Grant Final Report

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Monitoring Intensification of Treatment for Hyperglycemia and Hyperlipidemia in Patients with Diabetes

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Abstract

Purpose: To design and validate a process measure of quality of care of patients with diabetes that is a) tightly linked to patient outcomes and b) can be computed from the data available in electronic medical records.

Scope: This study evaluated treatment of over 20,000 of patients with diabetes treated in primary care practices affiliated with Brigham and Women's Hospital and Massachusetts General Hospital in Boston, MA.

Methods: We developed several natural language processing software applications to identify documentation of elements of care in narrative notes in electronic medical records that are not routinely available in structured electronic format. We subsequently utilized these applications to conduct a retrospective cohort study to evaluate the effect of different process measures of diabetes care on achievement of blood glucose, blood pressure and LDL cholesterol control.

Results: We have designed high-fidelity natural language processing tools for identification of treatment intensification in narrative text. In subsequent analysis we established that narrative and structured data sources provide complementary information about treatment intensification. We have confirmed that treatment intensification is strongly associated with faster achievement of both A1c and LDL control. High A1c and LDL levels were associated with higher probability of treatment intensification while government insurance and female gender were associated with lower rates of intensification. Both higher treatment intensification rate and higher A1c / LDL testing frequency were associated with higher probability of A1c control.

Key Words: electronic medical records, diabetes mellitus, quality of care, process measure, natural language processing

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Final Report

Purpose

This research project was funded to evaluate novel electronic process measures of treatment of patients with diabetes through the following four project aims:

Specific Aim 1. To test the hypothesis that an accurate measure of treatment intensification in the management of hyperglycemia and hyperlipidemia can be obtained through computational analysis of the text of physician notes in the EMR.

Specific Aim 2. To test the hypothesis that the measure of treatment intensification developed in Specific Aim 1 is related to glucose and lipid control.

Specific Aim 3. To identify specific patient and visit characteristics that affect the probability of anti-hyperglycemic and anti-hyperlipidemic treatment intensification at a given visit.

Specific Aim 4. To test the hypothesis that case mix-adjusted measure of intensification of treatment of hyperglycemia and hyperlipidemia is more strongly associated with clinical outcomes than currently used process measures of diabetes care.

Scope

Diabetes quality-of-care measurement is increasingly being used to evaluate quality improvement programs and to compare physicians and health plans. It is therefore important to know which measures are best associated with clinical outcomes. The most widely used process measures of diabetes quality-of-care, A1C and LDL screening rates, have multiple limitations. In this project we therefore aimed to develop and validate 1) a new diabetes quality-of-care process measure and 2) the technology for monitoring that measure using computational analysis of the free text of physician notes in the electronic medical record (EMR).

We planned to accomplish these tasks by expanding previously developed techniques developed by our group. In prior work we successfully designed and implemented an informatics application that allowed us to analyze the text of physician notes in the EMR to identify treatment intensification in management of hypertension. The measure derived from that work, frequency of anti-hypertensive treatment intensification, was strongly associated with blood pressure control. The objective of this project was to extend this innovative approach to develop and validate a technique that could be used for ongoing measurement of treatment intensification in care of hyperglycemia and hyperlipidemia.

There is a worldwide epidemic of diabetes – a costly disease that is a leading cause of morbidity and mortality in the U.S. Management of early disease in diabetes is an Institute of

Medicine priority area and there is strong evidence to support the benefit of glucose and lipid control in reducing diabetes complications. Despite this evidence, recommended glucose and cholesterol levels are not achieved in the majority of patients. In order to improve quality of care of diabetic patients, individual providers' and health care plans' adherence to process measures of diabetes care are increasingly monitored. However, the evidence that better adherence to the currently used process measures is associated with improvement in diabetes outcomes is limited. It is therefore important to develop a set of process measures of diabetes care that are strongly associated with outcomes.

An increasingly recognized contributor to suboptimal achievement of blood pressure, glucose and cholesterol goals is that treatment for these conditions is rarely intensified during physician visits. Low frequency of treatment intensification has been linked to increased prevalence of poor blood pressure and glucose control. Furthermore, interventions aimed at increasing the frequency of treatment intensification have been demonstrated to lower A1C levels. Therefore a validated metric that evaluates treatment intensification in management of hyperglycemia and hyperlipidemia potentially could provide a meaningful process measure that consumers could consider when choosing their clinicians, and clinicians to improve their outcomes.
The gold standard for identifying treatment intensification currently is resource-intensive manual record review. This hinders widespread measurement of treatment intensification. Growing prevalence of electronic medical record systems that include computerized text of physician notes provides an opportunity for a novel approach to monitoring treatment intensification. In this project we aimed to expand the work we previously carried out in hypertension to develop and validate a technique that can be used for ongoing measurement of treatment intensification in care of hyperglycemia and hyperlipidemia in diabetic patients.

Methods

Specific Aim 1

To test the hypothesis that an accurate measure of treatment intensification in the management of hyperglycemia and hyperlipidemia can be obtained through computational analysis of the text of physician notes in the EMR.

We developed natural language processing software applications to identify intensification of anti-hyperglycemic and anti-hyperlipidemic medications in the text of provider notes in the electronic medical record. This is particularly important for anti-hyperglycemic medications because insulin dosing regiments due to their complexity are frequently not recorded in prescriptions but only in narrative provider notes. The software design is represented schematically in Figure 1. The software was developed using an iterative process as illustrated in Figure 2. Sensitivity, specificity and positive predictive value for the software were ascertained by comparison to a set of manually reviewed narrative provider notes from the electronic medical record at Partners HealthCare.

We also conducted an analysis to determine whether narrative notes or structured medication records in electronic medical records should serve as the source for medication intensification information. To accomplish this we compared anti-hypertensive treatment intensification events

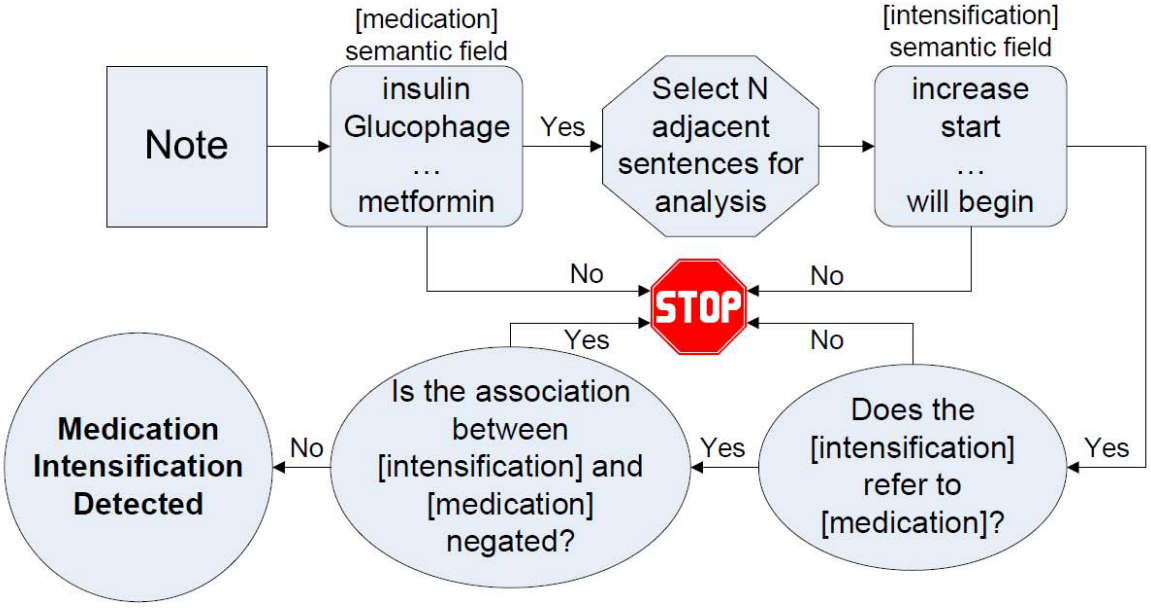
ascertained from structured medication records and narrative provider notes in Partners HealthCare EMR. As there is no gold standard data source for medication information, we clinically validated medication intensification information in both structured and narrative data sources by assessing the relationship between anti-hypertensive medication intensification and the patients' blood pressure using multivariable linear regression models that also adjusted for the patients' age, gender, race, and health insurance status, The models used the GLIMMIX procedure to adjust for clustering within individual physicians and repeated effects within patients.

Specific Aim 2

To test the hypothesis that the measure of treatment intensification developed in Specific Aim 1 is related to glucose and lipid control.

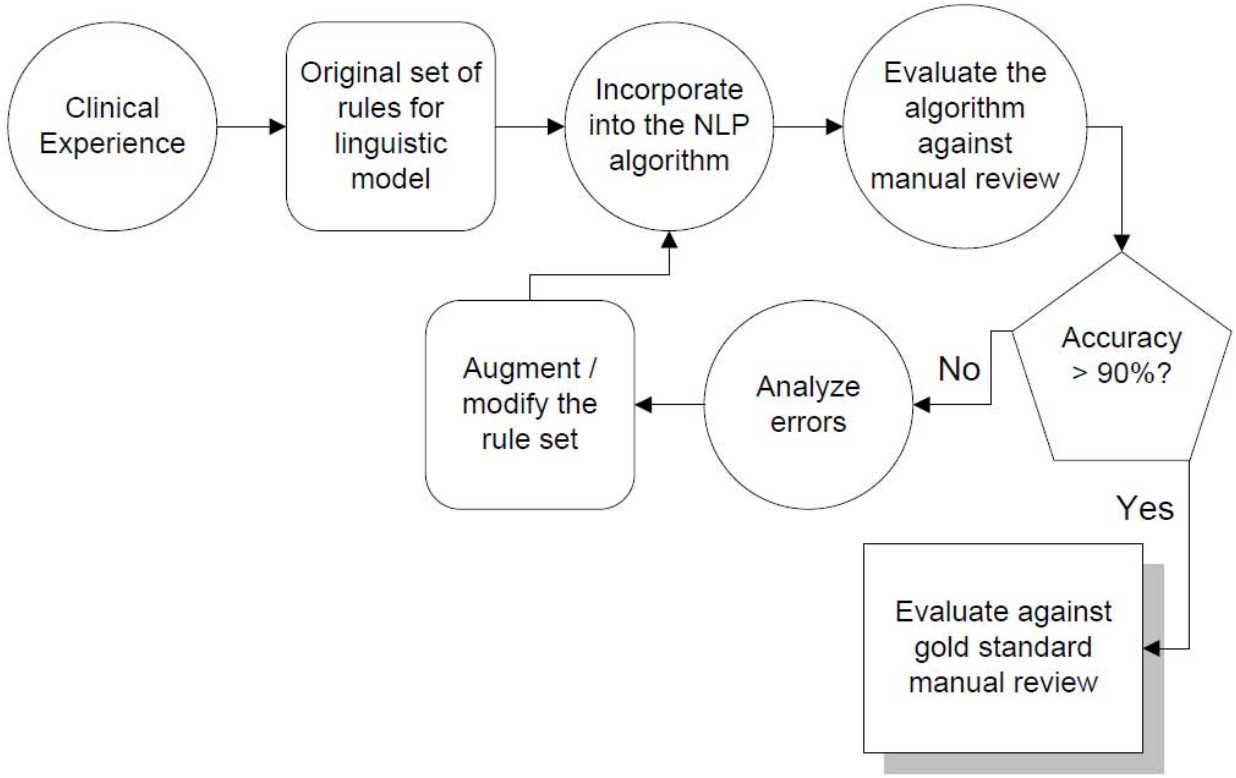
In order to determine whether the measure of treatment intensification obtained from a combination of narrative electronic notes and structured medication records in the EMR is related to glucose control, we conducted a retrospective cohort analysis of 14,293 hyperglycemic patients with diabetes. A unique hyperglycemic period, starting on the day of the first A1c measurement ≥ 7.0% and ending on the day of the first A1c measurement < 7.0% (or on the day of the last A1c study measurement if A1c never reached the target) served as the *unit of analysis*. Time from the first A1c ≥ 7.0% to the end of the hyperglycemic period served as the *primary outcome variable*. Monthly rate of anti-hyperglycemic treatment intensification served as the *predictor variable*. *Confounder variables* included patient age, gender, race, primary language, health insurance status, median income by zip code, frequency of encounters with their primary care physician and the highest A1c measured during the hyperglycemic period. We utilized marginal Cox proportional hazards models to account for clustering within providers and repeated measurements within patients.

Figure 1. Design of natural language processing software for identification of treatment intensification



In order to determine whether the measure of treatment intensification obtained from a combination of narrative electronic notes and structured medication records in the EMR is related to LDL cholesterol control, we conducted a retrospective cohort analysis of 15,739 hypercholesterolemic patients with diabetes. A unique hypercholesterolemic period, starting on the day of the first LDL cholesterol measurement ≥ 100 mg/dL and ending on the day of the first LDL measurement < 100 mg/dL (or on the day of the last LDL study measurement if LDL never reached the target) served as the *unit of analysis*. Time from the first LDL ≥ 100 mg/dL to the end of the hypercholesterolemic period served as the *primary outcome variable*. Monthly rate of anti-hypercholesterolemic treatment intensification served as the *predictor variable*. *Confounder variables* included patient age, gender, race, primary language, health insurance status, median income by zip code, frequency of encounters with their primary care physician and the highest LDL cholesterol measured during the hypercholesterolemic period. We utilized marginal Cox proportional hazards models to account for clustering within providers and repeated measurements within patients.

Figure 2. Iterative development process for natural language processing software



Specific Aim 3

To identify specific patient and visit characteristics that affect the probability of anti-hyperglycemic and anti-hyperlipidemic treatment intensification at a given visit.

In order to determine patient and visit characteristics that affect the probability of anti-hyperglycemic treatment intensification at a given visit, we conducted a retrospective cohort analysis of 14,293 hyperglycemic patients with diabetes. A unique provider-patient encounter during a hyperglycemic period served as the *unit of analysis*. Documentation of anti-hyperglycemic treatment intensification on the date of the encounter served as the *primary outcome variable*. Patient age, gender, race, primary language, health insurance status, median income by zip code, most recent A1c level and provider age served as *predictor variables*. We utilized GLIMMIX procedure to account for clustering within providers and repeated measurements within patients.

In order to determine patient and visit characteristics that affect the probability of anti-hypercholesterolemic treatment intensification at a given visit, we conducted a retrospective cohort analysis of 15,739 hypercholesterolemic patients with diabetes. A unique provider-patient encounter during a hypercholesterolemic period served as the *unit of analysis*. Documentation of anti-hypercholesterolemic treatment intensification on the date of the encounter served as the *primary outcome variable*. Patient age, gender, race, primary language, health insurance status, median income by zip code, most recent LDL cholesterol level and provider age served as *predictor variables*. We utilized GLIMMIX procedure to account for clustering within providers and repeated measurements within patients.

Specific Aim 4

To test the hypothesis that case mix-adjusted measure of intensification of treatment of hyperglycemia and hyperlipidemia is more strongly associated with clinical outcomes than currently used process measures of diabetes care.

In order to determine the relative effects of treatment intensification and frequency of A1c measurement on glucose control, we conducted a retrospective cohort analysis of 14,293 hyperglycemic patients with diabetes. A unique patient served as the *unit of analysis*. Achievement of A1c $\leq$ 7.0% at 2 years from the first elevated A1c level served as the binary *primary outcome variable*. Annual rate of anti-hyperglycemic treatment intensification and annual rate of A1c testing served as the *predictor variables*. *Confounder variables* included patient age, gender, race, primary language, health insurance status, median income by zip code, frequency of encounters with their primary care physician and the highest A1c measured during the hyperglycemic period. We utilized marginal Cox proportional hazards models to account for clustering within providers and repeated measurements within patients.

In order to determine whether the relative effects of treatment intensification and frequency of LDL measurement on LDL cholesterol control, we conducted a retrospective cohort analysis of 15,739 hypercholesterolemic patients with diabetes. A unique patient served as the *unit of analysis*. Achievement of LDL < 100 mg/dL at 2 years from the first elevated LDL cholesterol level served as the binary *primary outcome variable*. Annual rate of anti-hypercholesterolemic treatment intensification and annual rate of LDL cholesterol measurement served as the *predictor*

variables. *Confounder variables* included patient age, gender, race, primary language, health insurance status, median income by zip code, frequency of encounters with their primary care physician and the highest LDL cholesterol measured during the hypercholesterolemic period. We utilized marginal Cox proportional hazards models to account for clustering within providers and repeated measurements within patients.

Results

Specific Aim 1

To test the hypothesis that an accurate measure of treatment intensification in the management of hyperglycemia and hyperlipidemia can be obtained through computational analysis of the text of physician notes in the EMR.

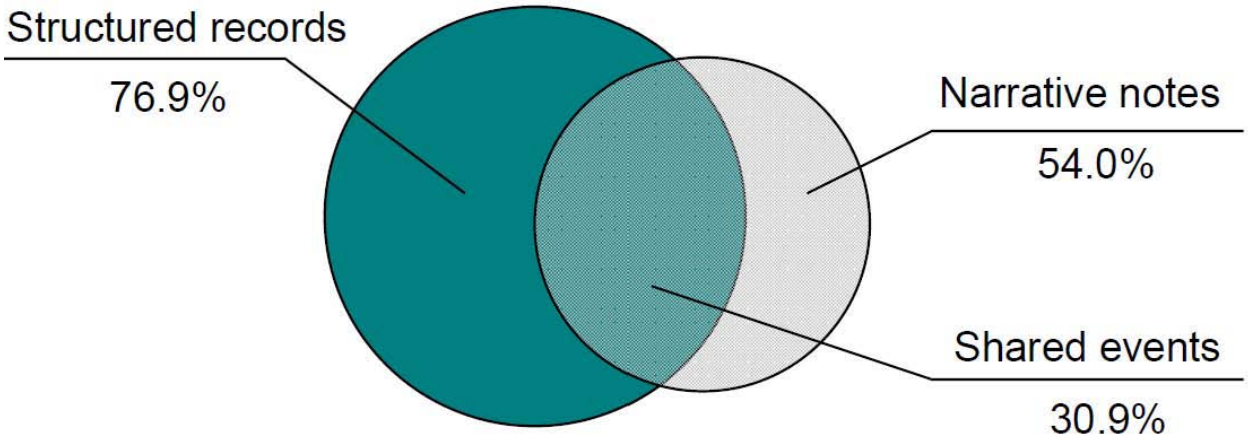
The software achieved high accuracy of extraction of medication intensification information from narrative text (Table 1).

We found that while narrative and structured records represented complementary data sources: approximately 1/3 of all intensification records were shared between the two sources, while the rest were unique to either one of them.

Table 1. Document-level accuracy of identification of anti-hyperglycemic and anti-hyperlipidemic medication intensification

Metric	Sensitivity	Specificity	Positive Predictive Value (Precision)
Anti-hyperglycemic medication intensification	97% (± 4.7%)	98% (± 1.8%)	90% (± 7.5%)
Anti-hyperlipidemic medication intensification	90% (± 13.1%)	99% (± 1.1%)	90% (± 12.8%)

Figure 3. Narrative and structured records as data sources for treatment intensification



Specific Aim 2

To test the hypothesis that the measure of treatment intensification developed in Specific Aim 1 is related to glucose and lipid control.

In univariate analysis, median time to A1c normalization (Figure 4a) gradually decreased from 1,708 days for patients whose anti-hyperglycemic treatment was intensified less than once every 12 months to 147 days for patients whose anti-hypertensive treatment was intensified more than once every 3 months ($p < 0.0001$). Similarly, median time to LDL cholesterol normalization (Figure 4b) decreased from 1,408 days for patients whose anti-hyperlipidemic treatment was intensified less than once a year to 89 days for patients whose anti-hyperlipidemic treatment was intensified more than once every 3 months ($p < 0.0001$).

Figure 4. Rate of treatment intensification and time to treatment target

Figure 4a. Kaplan-Meier curves for time to A1c target during a hyperglycemic period were plotted for different average rates of anti-hyperglycemic treatment intensification

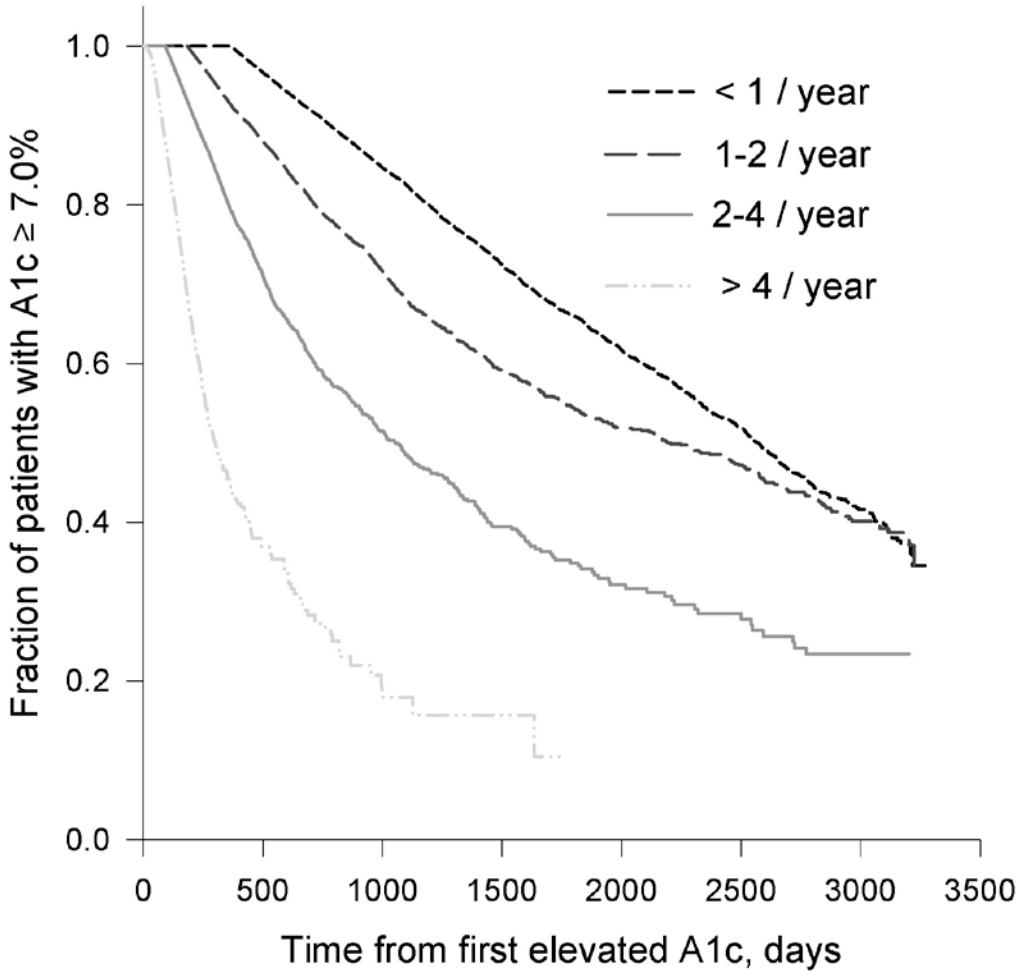
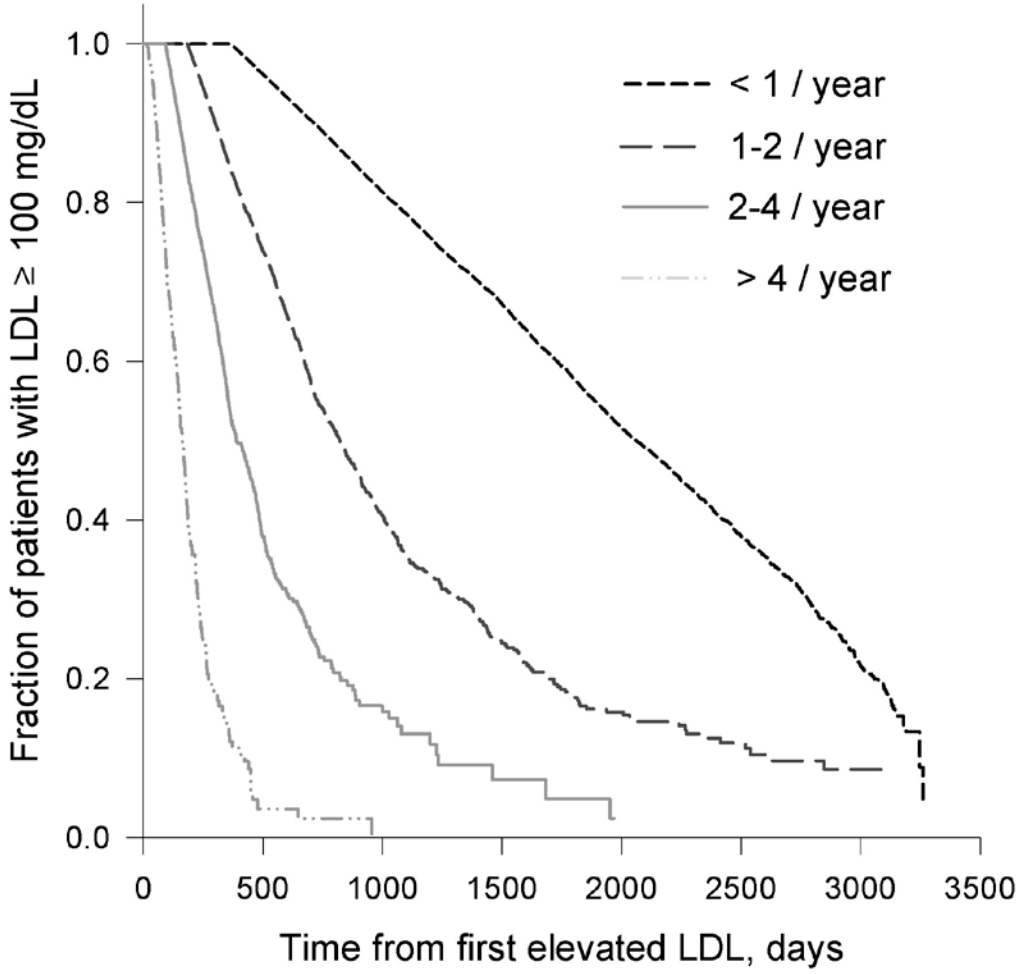


Figure 4b. Kaplan-Meier curves for time to LDL target during a hypercholesterolemic period were plotted for different average rates of anti-hypercholesterolemic treatment intensification



In a multivariable analysis that adjusted for patient age, gender, race, health insurance, median income by zip code, treatment with insulin, initial A1c and frequency of encounters with the primary care physician, an increase in one anti-hyperglycemic treatment intensification per month was associated with a hazard ratio of 44.9 (95% CI 36.3 to 55.6; $p < 0.0001$) for reaching A1c target. Similarly, multivariable analysis adjusted for patient age, gender, race, health insurance, median income by zip code, initial LDL cholesterol level and frequency of encounters with the primary care physician showed that an increase in one anti-hypercholesterolemic treatment intensification per month was associated with a hazard ratio of 50.2 (95% CI 23.1 to 109.4; $p < 0.0001$) for reaching LDL target.

Specific Aim 3

To identify specific patient and visit characteristics that affect the probability of anti-hyperglycemic and anti-hyperlipidemic treatment intensification at a given visit.

In multivariable analysis of the factors associated with anti-hyperglycemic treatment intensification for patients with A1c $\geq$ 7.0%, we found that treatment with insulin and higher A1c level were strongly associated with increased probability of intensification while government insurance (Medicare or Medicaid) and female gender were associated with lower probability of intensification (Table 2). After correction for multiple testing, race and median income by zip code were not significantly associated with anti-hyperglycemic treatment intensification.

Table 2. Patient and encounter characteristics and probability of anti-hyperglycemic treatment intensification

Variable	Odds of Treatment Intensification	p-value
InsulinRx	1.530	< 0.0001
A1c[1]	1.182	< 0.0001
Non-white	1.024	0.226
Income[2]	1.009	0.0575
Age[3]	0.978	0.0041
Medicaid[4]	0.875	< 0.0001
Medicare[4]	0.800	< 0.0001
Female[5]	0.867	< 0.0001
English[6]	0.861	< 0.0001

[1]For each additional 1.0%
[2]For each additional $10,000 annually
[3]For each additional 10 years
[4]Compared to private insurance
[5]Compared to male
[6]Listed as the primary language

Table 3. Patient and encounter characteristics and probability of anti-hyperlipidemic treatment intensification

Variable	Odds of Treatment Intensification	p-value
LDL[1]	1.097	< 0.0001
Non-white	1.113	< 0.0001
Income[2]	1.011	0.0067
Age[3]	1.088	< 0.0001
Medicaid[4]	0.992	0.0021
Medicare[4]	0.776	< 0.0001
Female[5]	0.75	< 0.0001
English[6]	0.933	0.0019

[1]For each additional 1.0%
[2]For each additional $10,000 annually
[3]For each additional 10 years
[4]Compared to private insurance
[5]Compared to male
[6]Listed as the primary language

In multivariable analysis of the factors associated with anti-hyperlipidemic treatment intensification for patients with LDL cholesterol ≥ 100 mg/dL, we found that higher LDL, non-white race, older age and higher income were strongly associated with increased probability of intensification while having a government insurance (Medicare or Medicaid), speaking English as the primary language and female gender were associated with lower probability of intensification (Table 3).

Specific Aim 4

To test the hypothesis that case mix-adjusted measure of intensification of treatment of hyperglycemia and hyperlipidemia is more strongly associated with clinical outcomes than currently used process measures of diabetes care.

In order to determine which process measure was more strongly associated with shorter time to A1c target, we constructed a logistic regression model to identify factors associated with achievement of A1c < 7.0% two years from the first elevated A1c measurement during the study period. In this model, which adjusted for patient demographics, highest A1c and frequency of provider-patient encounters, each additional monthly anti-hyperglycemic treatment intensification increased the odds of achieving A1c target by 63% ($p = 0.0083$) and decreasing the interval between A1c measurement by one month increased the odds by 42% ($p < 0.0001$).

In order to determine which process measure was more strongly associated with shorter time to LDL cholesterol target, we constructed a logistic regression model to identify factors associated with achievement of LDL cholesterol < 100 mg/dL two years from the first elevated LDL measurement during the study period. In this model, which adjusted for patient demographics, highest LDL level and frequency of provider-patient encounters, each additional monthly anti-hyperlipidemic treatment intensification increased the odds of achieving LDL cholesterol target 3.3-fold ($p = 0.0008$) and decreasing the interval between LDL measurements by one month increased the odds by 45%.

Based on these results, we conclude that both treatment intensification and measurement frequency are associated with higher rates of A1c and LDL target achievement.

List of Publications and Products

1. Turchin A, Wheeler HI, Labreche M, Chu JT, Pendergrass ML, Einbinder JS. (2008) Identification of Documented Medication Non-Adherence in Physician Notes. *Proc AMIA Symp* 2008; 732-6.

2. Turchin A, Shubina M, Breydo E, Pendergrass ML, Einbinder JS. (2009) Comparison of Information Content of Structured and Narrative Text Data Sources on the Example of Medication Intensification. *JAMIA*; 16:362-370.

3. Turchin A, Goldberg SI, Shubina M, Einbinder JS, Conlin PR. (2010) Encounter Frequency and Blood Pressure in Hypertensive Patients with Diabetes Mellitus. *Hypertension*; 56:68-74.

4. Kramer MH, Breydo E, Shubina M, Babcock K, Einbinder JS, Turchin A. (2010) Prevalence and factors affecting home blood pressure documentation in routine clinical care: a retrospective study. *BMC Health Services Research*; 10:139.