Diffusion of Information in Diabetes Care

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Project Title: Lower Extremity complications, Mortality, Healthcare Cost in Overweight Diabetes, PI: Elly Budiman-Mak, MD, MS, MPH
Objective

1. Do physicians vary in prescribing behavior?
2. What factors lead to the variation in this behavior?

HOW? Measure prescribing behavior in response to an FDA boxed warning for rosiglitazone, a glucose lowering drug, in the Department of Veterans Affairs (VA)

More generally:
• How do organizations and individuals learn?
• What explains the differences in their productivity?
FDA warning on rosiglitazone: timeline

- **May-21-07**
  - Nissen & Wolski NEJM pub
- **May-21-07**
  - FDA safety alert
- **Aug-14-07**
  - FDA adds black box warning
- **Oct-05-07**
  - VA removal from formulary

**Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes**

Steven E. Nissen, M.D., and Kathy Wolski, M.P.H.

**U.S. Food and Drug Administration**

FOR IMMEDIATE RELEASE
P07-88
May 21, 2007

**FDA Issues Safety Alert on Avandia**

**FDA Adds MI Warning to Rosiglitazone (Avandia) Black Box**

By Peggy Peck, Executive Editor, MedPage Today

**Rosiglitazone (Avandia) Deleted from VA Formulary for Diabetes**

By Peggy Peck, Executive Editor, MedPage Today
Published: October 30, 2007
About Diabetes

• A highly prevalent chronic disease: affects 25.8mil Americans
  ➢ Health Burden: 7th leading cause of death and serious side effects
  ➢ Financial Burden: $174B to U.S. economy (1/5 healthcare $$)

• Typically interventions focused on lowering glucose level
  ➢ Commonly used Test: glycated hemoglobin or HbA1c or A1c
  ➢ Diabetic if untreated A1c ≥ 6.5% (for older patients, it is 7%)

• Oral medications & Insulin
  ➢ Sulfonylureas (SUL), Metformin (MET) - first line agents
  ➢ Thiazolidinediones (2nd line): Rosiglitazone (ROSI), Pioglitazone (PIO)
    • Available since 1999, ROSI in VA formulary since 2003, PIO never in formulary
Literature

Geographical variation

- Dartmouth Atlas of Health Care Documented glaring variations in the use of medical resources
- Shah et al., 2010 (NEJM) state-level variation in ROSI use (CV=11%)

Learning

- L.Argote (2013): Organizational Learning (Springer)
- Nair et al., 2010 (J. Mktg Res) Effect of social network on physician learning
- Crawford & Shum, 2005 (E’metrica); Chintagunta et al., 2012 (J. Mktg Res) Bayesian Learning model for physician learning
- Syverson, 2011 (JEL) why businesses differ in their measured productivity levels?
- Clark et al., 2012 (Org Sci.) Learning from Customers: Individual and Organizational Effects
Hypothesis

H1 (organization learning)

• **H1a**: Facilities affiliated with a teaching hospital learn quicker
  ➢ Role of opinion leaders in information diffusion
• **H1b**: Facilities located in urban areas learn quicker

H2 (past history of events)

• **H2a**: A patient who has suffered more CV events in the past is less likely to receive rosiglitazone
• **H2b**: A patient belonging to a facility that has seen more patient-CV events is less likely to receive rosiglitazone
Data Source

Veterans Health Administration (VHA)

- Largest U.S. integrated healthcare delivery system
  - 8.57 mil enrollees, 152 hospitals, 817 outpatient clinics, 300 vet centers
- Held up as a model system for delivering diabetes care
  - High Prevalence: 1 in 4 veterans estimated to have diabetes
- Holistic Database: Access to patient’s full medical history
  - Demographics, Medications, Lab Data & Main event outcomes
- Access to organizational level characteristics at the facility level
  - 21 regions (VISNs), 128 parent stations, 719 facilities
- Physicians are salaried (mitigates agency issues)
- Coverage is excellent for veterans

**Cohort:** 550,959 patients w/diabetes, **Period:** 2003-08 (quarters), **Observations** ~ 9.8 mil.
Veterans Integrated Service Network (VISN)

- VISN regional structure established in 1995
- Autonomy in terms of conducting daily operations

http://www2.va.gov/directory/guide/map.asp?dnum=1
Variables

Outcome variable
- Indicator for whether patient was using rosiglitazone

Covariates
- Patient demographics at baseline
  - age, gender, race, marital status, and enrollment priority
  - Charlson comorbidity index at baseline, patient’s duration of diabetes
- Patient’s use of other glucose-lowering medications (binary):
  - Insulin; Oral medications: metformin, sulfonylurea, pioglitazone
- Lab results
  - \( \text{HbA}_{1c} \), triglycerides, cholesterol (HDL, LDL, total), blood pressure, BMI
- Indicator of whether patients experienced clinical complications:
  - cardiovascular (e.g. AMI), microvascular (e.g. amputation), hypoglycemia
  - Also includes the past history of events at the patient and facility-level
- Facility characteristics
  - VISN, # operating beds, affiliation with a teaching hospital, urban location, etc.
## Summary Stats (Baseline)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Male (%)</th>
<th>Married</th>
<th>Non-Hispanic White (%)</th>
<th>Non-Hispanic Black (%)</th>
<th>Age, yrs., mean±SD</th>
<th>Diabetes duration &lt;3 yrs (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>98.1</td>
<td>64.9</td>
<td>71.2</td>
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<td>66.9±10.5</td>
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</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>BMI, kg/m², mean±SD</th>
<th>HbA1C, %, mean±SD</th>
<th>LDL-C, mg/dL, mean±SD</th>
<th>SBP, mm Hg, mean±SD</th>
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<tr>
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<td>30.9±5.9</td>
<td>7.3±1.4</td>
<td>100.4±31.9</td>
<td>137.3±18.1</td>
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</table>

<table>
<thead>
<tr>
<th>Medication use</th>
<th>Sulfonylureas (%)</th>
<th>Metformin (%)</th>
<th>Rosiglitazone (%)</th>
<th>Pioglitazone (%)</th>
<th>Insulin (%)</th>
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<tr>
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<td>47.9</td>
<td>38.9</td>
<td>7.3</td>
<td>2.7</td>
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</table>

<table>
<thead>
<tr>
<th>Facility characteristics</th>
<th>Urban Location (%)</th>
<th>Teaching-Affiliated (%)</th>
<th>No. of outpatient beds ≥300 (%)</th>
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</thead>
<tbody>
<tr>
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<td>87.6</td>
<td>70.8</td>
<td>29.5</td>
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Results: Temporal variation (aggregate)

- **ROSI in VANF (Nov 03)**
- **FDA warnings (May 07)**
- **ROSI removed from VANF (Oct 07)**

<table>
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<tr>
<th>Time Period</th>
<th>Fraction of patients</th>
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<td>0%</td>
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<td>4%</td>
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<td>8%</td>
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<td>10%</td>
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<td>12%</td>
</tr>
<tr>
<td></td>
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</tr>
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<td></td>
<td>16%</td>
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</table>

- **Rosiglitazone**

**Time Period (Year, Quarter)**

**Fraction of patients**
Results: Cross-sectional variation

[Graph showing cross-sectional variation with Fraction of patients on the y-axis and Time Period (Year, Quarter) on the x-axis. The graph includes lines for different providers (1-23) with variations in the use of information. The Variation Factor (max use / min use) and Range (max use - min use) are also indicated.]
Statistical Model: Logistic Regression

\[ ROSI_{it} = \alpha_{11} + \beta_{11} VISN_i + \beta_{21} DEMO_i + \beta_{31} LAB_{it} \\
+ \beta_{41} MED_{it} + \beta_{51} MAIN_{it} + \beta_{61} FACIL_{it} + YQ_t + \epsilon_{it} \]

Outcome variable: \( ROSI_{it} \) (for patient \( i \) at time \( t \))

Covariates:

- Patient demographics at baseline: \( DEMO_t \)
- Patient’s use of other glucose-lowering medications: \( MEDI_{it} \)
- Lab results: \( LAB_{it} \)
- Indicator of whether patients experienced clinical events: \( MAIN_{it} \)
  - Use both current period indicator and past history
- Facility characteristics (incl. VISN): \( FACIL_i \)
- Time fixed effects: \( YQ_t \)
### VARIABLES

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**Observations**: 7,626,779

**Time fixed effects**: Yes, Yes, Yes, Yes

**VISN fixed effects**: Yes, Yes, Yes, Yes

**Patient event history**: Yes, Yes, Yes, Yes

**Facility main event history**: Yes, Yes, Yes, Yes

**Pseudo R2**: 0.0954, 0.106, 0.107, 0.107

*** p<0.001, ** p<0.01, * p<0.05; Estimates (Std Errors) are from logistics regression; All 20 time periods
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<td>Observations</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Pseudo R2</td>
<td>0.107</td>
<td>0.0923</td>
<td>0.136</td>
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</table>

*** p<0.001, ** p<0.01, * p<0.05; Estimates (Std Errors) are from logistics regression
Effect of Region (VISN)*

Pre-Warning Periods (2003Q4-2007Q1)

Post-Warning Periods (2007Q2-2008Q3)

Likelihood of ROSI Rx is HIGHER if

**Facility:**
- has a dedicated diabetes unit
- is a parent station
- is a VA medical center
- has low number of deaths

**Patient:**
- is male
- has duration of diabetes $\geq 2$ years
- has high glucose levels
- is taking other diabetes medications
- is not a senior (age $< 65$ years)
Conclusions

• **H1: false**
  - Teaching affiliation and urban location of the facility do not lead to a quicker reduction in rosiglitazone prescription
  - Local practice patterns dictate VA prescription patterns

• **H2: True**
  - AMI events at the patient level as well as the facility level reduce the likelihood of rosiglitazone prescription

• **Observations:**
  - Geographical variation in response to warnings (temporal & cross-sectional)
  - Likelihood of ROSI Rx correlated with facility & patient characteristics

**Future Direction:** Develop a Bayesian model of physician learning
Thank you
Diabetes Treatment in Action