Value-Based Reimbursement: Conceptual and Policy Issues

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October 2, 2007
Natural History of Technology

- First Technical Data
- FDA Approval
- Coverage Standard
- Discovery
- Initial Market Presence
- Clinical Standard of Care
- Sensitivity/Specificity/Accuracy +/- Clinical Effects
- Proven Clinical Effectiveness
- Broad Market Presence
Kaplan-Meier Survival by Treatment Group

Hazard Ratio = 0.69
Adjusted P=0.016

Total Mortality
CONV: 19.8%
ICD: 14.2%

31% reduction in risk of all-cause mortality
<table>
<thead>
<tr>
<th>Variable</th>
<th># Pts.</th>
<th>ICD:CONV Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>573</td>
<td></td>
</tr>
<tr>
<td>≥65 yr</td>
<td>659</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1040</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>192</td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤0.25</td>
<td>831</td>
<td></td>
</tr>
<tr>
<td>&gt;0.25</td>
<td>401</td>
<td></td>
</tr>
<tr>
<td>NYHA Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤II</td>
<td>867</td>
<td></td>
</tr>
<tr>
<td>&gt;II</td>
<td>350</td>
<td></td>
</tr>
<tr>
<td>QRS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.12s</td>
<td>603</td>
<td></td>
</tr>
<tr>
<td>0.12-0.15s</td>
<td>353</td>
<td></td>
</tr>
<tr>
<td>&gt;0.15s</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>769</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>463</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>1232</td>
<td></td>
</tr>
<tr>
<td>ICD Better</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Conventional Better</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SUBGROUP ANALYSES II: Mortality Endpoint

There is no significant difference in the hazard ratios between subgroups.
Kaplan-Meier Estimates of the Survival for Patients with QRS > 120 ms

Patients with pacemakers were excluded.
CMS analysis of the MADIT II dataset supplied by Guidant.

p-value=0.001
Kaplan-Meier Estimates of the Survival for Patients with QRS ≤ 120 ms

Patients with pacemakers were excluded.
CMS analysis of the MADIT II dataset supplied by Guidant.
CMS June 2003 ICD policy

- CMS covers MADIT-I patients and wide-QRS subgroup of MADIT-II
  - Single trial
  - Possible selection bias
  - IIa recommendation by ACC/AHA/NASPE

- Announced that NCD would be reconsidered following SCD-HeFT
Mortality by Intention-to-treat

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>97.5% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. Placebo</td>
<td>1.06</td>
<td>0.86, 1.30</td>
<td>0.529</td>
</tr>
<tr>
<td>ICD Therapy vs. Placebo</td>
<td>0.77</td>
<td>0.62, 0.96</td>
<td>0.007</td>
</tr>
</tbody>
</table>

SCD-HeFT Heart Failure Trial
## Meta-Analysis Results:
### ICD Therapy for Primary Prevention of SCD

*(DCRI, 2004)*

QRs $\geq 120$

<table>
<thead>
<tr>
<th>Study</th>
<th>Hazard Ratio (random)</th>
<th>Weight</th>
<th>Hazard Ratio (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>or sub-category</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>CABG-PATCH</td>
<td>16.15 [0.73, 1.64]</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>COMPANION</td>
<td>18.92 [0.48, 0.86]</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>DEFINITE</td>
<td>9.74 [0.26, 1.07]</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>DINAMIT</td>
<td>11.37 [0.82, 2.82]</td>
<td>1.52</td>
<td></td>
</tr>
<tr>
<td>MADIT-I</td>
<td>8.27 [0.12, 0.61]</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>MADIT-II</td>
<td>16.10 [0.38, 0.85]</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>19.43 [0.51, 0.88]</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.70 [0.52, 0.93]</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2 = 18.22$, df = 6 ($P = 0.008$), $I^2 = 67.1\%$

Test for overall effect: $Z = 2.44$ ($P = 0.01$)

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**Review:** Prevention of SCD  
**Comparison:** 01 ICD versus control  
**Outcome:** 10 QRs $\geq 120$ms
Meta-Analysis Results: ICD Therapy for Primary Prevention of SCD

(DCRI, 2004)

QRS < 120ms

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Hazard Ratio (random)</th>
<th>Weight %</th>
<th>Hazard Ratio (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG-PATCH</td>
<td>19.52</td>
<td>1.04</td>
<td>[0.70, 1.53]</td>
</tr>
<tr>
<td>DEFINITE</td>
<td>6.98</td>
<td>0.77</td>
<td>[0.40, 1.49]</td>
</tr>
<tr>
<td>DINAMIT</td>
<td>13.42</td>
<td>0.85</td>
<td>[0.53, 1.36]</td>
</tr>
<tr>
<td>MADIT-I</td>
<td>3.75</td>
<td>0.44</td>
<td>[0.18, 1.08]</td>
</tr>
<tr>
<td>MADIT-II</td>
<td>13.78</td>
<td>0.67</td>
<td>[0.42, 1.07]</td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>42.56</td>
<td>0.84</td>
<td>[0.64, 1.10]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.00</td>
<td>0.82</td>
<td>[0.69, 0.98]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2 = 4.03, df = 5$ ($P = 0.55$), $I^2 = 0\%$
Test for overall effect: $Z = 2.19$ ($P = 0.03$)
CMS ICD policy January 2005

- Medicare proposed decision to cover most pts with EF<35%
- SCD-HeFT make eligible pool 1M+
- Linked to submission of data to national ICD registry (CED)
- Intended goal of registry to get better information on patterns of use, real world event rates, risk stratification
CEA for ICDs

- NEJM Oct 6, 2005
  - Sanders, Hlatky, Owens,
- Markov model
  - based on meta-analysis of 8 trials
- 34K to 70.2K per life year saved
  - All sensitivity analyses below 100k/life-year
- Incremental cost $3-5B per year
- Called for better risk stratification
- Cheaper ICDs might also be worthwhile
Contact Information

- sean.tunis@cmtpnet.org
- www.cmtpnet.org
- 410-963-8876
Value-based options

- QOE high, MOB high, relative cost low
  - Covered without limitations
- QOE mod, MOB mod, relative cost mod
  - Differential co-pay
- QOE low, MOB high, relative cost high
  - Coverage with evidence development
- etc
Impact on Innovation

- Current pricing
  - Cost and risk of R&D
  - Resource use in delivering service
  - Reinvestment in innovation

- Value-based pricing
  - Amount of health benefit produced
  - Insensitive to risk, resources, innovation
Radiation for low-risk prostate CA

Comparative Clinical Effectiveness

Superior A
Incremental B
Comparable C
Pot/Unprov P/U
Inadequate I

Comparative Value
a High
b Reasonable/Comparable
c Low

Pearson / ICER

Aa     Ab     Ac
Brachytherapy
Bb     IMRT
C       C       C
Hypofract Rx
Pb     Pc
Proton Beam Therapy
Albuterol / Xopenex

- Levalbuterol is S-enantiomer of albuterol
- Good pharmacologic rationale for improved effectiveness with fewer side effects
- Initial clinical studies showed better FEV-1, reduced beta adrenergic effects
- Large RCTs suggested lower hospitalization, but unclear impact on FEV-1
- CMS process: LCA, NCD, 1847(a)(1)
- What would have made sense?
Evidence of Effectiveness

- Key limiting factor in determining value
- Use of observational data
  - Nurse’s Health / WHI, COURAGE, CATIE
- Pathophysiologic rationale
- Pragmatic trials, observational studies
Evidence-based Medicine (EBM): Original definition

“...Evidence-based medicine de-emphasizes intuition, unsystematic clinical experience, and patho-physiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research.”

Evidence-Based Medicine Working Group, JAMA (1992)
Quality of evidence

- prospective studies vs retrospective studies
- randomized vs observational studies
- concurrent vs. non-concurrent comparisons
- large studies vs. small studies
- blinded vs. unblinded observers
- effectiveness vs. efficacy
- hard outcomes / functional outcomes vs. intermediate outcomes