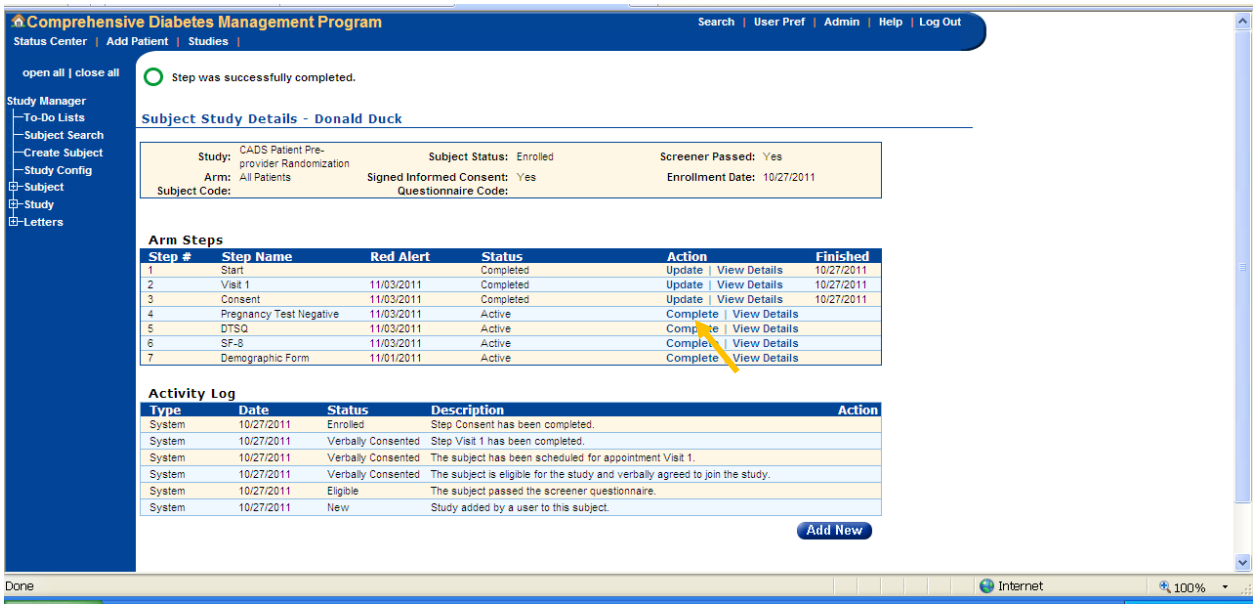

Click complete.



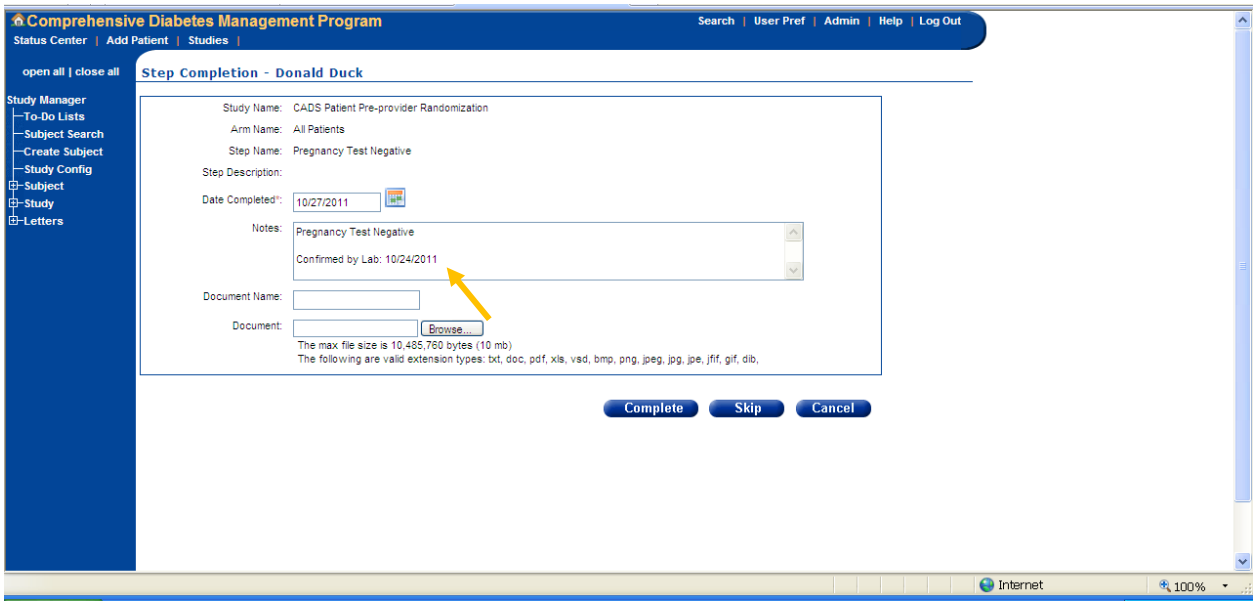

You are now going to upload the signed consent form. CLlick “Complete” in Step # 3 (Consent).



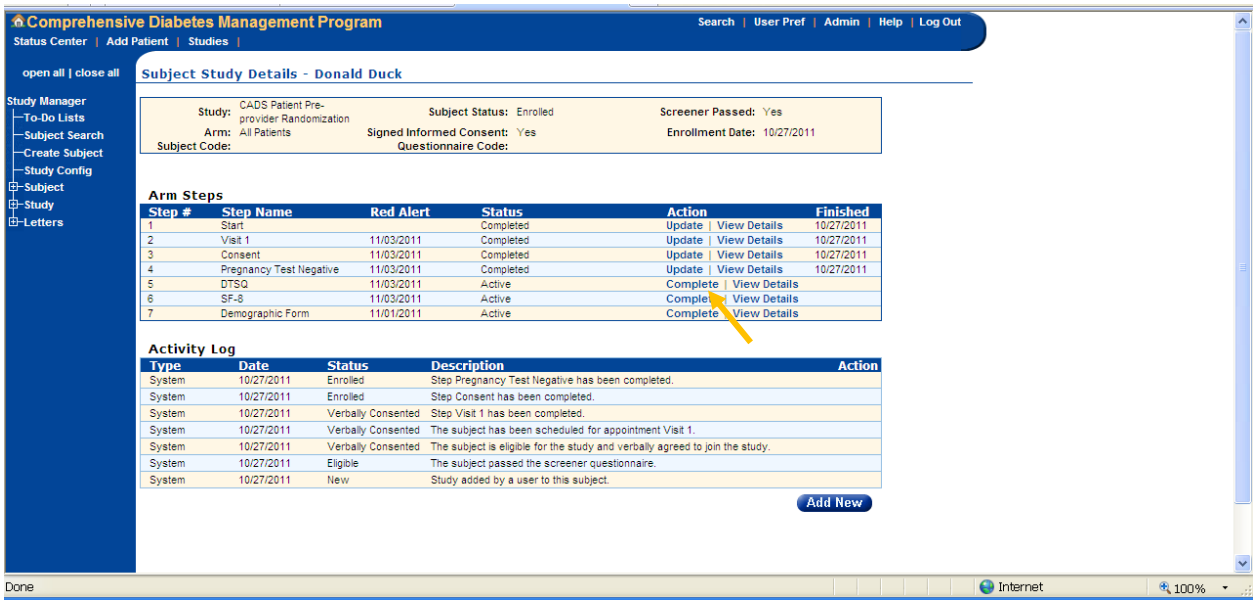

You will click “Browse” and choose Donald Duck’s signed Consent Form. Once that file name is in the Document: box you can complete this step.



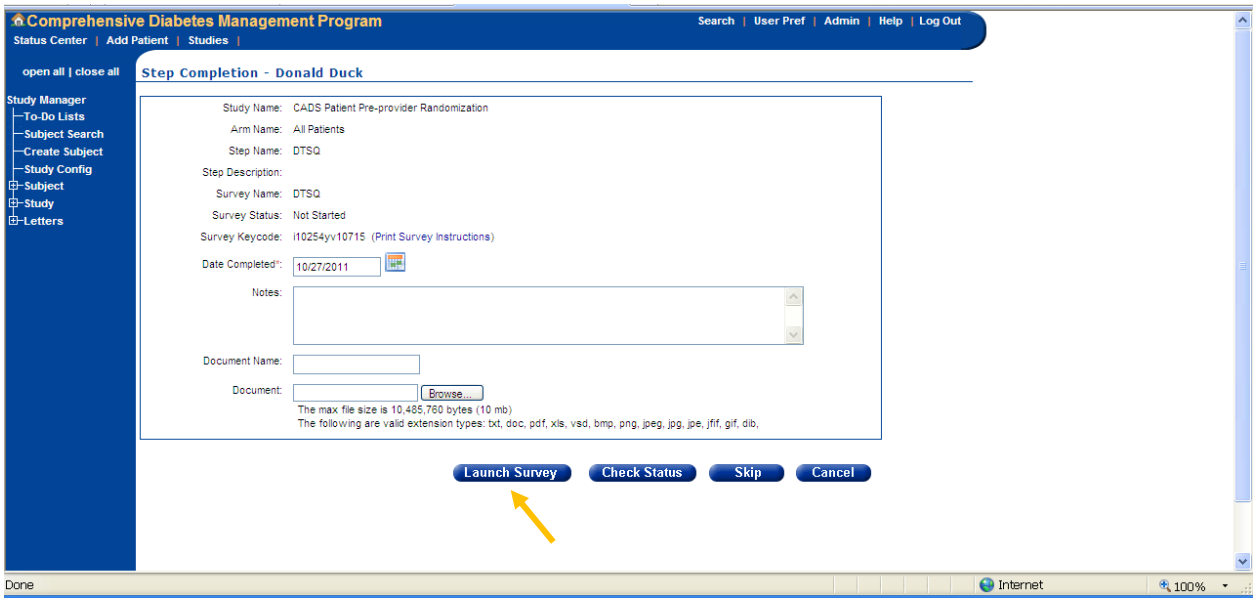

Continue to complete the Arm Steps for this study. Next is the pregnancy test.



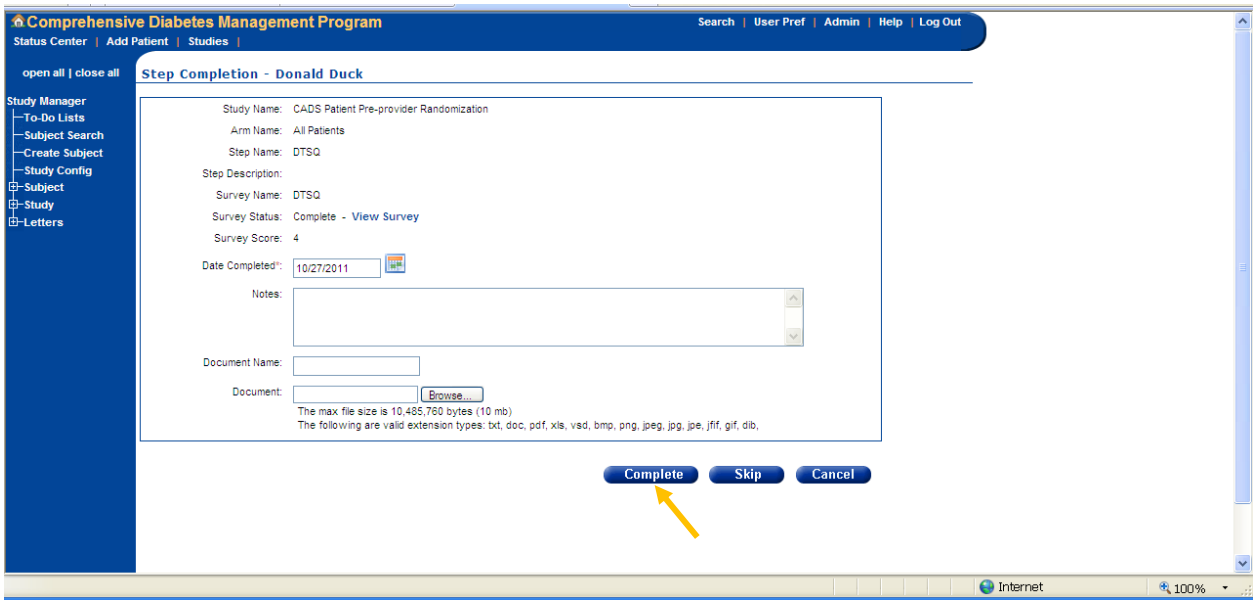

Type in the notes section information about the pregnancy test (it must be negative). In addition you can upload the test results in the same way you uploaded the signed consent form.



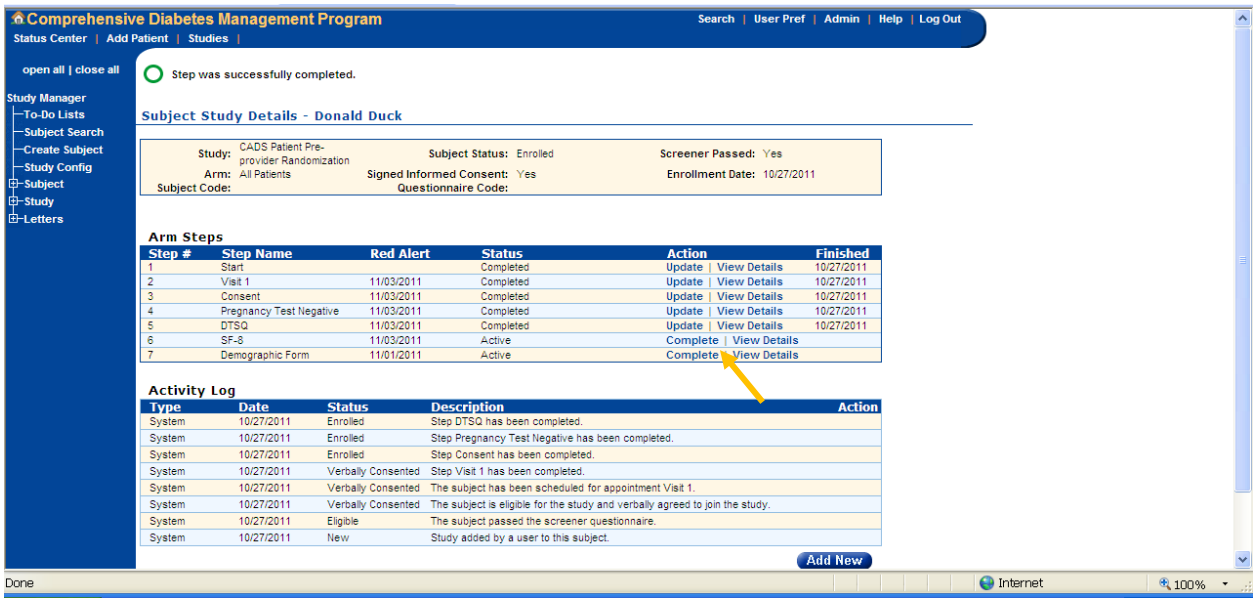

Now you will complete the DTSQ for the patient.



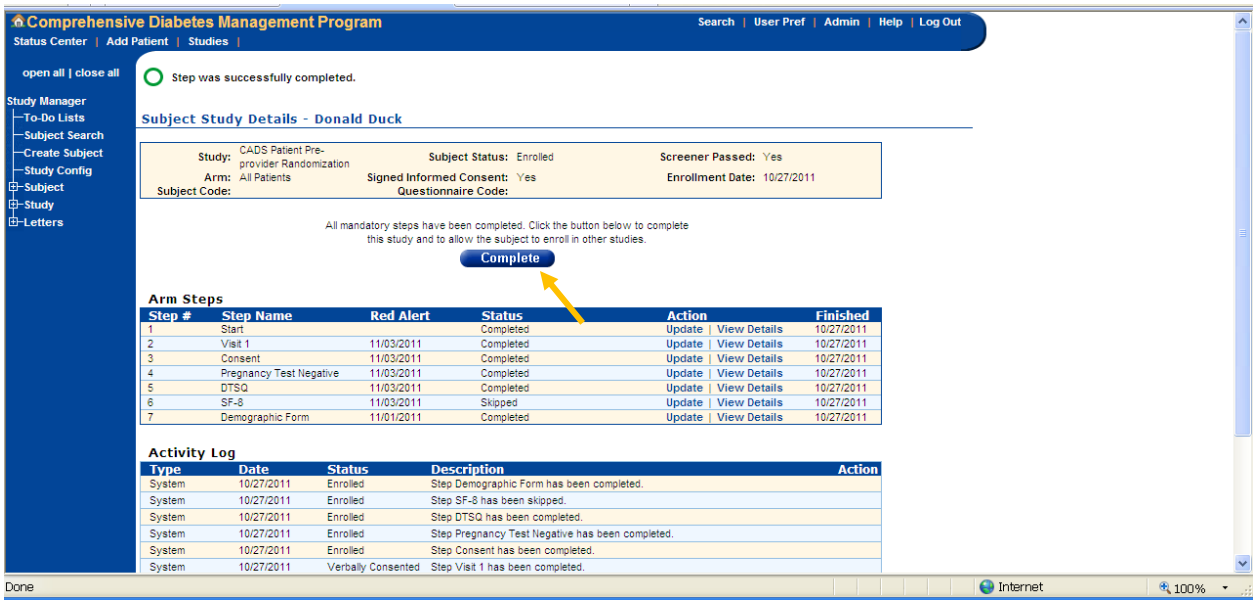

Launch the DTSQ by clicking “Launch Survey”




Once the survey is completed click Complete.

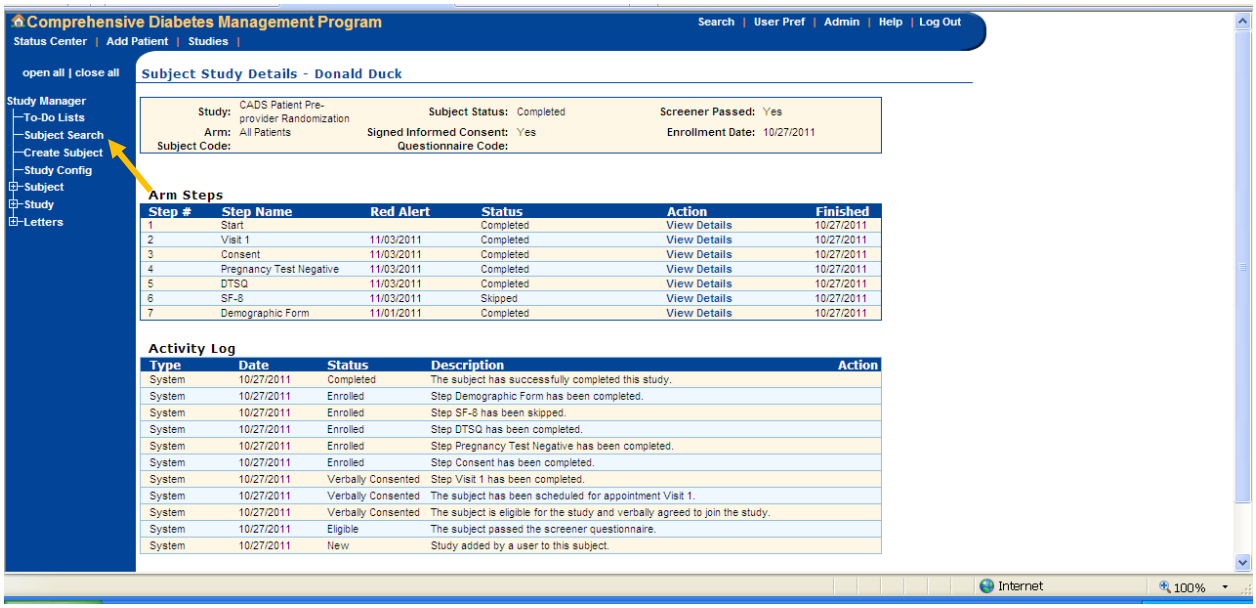



Now you will complete the SF-8.

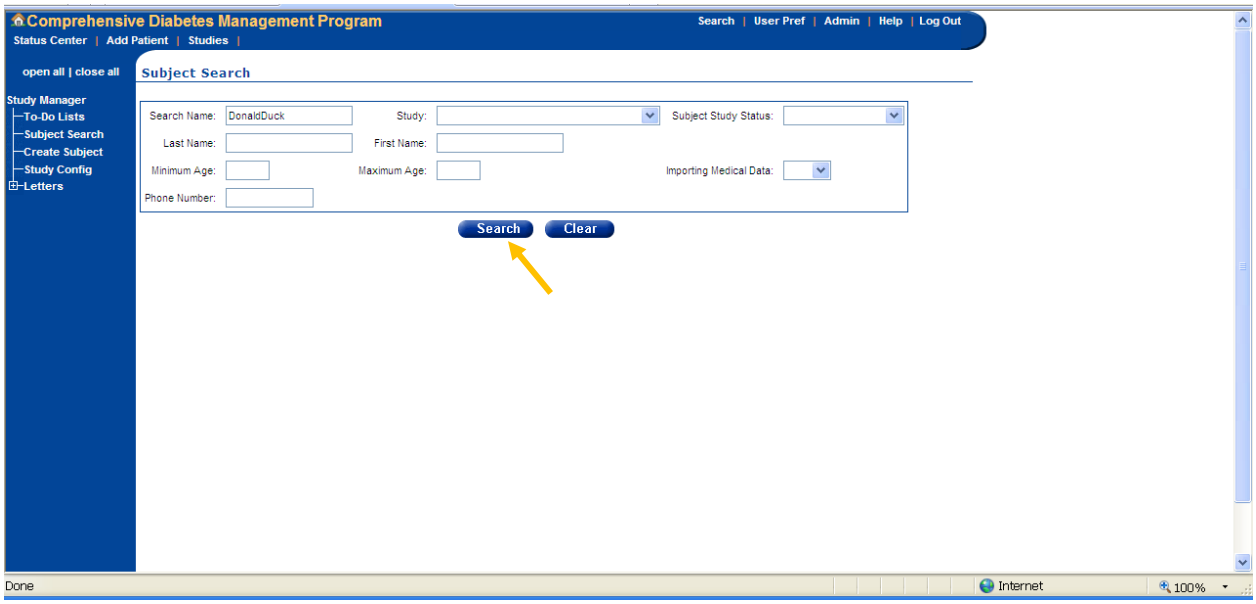



After completing all the Steps in the study, the Complete button will show above the Arm Steps. Click Complete to finish this study. When this study is complete CDMP will allow you to enroll Donald Duck in another study (this enrollment will happen after Donald's provider has been randomized so that Donald can be assigned to a group at that time).

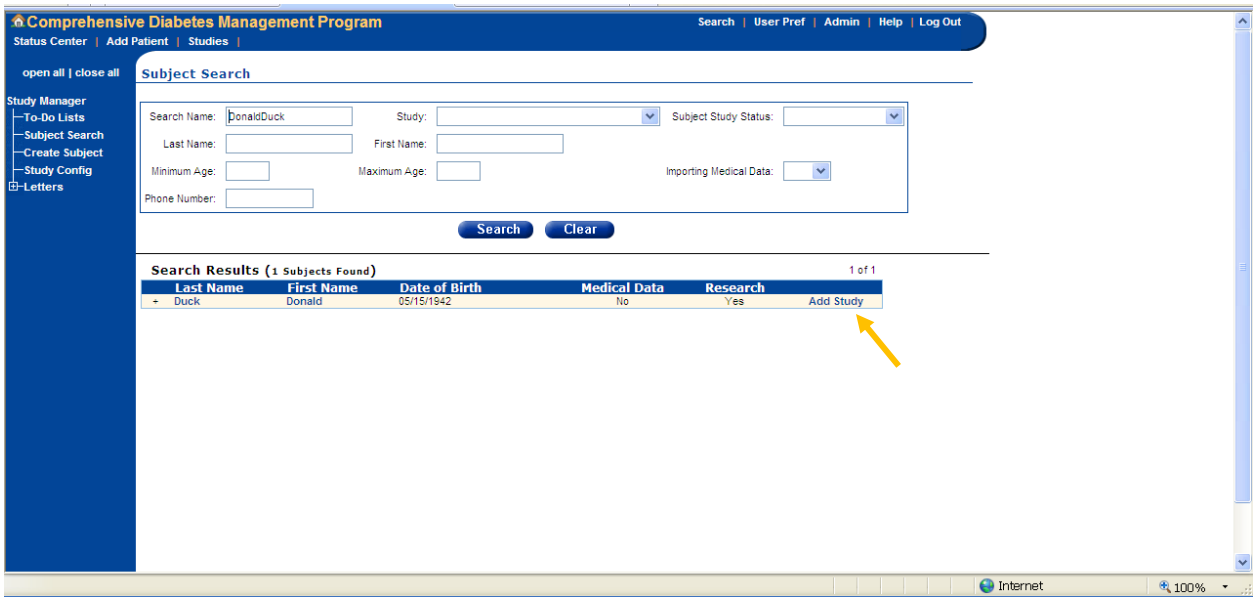
## ADDING ANOTHER STUDY (AFTER PROVIDER RANDOMIZATION)



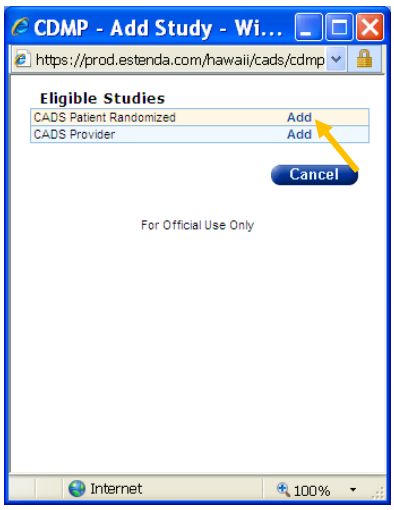

Donald's provider has been randomized, to add him to anther study go to Subject Search.



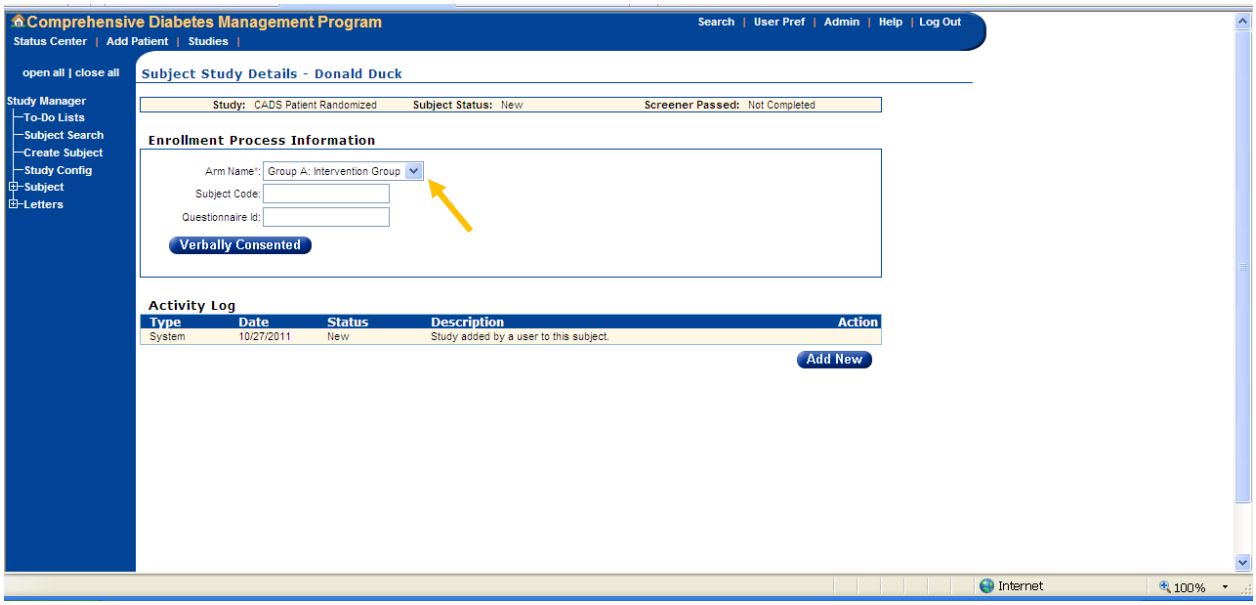

Enter the Search Name you created (here it is firstnamelastname)



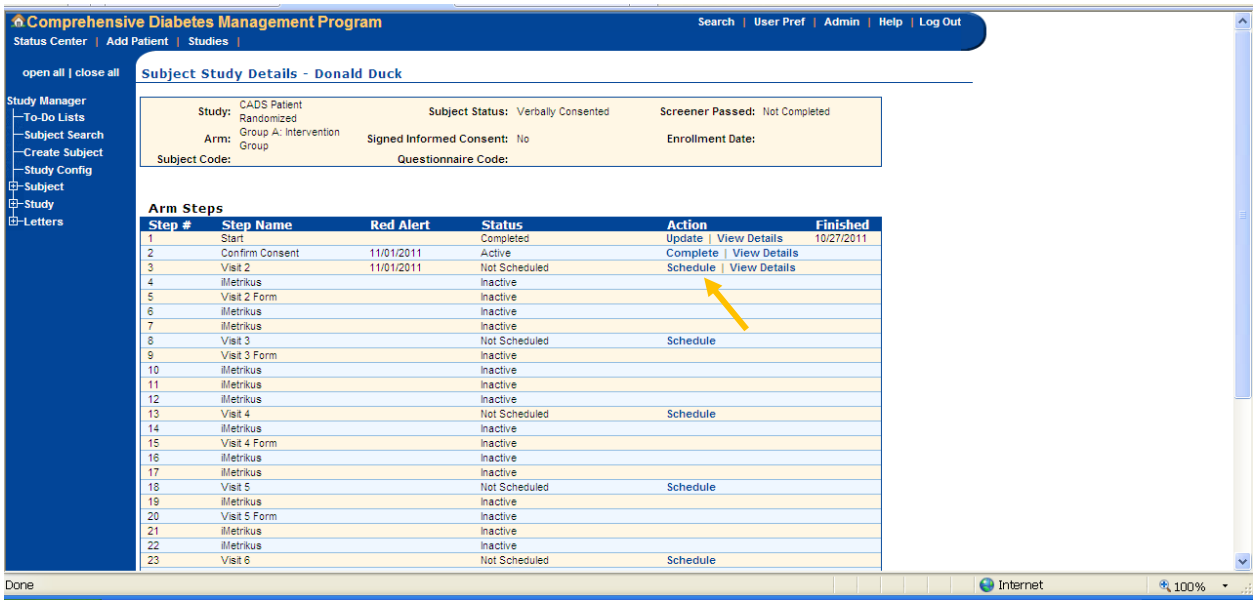

When you get to Donald's record, click on Add Study.




Add Donald to CADS Patient Randomized

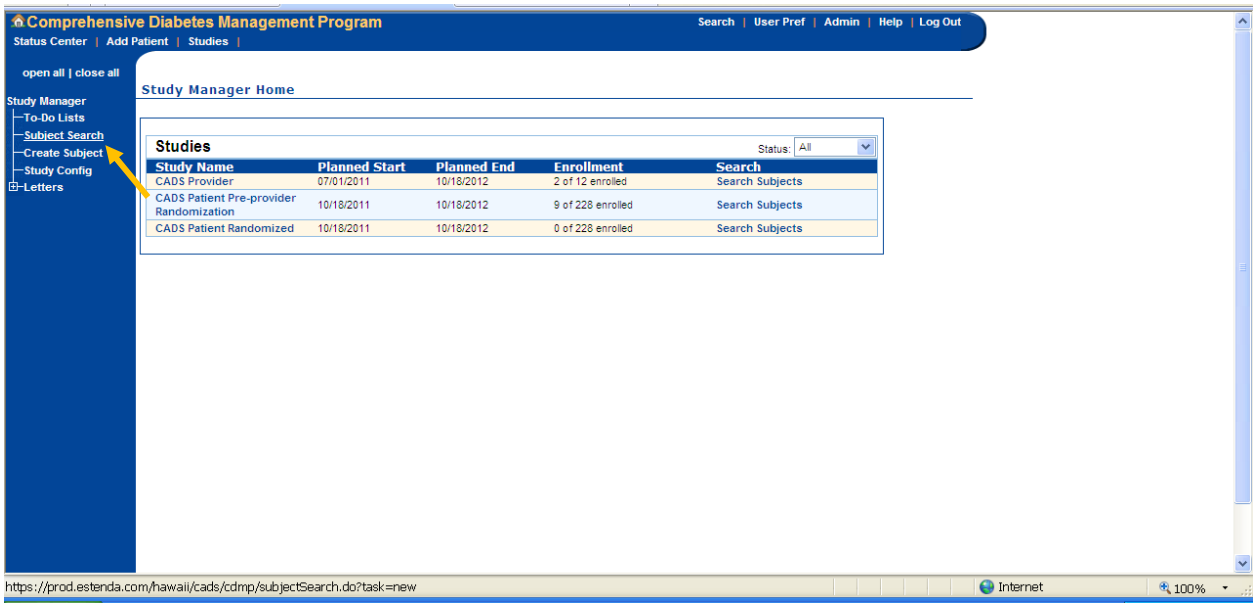


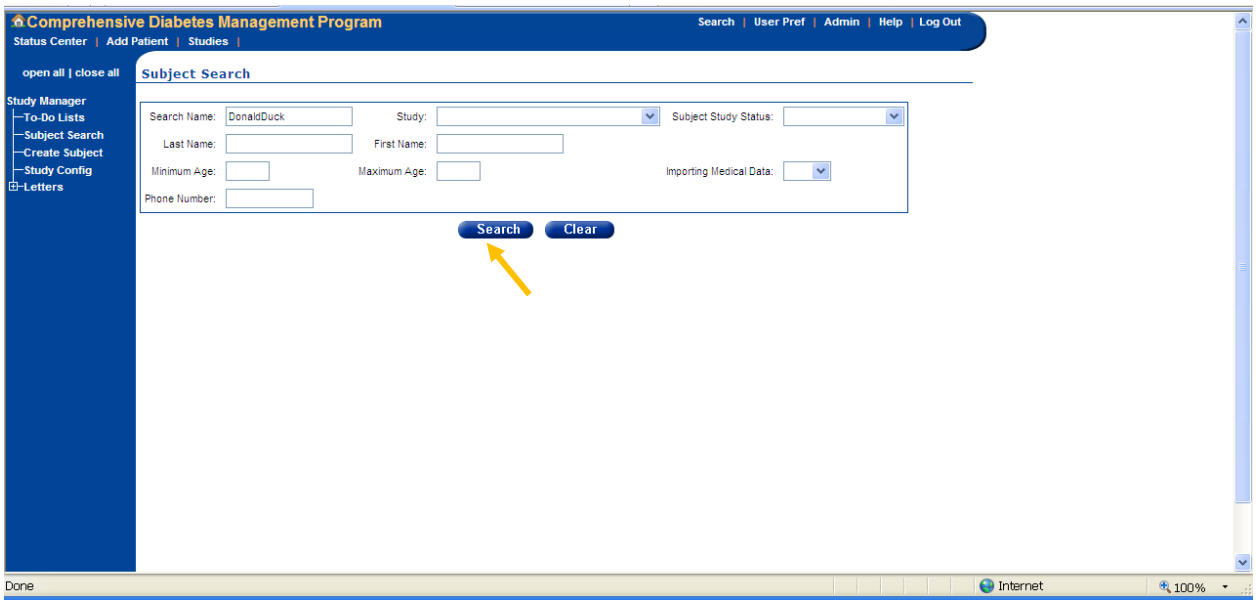

Choose the group to which Donald's provider has been assigned (in this example, Group A: Intervention Group). Enter in the subject code and questionnaire id that you have been assigned for this patient and click Verbally Consented.

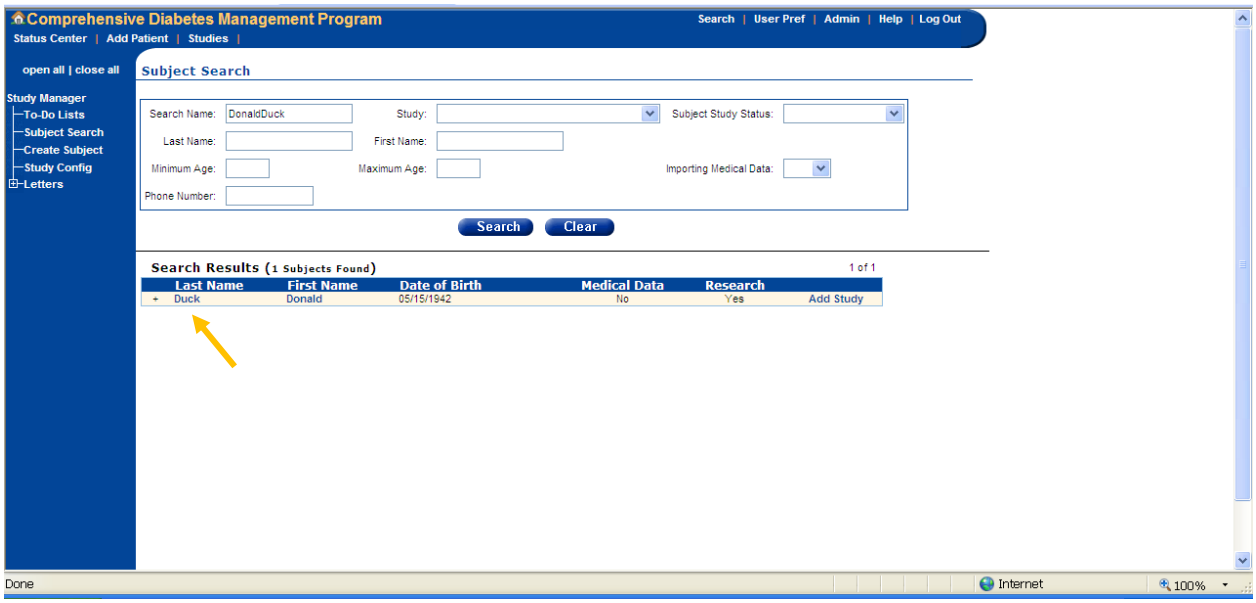



You will now repeat the process as you did for the previous study by scheduling appointments according to the Study Protocol and completing steps as they arise in your reminders and alerts.

## SEARCHING FOR A SPECIFIC SUBJECT




Comprehensive Diabetes Management Program
Search | User Pref | Admin | Help | Log Out
Status Center | Add Patient | Studies |
open all | close all
Subject Search
Study Manager
To-Do Lists
Subject Search
Create Subject
Study Config
Letters
Search Name: DonaldDuck
Study:
Subject Study Status:
Last Name:
First Name:
Minimum Age:
Maximum Age:
Importing Medical Data:
Phone Number:
Search
Clear
Search Results (1 Subjects Found)
1 of 1
Last Name
First Name
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Medical Data
Research
Duck
Donald
05/15/1942
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Yes
Add Study
Done
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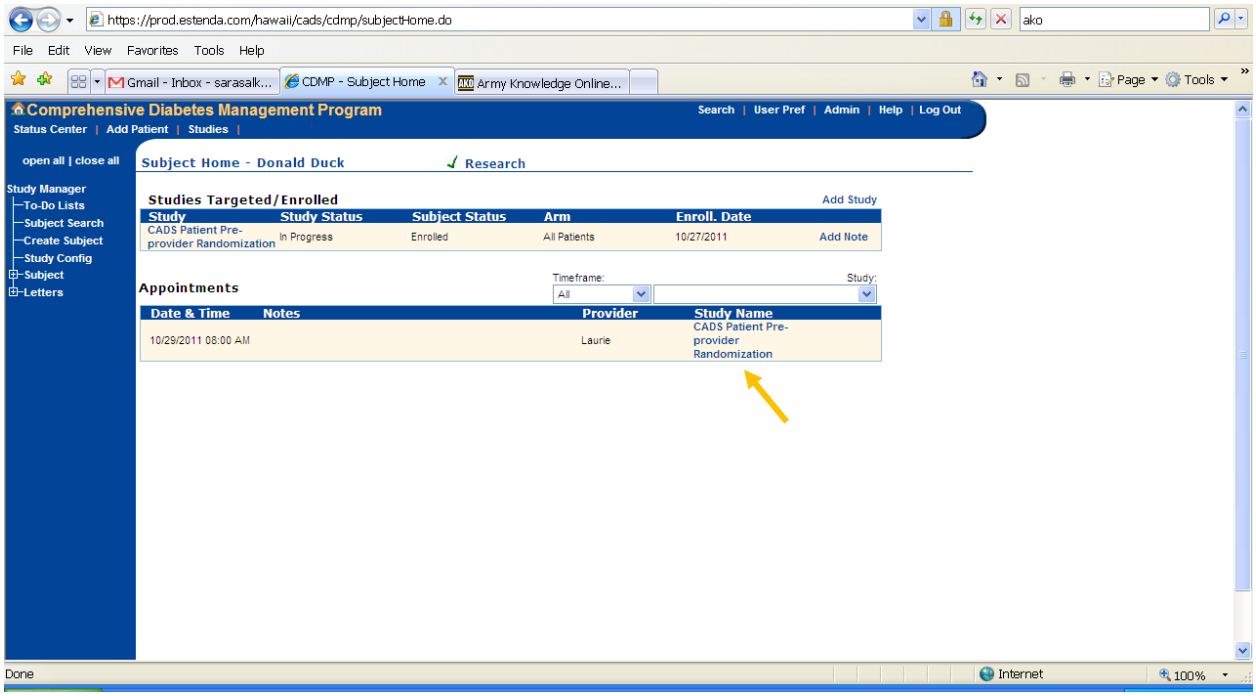
https://prod.estenda.com/hawaii/cads/cdmp/subjectHome.do
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Tools
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Subject Home - Donald Duck
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Study Manager
To-Do Lists
Subject Search
Create Subject
Study Config
Subject
Letters
Studies Targeted/Enrolled
Add Study
Study
Study Status
Subject Status
Arm
Enroll. Date
CADS Patient Pre-provider Randomization
In Progress
Enrolled
All Patients
10/27/2011
Add Note
Appointments
Timeframe:
All
Study:
Date & Time
Notes
Provider
Study Name
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Laurie
CADS Patient Pre-provider Randomization
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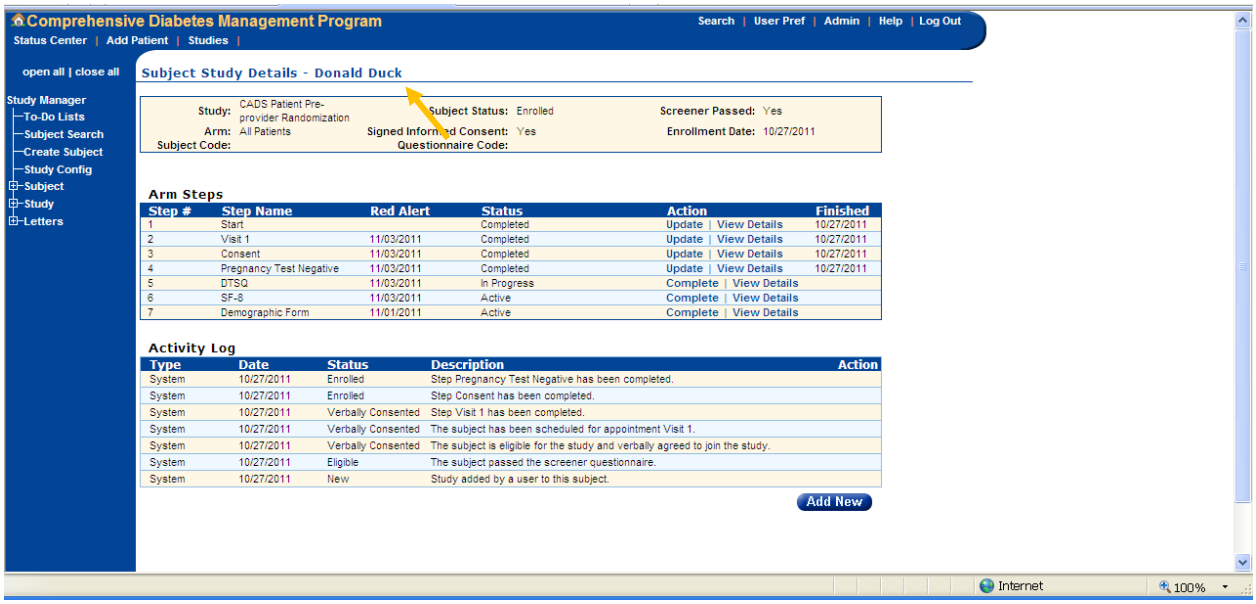
Comprehensive Diabetes Management Program
Search | User Pref | Admin | Help | Log Out
Status Center | Add Patient | Studies |
open all | close all
Study Manager
To-Do Lists
Subject Search
Create Subject
Study Config
Subject
Study
Letters
Subject Study Details - Donald Duck
Study: CADS Patient Pre-provider Randomization
Arm: All Patients
Subject Code:
Subject Status: Enrolled
Signed Informed Consent: Yes
Questionnaire Code:
Screener Passed: Yes
Enrollment Date: 10/27/2011
Arm Steps
Step # | Step Name | Red Alert | Status | Action | Finished
1 | Start | | Completed | Update | View Details | 10/27/2011
2 | Visit 1 | 11/03/2011 | Completed | Update | View Details | 10/27/2011
3 | Consent | 11/03/2011 | Completed | Update | View Details | 10/27/2011
4 | Pregnancy Test Negative | 11/03/2011 | Completed | Update | View Details | 10/27/2011
5 | DTSQ | 11/03/2011 | In Progress | Complete | View Details
6 | SF-8 | 11/03/2011 | Active | Complete | View Details
7 | Demographic Form | 11/01/2011 | Active | Complete | View Details
Activity Log
Type | Date | Status | Description | Action
System | 10/27/2011 | Enrolled | Step Pregnancy Test Negative has been completed.
System | 10/27/2011 | Enrolled | Step Consent has been completed.
System | 10/27/2011 | Verbally Consented | Step Visit 1 has been completed.
System | 10/27/2011 | Verbally Consented | The subject has been scheduled for appointment Visit 1.
System | 10/27/2011 | Verbally Consented | The subject is eligible for the study and verbally agreed to join the study.
System | 10/27/2011 | Eligible | The subject passed the screener questionnaire.
System | 10/27/2011 | New | Study added by a user to this subject.
Add New
Internet
100%

**Appendix C**
**Suggested Questions for CADS Focus Groups**

1. Topics for discussion:
2. Have you used the system (how much)?
3. Do you like the system (likert scale 1 to 5)
4. Have you encountered problems? If yes, what kind (more serious first)
5. Access
6. Understanding of outputs (which outputs)
7. Disagree with recommendations? Why
8. Utility of other features:
    a. Retrieval of laboratory data: A1C Creatinine BUN
    b. Retrieval of SMBG data
    c. Glucose statistics
    d. Glucose graphs
        1. By date
        2. By time of day
        3. Pie charts
        4. Stacked bar charts
            1. Which do you prefer – pie charts or stacked bar charts?
    e. Glucose Logbooks
    f. Display of current medications
    g. Medication history
    h. Data entry – side effects and contraindications
        1. Gi-, Renal-, hepatic-, cardiac-, other- side effects

9. How much time does it take to use the system for a typical patient visit?
10. How much time does it take to review the output for a typical patient visit, if using the system in that manner?
11. Which mode of operation would you prefer – using system online or viewing the output that has been emailed to you immediately before the patient visit?
12. Why?
13. Pros and cons of each (if having had chance to use both)?
14. What additional features would you like to see entered into the CADS system?
15. Is it comfortable to use the CADS system?
16. Would you recommend it to others?
17. Would you recommend it to the following types of potential users:
18. Physicians in general

19. NPs in general
20. PAs in general
21. Primary care physicians
    a. Internists
    b. Pediatricians
    c. OB/GYN
    d. Family Practitioners
22. NPs
23. PAs
24. Pharmacists
25. Diabetes Educators

26. Was the CADS system reasonably consistent (look and feel and mode of operation) with CDMP? With CIU? With AHLTA? With other systems with which you may be familiar? (specify system(s):

---

    a. _____
    b. _____
    c. _____

27. What did you like best about the CADS system?
28. What did you like least about the CADS system?
29. Is there anything that needs to be changed immediately with the system?
30. Open discussion: Topics the (focus group participants) would like to bring up?
31. Wrap-up:
32. Ask the participants to select a spokesperson to provide a wrap up or overview.

**Appendix D**
**Suggested Questions for Usual Care Focus Groups**

1. How do they like CDMP?
2. How do they like AHLTA
3. How frequently do they think that patients with T2DM should be testing SMBG
4. How many times per day
5. Do they like the idea of structured testing, e.g. 7 times per day, 3 days per week? Have they used that? Does that improve care and outcomes?
6. How do they analyze the patient data? Logbooks, computer printouts?
7. What graphs do they use and like? What percent of time do they have access to that?
8. If they had access to graphs and statistics, which ones would they want?
9. Would they want access to formulary? Prescribing information? Guidelines,? Medical literature? Instructions to patients? Other?
10. How much time do they spend with a typical patients?
11. How much time do they think they should spend with each patient, on average?
12. What tools or computer systems do they think they would like?
13. What percentage of clinic visits do you make a change in therapy?
14. What percentage of the changes in therapy that you make, are followed by an improvement within 3 months? Within 6 months?
15. How confident are you, that you can adjust therapy for patients with diabetes, in accord with the standard of practice in the community? In accord with the best practices?
16. Where can one find the “best practices”? – specify
    a. Are you aware of available guidelines or algorithms?
        a. If yes, where?
            1. ADA: guidelines or algorithms
            2. AACE: guidelines or algorithms
            3. DOD/VA: guidelines or algorithms
            4. Other: guidelines or algorithms
                1. Inzucchi – diabetes fact book
                2. Canadian
                3. Italian
                4. Brazilian
                5. other(?)
17. If the computer would make recommendations, what percentage of the time are you (they) likely to follow those recommendations?
18. What are the factors that would influence how you would respond to the recommendations?
    a. Who developed the system?

b. What the logic was based on?

c. Ease and speed of use?

d. Concern that this system might distract you from the patient and the doctor-patient relationship?

e. Concern that the patient might not accept the idea that you are using that system

f. If you had access to a clinical decision support systm, what would you want it to do?

g. Would you want it to provide a recommendation for a best course of action (e.g. change medication regimen, add insulin, etc.) or would you want to have it present a series of plausible alternatives?

19. How important would it be for the computer to provide an explanation of the recommendations that it is making?

20. Where do you normally go for advice, when you encounter a patient with a complex case, if you do not feel 95%+ confident that you can handle the case adequately by yourself?

    a. Fellow

    b. Resident

    c. Attending

    d. Endocrinology consult

    e. Library

    f. Online textbooks or reference sources

    g. Pubmed

    h. ePocrates

    i. PDR or equivalent

What are the biggest problems that you face when handling patients with type 2 diabetes?

Which – if any of those problems, do you think could be handled by a “clinical decision support” system?

What should such a system do?

How would you access it? Online, at time of visit? Online before the visit? Via email?

How often do you change therapy in your patients?

Every visit?

Every other visit

Every third visit, on average?

About once per year

Less often

In between office visits by email or telephone

How often do you think clinicians should change therapy

What is the A1C level that you regard as an appropriate target for most patients? How is that arrived at?

What factors should one consider when arriving at a target level of A1C?

(first do open ended)

Age of patient

- Life expectancy
- Duration of diabetes?
- Presence of known complications?
- History of hypoglycemia episodes? Frequency? Severity?
- Hypoglycemia unawareness
- Occupation
- Other medications

Other topics – chosen by group

Wrap-up by spokesman for the group

Wrap-up by session moderator