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Estimating Patient-Centered and Community-Centered Treatment Effects: Examples from Medical Care and Public Health

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Estimating Patient-Centered and Community-Centered Treatment Effects:
Examples from Medical Care and Public Health

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Acknowledgement

The Public Health Services & Systems Research Program and the Public Health Practice-Based Research Networks Program are national programs of the Robert Wood Johnson Foundation.

Funding for this research was provided by the Robert Wood Johnson Foundation.
Questions of interest

- Do the effects of interventions vary across patient and community subgroups based on health needs, vulnerabilities and risks?

- How can we estimate treatment heterogeneity at the level of the individual patient or community?

- Can we achieve larger and more equitable impacts with this knowledge, e.g. through enhanced targeting and tailoring of interventions?
  - Precision medicine
  - Precision public health
Instrumental variables: a review

- IVs influence treatment choices/exposures but are independent of factors that determine outcomes.
- IVs serve as natural randomizers: they approximate RCTs with observational studies.
- IVs can be used to estimate causal treatment effects while accounting for both observed and hidden confounding and selection bias.
Analysis of Observational Studies in the Presence of Treatment Selection Bias
Effects of Invasive Cardiac Management on AMI Survival Using Propensity Score and Instrumental Variable Methods

Thérèse A. Stukel, PhD
Elliott S. Fishor, MD, MPH
David E. Wennberg, MD, MPH
David A. Alter, MD, PhD
Daniel J. Gottlieb, MS
Marian J. Vormolen, MHSec

Context: Comparisons of outcomes between patients treated and untreated in observational studies may be biased due to differences in patient prognosis between groups, often because of unobserved treatment selection biases.

Objective: To compare 4 analytic methods for removing the effects of selection bias in observational studies: multivariable model risk adjustment, propensity score risk adjustment, propensity-based matching, and instrumental variable analysis.

Design, Setting, and Patients: A national cohort of 122,124 patients who were older (some RALJL aged) and hospitalized with acute myocardial infarction.

Unobserved confounder: Treatment selection of lower-risk patients.

Instrumental Variable
Regional catheterization rate

Differential distance to hospitals with cath labs

Treatment Invasive cardiac treatment

Relative Rate = 0.84
95% CI: 0.79-0.90

Outcome Long-term AMI Mortality rate

Observed confounders:
Age, sex, race, socio-economic status, comorbidities, inpatient treatments

IVs: a classic example
Treatment effect heterogeneity: fundamental empirical questions

- Which programs, interventions, policies, strategies *(mechanisms)*…
- Work best *(outcomes)*…
- In which institutional & community settings *(contexts)*…
- For whom *(populations and subgroups)*?

Pawson and Tilley 1997
Treatment effect heterogeneity

- Biological, behavioral, or structural mechanisms

- Average treatment effect from an RCT may not match the causal treatment effect found in observational data

- Average treatment effect may have little clinical utility and policy significance

- IV estimates may be difficult to interpret in the presence of treatment effect heterogeneity
Variations in policy design, implementation, enforcement

Estimated Effects of Smoke-free Policies on AMI admissions

<table>
<thead>
<tr>
<th>Study ID</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helena Montana</td>
<td>0.60 (0.21, 0.99)</td>
<td>1.76</td>
</tr>
<tr>
<td>Pueblo Colorado</td>
<td>0.73 (0.63, 0.85)</td>
<td>10.13</td>
</tr>
<tr>
<td>Piedmont Italy</td>
<td>0.89 (0.81, 0.98)</td>
<td>12.14</td>
</tr>
<tr>
<td>Bowling Green Ohio</td>
<td>0.61 (0.55, 0.67)</td>
<td>14.24</td>
</tr>
<tr>
<td>New York State</td>
<td>0.80 (0.80, 0.80)</td>
<td>17.20</td>
</tr>
<tr>
<td>Ireland</td>
<td>0.89 (0.81, 0.97)</td>
<td>12.56</td>
</tr>
<tr>
<td>Saskatoon Canada</td>
<td>0.87 (0.84, 0.90)</td>
<td>16.35</td>
</tr>
<tr>
<td>Rome Italy</td>
<td>0.89 (0.85, 0.93)</td>
<td>15.61</td>
</tr>
<tr>
<td>Overall</td>
<td>0.81 (0.76, 0.86)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

Glantz 2008
Treatment effect heterogeneity: estimation problems

- Treatment effects may vary over unobserved confounders
- “Essential heterogeneity”
- IV estimates may vary with specific IVs used

**Solution:** *local* IV methods to estimate marginal treatment effects (Heckman 1999, 2006)
Person-centered treatment effect estimation

- Treatment effects vary across patients based on factors observed by decision-makers
- Treatment is “sorted” across patients based in part on differential potential benefit
  - No single treatment effect
  - Average treatment effects vary across patient subgroups based on chosen treatment levels

Heckman et al. 2006; Basu et al. 2007
Person-centered treatment effect estimation

- PCTE is a conditional treatment effect that conditions on observed risk factors AND averages over the conditional distribution of unobserved risk factors, conditional on treatment choices
- Identifies individual-level treatment effect heterogeneity better than other methods
- Superior at identifying/controlling for self-selection
- Requires IVs to isolate distribution of unobserved risk factors

Heckman et al. 2006; Basu et al. 2007
Person-centered treatment effect estimation

Revisiting the CATIE Trial Results

PeT Effects of Generic Group vs Branded Group of AADs

Basu et al. 2013
## Person-centered treatment effect estimation

Revisiting the CATIE Trial Results

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Average annual number of hospitalizations (95% CI)</th>
<th>% change from Status-quo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status-quo</td>
<td>1.83 (1.81 – 1.85)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>All patients started on branded group of AADs</td>
<td>1.73 (1.59 – 1.87)</td>
<td>-5.5</td>
<td>0.15</td>
</tr>
<tr>
<td>All patients started on generic group of AADs</td>
<td>2.07 (1.91 – 2.23)</td>
<td>13.1</td>
<td>0.001</td>
</tr>
<tr>
<td>All patients started on optimal predicted therapy</td>
<td>1.32 (1.26 – 1.40)</td>
<td>-27.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Notes: P-values reflect comparisons of average annual number of hospitalizations under various scenarios to status quo.
Does treatment heterogeneity extend to public health services at the community-level?
Research questions of interest

- Which organizations contribute to the implementation of public health activities in local communities?
- How do these contributions change over time? Recession, recovery, ACA implementation?
- What are the health and economic effects of these activities?
  - Heterogeneity by population and delivery system characteristics?
Data: public health production

National Longitudinal Survey of Public Health Systems

- Cohort of 360 communities with at least 100,000 residents

Local public health officials report:
- **Scope**: availability of 20 recommended public health activities
- **Network**: types of organizations contributing to each activity
- **Effort**: contributed by designated local public health agency
- **Quality**: perceived effectiveness of each activity

** Stratified sample of 500 communities<100,000 added in 2014 wave
Cluster and network analysis to identify “system capital”

Cluster analysis is used to classify communities into one of 7 categories of public health system capital based on:

- **Scope of activities** contributed by each type of organization
- **Density of connections** among organizations jointly producing public health activities
- **Degree centrality** of the local public health agency

Estimating network effects

Dependent variables:

- **Quantity**: Percent of recommended public health activities performed in the community
- **Quality**: Perceived effectiveness of activities
- **Resource use**: Local governmental expenditures for public health activities
- **Health outcomes**: premature mortality (<75), infant mortality, death rates for heart disease, diabetes, cancer, influenza

Independent variables:

- **Contribution scores**: percent of activities contributed by each type of organization
- **Network characteristics**: network density, organizational degree centrality, betweenness centrality
Estimating network effects

Estimation:

- Log-transformed Generalized Linear Latent and Mixed Models
- Account for repeated measures and clustering of public health jurisdictions within states
- Instrumental variables address endogeneity of network structures

\[ \ln(\text{Network}_{z,ijt}) = \sum \alpha_z \text{Governance}_{ijt} + \beta_1 \text{Agency}_{ijt} + \beta_2 \text{Community}_{ijt} + \mu_j + \phi_t + \epsilon_{ijt} \]

\[ \ln(\text{Quantity/Quality/Cost}_{ijt}) = \sum \alpha_z \ln(\hat{\text{Network}}_z)_{ijt} + \beta_1 \text{Agency}_{ijt} + \beta_2 \text{Community}_{ijt} + \mu_j + \phi_t + \epsilon_{ijt} \]

All models control for type of jurisdiction, population size and density, metropolitan area designation, income per capita, unemployment, racial composition, age distribution, educational attainment, and physician availability.
## Delivery of recommended public health activities, 1998-2014

<table>
<thead>
<tr>
<th>Public Health Activity</th>
<th>1998</th>
<th>2014</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Community health needs assessment</td>
<td>71.5%</td>
<td>86.0%</td>
<td>20.2%**</td>
</tr>
<tr>
<td>2 Behavioral risk factor surveillance</td>
<td>45.8%</td>
<td>70.2%</td>
<td>53.2%**</td>
</tr>
<tr>
<td>3 Adverse health events investigation</td>
<td>98.6%</td>
<td>100.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>4 Public health laboratory testing services</td>
<td>96.3%</td>
<td>96.5%</td>
<td>0.2%</td>
</tr>
<tr>
<td>5 Analysis of health status and health determinants</td>
<td>61.3%</td>
<td>72.8%</td>
<td>18.7%**</td>
</tr>
<tr>
<td>6 Analysis of preventive services utilization</td>
<td>28.4%</td>
<td>39.4%</td>
<td>38.8%**</td>
</tr>
<tr>
<td>7 Health information provision to elected officials</td>
<td>80.9%</td>
<td>84.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td>8 Health information provision to the public</td>
<td>75.4%</td>
<td>83.8%</td>
<td>11.1%*</td>
</tr>
<tr>
<td>9 Health information provision to the media</td>
<td>75.2%</td>
<td>87.5%</td>
<td>16.3%**</td>
</tr>
<tr>
<td>10 Prioritization of community health needs</td>
<td>66.1%</td>
<td>82.3%</td>
<td>24.6%**</td>
</tr>
<tr>
<td>11 Community participation in health improvement planning</td>
<td>41.5%</td>
<td>67.7%</td>
<td>63.0%**</td>
</tr>
<tr>
<td>12 Development of community health improvement plan</td>
<td>81.9%</td>
<td>86.2%</td>
<td>5.2%</td>
</tr>
<tr>
<td>13 Resource allocation to implement community health plan</td>
<td>26.2%</td>
<td>43.2%</td>
<td>64.9%**</td>
</tr>
<tr>
<td>14 Policy development to implement community health plan</td>
<td>48.6%</td>
<td>57.5%</td>
<td>18.4%*</td>
</tr>
<tr>
<td>15 Communication network of health-related organizations</td>
<td>78.8%</td>
<td>84.8%</td>
<td>7.6%</td>
</tr>
<tr>
<td>16 Strategies to enhance access to needed health services</td>
<td>75.6%</td>
<td>50.2%</td>
<td>-33.6%**</td>
</tr>
<tr>
<td>17 Implementation of legally mandated public health activities</td>
<td>91.4%</td>
<td>92.4%</td>
<td>1.0%</td>
</tr>
<tr>
<td>18 Evaluation of public health programs and services</td>
<td>34.7%</td>
<td>38.4%</td>
<td>10.8%**</td>
</tr>
<tr>
<td>19 Evaluation of local public health agency capacity/performance</td>
<td>56.3%</td>
<td>55.0%</td>
<td>-2.4%</td>
</tr>
<tr>
<td>20 Implementation of quality improvement processes</td>
<td>47.3%</td>
<td>49.6%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Composite availability of assessment activities (1-6)</td>
<td>66.7%</td>
<td>77.6%</td>
<td>16.4%**</td>
</tr>
<tr>
<td>Composite availability of policy development activities (7-15)</td>
<td>60.2%</td>
<td>72.5%</td>
<td>20.4%</td>
</tr>
<tr>
<td>Composite availability of assurance activities (16-20)</td>
<td>64.4%</td>
<td>52.8%</td>
<td>-18.0%*</td>
</tr>
<tr>
<td>Composite availability of all activities (1-20)</td>
<td>63.8%</td>
<td>67.6%</td>
<td>6.0%*</td>
</tr>
</tbody>
</table>
Variation in Delivery of Recommended Public Health Services

National Longitudinal Survey of Public Health Systems

Percent of activities performed

Percent of U.S. communities

National Longitudinal Survey of Public Health Systems, 2014
Variation and Change in Delivery
Delivery of recommended public health activities, 2006-14

National Longitudinal Survey of Public Health Systems, 2014
Node size = centrality
Line size = % activities jointly contributed (tie strength)
Prevalence of Public Health System Configurations, 1998-2014

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Scope</th>
<th>Centrality</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster 1</td>
<td>High</td>
<td>Mod</td>
<td>High</td>
</tr>
<tr>
<td>Cluster 2</td>
<td>High</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Cluster 3</td>
<td>High</td>
<td>High</td>
<td>Mod</td>
</tr>
<tr>
<td>Cluster 4</td>
<td>Mod</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Cluster 5</td>
<td>Mod</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Cluster 6</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Cluster 7</td>
<td>Low</td>
<td>Low</td>
<td>Mod</td>
</tr>
</tbody>
</table>

Legend:
- Comprehensive (High System Capital)
- Conventional
- Limited
Prior Research: Mortality reductions attributable to local public health spending, 1993-2008

Hierarchical regression estimates with instrumental variables to correct for selection and unmeasured confounding

Mays et al. 2011
Prior Research: Medical cost offsets attributable to local public health spending 1993-2008

Offset elasticity = −0.088

Mays et al. 2013
Value of an additional dollar in public health

A. Under-spending
B. Equipoise spending
C. Over-spending
Analytic Approach

- Use the technique of local instrumental variables (LIV) estimation to estimate community-specific effects of public health spending.

- Compare the health & economic impact of increases public health spending between:
  - Low-income vs. higher-income communities
  - Agencies that deliver broad vs. narrow scope of public health activities


Local IV Approach

- Estimate predicted spending (P) as a function of all measured covariates (X) and instruments (Z)
- Model outcome (O) as nonlinear function of P(X,Z) and X
- Estimate $\frac{\partial O}{\partial P}$ the effect of a change in predicted spending on the outcome
- Find the distribution of P(X,Z) for the subset of communities of interest
- Estimate the average treatment effect for each subset as the average weighted value of $\frac{\partial O}{\partial P}$ across the subset


Analytical approach: IV estimation

- Identify exogenous sources of variation in spending that are unrelated to outcomes
  - Governance structures: local boards of health
  - Decision-making authority: agency, board, local, state

- Controls for unmeasured factors that jointly influence spending and outcomes
### Determinants of Local Public Health Spending Levels: Local IVs

<table>
<thead>
<tr>
<th>Governance/Decision Authority</th>
<th>Coefficient</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Governed by local board of health</td>
<td>0.131**</td>
<td>(0.061, 0.201)</td>
</tr>
<tr>
<td>State hires local PH agency head†</td>
<td>-0.151*</td>
<td>(-0.318, 0.018)</td>
</tr>
<tr>
<td>Local board approves local PH budget</td>
<td>0.388***</td>
<td>(0.576, 0.200)</td>
</tr>
<tr>
<td>State approves local PH budget†</td>
<td>-0.308**</td>
<td>(-0.162, -0.454)</td>
</tr>
<tr>
<td>Local govt sets local PH fees</td>
<td>0.217**</td>
<td>(0.101, 0.334)</td>
</tr>
<tr>
<td>Local govt imposes local PH taxes</td>
<td>0.190**</td>
<td>(0.044, 0.337)</td>
</tr>
<tr>
<td>Local board can request local PH levy</td>
<td>0.120**</td>
<td>(0.246, 0.007)</td>
</tr>
</tbody>
</table>

**Elasticity**  

\[ F = 16.4 \quad p < 0.001 \]

log regression estimates controlling for community-level and state-level characteristics.  

*\( p < 0.10 \)  \quad **\( p < 0.05 \)  \quad ***\( p < 0.01 \)

†As compared to the local board of health having the authority.

Mays et al. HSR 2009
Community-specific estimates of public health spending on heart disease mortality

Impact of 10% Increase in Public Health Spending/Capita Based on Income Per Capita in Communities

Log IV regression estimates controlling for community-level and state-level characteristics

Mays et al. forthcoming 2013
Community-specific estimates of public health spending on heart disease mortality

Impact of 10% Increase in Public Health Spending/Capita Based on Delivery System Comprehensiveness

Log IV regression estimates controlling for community-level and state-level characteristics

Mays et al. forthcoming 2013
Comprehensive systems do more with less

![Bar chart showing expenditures per capita and percentage of recommended activities performed for different types of delivery systems.]

- **Expenditures per capita**
  - Comprehensive: Moderate
  - Conventional: High
  - Limited: Moderate
  - Very limited: Low

- **Recommended activities performed**
  - Comprehensive: High
  - Conventional: High
  - Limited: Medium
  - Very limited: Low
Conclusions

- Sizable health & economic gains are attributable to local public health expenditures
- Gains are 21-44% larger in low-income communities
- Gains are 17-38% larger for communities with comprehensive delivery systems
- No evidence of over-spending
Implications for policy & practice

Increase the value of public health investments through:

- **Enhanced targeting**: low-resource, high-need communities

- **Enhanced infrastructure**: broad scope of core public health activities
  - Accreditation standards
  - Minimum package of services
Can Patient-Centered Treatment Estimation Help to Evaluate Community-level Programs?
Estimating Program ROI
Arkansas Community Connector Program

- Use community health workers & public health infrastructure to identify people with unmet social support needs
- Connect people to home and community-based services & supports
- Link to hospitals and nursing homes for transition planning
- Use Medicaid and SIM financing, savings reinvestment
- Costing with electronic time logs

Felix, Mays et al. 2011
http://content.healthaffairs.org/content/30/7/1366.abstract
The Community Connector Program (CCP)

- Quasi-experimental research design
- Measured expenditures one year before participation and up to 3 years after participation
- Statistically-matched comparison group of Medicaid recipients not served by CCP
- Difference-in-difference estimates of impact, controlling for time-varying covariates

Source: RWJF University of Wisconsin County Health Rankings 2014
# Estimates of Program Impact

Regression-Adjusted, Difference-in-Difference Estimates

<table>
<thead>
<tr>
<th>Time Period*</th>
<th>Average Spending Change from Baseline</th>
<th>PET Spending Change for Multimorbidity Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>-6.0%**</td>
<td>-9.6%**</td>
</tr>
<tr>
<td>Year 2</td>
<td>-13.4%**</td>
<td>18.2%**</td>
</tr>
<tr>
<td>Year 3</td>
<td>-15.3%**</td>
<td>21.4%**</td>
</tr>
</tbody>
</table>

After adjusting for baseline and time-varying differences between groups

*Reference year is one year prior to CCP participation

**p<0.05
Estimated Program ROI

Three Year Aggregate Estimates

- Combined Medicaid spending reductions: $3.515 M
- Program implementation costs: $0.896 M
- Net savings: $2.629 M
- ROI: $2.92
- ROI for multi-morbidity: $5.17

Felix, Mays et al. 2011
http://content.healthaffairs.org/content/30/7/1366.abstract


Heckman JJ, Vytlacil EJ. Local instrumental variables and latent variable models for identifying and bounding treatment effects. Proc Nat Acad Sci 1999; 96(8): 4730-34


Funded by Robert Wood Johnson Foundation: $10.5M to UK from 2011-2015

Intramural research activities
- Public Health Value: Cost estimation, economic evaluation
- Delivery System Reform: ACA effects on public health delivery, population health measurement, aligning public health & health care delivery

Extramural research programs (funded separately ≈ $30M)
- Practice-based Research Networks (PBRNs) across U.S.
- Investigator-initiated research awards
- Predoctoral/Postdoctoral & career development awards
- Quick Strike rapid-cycle studies