Final Progress Report

Title of Project: Comprehensive Analysis of Data from Testing the Re-engineered Hospital Discharge
Principal Investigator and Team Members: Veerappa K. Chetty, PhD
Organization: Boston Medical Center
Inclusive Dates of Project: 09/30/2009 – 09/29/2010
Federal Project Officer: Dr. James Battle
Acknowledgment of Agency Support: This work was funded by Agency for Healthcare Research and Quality grant 1R03 HS017354 01A2 (Dr. Chetty).

Grant Award Number: 1R03HS017354-01A2

Abstract Background: In our randomized trial, the "Re-Engineered Hospital Discharge" (RED), which had 10 mutually reinforcing components delivered using a tool called the "After Hospital Care Plan" (AHCP), reduced the 30-day rehospitalization rate by 30%. The main result is now published in the Annals of Internal Medicine. RED is accepted as a National Quality Forum "Safe Practice" (SP11) for all patients being discharged from the hospital. We have received many requests inquiring about 1) the effectiveness of our intervention among various subgroups, 2) the relative contributions of a discharge advocate and the pharmacist's follow-up call, and 3) a prediction model for risk stratification for testing the effects of the intervention on high-risk groups. An email we received today states: "I am now the medical director of a Medicaid and Medicare-Medicaid health plan in Michigan. The tool that I especially would be interested in hearing more about is the predictive modeling tool. With limited resources, our case managers have to do a really good job at stratifying the hospitalized members so that they only engage with a limited few that are especially high risk for readmission."

Goal: Perform a complete analysis of the 1,008 discharges of patients enrolled in the Re-Engineered Discharge trial, focusing on the risk (i.e., the probability of a readmission within 30 days after any discharge). We will also estimate the effects of RED for various subgroups and develop prediction models to identify high-risk patients for rehospitalization

who are also likely to benefit from the intervention. **Methods** Because patients may have more than one discharge, the statistical analysis should take into account possible correlation among repeated rehospitalizations for one person. Hence, we will treat repeated discharges for a patient as a cluster and estimate a mixed-effects logistic regression model using the "lmer" function in the "lme4" package developed by Bates et al., available in the free statistical software R, version 2.8.1. The threshold risk score will be determined using the estimated effect sizes and calculated intervention costs. The best performance model for each subgroup and the risk categories that will benefit will be chosen using net benefit analysis and software by Tobias Sing, Oliver Sander, Niko Beerenwinkel, and Thomas Lengauer (2007): "ROCR: Visualizing the performance of scoring classifiers," R package version 1.0-2 (http://rocr.bioinf.mpi-sb.mpg.de/).

Outcomes: Papers on efficient prediction and implementation of Project RED.

Objectives:

Specific Aim 1: To perform a comprehensive analysis of existing data in order to determine which subsets of patients are best served by the Re-Engineered Discharge in order to learn how to best market these tools.

In Project RED, we demonstrated that the 30-day readmission rate can be decreased by approximately 30% if our re-engineered discharge (RED) process is followed. However, it is possible that not all groups benefit from the RED. Furthermore, it is possible that the RED is detrimental to particular groups. As one may suspect, various factors contribute to a rehospitalization or an adverse event. Secondary analyses of these data will allow us to determine which specific subsets of the population are positively and/or negatively affected by the re-engineered discharge.

Specific Aim 2: To create a prediction model for rehospitalization. A prediction model has the potential to determine which particular patients have a significant likelihood of being rehospitalized.

Intense analyses of data, paying attention to particular individuals, are necessary in order to create such a model. However, the secondary analyses and a prediction model will allow us to determine which patients benefit from the RED, thus allowing us to best market the tools of the re-engineered discharge.

Scope: Setting and Participants

Two randomized controlled trials, Project RED and Project RED-LIT, were carried out with adult patients admitted to the general medical service of Boston Medical Center between January 2006 and October 2007.

A detailed description of the methods used in Project RED has been published previously . In brief, patients were randomized to receive either 1) usual care or 2) a patient-centered hospital intervention. The initial part of the intervention was delivered by a research nurse called the Discharge Advocate, whose role was to provide patients with information about medications and diagnoses, arrange follow-up appointments at times convenient for patients, and provide patients with information and instructions on self-care after discharge. All of this information was incorporated into a personalized After Hospital Care Plan booklet, which was given to patients and used as an educational tool by the Discharge Advocate prior to discharge. These patients also received a follow-up telephone call from a pharmacist within 2 to 6 days of hospital discharge.

Project RED was designed to study the risk of hospital utilization (hospitalization and emergency department visits) in the 30-day period after discharge from the index admission. Participants in the intervention group for Project RED (n = 370) had a lower rate of hospital utilization than those receiving usual care (n = 368) (0.314 vs. 0.451 visit per person per month; incidence rate ratio, 0.695 [95% CI, 0.515 to 0.937]; p= 0.009). The intervention was most effective among participants with hospital utilization in the 6 months before index admission (p = 0.014). Project RED-LIT was designed to study the effects of an intervention that was the same as in Project RED except for the following differences: 1) An embodied conversation agent was provided to the subjects in the intervention arm. 2) In the first phase of the trial, RED-LIT-1, the follow-up after discharge was through a telephone linked system instead of from a pharmacist. 3) In the second phase, the telephone system was replaced by a pharmacist as in Project RED.

We used the 329 subjects in the *control* arms of RED-LIT-1 and -2 to identify risk factors for readmission and develop prediction rules for selecting patients for cost-effective implementation of Project RED in a *new* group of patients. Because we also have the outcomes of the Project RED trial for the chosen risk categories, we can use part of the intervention group (e.g., the first 100 patients, or 100 randomly selected patients from the intervention arm by rank order of the reductions in the readmission rates---i.e., the effectiveness of the intervention for the risk categories) and provide the intervention only to subgroups for which it is effective. We kept the remaining 266 subjects in each arm of Project RED for testing our prediction rules.

Methods: Figure 1 shows the research model for the experiment. The independent variables, intermediate clinical variables, baseline variables, and outcome variables are shown in the schematic below.

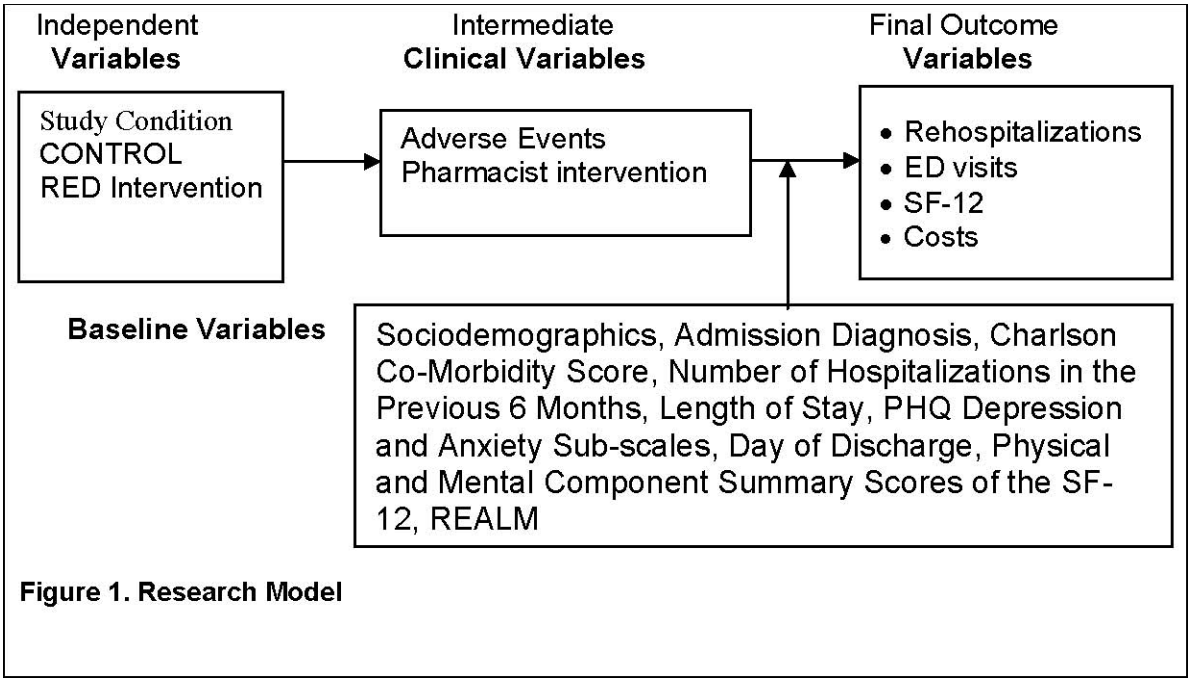


Figure 1. Research Model

Implementation Methods

We study seven methods of implementing Project RED: 1) Replicate Project RED. 2) Using data available at the time of admission, identify risk factors for readmission, develop risk categories, and provide the intervention to selected high-risk groups. We will study two methods to create risk categories: i) estimate a logistic regression model and create risk scores; and ii) create a "flat" table of incidence rates (for readmission) for the risk categories identified in the logistic regression model and/or other clinical evidence and use the flat table to rank the risk categories. 3) Enroll 200 patients for a pilot study, randomize them into intervention and usual-care arms, provide the intervention to the 100 patients in the intervention arm, identify the subgroups with the chosen risk factors that benefit by the intervention by comparing the *average* readmission rates for corresponding subgroups in the two arms, and provide the intervention only to the subgroups that benefit. 4) Modify the previous method 3 to provide the intervention only to few, say five, subgroups that benefit most from the intervention.

We have two methods to create risk categories, one using quantitative risk scores from a logistic regression model and the other using tabulation of incidence rates for clinically useful or readily observable risk categories, such as homeless or those with diabetes, identified by regression models or clinical observations. We have three ways to implement Project RED: 1) Provide intervention to selected subgroups by one of the risk stratification methods without conduction a pilot trial. 2) Conduct a pilot study and provide intervention-only subgroups that benefit, identified again by one of the risk stratification methods. 3) Modify the previous method to select few, say five, subgroups, that benefit most. We have then 3 x 2 = 6 different methods of implementing Project RED. Including simple replication of Project RED, there are seven different ways.

We will study the comparative effectiveness of the seven methods using two sets of data from the same population of adult patients admitted to the general medical service of Boston Medical Center between January 2006 and October 2007.

Statistical Methods for Selecting Subgroups

We used 325 observations from the control arms of RED-LIT-1 and -2 to identify subgroups of patients with high risk for readmission within 30 days after discharge. We estimated a Poisson regression model using total hospital utilization as the dependent variable and assessed effects of sex, marital status, homeless (or housed), previous hospital utilization (Fr.Fly), depression diagnosis (Dep), and one or more of three chronic conditions (type 2 diabetes, hypertension, and asthma [DM-BP-Asthma]).

Previous hospital utilization, homeless, and depression diagnosis were found to be significant risk factors, with P-values less than 0.1. We included the three chronic conditions, DM-BP-Asth, as one clinically significant risk factor. All data were analyzed using R- version 2.11.1 (R Development Core Team [2010]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org).

Thus, four risk factors were identified. Depending on the presence or absence of each risk factor, 2 x 2 x 2 x 2 = 16 mutually excusive subcategories of patients were created. Risk scores for these categories can be calculated using the incidence rates estimated using the Poisson regression model.

Assuming that the risks are proportional to the incidence rates, normalizing the total risk for the four risk factors to sum to 100 and approximating them by the nearest multiple of five, we have the following risk scores: Fr.Fly = 30, Dep = 25, Homeless = 30, and DM-BP-Asthma = 15. Scores for various combinations of risk categories are calculated by adding the corresponding risk scores. The resulting 12 risk categories are 0, 15, 25, 30, 40, 45, 55, 60, 70, 75, 85, and 100. The risk score categories are only 12 and not 16, because some of the categories, such as DM-BP-Asthma + Homeless and DM-BP-Asthma + FR.Fly, have the same score of 45. Although the risk scores for these two groups are the same, the effectiveness of the intervention may differ between the two subgroups. Hence, treating the two groups as one may decrease the effectiveness of the intervention, especially if it is not effective in one group.

Alternatively, we can use all the 16 mutually exclusive risk categories without quantifying the risk but using the readmission rates to rank them.

To validate the usefulness of the risk categories, we use the outcomes from the Project RED trial. As noted earlier in Table 1, the IRR varies among subgroups (with at least five patients) from a minimum of 0.333 to a maximum of 1.432. Also, the readmission rate for the “no-risk--usual care” subgroup is 0.275, indicating that the risk assessment is not perfect. The readmission rate for the “no-risk” intervention group is 0.149, indicating the effectiveness of the intervention.

Because the intervention is not uniformly effective across subgroups, it may be useful to conduct a “mini trial” (e.g., with 100 patients in each arm) to identify the subgroups for which the intervention is effective. The intervention can then be given only to those subgroups for which it is effective.

To validate this method, we selected the first 100 patients or alternatively random samples of 100 patients from each arm, calculated the effectiveness of the intervention for each subgroup, and provided the intervention to “effective” subgroups. The efficiency of this “sequential” procedure is determined using only the outcomes for the effective subgroups in both arms from the remaining 527 patients from Project RED. When random samples are taken, the procedure can be repeated a large number of times (e.g., 1,000 mini trials) to validate this “bootstrap” method. Another variation is to provide the intervention only to a subset among the effective groups (e.g., to the best five subgroups). In the next section, we present the results for all the selection rules.

Table 1. Incidence Rate Ratios for Subgroups: Project RED

Risk Categories	n-Usual Care	ReadmnRate-UsualCare	n-Treat	ReadmnRate-Treat	Incidence Rate Ratio
NoRisk	69.000	0.275	67.000	0.149	0.542
Homeless	8.000	0.375	8.000	0.125	0.333
Fr.Fly	25.000	0.560	23.000	0.478	0.854
Dep	25.000	0.520	22.000	0.500	0.962
DM-BP-Asth	84.000	0.190	95.000	0.189	0.995
DM-BP-Asth-Dep	26.000	0.308	46.000	0.391	1.272
DM-BP-Asth-Fr.Fly	51.000	0.686	36.000	0.694	1.012
DM-BP-Asth-Homeless	4.000	0.500	2.000	1.000	2.000
Dep-Fr.Fly	18.000	0.444	11.000	0.636	1.432
Dep-Homeless	2.000	0.000	3.000	0.000	
Fr.Fly-Homeless	3.000	0.333	3.000	0.000	0.000
DM-BP-Asth-Dep-Fr.Fly	25.000	1.160	29.000	0.724	0.624
DM-BP-Asth-Dep-Homeless	3.000	0.000	5.000	0.200	Inf
DM-BP-Asth-Fr.Fly-Homeless	11.000	0.727	6.000	0.500	0.688
Dep-Fr.Fly-Homeless	4.000	3.250	2.000	0.000	0.000
DM-BP-Asth-Dep-Fr.Fly-Homeless	5.000	3.400	6.000	0.667	0.196

Results

Project RED intervention can be implemented in several ways. As noted earlier, adopting new models of care such as RED will require realignment and, at least initially, additional hospital resources. As a result, hospitals will try to maximize the impact of the intervention by identifying specific patient populations that will benefit from the resources and effort expended. Limited resources may often lead to providing the intervention to selected patients, at least at the start. A systematic method to identify such subgroups using readily available data and clinical experience will help achieve this aim and increase the chance of adapting new models of care.

Using outcomes from Project RED, we have calculated the comparative effectiveness of the following seven methods of adopting the intervention: 1) Provide to all patients, repeating the Project RED intervention. 2) Identify risk categories using discharge diagnosis and other sociodemographic characteristics and provide only to selected risk categories. 3) Calculate risk scores for all admitted patients and provide only to selected risk *score* categories. 4) Conduct a pilot study, calculating effectiveness of the intervention for all subgroups using qualitative risk categories, and provide only to subgroups benefiting from the intervention. 5) Provide according to the same approach as in method 4, but use risk score categories. 6) Provide only to the five most effective subgroups identified in method 4. 7) Provide only to the five most effective subgroups identified in method 5.

The results are given in Table 2. When Project RED is given to all, the incidence rate ratio (IRR) is 0.707, reflecting an approximately 30% reduction in the 30-day readmission rate, as was observed in Project RED. When the intervention is given only to patients at risk for readmission, as determined by risk categories, the IRR increases to 0.723. The exclusion of the “no-risk” group from the intervention *increases* the IRR. This is because, although our risk stratification indicates that this group of patients is unlikely to be readmitted, some patients are readmitted (the observed readmission rate for this group is

0.275, which is less than readmission rate for the whole control group, 0.542.) Thus the "no-risk" group includes some patients who are readmitted, and the observed IRR for the "no-risk" group is 0.542, indicating the effectiveness of the intervention for this group. Similarly, providing the intervention only to 11 risk score categories also increases the IRR.

When the intervention is given only to effective subgroups based on the outcomes from the pilot study of 100 patients, the IRR decreases significantly to 0.581 for qualitative risk categories and to 0.558 for quantitative risk score categories. The reduction is really remarkable when the intervention is given only to the five most effective risk categories. The IRR is 0.153 (i.e., there is an 84.7% reduction in the readmission compared with the same five subgroups receiving usual care). The IRR for the five most effective risk score categories also decreases, though not as much as in the qualitative risk stratification method, to 0.241. As noted in the previous section, the smaller decrease for the risk score categories is due to combining subgroups with varying effectiveness.

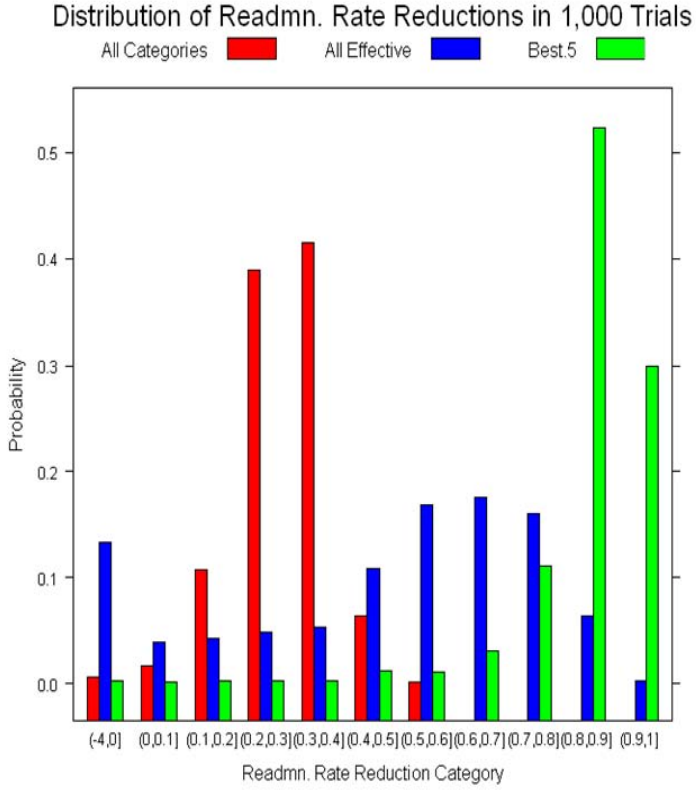
Table 2. Comparative Effectiveness of Prediction Rules

Subgroups	IRR	95 % CI	P (Effective)*
All (Repeat RED)	0.707	(0.61,0.80)	
15 Risk Categories	0.723	(0.61,0.84)	
11 Risk Score Categories	0.735	(0.63, 0.84)	
Effective Risk Categories	0.581	(0.18, 1.33)	0.872
Effective Risk Score Categories	0.558	(0.17, 1.41)	0.848
5 Best Effective Risk Categories	**0.153**	**(0.06, 0.35)**	**0.998**
5 Best Effective Risk Score Categories	0.241	(0.10,0.49)	0.993

*In 1,000 bootstrap samples, the fraction of samples with IRR < 1

Because we have an IRR for each bootstrap sample, we have a total of 1,000 IRRs for each method. The reduction in readmission rate associated with an IRR is given by 1 – IRR. We grouped these readmission rate reductions into 10 equally divided categories, from 0 to 1. The frequency distributions of these rate reductions for the following three methods are shown in the figure below: 1) Project RED (red), 2) effective risk categories (blue), and 3) five best effective risk categories (green).

The distribution of the rate reduction for Project RED is concentrated in the range of 20% to 40%, which is consistent with the observed average reduction of 30%. When the intervention is restricted to effective categories, the distribution shifts to the right, with concentration in the range of 50% to 80% reduction. When the intervention is to the best five effective categories, the distribution shifts further to the right, with concentration in the 80% to 100% range.



List of Publications and Products:

Family Physician Geographic Density is Associated with Lower Hospital Readmission Rates and Costs, by V.K. Chetty, Larry Culpepper, Robert Phillips, Jennifer Rankin, Imam Xierali, Sean Finnegan, and Brian Jack. Accepted for publication in *American Family Physician.*