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Reply: The Benefit of Cardiac Resynchronization Therapy Is Not Hindered by the Number of Comorbidities

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We appreciate the thoughtful commentary by Dr. Barra and colleagues in response to our analysis of cardiac resynchronization therapy defibrillator (CRT-D) over implantable cardioverter-defibrillator (ICD) alone in patients with multiple comorbidities enrolled in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). Our findings support the ongoing use of CRT-D in qualifying ICD-eligible patients across a range of common comorbidities (1). Dr. Barra and colleagues have done a complementary analysis demonstrating a similar finding in a large "real-world" population in a clinical practice registry. This is important for 2 major reasons. First, the patients and health care in clinical trials are often different from those seen in clinical practice. Second, registry data from current clinical practice incorporate contemporary devices, programming, and patient selection. Thus, the data from Dr. Barra and colleagues add external validity to our findings (1).

As in our analysis, Dr. Barra and colleagues evaluated the association of CRT response with 6 common comorbidities including some comorbidities not incorporated in our analysis (i.e., previous malignancy) and others that were similar but not identical (e.g., atrial fibrillation vs. atrial arrhythmias). Despite these differences, similar patterns emerged. Unsurprisingly, patients with the greatest comorbidity burden had the highest mortality. Dr. Barra and colleagues found no interaction between comorbidity burden and response to CRT in patients with ≤2 comorbidities, whereas attenuated response was seen in those with ≥3 comorbidities. However, nearly 50% of the cohort assessed by Dr. Barra and colleagues had New York Association functional class III or IV heart failure, whereas MADIT-CRT enrolled patients with New York Association functional class I or II only 2, 3; this difference may explain the attenuated response.

Traditional randomized clinical trials serve an essential role in the evaluation of medical therapies, but these trials are often limited in providing information on diverse patient populations in a real-world setting. Real-world data from sources such as electronic health records, clinical registries, claims databases, and others can therefore complement and enrich our understanding (4). Until data from clinical trials and clinical practice can be

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seamlessly acquired, integrated, and compared, post hoc analyses like ours and analyses of clinical practice registries like the one by Dr. Barra and colleagues can provide meaningful data to help inform clinical decision making.

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