

Online Supplementary Appendices

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Appendix S1.

Equilibrating the KCCQ and MLWHF to define a responder definition for the MLWHF

While there are well established thresholds for what is a clinically meaningful changes in the KCCQ scores, evidence as to what is meaningful in the MLWHF is more sparse.

Bennet et al did report -4.8 +/- 17.43 point change as associated with a minimal clinical change but this was in a small sample (n=165) and given the very high standard deviation was felt to be unreliable.[3] For this reason we attempted to estimate what a 5, 10, and 15 point change in KCCQ at 3 months would be for the MLWHF.

A regression analysis yielded the equation:

$MLWHF \text{ change at 3 months} = KCCQ \text{ change at 3 months} * (-0.74902) - 2.92430$

Using this equation the following assumptions were created:

0 point change in KCCQ = -2.92430 point change in MLWHF

5 point change in KCCQ = -6.6694 point change in MLWHF

10 point change in KCCQ = -10.4145 point change in MLWHF

20 point change in KCCQ = -17.9047 point change in MLWHF

Table S1. Quality of Life Measurements and Time points of Collection by Trial.

| | CARE- HF n = 813 | MIRACLE n = 541 | MIRACLE- ICD n = 555 | RAFT n = 1798 | REVERSE n = 610 | Total n = 4317 |
|-----------------------|---------------------------------|----------------------------|-------------------------------------|--------------------------|----------------------------|---------------------------|
| KCCQ at 3 months | 0 | 0 | 0 | 0 | 514 | 514 |
| KCCQ at 6 months | 0 | 0 | 0 | 0 | 512 | 512 |
| KCCQ at 9 months | 0 | 0 | 0 | 0 | 0 | 0 |
| KCCQ at 12 months | 0 | 0 | 0 | 0 | 507 | 507 |
| KCCQ at 15 months | 0 | 0 | 0 | 0 | 0 | 0 |
| KCCQ at 18 months | 0 | 0 | 0 | 0 | 162 | 162 |
| MLWHF at 3 months | 658 | 507 | 525 | 1450 | 576 | 3716 |
| MLWHF at 6 months | 0 | 480 | 509 | 1574 | 574 | 3137 |
| MLWHF at 9 months | 0 | 0 | 260 | 895 | 0 | 1155 |
| MLWHF at 12 months | 0 | 363 | 423 | 1528 | 567 | 2881 |
| MLWHF at 15 months | 0 | 0 | 0 | 729 | 0 | 729 |
| MLWHF at 18 months | 546 | 144 | 238 | 1334 | 222 | 2484 |

Values are shown as absolute numbers. MLWHF = Minnesota Living with Heart Failure;
KCCQ = Kansas City cardiomyopathy questionnaire

Table S2. Characteristics of patients deceased prior to 3 months versus those in analytic cohort.

| | Died prior to 3 months n=98 | Study Cohort n=3614 | p-value |
|---------------------------|--|--------------------------------|----------------|
| Age (y) | 67.6 ± 10.3 | 65.2 ± 10.3 | 0.020 |
| Male | 80 (81.6%) | 2827 (78.2%) | 0.419 |
| QRS width (ms) | 160.4 ± 23.2 | 162.2 ± 24.2 | 0.454 |
| Left bundle branch block | 74 (77.1%) | 2722 (75.8%) | 0.764 |
| CRT | 47 (48.0%) | 1890 (52.3%) | 0.396 |
| Implantable defibrillator | 48 (49%) | 1890 (52.3%) | <0.001 |
| NYHA Class | | | |
| II | 21 (21.4%) | 1819 (50.3%) | <0.001 |
| III | 60 (61.2%) | 1685 (46.6%) | |
| IV | 17 (17.3%) | 110 (3.0%) | |
| Left ventricular EF | 22 ± 7 | 24 ± 6 | 0.004 |
| Ischemic cardiomyopathy | 72 (73.5%) | 2100 (58.1%) | 0.002 |
| Diabetes mellitus | 33 (42.1%) | 888 (30.0%) | 0.022 |
| MLWHF at baseline | 57.5 ± 23.5 | 42.5 ± 23.5 | <0.001 |
| ACE-I/ARB | 81 (84.4%) | 3445 (95.3%) | <0.001 |
| Beta blocker | 54 (55.1%) | 2841 (78.6%) | <0.001 |

Table S3. Characteristics of patients with missing QoL data versus those in the analytic cohort.

| | Missing QoL Data n=505 | Study Cohort n=3614 | p-value |
|----------------------------|---------------------------------------|--------------------------------|----------------|
| Age (y) | 65.4 ± 9.9 | 65.2 ± 10.3 | 0.597 |
| Male | 404 (80.0%) | 2827 (78.2%) | 0.363 |
| QRS width (ms) | 160.7 ± 24.7 | 162.2 ± 24.2 | 0.200 |
| LBBB | 381 (77.6%) | 2722 (75.8%) | 0.371 |
| CRT | 254 (50.3%) | 1890 (52.3%) | 0.399 |
| ICD | 364 (72.1%) | 1890 (52.3%) | 0.003 |
| NYHA Class | | | |
| II | 287 (56.8%) | 1819 (50.3%) | <0.001 |
| III | 192 (38.0%) | 1685 (46.6%) | |
| IV | 19 (3.8%) | 110 (3.0%) | |
| Left ventricular EF | 24 ± 6 | 24 ± 6 | 0.107 |
| Ischemic cardiomyopathy | 293 (58.0%) | 2100 (58.1%) | 0.970 |
| Diabetes mellitus | 150 (33.2%) | 888 (30.0%) | 0.164 |
| MLWHF at baseline | 40.0 ± 25.0 | 42.5 ± 23.5 | 0.05 |
| ACE-I/ARB | 472 (95.4%) | 3445 (95.3%) | 0.976 |
| Beta blocker | 420 (83.2%) | 2841 (78.6%) | 0.018 |

Table S4. Baseline characteristics of Cardiac Resynchronization Therapy vs. control

| | CRT N = 1890 | Control N = 1724 | p-value |
|-------------------------|-----------------|---------------------|---------|
| Male | 1486 (78.6%) | 1341 (77.8%) | 0.541 |
| Age | 65.0 ± 10.3 | 65.3 ± 10.3 | 0.413 |
| QRS width (ms) | 161.6 ± 24.2 | 162.9 ± 24.2 | 0.129 |
| LBBB | 1441 (76.6%) | 1281 (74.9%) | 0.235 |
| MLWLHF | 42.2 ± 23.5 | 42.5 ± 23.2 | 0.741 |
| Systolic Blood Pressure | 118.3 ± 18.1 | 117.8 ± 17.7 | 0.443 |
| Medical history | | | |
| ICD | 1246 (65.9%) | 1123 (65.1%) | 0.619 |
| NYHA II | 987 (52.2%) | 832 (48.3%) | 0.017 |
| NYHA IV | 61 (3.2%) | 49 (2.9%) | 0.500 |
| Ejection fraction | 24.0 ± 6.3 | 24.0 ± 6.1 | 0.795 |
| Ischemic CM | 1112 (58.8%) | 988 (57.3%) | 0.352 |
| Diabetes | 456 (29.0%) | 432 (31.0%) | 0.229 |
| Baseline Medications | | | |
| ACE/ARB Usage | 1805 (95.5%) | 1640 (95.1%) | 0.593 |
| Beta blockers | 1518 (80.3%) | 1323 (76.7%) | 0.008 |
| Spironolactone | 752 (42.3%) | 725 (45.2%) | 0.091 |

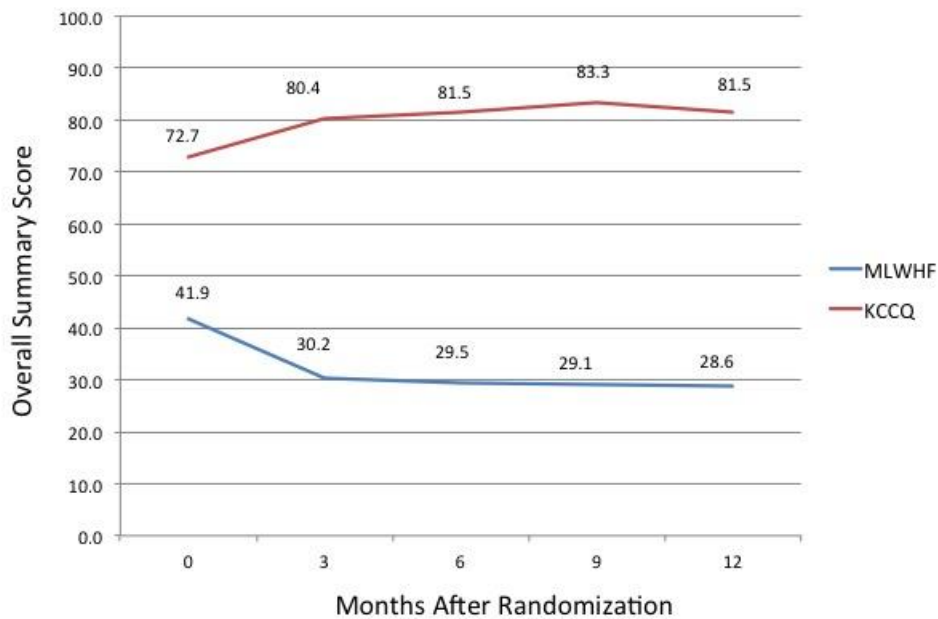
Values are shown as absolute numbers (percentages), mean ± SD. NYHA, New York Heart Association; MLWHF, Minnesota Living with Heart Failure; ACE-I, angiotensin converting enzyme-inhibitor; ARB, angiotensin II receptor blocker

Table S5. Clinically meaningful changes in quality of life of CRT versus control

| QOL Change Category | CRT n=1890 | Control n=1724 | p-value |
|----------------------------|-----------------------|---------------------------|----------------|
| Large deterioration | 7.6 | 10.0 | <0.001 |
| Moderate deterioration | 6.5 | 11.3 | |
| Small deterioration | 7.0 | 7.3 | |
| No change | 16.5 | 19.2 | |
| Small improvement | 9.5 | 8.8 | |
| Moderate improvement | 14.1 | 12.9 | |
| Large improvement | 38.7 | 30.6 | |

Values are shown as percentages. CRT, cardiac resynchronization therapy

Figure S1. Quality of Life Over time measure by Minnesota Living With Heart Failure and Kansas City Cardiomyopathy Questionnaire



Values shown as mean overall scores. MLWHF = Minnesota living with heart failure; KCCQ = Kansas City Cardiomyopathy Questionnaire.

*The KCCQ overall summary scored is 0-100 with higher numbers reflecting better quality of life. The MLWHF is scored 0-105 with lower scores representing better quality of life.

Figure S2. Observed versus predicted probability of no change in quality of life at 12 months

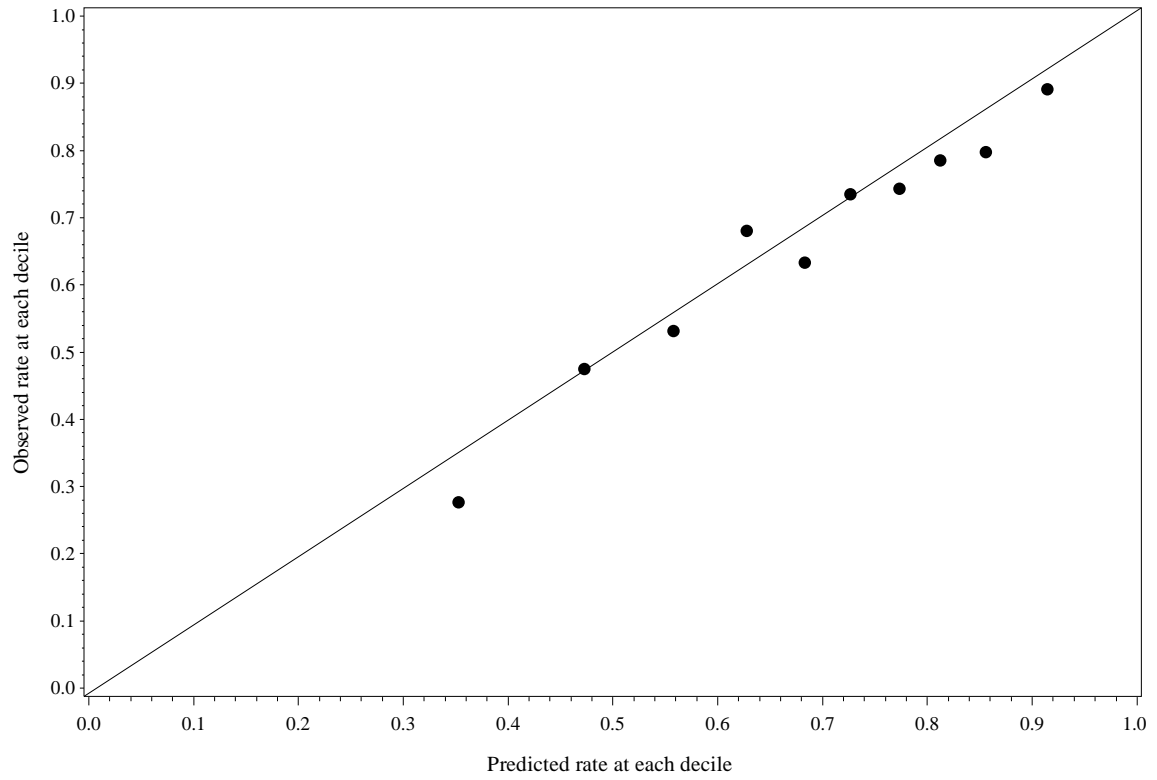


Figure S3. Observed versus predicted probability of a small improvement in quality of life at 12 months

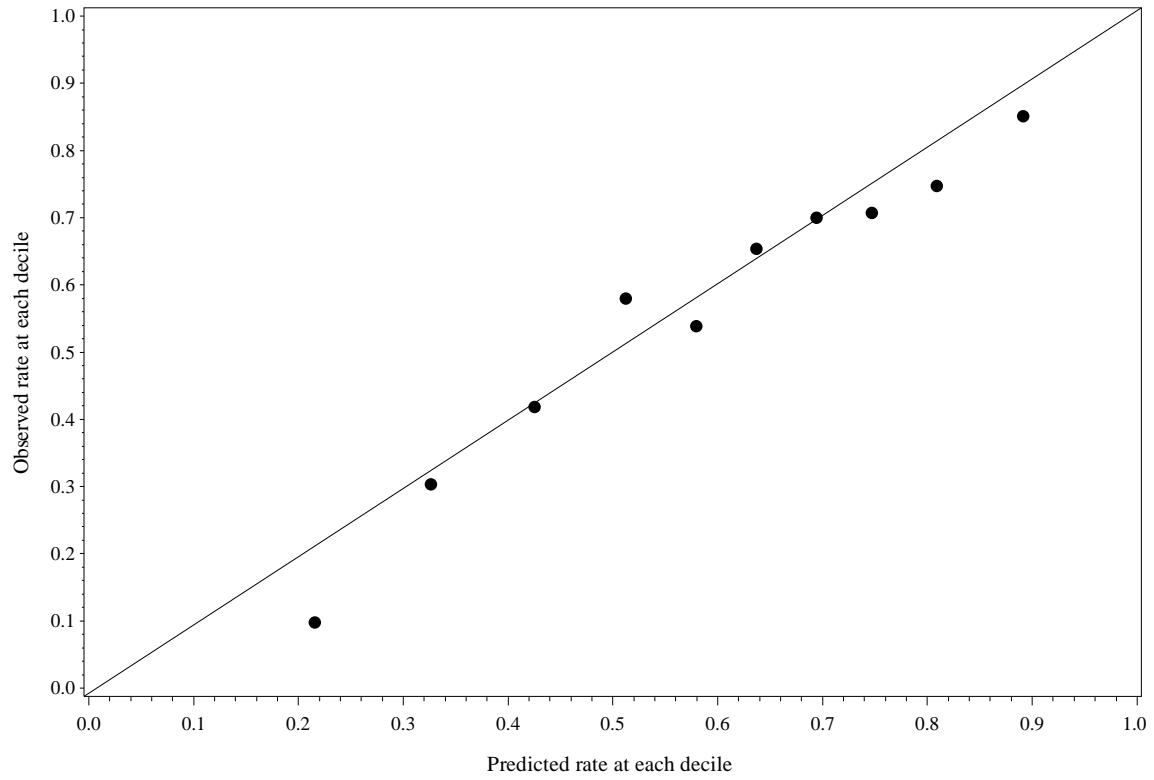


Figure S4. Observed versus predicted probability of a moderate improvement in quality of life at 12 months

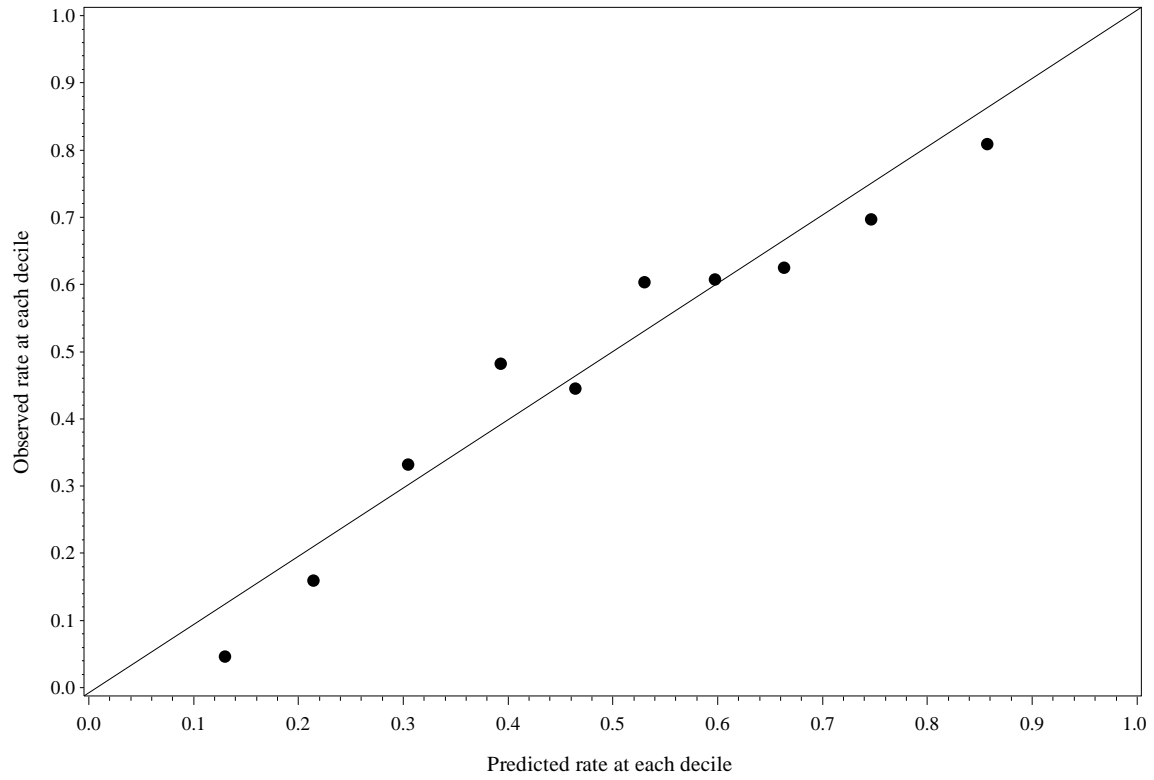


Figure S5. Observed versus predicted probability of a large improvement in quality of life at 12 months

