ew cardiac procedures are often used excessively, suggesting that physicians tend to overestimate the benefits of new procedures. Randomized trial reports may contribute to this problem by exaggerating procedural benefits. I have previously noted that a variety of rhetorical strategies that emphasize device benefits were used in reporting implantable cardioverter defibrillator (ICD) primary prevention trials, including message framing, underreporting of complications, and interpretation bias. Other investigators have also noted widespread use of such techniques in randomized trial reports. The purpose of this report was to determine the extent to which rhetorical strategies were used to emphasize device benefits in cardiac resynchronization therapy (CRT) trial reports.

### Methods

The methods used in this study have been described in detail previously. In brief, MEDLINE, the Cochrane Trial Register and Library, and CRT reviews were searched for all randomized trials in which CRT was compared with no pacing; enrollment was more than 100 patients; and the primary outcome was survival, functional capacity, and/or hospitalization.

Publications were analyzed for the presence of four rhetorical strategies that can be used to emphasize treatment efficacy: message framing, use of ratios rather than absolute values to report results, underreporting of harms, and interpretation bias. Message framing was considered present when the trial objective, stated in the abstract or introduction, failed to include the evaluation of CRT harms and/or the introduction only included background information supporting CRT efficacy.

The exclusive use of ratios to present primary outcome results was considered evidence that ratios were used to emphasize CRT benefits. Complication data were considered to be underreported when the abstract did not include information about CRT complications and/or the results section did not contain complete information about the rates of unsuccessful device implantation, procedural complications, and/or postimplant complications. Interpretative bias was considered present when (1) important trial limitations were not mentioned and discussed; (2) CRT complications were not discussed despite the presence of significant device complications in the study population; (3) the risks vs benefits of CRT therapy were not compared, including how the frequency of risks should alter use of CRTs; (4) there was no mention that CRT benefits are likely to be less in clinical practice than in a clinical trial; and/or (5) trial conclusions indicated that CRT therapy is unequivocally beneficial despite failure of the trial to demonstrate a significant effect on the primary efficacy end point.

### Results

The search criteria identified 10 trial publications. Evidence of message framing was noted in both abstracts and introductory sections. In 8 abstracts and 9 introductory sections, the stated objective of the trial was to evaluate CRT benefits with no mention of evaluating CRT harms. In 7 introductory sections, only background information that supported CRT efficacy is noted, with no mention of negative CRT study findings or reports of high CRT complication rates. Primary end point data were reported using absolute values in the results section of 9 publications.

Device-related adverse events were underreported. Adverse events from CRT are not mentioned in 8 of the publication abstracts. Unsuccessful initial CRT implant rates are described in all publications, with a mean 8% of patients having an unsuccessful implant (range, 1%-14%). Procedural complication rates and a description of the complications are provided in only 6 publications, with a mean 15.7% of patients experiencing complications (range, 4%-28%). Three additional publications provide partial descriptions of procedural complications. Postimplant complication data are clearly reported in only 4 publications, with a mean 26.1% of patients experiencing complications (range, 7%-46%). In 1 publication, annualized complication event rates are noted but without describing specific complications. In 1 publication, composite procedural and postprocedural complications rates are reported. In all 10 publications, only 1 table of a total 51 tables and figures is used to describe adverse events.

Trial interpretation in all publications appeared to be biased in favor of CRT efficacy. Six of the publications contain no mention of device adverse effects in the discussion section. The other 4 publications mention CRT adverse effects but do not include any further commentary such as a comparison of the percentage of patients who improved with CRT therapy vs the percentage who experienced device adverse effects.
any discussion of how the presence of adverse effects should influence device use, or any comment that CRT benefits are likely to be less in clinical practice than in a randomized trial.

In the MIRACLE (Multicenter InSync Randomized Clinical Evaluation), MIRACLE ICD (Multicenter InSync ICD Randomized Clinical Evaluation), MIRACLE ICD II, and REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trials, patients were randomized only after successful device implantation with no discussion of how such a design reduces the ability to generalize results. The CONTAK CD study was changed from a crossover to a parallel design, and the primary end point altered with no discussion of the impact on trial analysis.

Comment. Cardiac resynchronization therapy is a relatively new treatment for heart failure that was first approved by the US Food and Drug Administration in 2001. This approval is based on the pivotal clinical trials that discuss risks and benefits of CRT.

My analysis of these trials and publications suggests that rhetorical techniques were used to emphasize the benefits and minimize the harms of CRT. My recent analysis of implantable defibrillator primary prevention trial reports led to similar conclusions. In fact, the use of specific rhetorical strategies was strikingly similar in the CRT and ICD reports, particularly the tendency to underreport complications and to ignore device complications in discussion sections.

This use of rhetoric has likely contributed to an overly optimistic view of CRT and ICD benefits and may help to explain why cardiac devices are frequently implanted in patient groups that were excluded from device trials, such as patients older than 80 years, and why device implant complication rates in the Medicare population are higher than expected.

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9. Young JB, Abraham WT, Smith AL, et al; Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined car-
Etiology of Febrile Episodes in Patients With Acute Myeloid Leukemia: Results From the Hema e-Chart Registry

Several studies have attempted to analyze the epidemiologic patterns of infectious complications in patients with acute myeloid leukemia (AML), although the power of these studies was frequently limited by their retrospective design.\(^1,2\)

A lively debate currently focuses on the potential of Internet-based software and associated technologies, such as electronic medical records, to simplify reporting, to improve database content, and to optimize the timing of interventions.\(^3,4\) Because a well-designed surveillance system is essential for the systematic collection, analysis, and dissemination of data, we designed an electronic medical record system.

**Methods.** From March 2007 to March 2009, all newly diagnosed AML candidates for conventional chemotherapy from 17 hematology units in Italy were enrolled in the Hema e-Chart and followed-up prospectively to assess the incidence of febrile events (FEs). Data were entered prospectively into electronic case report forms using previously described methods.\(^5\) Enrolling a patient in the Hema e-Chart registry had no impact on the standard clinical practice of each hematology unit.

**Results.** In the 747 adults with AML treated with conventional chemotherapy, 528 FEs were registered: 208 of them (39.3%) were classified as fever of unidentified origin (FUO), while there were 21 (3.9%) disease/treatment-related fevers (DTRF). The remaining 299 FEs (56.6%) were associated with infections.

Bacterial infections were identified in 223 cases. After we excluded 20 cases of mixed infections, 203 patients had a bacterial infection only. Thirty-one patients had possible bacterial pneumonia (ie, no etiologic agents were isolated and the patients were successfully treated with antibiotic therapy only). Overall, 192 patients had a microbiologically proven bacterial infection, and in 20 of them, 1 or more other agent was identified as a concomitant cause of fever. Among the 192 FEs with an identified bacterial agent, 147 infections were caused by a single agent (83 from gram-positive [36.5%] and 64 from gram-negative [43.5%] bacteria). Two or more bacterial agents were associated in 45 episodes.

Of 528 patients, 93 invasive fungal diseases (IFDs) were identified (17.6%), with an incidence of 12.4% in the examined population. Molds and yeasts were detected in 80 (86%) and 12 (13%) cases, respectively. Invasive fungal diseases were proven in 24 cases (25.7%), probable in 20 cases (21.6%), and possible in 49 cases (52.7%). In all cases of possible IFD, the suspected etiological agent was a mold. Proven or probable cases comprised 12 yeast (all *Candida* spp), 31 mold (all *Aspergillus* spp), and 1 dimorphic fungus (*Histoplasma capsulatum*) infection. In 73 of 93 IFDs, a single fungal infection was detected; in the remaining 20 cases, a mixed infection was diagnosed. Viral infections resulted to be the cause of fever in 4 cases only, with a very low incidence in the overall population (4 of 747 AML cases [0.5%]).

During the study period, only 34 FEs were recognized as the cause of death, with an overall incidence in AML cases of 6.4% (34 of 528). The highest attributable mortality rate (11 of 73 [15.1%]) was observed in the IFD group. Overall, 10 deaths were registered in the FUO group (4.8%), 10 in the bacterial group (4.9%), and 3 in the mixed-infection group (14.3%). No deaths were observed either in the viral infection or in the DTRF group. Of 21 patients with mixed infection, 3 patients died (attributable mortality rate [AMR], 14.3%) (**Table**).

**Comment.** Our study shows that FUO and fungal and bacterial infections were most frequently observed in AML cases. The etiology of FUO, detected in over 38% of episodes, remains unknown despite the use of currently avail-

**Table. Distribution of FEs Among 747 Patients With AML**

<table>
<thead>
<tr>
<th>Event</th>
<th>FE, No. (%)</th>
<th>AMR, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FUO</td>
<td>208 (39.4)</td>
<td>10 (4.8)</td>
</tr>
<tr>
<td>DTRF</td>
<td>21 (4.0)</td>
<td>0</td>
</tr>
<tr>
<td>Bacterial</td>
<td>203 (38.4)</td>
<td>10 (4.9)</td>
</tr>
<tr>
<td>Fungal</td>
<td>73 (13.8)</td>
<td>11 (15.1)</td>
</tr>
<tr>
<td>Viral</td>
<td>2 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Mixed</td>
<td>21 (4.0)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Fungal and bacterial</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Bacterial and viral</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fungal and viral</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AMR, attributable mortality rate; DTRF, disease/treatment-related fever; FE, febrile events; FUO, fever of unidentified origin.