

Response Form for the Final Performance Review Report*

1. Name of Grantee: Geisinger Clinic – Weis Center for Research
2. Year of Grant: 2010 Formula Grant

A. For the overall grant, briefly describe your grant oversight process. How will you ensure that future health research grants and projects are completed and required reports (Annual Reports, Final Progress Reports, Audit Reports, etc.) are submitted to the Department in accordance with Grant Agreements? If any of the research projects contained in the grant received an “unfavorable” rating, please describe how you will ensure the Principal Investigator is more closely monitored (or not funded) when conducting future formula funded health research.

The overall research program is overseen by a panel of scientists and administrators at Geisinger Clinic that includes the following individuals: David Ledbetter, PhD, EVP-Chief Scientific Officer; Judith Argon, Chief, Research Administration, Geisinger Clinic; Cathy J. Beinlich, PhD, Associate Vice President, Weis Center for Research; Gregg Bloomquist, Director, Office of Sponsored Projects; Edwin Bommel, Director, Research Finance, Geisinger Clinic; Dorothy Sellers, Director, Office of Research Compliance; and David J. Carey, PhD, Associate Chief Research Officer, Geisinger Clinic. These individual are responsible for ensuring that projects are completed and the required reports are filed.

* Please note that for grants ending on or after July 1, 2007, grantees' Final Performance Review Reports, Response Forms, and Final Progress Reports ***will be made publicly available on the CURE Program's Web site.***

Project Number: 1084901

Project Title: Rare Genetic Variants in Patients with Abdominal Aortic Aneurysm

Investigator: Carey, David

B. Briefly describe your plans to address each specific weakness and recommendation in Section B of the Final Performance Summary Report using the following format. As you prepare your response please be aware that the Final Performance Review Summary Report, this Response Form, and the Final Progress Report will be made publicly available on the CURE Program's Web site.

Reviewer Comment on Specific Weakness and Recommendation (*Copy and paste from the report the reviewers' comments listed under Section B - Specific Weaknesses and Recommendations*):

Response (*Describe your plan to address each specific weakness and recommendation to ensure the feedback provided is utilized to improve ongoing or future research efforts*):

Reviewer 1:

1. Recent experience through large-scale exome sequencing projects and targeting sequencing projects suggests that less common variants with very strong effects are not as common as one would hope. Identifying rare variants that associate with disease requires the study of tens of thousands of subjects, especially if the goal is to identify a profile of variants for risk prediction. Firmer plans of collaborations with other groups with large sample sets related to AAA and interested in sequencing should be pursued and described. The collaboration with deCODE noted in the PI's relevant recent publication is a great start and includes many other groups with large sample sets. Has this collaboration persisted and could it be leveraged for the next step?

Response:

We are actively seeking collaborations with other sites to expand the sample size available for analysis. This includes collaborations through the eMERGE (electronic Medical Records and Genomics) Network, an NIH-National Human Genome Research Institute-sponsored consortium of 9 institutions (Geisinger is one of the network members), continued collaboration with DeCODE, as well as with other collaborators in the UK and in New Zealand.

2. The identification of pathogenic variants through large-scale whole genome sequencing remains cost prohibitive. It may be more worthwhile to pursue large-scale targeted re-sequencing of linkage and GWAS susceptibility loci for AAA (e.g., 9p21) among cases of AAA and suitable controls in addition to whole exome sequencing until there is a more dramatic price drop in whole genome sequencing.

Response:

As suggested by the reviewer, we are pursuing other approaches to identifying AAA-associated genetic variants. Plans are underway to perform whole-exome sequence analysis of AAA cases and controls. We have also performed genotyping of AAA cases and controls using the Illumina exome array, which interrogates approximately 240,000 non-synonymous variants in coding regions of the genome, and includes a large number of low frequency and rare variants. Those data are currently being analyzed

Reviewer 2:

1. Establish investigator data analysis program.

Response:

We are working to enhance our internal data analysis capabilities. This includes creating a Biostatistics Section, which currently has 3 PhD level biostatisticians, and a Bioinformatics Section, currently with one PhD and 2 MS level analysts. Future recruitment efforts will seek to enlarge our internal expertise in this area

2. Recruit new, outstanding young investigators or students into this program.

Response:

Geisinger is not a degree-granting institution and graduate students are not available to participate in the research. We are actively involving undergraduate students from local and regional universities, as well as residents and fellows from clinical training programs in our clinic and hospital. Future efforts will focus on recruiting junior faculty with expertise in cardiovascular biology, genetic, or bioinformatics to participate in the research.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response:

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response:

Project Number: 1084902

Project Title: The Natural History and Comparative Effectiveness of Electronic Alerts in Geisinger Health System's Electronic Health Record

Investigator: Stewart, Walter

B. Briefly describe your plans to address each specific weakness and recommendation in Section B of the Final Performance Summary Report using the following format. As you prepare your response please be aware that the Final Performance Review Summary Report, this Response Form, and the Final Progress Report will be made publicly available on the CURE Program's Web site.

Reviewer Comment on Specific Weakness and Recommendation (*Copy and paste from the report the reviewers' comments listed under Section B - Specific Weaknesses and Recommendations*):

Response (*Describe your plan to address each specific weakness and recommendation to ensure the feedback provided is utilized to improve ongoing or future research efforts*):

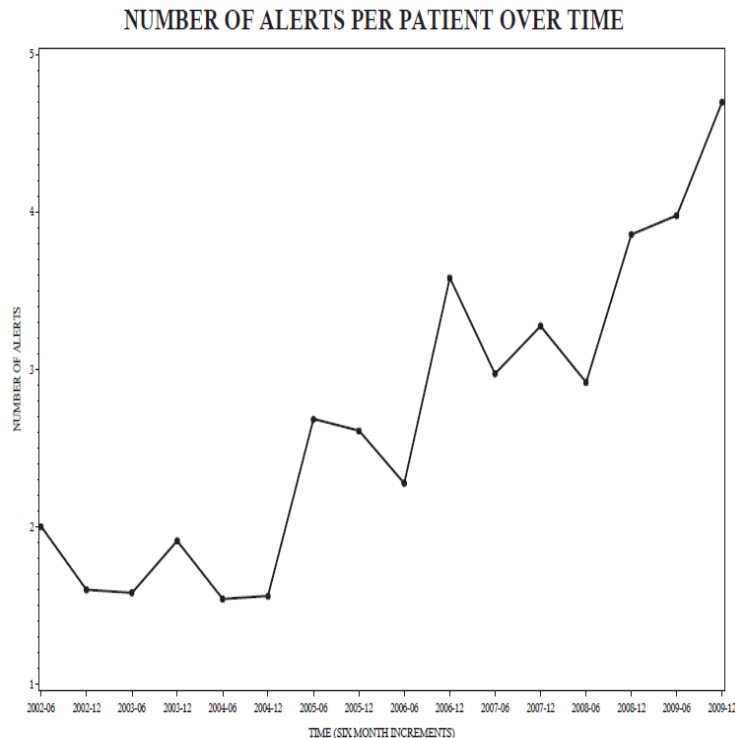
Reviewer 1:

1. Figure 2 appears to be a typo; it is a duplicate of Figure 1 and should be replaced with the correct figure.

Response:

This was a typo and the corrected figure is displayed below.

Figure 2: Average number of BPAs fired per patient from 2002-2009



2. Figures 3 and 4 should be merged for clarity.

Response: The figures were separated due to scaling issues. In 2005 Geisinger began to roll out an increasing number of Best Practice Alerts, and the numbers continued to rise exponentially after that point. The figures were separated in order to display the granularity of alerts by provider types prior to 2005.

3. Reasons for not completing Aim 3 as planned, which arguably is the analytic centerpiece of the proposal, should be provided. The planned analysis was ambitious to begin with and probably unrealistic in a small grant project like this one, and this should be better identified in the future. It would have been reasonable just to develop the database and validate it for this grant. The investigators may have been overly ambitious in the proposal, and as a result the proposed deliverables were not completed.

Response:

Originally we had planned to classify all alerts according to two criteria for an “effective” alert: 1) whether the alert was acknowledged (i.e., did the physician click on and open it), and 2) whether the alert was satisfied based on some action (e.g., medication order, diagnostic test). We then planned to utilize these definitions of “effective” as a dependent variable in regression-based analyses to determine factors associated with effective alerts. After obtaining and working with the data, we determined that limited information was available to inform either 1 or 2 above. While we were expecting to use available audit trail data to determine whether or not an alert was viewed, in reality it was not possible to identify whether an alert was acknowledged (i.e., clicked on and opened) based on the available log files. Additionally, determining whether or not an alert was satisfied would have required resources outside of the scope of this project as each unique alert had its own logic-based criterion for firing and this information was stored in free text within the EHR, not as an extractable data point. Due to these challenges, we decided to utilize a simplified and achievable definition of effectiveness based on the alert “re-fire” rate, but did not have required resources to complete the remaining regression-based analyses utilizing this definition after overcoming these data obstacles .

4. Explain why results were only provided through 2009.

Response:

The data were pulled from an enterprise wide data warehouse, and at the time of the data pull the tables which stored these data were only updated through 2009. Updating these tables would have required resources (staff, funding) outside of the scope of this project, so the decision was made to utilize data through 2009.

5. Propose a plan in the future to complete Aim 3 as initially proposed, to show the effectiveness of alerts. No clear plan is presented, and there is a high risk that this analysis will not be picked up in the future under a different mechanism. If it is not moved forward, the development of the database under Aim 1 will have been a futile effort.

Response:

Completing Aim 3 as initially proposed will require large scale resources, as well as a change in the way in which audit logging parameters are set within the system EHR. While potentially achievable and a worthwhile endeavor, we have no existing plans to move forward with the analysis as originally planned in Aim 3. The database developed in Aim 1, however, remains a useful resource, and we plan to pursue additional funding to complete the regression analyses utilizing our working definition of “effectiveness”.

Reviewer 2:

1. Provide the average number of alerts fired per patient as indicated in Aim 2 but not reported.

Response:

The average number of alerts per patient per encounter grew from 2 alerts in 2002 to nearly 5 per patient per encounter in 2009 (see figure 2 above).

2. Continue to define "alert effectiveness" and "alert closure."

Response:

Please see response to Reviewer 1’s comment number 3.

3. Complete the regression analysis to examine how alerts were impacted by factors at the clinic, provider and patient levels. Publish these important results.

Response:

Please see response to Reviewer 1’s comment number 5.

Reviewer 3:

1. The project failed to provide a natural history of the use of alerts at Geisinger Clinic for the time period 2002-2009. The project failed to associate alerts usage with health outcomes. No data was presented on health outcomes. No data was provided on consequences of the research.

Response:

The main objective of this project was to identify the various types of alerts that have been deployed in clinical practice, describe the frequency with which they are used, and characterize their effectiveness in achieving the desired clinical outcome (e.g., an alert’s effectiveness in prompting a doctor to order a vaccination). We did not propose to associate alerts with health outcomes.

2. Additional details regarding the alerts database should be provided. Statistical analysis should be conducted to characterize the natural history of the alerts over time at Geisinger (Aim 2) and presented in a peer-reviewed publication. There are many interesting questions that can be explored using the dataset assembled in Aim 1. Why did alerts drop for physicians in 2008? Do nurses and physicians respond differently to alerts? How? What do all the alerts look like (not just BPAs)?

Response:

We agree that there are many interesting and important questions that can be explored using the database created in Aim 1. We plan to seek additional funding for a more robust study design and analytic support to begin to understand these issues, and to publish the results.

3. Significant additional statistical analyses should be conducted to determine the relationship of alerts to health outcomes. When are alerts effective? When are they ineffective? These are fundamental questions that Geisinger Clinic may be in a position to address. Additional statistical expertise should be brought to bear on the data to formulate specific questions and conduct analyses.

Response:

We agree that there is an opportunity to explore the relationship between alerts and health outcomes. As noted above, we did not propose to analyze health outcomes in this initial project. However, the creation of the database as part of Aim 1 provides an opportunity to consider this type of analysis in the future, without the need to duplicate the initial work required to build this data asset. We plan to seek additional funding for a more robust study design and analytic support to begin to understand these issues, and to publish the results.

4. Results from the study should be published in a peer-reviewed journal.

Response:

We strongly agree that future work done using these data should be published in a peer-reviewed journal. As we seek funding to support additional work with these data, all proposals will include publishing the results in a peer-reviewed journal as a specific aim.

5. Results of the study should be used to alter the deployment of alerts at Geisinger Clinic. Once the natural history is well characterized and specific findings regarding alerts related to improving health outcomes have been determined, the institution should use those results to improve its deployment of alerts and hence its ability to deliver quality health care.

Response:

The original vision behind this proposal was to use the results to influence how alerts are deployed within the Geisinger Clinic. As noted, we are seeking additional funding so that we can continue to use the database built as part of Aim 1 to help achieve this vision.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response:

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response: