Introductions and Agenda

- Today’s Presenters
  Thomas F. Goss, PharmD, Sr. VP Boston Healthcare Associates
  Liesl Cooper, PhD, VP Global Healthcare Economics & Reimbursement, Covidien
  Sheri Dodd, MSc, Medtronic Cardiac Rhythm Disease Management
  Bernd Brüggenjürgen, MD, MPH Managing Director Boston Healthcare International GmbH

- Agenda
  The Value Environment and Implications for Innovators
  Capturing Value in an Evidence-driven Environment Case Studies
  Q&A
Polling Question 1

• Does your company currently have formalized processes for evaluating evidence standards or requirements incorporating stakeholder perspectives throughout the technology development and commercialization lifecycle?

  1. No
  2. Yes

Polling Question 2

• Does your company routinely evaluate evidence requirements to support optimal reimbursement as part of its M&A and Portfolio Management Processes?

  1. No
  2. Yes
Health Care Stakeholders are Seeking Value, Reshaping Policy and Payment Mechanisms around Clinical and Economic Evidence

- Outcomes- or performance-driven coverage and payment
  - e.g. quality incentives
    - Day case tariffs higher than inpatient, pt. assessments, etc.
    - Regional/hospital risk sharing agreements

- Valued-based purchasing
  - Pay-for-reporting, pay-for-performance

- Comparative effectiveness*
  - Objective: Evaluate medical innovations and technologies to determine which ones represent value added, which offer little improvement over the current options, which fail to provide added benefits, and which work for some patients and not for others

- Expansion of the “financial episode of care”
  - Looking beyond a hospital stay as a clinical and financial risk event
  - Alignment of economics with outcomes

Supporting the drive for value, there is a growing demand for evidence from purchasers and customers on a global scale

*Source: AHRQ
Global Health Systems are Evolving to More Cost-effectiveness Evidence-Driven Value Models

- Countries spending more per capita on health care tend to use prospective payment mechanisms, and have the infrastructure to implement cost-effectiveness health care initiatives
- These countries will have higher demands for clinical and economic evidence

Hospital Payment Mechanisms In Relation to Total Expenditure on Healthcare Per Capita in 2005 for Countries Profiled*  

**Data are expressed in US dollars adjusted for purchasing power parities (PPPs), which provide a means of comparing spending between countries on a common base

In this Environment, Evidence-based Value (EbV) is an Essential Component of Overall Innovation Value

Product value may be driven by a number of factors. Demonstrating Evidence-based Value can support provider adoption, payer coverage, and premium pricing resulting in routine optimal payment and market access

In this environment, an understanding of Evidence-based Value can inform technology investment decisions
To Address This Issue, Innovators Should Conduct Stage-appropriate Evidence-based Value Analysis

Typical Issues Addressed in an EbV Analysis

- Does the product’s design, format, and use fit easily into existing reimbursement systems, or will it need new codes, tariffs or policies that require an investment of time and money to achieve?

- Are there opportunities to access additional reimbursement due to the innovative nature of the technology or the reimbursement structure of the target market?

- Is the target selling price compatible with available reimbursement, as well as the value perceived by each key clinical and/or economic stakeholder?

- What clinical and economic evidence will funding authorities require to establish optimal patient access at the targeted price?

At each stage gate, these questions are refined as additional evidence is available from the development team, further informed by the evidence-based value opportunity.
An Understanding of the Clinical and Economic Impact Correlates Directly to Reimbursement and Market Access Potential and Risk

Typically relies on existing payment paradigms

- Incremental payment for an incremental innovation
- Demonstrating clinical and economic practice advantages within a given case
- More likely to demand a practice-level economic understanding

Often demands a substantial effort to secure unique, value-based, payment

- Typically will require new reimbursement paradigms including novel policy approaches and novel coding
- More likely to demand a population-level economic understanding

This distinction is particularly important in developed health care systems, where an understanding of cost and demand will drive an assessment of clinical and economic impact of a new technology.

A Comprehensive Approach to Value Environment Assessment

Objective:
Examine the range of factors that influence patient/provider access and reimbursement success on a global scale

Evidence Environment
Clinical and Economic Evidence in published literature

Policy / Coverage Landscape
Policy environment that restricts access to medical technologies or services

Coding and Payment Structure
Country-specific Mechanics of reimbursement

Stakeholder Insight
Value perspectives and evidence needs of clinical adoption and financial stakeholders

- Literature Review
- Secondary Data
- Policy Analysis
- Coding and Payment Analysis
- Primary research driven analysis

Strategic Approach to Evidence Development, Optimal Access, and Routine Payment for the Technology
Case Studies: Applications of Evidence-based Value Assessment

- Case Study 1 - Evidence-Based Value Assessment: Incorporating EBV Assessment in M&A Due Diligence Activities
  Liesl Cooper, PhD  
  VP, Global Healthcare Economics & Reimbursement  
  Covidien

- Case Study 2 - Evidence-Based Value Assessment: “Hands-On” Planning for the Payer
  Sheri Dodd, MSc  
  Vice President, Clinical Research, Healthcare Economics and Policy  
  Cardiac Rhythm Disease Management (CRDM)  
  Medtronic, Inc

- Case Study 3: What Evidence at What Time? Three Evidence Case Examples
  Bernd Brueggenjuergen, MD, MPH  
  Managing Director, Boston Healthcare GmbH

Case Study 1

Evidence-Based Value Assessment  
“Value Determination”: HE&R Due Diligence Input
Diligence Example: Economic, Reimbursement, and Policy Analysis

Liesl Cooper, PhD
VP, Global Healthcare Economics & Reimbursement

General Stages of Pre-Signing M&A Processes
Establishing Early Value Parameters for Disease and Treatment

Strategy & BDL Core Objectives
- Market & competitor evaluation
- Desired market participation
- Key success factors
- Gaps & imperatives
- Internal vs. external assessment
- Strategic objectives mapped to acquisition strategies
- Multi-year acquisition plans hypothesized
- Criteria established for evaluating targets
- Target landscaping conducted

HE&R Evaluation Requirements
- Disease area and current standards of care
  - Prevalence and economic impact
  - Current treatment options / value proposition
  - Site of care
  - Unmet needs
- Stakeholder and ‘gatekeeper’ reviews
  - Drivers and incentives
  - Financial risks and decision-making
- Reimbursement environment for current treatment
  - Coding, coverage & payment
  - Technology assessments

Differentiation and Stakeholder Value Statements

Core Objectives
- Further refinement of target assessment criteria
- Further refinement of target landscaping
- Screening of targets
- Initial assessments of targets
- Initial dialogue with target management

HE&R Evaluation Requirements
- Stakeholder reactions and impact
  - Technology and innovation perspective
  - Incremental or disruptive
  - “Reasonable and necessary”
  - Changes to care standards, site or costs
- Access issues in related areas
- Evidence needs and availability
  - Clinical and economic data quality
  - Technology assessments and outcome
  - Risks and opportunities for technology
- Refine landscaping done in strategy phase
- Policy and access leadership assessment
**Critical Input to “Go/No Go” and Valuation Inputs**

**Acquisition Team’s Core Objectives**
- Preliminary go/no go decision
  - key success drivers of base business identified
  - value-driving integration decisions vetted
- Vision for post-close business management discussed (e.g., degree of consolidation)
- Pro forma & valuation drafted

**HE&R Evaluation Requirements**
- Reimbursement landscape detail
  - Coding, coverage & payment
  - Investment required for access
  - Clinical evidence risks
  - Regional characteristics
  - Revenue impacts
  - Cost of capabilities build-out
  - Consequences of timing

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**Finalize Inputs Into Valuation and Begin Integration Planning**

**Acquisition Team’s Core Objectives**
- Final go/no go decision
  - potential risks and liabilities highlighted
- Vision for post-close business management defined (e.g., degree of consolidation)
- Pro forma & valuation finalized
  - further definition and testing of integration objectives
- Contract terms negotiated & finalized

**HE&R Evaluation Requirements**
- Validation of all assessments
- Deep-dive into key clinicals
- Stakeholder / payer interviews
- Staffing and project assessment
- Integration planning
Barrett’s Esophagus – Minimally Invasive Treatment Option

Clinical Unmet Needs: RF Ablation for Barrett’s Esophagus

- 91% complete eradication of low grade dysplasia
- 81% complete eradication of high grade dysplasia
- 87% lower cancer incidence than control patients
- Tissue dysplasia remained completely eradicated in 85% after 3-year follow-up without maintenance RFA

Efficacy

- Cumulative stricture rate with RFA of 0.17%
- Perforation rate with RFA 0.01%
- Cumulative reportable event rate per procedure of 0.22%

Safety/ Morbidity

- Prevalence of 3.3 million over age 50 in US (0.4 – 1.3%)
- 13% of Caucasian men over 50 with GERD will develop BE - a risk factor for cancer
- Incidence of adenocarcinoma and death are increasing
- With aggressive treatment 5-year survival from adenocarcinoma is around 17%

Imperative to Treat

- Patients receiving treatment have less worry about cancer and esophagectomy and significantly reduced depression and impact on work and family life

Payer Mix for Barrett’s Esophagus (U.S.)

- Estimated that majority of patients have private insurance
- Most people with the disease are between 55 and 70. The risk is much lower for patients under 40 (Mayo Clinic).
- Most people who develop esophageal cancer are in their 50’s to 70’s (ACS).

### Payer Coverage Analysis for Barrett's Esophagus (U.S.)

<table>
<thead>
<tr>
<th>Plan</th>
<th>Coverage Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aetna</td>
<td><strong>Clinical Policy Bulletin #0728 Barrett's Esophagus Surgery</strong> – Aetna considers [Radiofrequency Ablation] <strong>medically necessary</strong> for the treatment of members with high grade dysplasia Barrett's esophagus</td>
</tr>
<tr>
<td>Blue Cross of ID</td>
<td><strong>MP2.01.80 Endoscopic RFA for Barrett’s Esophagus</strong> – RFA is considered <strong>medically necessary</strong> as a treatment for high grade dysplasia Barrett’s esophagus and <strong>investigational</strong> for low grade dysplasia</td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td><strong>Surg.00106 Radiofrequency Ablation as a Treatment for Barrett’s Esophagus</strong> – RFA <strong>medically necessary</strong> as a treatment for high grade Barrett’s esophagus and for low grade with 2 independent biopsy confirmations.</td>
</tr>
<tr>
<td>Medicare</td>
<td>No specific National or Local coverage policy for RFA. Absence of policies default to positive coverage environment.</td>
</tr>
<tr>
<td>CIGNA</td>
<td>No published policy on RFA for Barrett’s esophagus</td>
</tr>
</tbody>
</table>

### Technology / Procedure Assessments Global

<table>
<thead>
<tr>
<th>Source</th>
<th>Coverage Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK NICE</td>
<td><strong>Guidance IPG244 – Circumferential epithelial RFA for Barrett’s oesophagus – Dec07</strong></td>
</tr>
<tr>
<td></td>
<td>• Evidence on the safety and efficacy of circumferential RF ablation for Barrett’s oesophagus is currently inadequate. Therefore this procedure should only be used in context of research.</td>
</tr>
<tr>
<td></td>
<td>• 2010 NICE guidance IPG 344: Barrett’s oesophagus: ablative therapy for the treatment of Barrett’s oesophagus</td>
</tr>
<tr>
<td></td>
<td>• Adequate for high grade dysplasia</td>
</tr>
<tr>
<td></td>
<td>• Inadequate for low grade dysplasia</td>
</tr>
<tr>
<td>Clinical Trials.gov</td>
<td>9 studies found [Barrett's esophagus &amp; Halo]</td>
</tr>
<tr>
<td>Hayes</td>
<td>No technology assessments found</td>
</tr>
<tr>
<td>ASGE</td>
<td>No clinical guidelines on ASGE website</td>
</tr>
<tr>
<td>BCBS TEC</td>
<td>Not adequate evidence for low grade dysplasia</td>
</tr>
</tbody>
</table>
### Procedure & Device Coding Analysis United States

<table>
<thead>
<tr>
<th>CPT™</th>
<th>Description</th>
<th>ICD-9</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>43228</td>
<td>Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
<td>42.33</td>
<td>Endoscopic excision or destruction of lesion or tissue of esophagus</td>
</tr>
<tr>
<td>43258</td>
<td>Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
<td></td>
<td>• CPT 43228 recommendation by the ASGE on 5/22/06</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• CPT™ Codes are used by hospital outpatient departments, ASCs, and physicians</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ICD-9 Codes are used by hospitals to report procedures performed in the hospital inpatient setting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No device specific HCPCS or C-codes were identified.</td>
</tr>
</tbody>
</table>

Halo™ system is well described in available coding systems

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### Site of Service Mix for Barrett’s Esophagus (U.S. 2009)

- **2009 Medicare National Average Rates** (private insurers generally pay higher)
  - Hospital Outpatient Department reimbursement is $1,676
  - Ambulatory Surgery Center reimbursement is $730
### Payment Analysis United States

<table>
<thead>
<tr>
<th>CPT™</th>
<th>Description</th>
<th>HOPD</th>
<th>ASC</th>
<th>Phys Facility</th>
<th>Phys Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>43228</td>
<td>Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
<td>$1,676</td>
<td>$730</td>
<td>$216</td>
<td>$216</td>
</tr>
<tr>
<td>43258</td>
<td>Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with ablation of tumor(s), poly(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
<td>$572</td>
<td>$423</td>
<td>$258</td>
<td>$258</td>
</tr>
</tbody>
</table>

• Procedure is not reimbursed in the hospital inpatient setting

### Price Sensitivity Analysis United States

<table>
<thead>
<tr>
<th>CPT™</th>
<th>Description</th>
<th>HOPD</th>
<th>Halo360 per procedure Revenue</th>
<th>Halo360 per procedure Revenue</th>
<th>Halo90 per procedure Revenue</th>
<th>Halo90 per procedure Revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>43228</td>
<td>Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
<td>$1,676</td>
<td>$1,496</td>
<td>$727</td>
<td>$727</td>
<td></td>
</tr>
</tbody>
</table>

• The device portion of procedure reimbursement should generally not exceed 50% - 25% to 40% is a healthy percent share

• Provider reimbursement rates are generally all inclusive – meaning one payment covers all costs, including personnel, supplies, medication, etc...
### Preliminary Findings and Next Steps

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>PRELIMINARY FINDINGS</th>
<th>NEXT STEPS</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payer Mix</td>
<td>Private payer dominance in U.S. will allow for better payment rates but will require coverage.</td>
<td>Confirm U.S. payer mix and expand to EMEA</td>
<td>Positive</td>
</tr>
<tr>
<td>Site of Service Mix</td>
<td>Hospital outpatient primary site of service in the US</td>
<td>Confirm U.S. site of service mix and expand to EMEA</td>
<td>Neutral</td>
</tr>
<tr>
<td>Coverage</td>
<td>Private payer coverage policies in U.S. clearly state RFA for Barrett's Esophagus is experimental and investigational for low-grade</td>
<td>Expand coverage analysis to EMEA</td>
<td>Neutral</td>
</tr>
<tr>
<td>Coding</td>
<td>U.S.: ASGE states CPT 43228 is appropriate for use with Halo RFA procedures. ICD-9 42.33 available also.</td>
<td>Expand coding analysis to EMEA</td>
<td>Positive</td>
</tr>
<tr>
<td>Payment</td>
<td>U.S.: Hospital Outpatient and ASC payment rates inadequately reimburse providers for the cost of procedure.</td>
<td>Expand payment analysis to EMEA</td>
<td>Negative</td>
</tr>
<tr>
<td>Conclusion</td>
<td>Mixed coverage policies and inadequate reimbursement rates trump the positive side of coding, payer, and site of service mix. Poor coverage and low payment rates could prevent expansion of technology. To address this situation dedicated reimbursement resources will be required (FTE or Consultant).</td>
<td></td>
<td>Neutral</td>
</tr>
</tbody>
</table>

### Case Study 2

**Evidence-Based Value Assessment: “Hands-On” Planning for the Payer**
Case Study 3

What evidence at what time? Three evidence case examples:

• A registry case
• A prospective controlled trial case
• A randomized controlled prospective trial case

1. The DESDE Registry Case Example - Background and Objectives

Background:
• Significant reduction of coronary re-intervention following drug-eluting stent implantation shown in randomised trials
• Can results of efficacy trials be realised in usual medical practice?
• Insufficient cost effectiveness data for treatment with DES

Objectives:
• Cost effectiveness of drug-eluting stents (DES) compared to bare-metal stents (BMS)
• Major adverse cardiac and cardiovascular events after DES
• Health related quality of life
The DESDE Registry Case Example - Cooperating Partners

- Centre recruitment
- Logistics
- DES.de Registry
- Follow-up

The DESDE Registry Case Example - Study Design

Recruitment DES

Follow-up

Recruitment BMS

Follow-up

- DES: Indication for drug-eluting stent implantation (Taxus/ Cypher)
- BMS: Indication for BMS implantation - Only BMS implanted
  - Eligible medical conditions:
    - Acute Coronary Syndrome, Diabetes Mellitus, Previous Percutaneous Coronary Intervention/ Coronary Artery Bypass Graft, 3-Vessel Diseases,
The DESDE Registry Case Example - Baseline Issues

<table>
<thead>
<tr>
<th></th>
<th>BMS (n=457)</th>
<th>DES (n=3516)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male %)</td>
<td>74</td>
<td>75</td>
<td>0.688</td>
</tr>
<tr>
<td>Age in years (mean ± SD)</td>
<td>67 ± 11</td>
<td>65 ± 11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>26</td>
<td>22</td>
<td>0.127</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>84</td>
<td>84</td>
<td>0.681</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>76</td>
<td>81</td>
<td>0.017</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>33</td>
<td>32</td>
<td>0.749</td>
</tr>
<tr>
<td>Previous myocardial infarction (%)</td>
<td>26</td>
<td>30</td>
<td>0.064</td>
</tr>
<tr>
<td>Previous bypass (%)</td>
<td>16</td>
<td>15</td>
<td>0.326</td>
</tr>
<tr>
<td>Lesion type C (%)</td>
<td>27</td>
<td>27</td>
<td>1.0</td>
</tr>
<tr>
<td>Stent diameter (mean ± SD)</td>
<td>3.1 ± 0.5</td>
<td>3.0 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stent length (mean ± SD)</td>
<td>16.1 ± 5.7</td>
<td>19.2 ± 7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3-vessel disease (%)</td>
<td>46</td>
<td>39</td>
<td>0.008</td>
</tr>
<tr>
<td>Number of stents (mean ± SD)</td>
<td>1.4 ± 0.7</td>
<td>1.4 ± 0.7</td>
<td>0.543</td>
</tr>
</tbody>
</table>

Willich, Annual German Cardiology Society - Meeting 2008

Evidence Requirements in Medical Device Development - First Conclusions

Preliminary 6-month follow-up indicated that
- DES is clinically superior to BMS
- DES is associated with higher costs
- Compared to previous studies, cost effectiveness seems to improve with declining DES surcharges

Evidence requirements Issues:
- Control group without statistical power calculation basis
- Even with multivariate adjustment impact of selection bias highly probable
- Generates evidence with regard to device usage characteristics in Germany
2. The GERSHWIN Prospective Study Case Example – Background and Objectives

Background:
- Significant reduction of coronary re-intervention following sirolimus-eluting stent (SES) implantation shown in randomised trials
- Can results of efficacy trials be realised in usual medical practice?
- Insufficient long-term medical and cost benefit data for treatment with SES

Objectives:
- Cost equivalence over the long-term, despite the higher initial cost of SES compared to bare metal stents
- Major adverse cardiac events after SES (death, myocardial infarct, bypass, re-PCI)
- Patient quality of life
- Follow-up medical care

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GERSHWIN Study Concept: German Stent Health Outcome and Economics Within Normal Practice

Control strategy (sequential design, 1:2 ratio)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td>24</td>
<td>36 months</td>
</tr>
</tbody>
</table>

Willich, Annual ESC-Meeting 2007
The GERSHWIN Prospective Study Case Example -
Patient Selection

Inclusion criteria

Diabetics
- De novo lesion
- Lesion length ≤ 30 mm

Non diabetics
- De novo lesion with
- Lesion length 12-30 mm
  OR
- RVD 2.5-3 mm, proximal lesions 2.25-3 mm

Exclusion criteria

- Acute MI
- Lesion length > 30 mm
- In-stent restenosis
- Distal lesion RVD < 2.25 mm
- Lesion in left main or CABG or treated with brachytherapy
- Contraindications

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The GERSHWIN Prospective Study Case Example -
Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>BMS n=294</th>
<th>p</th>
<th>SES n=658</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male %)</td>
<td>79</td>
<td>0.003</td>
<td>87</td>
</tr>
<tr>
<td>Age in years (mean ± SD)</td>
<td>64 ± 10</td>
<td>0.122</td>
<td>63 ± 9</td>
</tr>
<tr>
<td>Single-person household (%)</td>
<td>16</td>
<td>0.034</td>
<td>11</td>
</tr>
<tr>
<td>Employed (%)</td>
<td>29</td>
<td>ns</td>
<td>33</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>59</td>
<td>ns</td>
<td>63</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>82</td>
<td>ns</td>
<td>80</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>85</td>
<td>ns</td>
<td>86</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>20</td>
<td>ns</td>
<td>24</td>
</tr>
<tr>
<td>Body Mass Index &gt; 30kg/m2 (%)</td>
<td>24</td>
<td>ns</td>
<td>20</td>
</tr>
<tr>
<td>Angina pectoris (%)</td>
<td>85</td>
<td>ns</td>
<td>86</td>
</tr>
<tr>
<td>Previous myocardial infarct (%)</td>
<td>31</td>
<td>ns</td>
<td>36</td>
</tr>
<tr>
<td>Previous bypass (%)</td>
<td>10</td>
<td>ns</td>
<td>12</td>
</tr>
<tr>
<td>3-vessel disease (%)</td>
<td>32</td>
<td>0.229</td>
<td>38</td>
</tr>
<tr>
<td>Number of stents (mean ± SD)</td>
<td>1.3 ± 0.6</td>
<td>&lt;0.001</td>
<td>1.6 ± 0.9</td>
</tr>
</tbody>
</table>

Willich, Annual ESC-Meeting 2007c

The GERSHWIN Prospective Study Case Example - Clinical Events 0 - 18 Months

- **MACE**
  - SES < BMS after 18 months
- **Patient quality of life**
  - SES > BMS
- **Costs**
  - Initial hospitalisation: SES > BMS
  - Follow-up costs: SES = BMS
  - Total costs after 18 months: SES > BMS
- At 18 months SES clinically superior to BMS but with higher total costs

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Further Issues - Development of Unit Costs in Longitudinal Settings

![Graph showing price indexes for original products across different countries and time periods.](image)
Further Issues - Development of Unit Costs in Longitudinal Study Settings

Evidence Requirements in Medical Device Development - Further Conclusions

- A control design is an essential element for generating evidence.
- However, the non-feasibility of introducing a randomization at that time of market launch introduced some selection bias.
- Despite a multi-variate adjustment being performed a remaining selection bias could not be excluded.
- The German IQWiG embarks merely on randomized approaches, even if a feasibility is not given.
- In longitudinal setting development of cost units is a further issue.
- Simulation of final costing year or publication year reasonable.
3. The OptiLink HF Randomized Study Case Example

- OptiLink HF Study: Optimization of Heart Failure Management Using Medtronic OptiVol Fluid Status Monitoring and Medtronic CareLink Network (OptiLink-HF)

- Patients suffering from heart failure and a markedly reduced pumping capacity and sometimes desynchronization of the lower chambers of the heart have a higher risk of suffering sudden cardiac death.

- Medtronic ICD- and CRT-D-Systems incorporated with fluid measuring coupled with modern data transmitting technology (CareLink)
  - Automatic information in case of a worsening of the cardiac status can be sent to caregivers.

- The study examines to which extent this new technology prevents potentially adverse cardiac situations and / or hospitalizations and has an influence of the duration of patient’s lives.

(http://clinicaltrials.gov/ct2/show/NCT00769457)

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The OptiLink HF Randomized Study Case Example

- OptiLink HF Study: Optimization of Heart Failure Management Using Medtronic OptiVol Fluid Status Monitoring and Medtronic CareLink Network (OptiLink-HF)

- Objective: Evidence generating whether the use of event-triggered HF-disease management through Medtronic’s OptiVol® fluid status monitoring with an automatically generated wireless CareAlert® notification ...can reduce cardiovascular related hospitalizations and the number of deaths ...compared to standard clinical assessment

- Primary Outcomes Measure: All-cause of death or unplanned admission to hospital for cardiovascular reason from day of patient informed consent sign off [ Time Frame: 18 Months ]

- Study Type: Interventional Study
- Allocation: Randomized
- Endpoint Classification: Efficacy Study
- Intervention Model: Parallel Assignment

- Patients to be included: 1000

(http://clinicaltrials.gov/ct2/show/NCT00769457)
Evidence Requirements in Medical Device Development - Conclusions

- Medical device assessment ideally part of full process assessment
- A control design is an essential element for generating evidence. However, despite a multi-variate adjustments selection bias can not be excluded
- A randomized design is considered even for medical devices as the only way demonstrating causal inference
- Registries might contribute to resource utilization and cost features understandings
- France (HAS) also focuses on clinical utility and comparative effectiveness to control costs
- UK (NICE) applies comprehensive reviews in order to obtain cost effectiveness results. So far most transparent international body
- The German IQWiG embarks merely on randomized approaches, even if a feasibility is not given with a strong focus on clinical benefit (not yet mandatory process)