Impact of Multiple Chronic Conditions on Therapeutic Outcomes in Patients with Implantable Cardioverter Defibrillators

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Alan S. Go, MD
Mary Tinetti, MD
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The MCC-ICD:
Exploring Therapeutic Outcomes in ICD Recipients with Multiple Chronic Conditions

A collaboration of Kaiser Permanente Northern California and the Yale Older Americans Independence Center

AGING Initiative Pilot Plus+ Webinar
October 27, 2016
Objectives

Discuss relevance of MCCs in the context of implantable cardioverter defibrillators (ICDs)

Examine association of MCCs with receipt of ICD therapies

Discuss implications for shared decision-making in multimorbid patients considering ICDs
Alan Go, MD (senior PI)
Jerry Gurwitz, MD
Frederick Masoudi, MD, MSPH
Robert Greenlee, PhD, MPH
David Magid, MD, MPH
Grace Tabada, MPH
Sue Hee Sung, MPH
Alda Inveiss, MPH
OAIC (Pepper) Sites

Alexandra Hajduk, PhD, MPH (Junior PI)
Thomas Gill, MD
Heather Allore, PhD
The Rise of ICDs

175,000 ICD implants in 2011
50% over age 65

Reduce risk of sudden cardiac death 25-60%

CMS Indications:
- Nonischemic heart disease
- Ischemic heart disease + MI
- EF <35%
- Life expectancy >1 year

Kramer, et al., Circ Cardiovasc Qual Outcomes, 2015; CMS Decision Memo CAG-00157R3
Average patient hospitalized with HF and EF<35 is 75 y.o., has 2 comorbidities and one-year mortality risk of 30%.

Moss, et al., NEJM 2002; Epstein, et al., JACC, 2013
Over half of ICD recipients >65 years die or are in hospice within five years of implantation.

The majority of older adults with ICDs die of non-arrhythmic causes.

Figure 3. The association between mode of cardiac death and total mortality with the Charlson Comorbidity Index (CCI) in heart failure. **White bars:** Mortality from sudden death (SD). The *P*-value for trend was .03 as the CCI increased. **Gray bars:** Mortality from non-SD. The *P*-value for trend was <.001 as the CCI increased. **Black bars:** Total mortality. The *P*-value for trend was <.001 as the CCI increased.
MCCs, ICDs, and Mortality

Steinberg, et al., JACC HF, 2014
The Downside of ICDs

- Complications
- End-of-life issues
- Price
- Inappropriate therapy

Inappropriate ICD therapies

1/3 of ICD therapies are inappropriate

Shocks or ATP can be inappropriate

10-21% of ICD patients receive inappropriate therapy

Daubert, et al., JACC 2014; Westerdahl, et al., Circ 2014; unpublished LS-ICD data
Sequelae of inappropriate ICD therapy

↑ patient pain and anxiety  (Marcus, et al., PACE 2011, Morken, et al., PACE 2012)

↓ quality of life  (Mark, et al., NEJM 2008; Magnusson, et al., Health Qual Life Outcomes, 2016)

↑ health care utilization  (Medtronic, Heart Rhythm 2010; Bhavnani, et al., PACE 2014)

Injury to myocardium  (Sham’a, et al., PACE 2014)

↑ mortality  (Poole, et al., NEJM 2008; Van Rees, et al., JACC 2011)
<table>
<thead>
<tr>
<th>Appropriate</th>
<th>Inappropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>Age &lt;65</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>Diastolic hypertension*</td>
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<tr>
<td></td>
<td>Atrial fibrillation*</td>
</tr>
<tr>
<td></td>
<td>Prior MI*</td>
</tr>
<tr>
<td></td>
<td>SVT*</td>
</tr>
<tr>
<td></td>
<td>EF &lt;25%</td>
</tr>
<tr>
<td></td>
<td>Prior appropriate shock</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
</tr>
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<td></td>
<td>Device malfunction/oversensing</td>
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</tbody>
</table>

How do MCCs affect risk of appropriate and inappropriate therapy in ICD recipients?
Longitudinal Study of ICDs

2,787 primary prevention ICD recipients
Implantation: January 2006 to December 2009
14 hospitals in the HCSRN
Follow-up: 2.6 years (range: 2 to 3 years)
LS-ICD Data Collection

NCDR ICD Registry

LS-ICD

HCSRN VDW

ICD Therapy Data Repository*

Masoudi, et al., *Circ Cardiovascular Qual Outcomes*, 2012
<table>
<thead>
<tr>
<th><strong>CMS-identified Conditions</strong></th>
<th><strong>Other Priority Conditions</strong></th>
</tr>
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<tbody>
<tr>
<td>Arthritis</td>
<td>Anemia</td>
</tr>
<tr>
<td>Asthma</td>
<td>Aortic valvular disease</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>Cancer</td>
<td>Mobility impairment</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Peripheral artery disease</td>
</tr>
<tr>
<td>COPD/Asthma</td>
<td>Previous GI bleed</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Previous valvular surgery</td>
</tr>
<tr>
<td>Dementia</td>
<td>Sinus node dysfunction</td>
</tr>
<tr>
<td>Depression</td>
<td>Thyroid dysfunction</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Ventricular tachycardia</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
</tr>
</tbody>
</table>
MCC Counts

0 to 3
4 to 5
6 to 7
8+
MCC Clusters
Clustering Methods

Agglomerative

Jaccard Coefficient

Ward’s Minimum Variance

Outcome: ICD therapies

Therapies: shocks and anti-tachycardia pacing (ATP)

Abstraction at study site → Central clinical review → Expert external adjudication → Any ICD Therapy → Appropriate


Any ICD Therapy → Inappropriate
Analytic Approach

**Time to first therapy**: Cox proportional hazards regression

**Total burden of therapy**: Poisson regression

**Inappropriate vs. appropriate therapy**: relative risk regression

Covariates: duration of follow-up, study site, demographics, medical history, NYHA classification, LVEF, smoking status, vital signs, lab results, medication use, ICD type
Initial Sample of Adults receiving Primary Prevention ICD Between 2006-2009
N = 2787

Exclusions (not mutually exclusive):
- <12 months continuous membership before implant date (N = 545)
- <21 years old at implant date (N = 3)
- Death or missing status during index procedure (N = 7)

Final Eligible Cohort
N = 2235
## Sample Characteristics

<table>
<thead>
<tr>
<th>Sample Characteristics</th>
<th>N=2235</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69 ±11 years</td>
</tr>
<tr>
<td>Women</td>
<td>567 (25%)</td>
</tr>
<tr>
<td>Race, White/European</td>
<td>1711 (77%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>313 (14%)</td>
</tr>
<tr>
<td>ICD Device Type</td>
<td></td>
</tr>
<tr>
<td>Single Chamber</td>
<td>728 (33%)</td>
</tr>
<tr>
<td>Dual Chamber</td>
<td>797 (36%)</td>
</tr>
<tr>
<td>Biventricular</td>
<td>710 (32%)</td>
</tr>
<tr>
<td>Chronic HF</td>
<td>2146 (96%)</td>
</tr>
<tr>
<td>Pre-implantation EF</td>
<td>25.2 ±6.6%</td>
</tr>
<tr>
<td># Comorbidities (median, IQR)</td>
<td>6 (4-8)</td>
</tr>
<tr>
<td>MCC Categories</td>
<td></td>
</tr>
<tr>
<td>0 to 3</td>
<td>317 (14%)</td>
</tr>
<tr>
<td>4 to 5</td>
<td>650 (29%)</td>
</tr>
<tr>
<td>6 to 7</td>
<td>381 (30%)</td>
</tr>
<tr>
<td>8+</td>
<td>587 (26%)</td>
</tr>
</tbody>
</table>
Comorbidities

- Dyslipidemia
- Hypertension
- Coronary artery disease
- Chronic kidney disease
- Diabetes mellitus
- Aortic valvular disease
- Atrial fibrillation or flutter
- Arthritis
- Chronic obstructive pulmonary disease
- Anemia
- Depression
- Abnormal sinus node function
- Ventricular tachycardia
- Cerebrovascular disease
- Asthma
- Abnormal thyroid function
- Chronic cancer
- Osteoporosis
- Previous valvular surgery
- Dementia
- Chronic liver disease
- Mobility impairment
- Peripheral artery disease
- Gastrointestinal hemorrhage

Percent (%)
ICD therapies, by MCC Count
Outcomes, by MCC Count

- At least 1 shock/ATP
  - 0-3 comorbidities (Reference): 26.8%
  - 4-5 comorbidities: 26.6%
  - 6-7 comorbidities: 25.0%
  - 8-16 comorbidities: 30.2%

- At least 1 appropriate shock/ATP
  - 0-3 comorbidities: 20.2%
  - 4-5 comorbidities: 18.5%
  - 6-7 comorbidities: 16.6%
  - 8-16 comorbidities: 19.3%

- At least 1 inappropriate shock/ATP
  - 0-3 comorbidities: 7.3%
  - 4-5 comorbidities: 10.5%
  - 6-7 comorbidities: 9.7%
  - 8-16 comorbidities: 10.9%
Adjusted for age, gender, race, site, tobacco use, NYHA class, family history of sudden cardiac death, chronic heart failure, systolic blood pressure, body mass index, estimated glomerular filtration rate, hemoglobin, potassium, left ventricular ejection fraction, ICD device type, ACEI, ARB, aspirin, beta-blockers, warfarin, digoxin, statin, and antiplatelet agent
MCCs and Burden of ICD Therapy

Adjusted for age, gender, race, site, tobacco use, NYHA class, family history of sudden cardiac death, chronic heart failure, systolic blood pressure, body mass index, estimated glomerular filtration rate, hemoglobin, potassium, left ventricular ejection fraction, ICD device type, ACEI, ARB, aspirin, beta-blockers, warfarin, digoxin, statin, and antiplatelet agent
MCC Counts and Risk of Inappropriate vs. Appropriate Therapy

Adjusted for age, gender, race, site, tobacco use, NYHA class, family history of sudden cardiac death, chronic heart failure, systolic blood pressure, body mass index, estimated glomerular filtration rate, hemoglobin, potassium, left ventricular ejection fraction, ICD device type, ACEI, ARB, aspirin, beta-blockers, warfarin, digoxin, statin, and antiplatelet agent.
MCC Cluster Results

Cluster Analysis

Cluster Analysis diagram showing a dendrogram with various conditions such as dyslipid, hypertension, CKD, CAD, arthritis, flutter, prewalsesurg, osteop, diabetes, cvdisease, cancer, PAD, asthma, _cnt_vt, thyroid, dementia, hem_gi, valvular, copd, _anemia2, depress, sinusnodef, frailty, and liver. The diagram illustrates the semi-partial R-Squared values along the x-axis.
Identifying Patterns of Multimorbidity in Older Americans: Application of Latent Class Analysis

Heather E. Whitson, MD, MHS, Kimberly S. Johnson, MD, Richard Sloane, MPH, Christine T. Cigolle, MD, MPH, Carl F. Pieper, DrPH, Lawrence Landerman, PhD, and Susan N. Hastings, MD, MHS (JAGS, 2016)
Higher comorbidity burden ↑ probability of ICD therapy

Higher comorbidity burden associated with ↑ risk of inappropriate, but not appropriate, therapy

Risk of inappropriate therapies highest among patients with 8+ comorbidities
Potential Mechanisms

MCCs $\rightarrow$ inflammation $\rightarrow$ arrhythmias

Accumulating, multifactorial etiology

Individual comorbidities

Strengths and Challenges

Large, contemporary, population-representative cohort
Wide range of comorbidities
Robust double-adjudicated review of ICD therapies

15% of ICD therapies could not be classified
No data on ICD models/programming strategies
Limited data on severity of comorbidities
Encourage shared decision-making for ICD implantation
- discuss goals of care, then risks and benefits
- consider alternative treatments

For patients who wish to proceed:
- consider ICD types and settings
- discuss potential for deactivation
AGING Initiative (NIA R24 AG045050)

AHRQ, US DHHS DEcIDE Program Contract No. 290-05-0033
American College of Cardiology Foundation
Cardiovascular Research Network (NHLBI U19HL091179)
Yale Pepper Center (NIA P30 AG021342)
Yale Training Program in Geriatric Clinical Epidemiology (NIA T32 AG019134)
Patient health priorities (goals)-based care for adults with multiple and complex conditions

Mary Tinetti, MD
Gladys Phillips Crofoot Professor of Medicine (Geriatrics) and Professor in the Institution for Social and Policy Studies; Section Chief, Geriatrics; Yale School of Medicine
- Describe limitations of the current decision-making and care for persons with multiple and complex conditions (as illustrated by Drs. Go’s & Hadjuk’s study results)

- Suggest where we need to go in research and care for persons with multiple and complex conditions
83-year-old man who complains of fatigue, decreased appetite, and weakness; feels burdened by his health care tasks
Mr. T: Multiple conditions (N=10) requiring 14 guideline-recommended medications

- Prior MI
- Diabetes
- Hypertension
- Depression
- Heart failure
- Atrial fibrillation
- Osteoporosis
- Chronic kidney disease
- COPD
- Peptic ulcer disease
Mr. T’s Evidence-based guideline treatments

- **Cardiologist:** Increase β-blocker, warfarin, diuretic, statin get a defibrillator
- **Endocrinologist:** Start insulin, bisphosphonate
- **Nephrologist:** start dialysis soon
- **Psychiatrist:** Decrease β-blocker, add 2\textsuperscript{nd} antidepressant
- **Gastroenterologist:** Stop or decrease warfarin
- **Disease outcomes** – Avoid sudden death, stroke, MI, fracture, re-hospitalization for heart failure, GI bleed; BP and HR control; improve depression
Result of care for Mr. T:

- Conflicting recommendations;
- Burdened by care tasks:
  - ~20 visits/month + lab
  - Self-management tasks
  - 12 medications
  - More procedures (dialysis, ICD)
- Still fatigue, weakness, ↓ appetite
18,500,000 (37%) Medicare beneficiaries with $4^+$ chronic conditions consume 74% of Medicare budget (CMS, 2012)

All adults: Majority of health care used by those with $\geq 2$ conditions (Anderson G, RWJF.org)

Multiple conditions is the norm; single disease is the outlier
Older adults with multiple and complex conditions receive a lot of care...

- Fragmented across providers and settings
- Each clinician focuses on subset of patient’s conditions
- Potentially harmful
- Of unclear benefit
- Not always targeted at what matters to patients
The care is fragmented

- **For patients:**
  - See average of 7 MDs/year, focus on individual conditions

- **For providers:**
  - Typical 1° care clinician coordinates care with 229 providers.

Pham, Ann Inter Med, 2009
The care is of uncertain benefit

- **Excluded from RCTs:**
  - Participants healthier & younger than clinical populations

- **With multiple conditions**
  - What outcome defines benefit?
The care is of potential harm

- 20% receive ≥ 1 “guideline” medication that may harm coexisting condition
  
  Lorgunpai, Tinetti, PLoS ONE, 2014

- Risk of adverse drug effect
  - ↑10% per drug;
  - ~100% with 10+ drugs

  Gandhi, NEJM, 2003
Care may be burdensome

- Medication complexity, self-management (Boyd)
- Ave. 25 contact days/yr.* (Bynum)
- “Caring for my chronic conditions is more burdensome than the conditions” (Montori)

### Table 3. Treatment Regimen Based on Clinical Practice Guidelines for a Hypothetical 79-Year-Old Woman With Hypertension, Diabetes Mellitus, Osteoporosis, Osteoarthritis, and COPD

<table>
<thead>
<tr>
<th>Time</th>
<th>Medications†</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 AM</td>
<td>Ipratropium metered dose inhaler 70 mg/vial of albuterol</td>
<td>Check test; Sit upright for 30 min on day when albuterol is taken</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Check blood sugar</td>
</tr>
<tr>
<td>8:00 AM</td>
<td>500 mg of calcium and 200 IU of vitamin D 12.5 mg of hydrochlorothiazide 40 mg of lisinopril 10 mg of gluburide 81 mg of aspirin 850 mg of metformin 250 mg of naproxen 20 mg of omeprazole</td>
<td>Eat breakfast; 2.4 g/d of sodium; 90 mmol/d of potassium; Low intake of dietary saturated fat and cholesterol; Adequate intake of magnesium and calcium; Medical nutrition therapy for diabetes: DASH‡</td>
</tr>
<tr>
<td>12:00 PM</td>
<td></td>
<td>Eat lunch; 2.4 g/d of sodium; 90 mmol/d of potassium; Low intake of dietary saturated fat and cholesterol; Adequate intake of magnesium and calcium; Medical nutrition therapy for diabetes: DASH‡</td>
</tr>
<tr>
<td>1:00 PM</td>
<td>Ipratropium metered dose inhaler 500 mg of calcium and 200 IU of vitamin D</td>
<td></td>
</tr>
<tr>
<td>7:00 PM</td>
<td>Ipratropium metered dose inhaler 850 mg of metformin 800 mg of calcium and 200 IU of vitamin D 40 mg of losartan 250 mg of naproxen</td>
<td>Eat dinner; 2.4 g/d of sodium; 90 mmol/d of potassium; Low intake of dietary saturated fat and cholesterol; Adequate intake of magnesium and calcium; Medical nutrition therapy for diabetes: DASH‡</td>
</tr>
</tbody>
</table>
| 11:00 PM   | Ipratropium metered dose inhaler As needed Albuterol metered dose inhaler | As needed; Albuterol metered dose inhaler

Abbreviations: ADA, American Diabetes Association; COPD, chronic obstructive pulmonary disease; DASH, Dietary Approaches to Stop Hypertension.†Clinical practice guidelines used: (1) Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; (2) ADA; (3) American College of Cardiology; (4) American Heart Association; (5) National Osteoporosis Foundation; (6) National Heart, Lung, and Blood Institute and World Health Organization.‡Days spent in hospital or ambulatory visit, procedure, imaging or lab test.

* Taken orally unless otherwise indicated. The medication complexity score of the regimen for this hypothetical woman is 14, with 19 doses of medications per day, assuming 2 as needed doses of albuterol metered dose inhaler plus 70 mg/vial of albuterol.
ICDs: Illustrates greater risk of harms & burden of care for persons with MCC

<table>
<thead>
<tr>
<th>No. conditions</th>
<th>AHR inappropriate therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>1</td>
</tr>
<tr>
<td>4-5</td>
<td>1.94 [1.14-3.31]</td>
</tr>
<tr>
<td>6-7</td>
<td>2.25 [1.25-4.05]</td>
</tr>
<tr>
<td>8+</td>
<td>2.91 [1.54-5.50]</td>
</tr>
</tbody>
</table>
“Inappropriate therapy” with ICDs...

Care may not address what matters most to persons with MCC

- Clinicians’ focus on discrete disease-specific outcomes
  - "inappropriate therapy” (clinician- not patient-centric)

- That are not targeted what matters to patients
  - Reduce risk of sudden death (is this the person’s outcome priority?)
Older adults with MCCs vary in what matters most when faced with tradeoffs:

- Maintain function: 42%
- Relief of pain or other symptoms: 32%
- Keep alive: 27%

Where to we need to go in research and practice?
Patients, caregivers, clinicians, national provider and patient organizations, health systems, payers
*CaRealign*

(Patient Priorities Care Initiative)

- **Asked them:**
  - To identify issues to be addressed to improve care and outcomes of persons with multiple conditions
  - To design a feasible, sustainable approach that addresses these issues → better care & outcomes
Patients’ health goals should drive care

Most treatments preference sensitive but doctors don’t see it that way, “Doctors think they know best what patients should do”

Patient defines what is a “bad outcome”

Everybody needs “a somebody”

People differ in whether treatment burden is worth the outcome (vary in care preferences as well as outcome)
Primary & specialty clinicians: Key themes

- Incentives (financial and nonfinancial) to support complex care
- Clear roles and responsibilities; framework for communication
- Smaller networks of providers
- Quality metrics that are patient, not disease-oriented
- Evidence of what works in this population
- Liked idea of knowing patients’ wants prior to visits
- Want other clinicians to honor changes they make in response to patient requests
Health systems leaders: Key themes

- Provide care more efficiently and cost-effectively
- Needs to fit their mission
- Don’t know how to do that for this population
- Do not want to add staff, rather change what staff do
Clinical decisions & research should be based on intersect

Recommended approach to address these issues:

Patient Health Priorities Aligned Care
A Move from...

Disease-outcome centered care & research

TO

Patient-health priorities-centered care & research
What is patient health priorities aligned care?

- Member of health team helps patients identify (construct) their health priorities

- Clinicians align their care with achieving these health priorities (Decision-making predicated on achieving patient’s health outcome goals within context of care preferences)
What are health outcome goals?

Outcome goals patients want from health care:

- **Specific, Measurable, Actionable, Reliable, Timebound (SMART) goals**
- Example: Able to walk at > 2 blocks or 1 flight daily without stopping for SOB
- Distinct from behavioral goals such as stop smoking and disease goals such as improving HbA1c or BP)
What are care preferences?

<table>
<thead>
<tr>
<th>Domains (examples) of care preferences**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health care utilization</strong></td>
</tr>
<tr>
<td>(e.g. # visits, hospitalizations; clinicians; diagnostics)</td>
</tr>
<tr>
<td><strong>Medication management</strong></td>
</tr>
<tr>
<td>(e.g., complexity; adverse effects; monitoring)</td>
</tr>
<tr>
<td><strong>Self-management</strong></td>
</tr>
<tr>
<td>(e.g., diet, exercise, check weights, bp, glucose)</td>
</tr>
<tr>
<td><strong>Procedures</strong></td>
</tr>
<tr>
<td>(time, discomfort, anxiety, complications; time to recover)</td>
</tr>
</tbody>
</table>

** patient activity/workload; what willing & able to tolerate to achieve outcomes; care or treatment burden if unacceptable
Guiding principles for patient priorities aligned care

- Patients health priorities drive all care & communications
- Everyone focuses on same outcome(s)
- Roles and responsibilities are agreed to
- Decision-making acknowledges:
  - Uncertainty
  - Health trajectory
  - Tradeoffs
- Clinicians integrate care across conditions
FROM Disease-based:

Current care: “You need______ for your______”
Research: Does X treatment improve Y disease measure?

TO Patient priorities-based research that gives clinicians the information to say:

“There are several things we could do, but knowing your health priorities, your conditions, and what’s important to you, I suggest we ______”
Ascertain his health outcome goals & care preferences:
- Fewer symptoms & better function not life prolongation
- Fewer meds, fewer clinicians & visits; only procedures that help function & symptoms

Health priorities-aligned care:
- Reduce or stop several medications
- Eliminate dietary restrictions
- No defibrillator
- Try dialysis but stop if symptoms & function don’t improve

Integrate decision-making across his clinicians
Where we need to go in research for persons with multiple & complex conditions

- Multiple stakeholders (patients, caregivers, clinicians) members of research team
- Outcomes that patients care about (function & symptoms)
- Incorporate patient goals, preferences, life context into the research
- Measure burden of intervention as well as benefit
- Sufficient sample size to look at key subgroups based on conditions & other factors