CAN MACRODATA PREDICT RESPONSE TO THERAPY?

Larry Allen, MD, MHS
Associate Professor, Medicine
Associate Head, Clinical Affairs, Cardiology
Medical Director, Advanced Heart Failure
Denver, CO
Can Macrodata Predict Response to Therapy?

Larry A. Allen, MD, MHS
University of Colorado School of Medicine
Presenter Disclosure Information

• I will not discuss off label use or investigational use in my presentation.

• I have financial relationships to disclose:
  • Employee of: University of Colorado
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  • Stockholder in: None
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  • Honoraria from: None
“Every day, millions of people are taking medications that will not help them. The top ten highest-grossing drugs in the United States help between 1 in 25 and 1 in 4 of the people who take them. For some drugs, such as statins — routinely used to lower cholesterol — as few as 1 in 50 may benefit.”
HFrEF now enjoys an …

embarrassment of riches (or choice)

phrase of embarrassment

1. more options or resources than one knows what to do with.
   "picking a highlight from such an embarrassment of riches is hard"
## 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: *Answers to 10 pivotal questions about heart failure with reduced ejection fraction*

<table>
<thead>
<tr>
<th>Target</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin-angiotensin system</td>
<td>ACEi, ARBs, ARNI</td>
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<tr>
<td>Sympathetic nervous system</td>
<td>Beta blockers</td>
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<tr>
<td>Aldosterone</td>
<td>aldosterone antagonists</td>
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<tr>
<td>Vasoactive peptides</td>
<td>ARNI</td>
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<td>Heart rate (in sinus rhythm, on optimal beta blocker dose)</td>
<td>Ivabradine</td>
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<td>Balanced vasodilation and oxidative stress modulation in African Americans</td>
<td>HYD/ISDN</td>
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<tr>
<td>Arrhythmic sudden death</td>
<td>Implantable cardioverter-defibrillators</td>
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<td>Ventricular dyssynchrony due to conduction abnormalities</td>
<td>Cardiac resynchronization therapy</td>
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<tr>
<td>Congestion</td>
<td>Diuretics, chronic ambulatory pulmonary artery pressure monitoring in select patients</td>
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<tr>
<td>Reduced Aerobic capacity</td>
<td>Exercise training/cardiac rehab</td>
</tr>
</tbody>
</table>
HF is not the only problem

- 23,435 identified with HF
- Multimorbidity common – addition to HF:
  - 2%: no comorbidity
  - 76%: 3+ co-occurring conditions
  - 52%: 5+ co-occurring conditions
- HFpEF compared to HFrEF:
  - 53% v. 47%
  - mean 4.5 vs 4.4 comorbidities
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More than half of people 65 and older have 3+ chronic conditions

Patterns of Comorbidity in Older Adults with Heart Failure: The Cardiovascular Research Network PRESERVE Study

Jone S. Szczepaniak, PhD,1,2,3 Alan S. Go, MD,1,2,3 David J. Magid, MD,1,2,3 David H. Smith, PhD,1
David D. MacManus, MD,1,2,3 Larry Allen, MD,1 Jessica Ojovick, MS,1 Robert J. Goldberg, PhD,1,2
and Jerry H. Gattis, MD,1,2

Boyd, CM, Fortin M. Public Health Reviews, 2011.
Medications for multimorbidity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall Sample, N = 23,435</th>
<th>Preserved Ejection Fraction, n = 12,407</th>
<th>Reduced Ejection Fraction, n = 11,028</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic variables</strong></td>
<td></td>
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<tr>
<td>Age, mean ± SD</td>
<td>73.7 ± 12.4</td>
<td>75.6 ± 11.6</td>
<td>71.8 ± 12.8</td>
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<tr>
<td><strong>Cardiovascular diseases</strong></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>58.9</td>
<td></td>
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<tr>
<td>Anemia</td>
<td>55.8</td>
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<tr>
<td>Dyslipidemia</td>
<td>44.6</td>
<td></td>
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<tr>
<td>Visual impairment</td>
<td>43.2</td>
<td></td>
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<tr>
<td>Lung disease</td>
<td>30.9</td>
<td></td>
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<tr>
<td>Atrial fibrillation or flutter</td>
<td>25.3</td>
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<tr>
<td>Aortic valvular disease</td>
<td>22.9</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>22.8</td>
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<tr>
<td>Hearing impairment</td>
<td>21.7</td>
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<tr>
<td>Diabetes mellitus</td>
<td>19.2</td>
<td></td>
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<tr>
<td>Coronary heart disease (acute)</td>
<td>16.9</td>
<td></td>
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<tr>
<td>Myocardial infarction or unstable angina pectoris</td>
<td></td>
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<tr>
<td>Depression</td>
<td>17.5</td>
<td></td>
<td></td>
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<tr>
<td>Dementia</td>
<td>13.8</td>
<td></td>
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<tr>
<td>Peripheral arterial disease</td>
<td>9.8</td>
<td></td>
<td></td>
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<tr>
<td>Cancer</td>
<td>7.8</td>
<td></td>
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<tr>
<td>Thromboembolic disorder</td>
<td>6.9</td>
<td></td>
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<tr>
<td>Gastrointestinal hemorrhage</td>
<td>5.8</td>
<td></td>
<td></td>
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<tr>
<td>Ventricular fibrillation or tachycardia</td>
<td>3.1</td>
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</tbody>
</table>
Medication Overload

6.8 prescription meds
10.1 doses daily
(up 50% 1988-2008)

88% OTC
35% herbals
65% vitamins

Dismal Prescribing

- Patients with HFrEF are frequently on suboptimal medical therapies.

- Low uptake of newer therapies (aldosterone antagonists, ARNI)

Of 21,078 patients hospitalized with HFrEF during the study period, 495 (2.3%) were prescribed ARNIs at discharge.
Consistently <50% of medications are taken!
Can Macrodata Predict Response to Therapy?
#1: EHR data to predict response
Health Care Is Next Frontier for Big Data

By BEN ROONEY
January 19, 2012

Big Data—the ability to collect, process and interpret massive amounts of information—is one of today’s most important technological drivers. While companies see it as a way of detecting weak market signals, one of the biggest potential areas of application for society is health care.
“Big data has the potential to create significant value in health care by improving outcomes while lowering costs.”

“By discovering associations and understanding patterns and trends within the data, big data analytics has the potential to improve care, save lives and lower costs”
“Big data has arrived, but big insights have not.”

“Who cares about causation or sampling bias, though, when there is money to be made?”
“Through predictive analytics, we can reduce total population medical expense and 30 day readmissions by 10-25%. Our performance improvement solution can identify cost savings opportunity of 10% to 40% in targeted areas while improving quality.”
The statistics for the retrospective and prospective predictions were 0.710 and 0.704 respectively.

The summary above shows that this 59 year old female had 14 ED visits in the last 12 month period.

The chart shows the timing of each encounter along with the risk scores increasing over time.
Law of Diminishing Returns (=multicollinearity)
“Big data solutions are not yet connected to care”

“Without consideration of social uses and clinical practices, big data will fail to cure the woes of the U.S. healthcare system”

Gina Neff
Department of Communication
University of Washington, Seattle, Washington
Big Data Analytics in Healthcare

Volume

Variety

Velocity

Veracity

Clinical insights

Implementation

Impact

Better care,
Better health,
Better outcomes,
Lower costs
#2: Variable benefit against fixed risks
Value = Benefit - Risk

**VARIABLE:**
Dependent on absolute event rates (and RRR)

**RELATIVELY FIXED:**
Side effects, adverse events, and costs of therapy often occur to all exposed
The substantial benefits of intensive systolic BP lowering observed in SPRINT came at a cost of an increase in serious adverse events such as acute kidney injury (or acute renal failure), syncope, and hypotension and electrolyte disturbances (intensive vs. standard group: 4.7% vs. 2.5%).

SPRINGT example in Hypertension Rx

• **Methods** Stratify by quartiles of baseline 10-year CVD risk.
• **Results** Within each quartile, there was a lower rate of primary outcome events in the intensive treatment group, with no differences in all-cause SAEs. From the first to fourth quartiles, the number needed to treat to prevent primary outcomes decreased from 91 to 38. The number needed to harm for all-cause SAEs increased from 62 to 250.
• **Conclusions** In SPRINGT, those with lower baseline CVD risk had more harm than benefit from intensive treatment, whereas those with higher risk had more benefit.
Recognize uncertainty for the individual
Population Medicine v. Individual Care

\[ \Delta x \Delta p \geq \frac{h}{4\pi} \]

THE UNCERTAINTY PRINCIPLE
Should my patient go to hospice?

Common HF Risk Models: SHFM and MAGGIC

Levy et al. Seattle Heart Failure Model. Circulation. 2006;113:1424
http://depts.washington.edu/shfm/
11,000 patients with HF followed for 1 year
11,000 patients with HF followed for 1 year
What does a c index of 0.69 look like?

Randomly pick 1 alive and 1 dead patient:
What does c index of 0.69 look like?

Randomly pick 1 alive and 1 dead patient: 69% of the time score for alive person is lower than for the dead person.

SHFM 1-Year Estimated Risk of Death

What does a c-index of 0.69 look like?

Randomly pick 1 alive and 1 dead patient: 31% of the time score for alive person is higher than for the dead person.
What does c index of 0.69 look like?

Accurate Prediction for individual

Inaccurate Prediction for individual

“Attempts to determine through data collection which patients have a low or zero chance of survival have been largely unsuccessful.”

Shared decision making = “A meeting of two experts”

**PATIENT** is expert on:
1. Values and priorities
2. Hopes and fears

**CLINICIAN** is expert on:
1. What options are medically reasonable
2. Best, worst, and likely outcome for each option
Our 2 challenges

- Big data
- Omics

Predictive Certainty vs. Data

Uncertainty