**Cost-Effectiveness of Biventricular Pacing versus Right Ventricular Pacing in Patients with Atrioventricular Block and Reduced Ejection Fraction: Data Analysis based on the BLOCK HF**

**Supplementary Appendix**

**Supplementary Table S1**: Additional Input Parameters (Adverse Events, Health-Related Quality of Life and Device Longevity)

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Value** | **Source** |
| *Lead displacement rates* | | |
| RV-P | 2.10% | BLOCK-HF data on file |
| BiV-P | 3.30% | BLOCK-HF data on file |
| RV-D | 4.00% | BLOCK-HF data on file |
| BiV-D | 1.90% | BLOCK-HF data on file |
| *Other device related surgery rates* | | |
| RV-P | 3.60% | BLOCK-HF data on file |
| BiV-P | 1.60% | BLOCK-HF data on file |
| RV-D | 4.00% | BLOCK-HF data on file |
| BiV-D | 5.60% | BLOCK-HF data on file |
| *NYHA class specific utility decrements* | | |
| NYHA I | 0.000 | Gohler et al. 2009 |
| NYHA II | -0.071 | Gohler et al. 2009 |
| NYHA III/IV | -0.161 | Gohler et al. 2009 |
| HF related hospitalization | -0.100 | Assumption |
| Other hospitalization | -0.100 | Assumption |
| *Parameters used to model time to first battery replacement (ICD)* | | |
| Lambda | 1.39x10-7 | NICE submission |
| Gamma | 1.943 | NICE submission |
| *Parameters used to model time to first battery replacement (CRT-P)* | | |
| Lambda | 6.24x10-7 | NICE submission |
| Gamma | 1.689 | NICE submission |
| *Parameters used to model time to first battery replacement (CRT-D)* | | |
| Lambda | 1.92x10-7 | NICE submission |
| Gamma | 1.935 | NICE submission |

**Supplementary Table S2**: Cost Input Parameters

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Value** | | **Source** |
| *Total Device Cost* | | | |
| CRT-P | $16,545.23 | | Medicare FY2014 |
| CRT-D | $35,588.58 | | Medicare FY2014 |
| ICD | $35,120.26 | | Medicare FY2014 |
| RV pacemaker | $13,638.40 | | Medicare FY2014 |
| LV lead | $0.00 | | Medicare FY2014 |
| *Other Cost* | | | |
| Physician payment (CRT-D) | $98.00 | | Medicare FY2014 |
| Physician payment (CRT-P) | $98.00 | | Medicare FY2014 |
| HF Admission/Re-Admission | $6,392.14 | | Medicare FY2014 |
| Total Admission/Re-Admission | $6,511.46 | | Medicare FY2014 |
| ED visit | $359.00 | | Medicare FY2014 |
| *Drug Cost* | | | |
| ACE-Inhibitors | | $33.75 | Medicare FY2014 |
| ARBs | | $91.06 | Medicare FY2014 |
| Beta blockers | | $54.48 | Medicare FY2014 |
| Vasodilators/Nitrates | | $1.22 | Medicare FY2014 |
| Aldosterone receptor antagonists | | $92.77 | Medicare FY2014 |
| Spironolactone | | $0.00 | Medicare FY2014 |
| Diuretics | | $9.73 | Medicare FY2014 |
| Digoxin | | $0.00 | Medicare FY2014 |
| *Adverse Event Cost* | | | |
| Lead dislodgement | $5,980.10 | | Medicare FY2014 |
| *Battery Replacement Cost* | | | |
| Battery upgrade (CRT-D) | $35,120.26 | | Medicare FY2014 |
| Battery upgrade (CRT-P) | $13,638.40 | | Medicare FY2014 |
| Battery upgrade (ICD) | $35,120.26 | | Medicare FY2014 |
| Battery upgrade (RV) | $13,638.40 | | Medicare FY2014 |

**Supplementary Table S3**: Statistical Models Used for All-Cause Mortality; Gompertz function in Model “Base-Case”

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All Patients** | | | | | |  | **Defibrillator Patients** | | | | | |  | **Non-Defibrillator Patients** | | | | | |
|  | **Model 1** | | | **Model 2** | | |  | **Model 1** | | | **Model 2** | | |  | **Model 1** | | | **Model 2** | | |
| **Event** | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |
| *Weibull Function* | | | | | | | | | | | | | | | | | | | | |
| **Intercept** | **-9.311** | **N/A** | **<0.001** | **-9.792** | **N/A** | **<0.001** |  | **-7.322** | **N/A** | **<0.001** | **-8.069** | **N/A** | **<0.001** |  | **-10.069** | **N/A** | **<0.001** | **-10.452** | **N/A** | **<0.001** |
| BiV Usage | -0.251 | 0.78 | 0.13 | -0.224 | 0.8 | 0.146 |  | -0.228 | 0.8 | 0.424 | -0.244 | 0.78 | 0.395 |  | -0.265 | 0.77 | 0.149 | -0.227 | 0.8 | 0.217 |
| **Starting age (per year)** | **0.039** | **1.04** | **<0.001** | **0.033** | **1.03** | **<0.001** |  | 0.031 | 1.03 | 0.086 | 0.024 | 1.02 | 0.181 |  | **0.04** | **1.04** | **<0.001** | **0.034** | **1.03** | **<0.001** |
| Male gender | 0.303 | 1.35 | 0.114 | 0.288 | 1.33 | 0.134 |  | -0.095 | 0.91 | 0.816 | 0 | 1 | 0.999 |  | 0.407 | 1.5 | 0.065 | 0.381 | 1.46 | 0.086 |
| Baseline NYHA I | **-0.62** | **0.54** | 0.01 | -0.199 | 0.82 | 0.433 |  | -0.414 | 0.66 | 0.323 | -0.002 | 1 | 0.996 |  | **-0.75** | **0.47** | **0.013** | -0.343 | 0.71 | 0.282 |
| Baseline NYHA III | **0.699** | **2.01** | <0.001 | 0.269 | 1.31 | 0.128 |  | 0.422 | 1.53 | 0.188 | -0.153 | 0.86 | 0.651 |  | **0.827** | **2.29** | **<0.001** | **0.472** | **1.6** | **0.022** |
| NYHA II | N/A | N/A | N/A | **0.731** | **2.08** | **0.04** |  | N/A | N/A | N/A | 0.938 | 2.55 | 0.22 |  | N/A | N/A | N/A | 0.639 | 1.89 | 0.116 |
| NYHA III | N/A | N/A | N/A | **1.773** | **5.89** | **<0.001** |  | N/A | N/A | N/A | **2.176** | **8.81** | **0.005** |  | N/A | N/A | N/A | **1.616** | **5.03** | **<0.001** |
| 2nd degree AV block | -0.014 | 0.99 | 0.947 | 0.081 | 1.08 | 0.703 |  | -0.114 | 0.89 | 0.743 | 0.006 | 1.01 | 0.986 |  | 0.082 | 1.09 | 0.771 | 0.162 | 1.18 | 0.565 |
| 3rd Degree AV block | -0.014 | 0.99 | 0.947 | 0.083 | 1.09 | 0.691 |  | -0.19 | 0.83 | 0.595 | -0.139 | 0.87 | 0.702 |  | 0.113 | 1.12 | 0.676 | 0.21 | 1.23 | 0.441 |
| LVEF >35% | -0.047 | 0.95 | 0.777 | -0.022 | 0.98 | 0.894 |  | 0.17 | 1.18 | 0.598 | 0.058 | 1.06 | 0.857 |  | -0.161 | 0.85 | 0.532 | -0.135 | 0.87 | 0.601 |
| Gamma | 1.301 | N/A | N/A | 1.247 | N/A | N/A |  | 1.059 | N/A | N/A | 1 | N/A | N/A |  | 1.438 | N/A | N/A | 1.39 | N/A | N/A |
| *Gompertz Function* | | | | | | | | | | | | | | | | | | | | |
| Intercept | -8.887 | N/A | <0.001 | -9.389 | N/A | <0.001 |  | -7.233 | N/A | <0.001 | -8.096 | N/A | <0.001 |  | -9.362 | N/A | <0.001 | -9.704 | N/A | <0.001 |
| BiV Usage | -0.255 | 0.78 | 0.098 | -0.233 | 0.79 | 0.131 |  | -0.226 | 0.8 | 0.427 | -0.243 | 0.78 | 0.396 |  | -0.273 | 0.76 | 0.136 | -0.239 | 0.79 | 0.192 |
| Starting age (per year) | **0.041** | **1.04** | <0.001 | **0.034** | **1.03** | **<0.001** |  | 0.031 | 1.03 | 0.084 | 0.024 | 1.02 | 0.18 |  | **0.044** | **1.04** | <0.001 | **0.036** | **1.04** | <0.001 |
| Male gender | 0.317 | 1.37 | 0.099 | 0.297 | 1.35 | 0.122 |  | -0.103 | 0.9 | 0.801 | -0.004 | 1 | 0.992 |  | 0.424 | 1.53 | 0.055 | 0.396 | 1.49 | 0.075 |
| Baseline NYHA I | **-0.655** | **0.52** | 0.007 | -0.258 | 0.77 | 0.31 |  | -0.419 | 0.66 | 0.318 | -0.006 | 0.99 | 0.99 |  | **-0.802** | **0.45** | 0.008 | -0.432 | 0.65 | 0.175 |
| Baseline NYHA III | **0.703** | **2.02** | <0.001 | 0.284 | 1.33 | 0.107 |  | 0.414 | 1.51 | 0.198 | -0.153 | 0.86 | 0.652 |  | **0.84** | **2.32** | <0.001 | 0.495 | 1.64 | 0.016 |
| NYHA II | N/A | N/A | N/A | **0.705** | **2.02** | **0.047** |  | N/A | N/A | N/A | 0.936 | 2.55 | 0.22 |  | N/A | N/A | N/A | 0.594 | 1.81 | 0.144 |
| NYHA III | N/A | N/A | N/A | **1.728** | **5.63** | **<0.001** |  | N/A | N/A | N/A | **2.171** | **8.76** | **0.005** |  | N/A | N/A | **N/A** | **1.552** | **4.72** | <0.001 |
| 2nd degree AV block | -0.048 | 0.95 | 0.823 | 0.05 | 1.05 | 0.815 |  | -0.114 | 0.89 | 0.744 | 0.007 | 1.01 | 0.985 |  | 0.029 | 1.03 | 0.918 | 0.107 | 1.11 | 0.704 |
| 3rd Degree AV block | -0.02 | 0.98 | 0.924 | 0.076 | 1.08 | 0.717 |  | -0.188 | 0.83 | 0.599 | -0.137 | 0.87 | 0.705 |  | 0.105 | 1.11 | 0.697 | 0.195 | 1.22 | 0.474 |
| LVEF >35% | -0.05 | 0.95 | 0.76 | -0.021 | 0.98 | 0.9 |  | 0.173 | 1.19 | 0.59 | 0.061 | 1.06 | 0.85 |  | -0.152 | 0.86 | 0.553 | -0.127 | 0.88 | 0.624 |
| Gamma | 0.019 | N/A | N/A | 0.016 | N/A | N/A |  | 0.005 | N/A | N/A | 0.001 | N/A | N/A |  | 0.024 | N/A | N/A | 0.022 | N/A | N/A |

Model 1: NYHA class included solely via baseline value; Model 2: NYHA class included as both baseline and current values; N/A: Not applicable; bold values indicate statistically significant coefficients (p<0.05).

**Supplementary Table S4**: Statistical Models Used for Prediction of NYHA Class Patient Allocation over Time (Multinomial Logistic Regression Models)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All Patients** | | |  | **Defibrillator Patients** | | |  | **Non-Defibrillator Patients** | | |
| **Event** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** |
| *NYHA Class I* | | | | | | | | | | | |
| **Intercept** | 0.02 | N/A | **0.837** |  | -0.267 | N/A | **0.694** |  | 0.967 | N/A | **0.023** |
| BiV Usage | -0.218 | 0.8 | 0.289 |  | -0.245 | 0.78 | 0.309 |  | -0.192 | 0.83 | 0.43 |
| **ln(time)a** | **-0.229** | **0.8** | **0.002** |  | -0.212 | 0.81 | 0.163 |  | **-0.244** | **0.78** | **0.003** |
| BiV \* ln(time)a | 0.157 | 1.17 | 0.246 |  | 0.205 | 1.23 | 0.187 |  | 0.141 | 1.15 | 0.328 |
| Starting age (per year) | **-0.022** | **0.98** | <0.001 |  | **-0.02** | **0.98** | 0.023 |  | **-0.023** | **0.98** | **<0.001** |
| Male gender | 0.156 | 1.17 | 0.371 |  | 0.112 | 1.12 | 0.755 |  | **0.263** | **1.3** | **0.024** |
| Baseline NYHA I | **1.75** | **5.75** | <0.001 |  | **1.401** | **4.06** | <0.001 |  | **1.956** | **7.07** | <0.001 |
| Baseline NYHA III | **-0.343** | **0.71** | 0.016 |  | -0.264 | 0.77 | 0.355 |  | -0.367 | 0.69 | 0.056 |
| 2nd degree AV block | **0.261** | **1.3** | 0.055 |  | 0.343 | 1.41 | 0.075 |  | -0.229 | 0.8 | 0.191 |
| 3rd Degree AV block | **0.319** | **1.38** | 0.016 |  | 0.311 | 1.36 | 0.131 |  | -0.106 | 0.9 | 0.517 |
| LVEF >35% | -0.033 | 0.97 | 0.319 |  | -0.149 | 0.86 | 0.44 |  | **-0.542** | **0.58** | <0.001 |
| *NYHA Class III* | | | | | | | | | | | |
| **Intercept** | -1.578 | N/A | <0.001 |  | -2.195 | N/A | <0.001 |  | -1.074 | N/A | 0.014 |
| BiV Usage | **-0.401** | **0.67** | 0.039 |  | -0.15 | 0.86 | 0.534 |  | **-0.554** | **0.57** | <0.001 |
| **ln(time)a** | 0.099 | 1.1 | 0.406 |  | 0.145 | 1.16 | 0.28 |  | 0.075 | 1.08 | 0.767 |
| BiV \* ln(time)a | **0.224** | **1.25** | **0.023** |  | 0.195 | 1.22 | 0.188 |  | **0.261** | **1.3** | **0.002** |
| Starting age (per year) | **0.008** | **1.01** | 0.056 |  | **0.018** | **1.02** | 0.022 |  | 0.006 | 1.01 | 0.197 |
| Male gender | 0.073 | 1.08 | 0.123 |  | -0.386 | 0.68 | 0.053 |  | 0.165 | 1.18 | 0.097 |
| Baseline NYHA I | **-0.64** | **0.53** | **<0.001** |  | **-0.779** | **0.46** | **<0.001** |  | **-0.599** | **0.55** | **<0.001** |
| Baseline NYHA III | **1.82** | **6.17** | <0.001 |  | **1.935** | **6.93** | <0.001 |  | **1.74** | **5.7** | **<0.001** |
| 2nd degree AV block | **-0.33** | **0.72** | 0.009 |  | **-0.462** | **0.63** | 0.008 |  | **-0.376** | **0.69** | 0.004 |
| 3rd Degree AV block | **-0.216** | **0.81** | 0.045 |  | -0.101 | 0.9 | 0.548 |  | **-0.328** | **0.72** | 0.009 |
| LVEF >35% | -0.045 | 0.96 | 0.443 |  | 0.516 | 1.68 | 0.001 |  | **-0.305** | **0.74** | 0.021 |

a: time measured in units of six months; Bold values indicate statistically significant coefficients (p<0.05).

**Supplementary Table S5**: Statistical Models Used for Prediction of Heart Failure-Related Hospitalization Rates

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All Patients** | | | | | |  | **Defibrillator Patients** | | | | | |  | **Non-Defibrillator Patients** | | | | | |
|  | **Model 1** | | | **Model 2** | | |  | **Model 1** | | | **Model 2** | | |  | **Model 1** | | | **Model 2** | | |
| **Event** | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** | **Coefficient** | **RRR** | ***p*-Value** |
| *Weibull Function* | | | | | | | | | | | | | | | | | | | | |
| Intercept | -2.83 | N/A | 0.951 | **-2.994** | **N/A** | **<.0001** |  | **-2.813** | **N/A** | **0.002** | **-3.064** | **N/A** | **<.0001** |  | **-2.912** | **N/A** | **<.0001** | **-3.075** | **N/A** | **<.0001** |
| BiV Usage | -0.091 | 0.91 | 0.294 | -0.073 | 0.93 | 0.311 |  | -0.009 | 0.99 | 0.964 | -0.031 | 0.97 | 0.495 |  | -0.121 | 0.89 | 0.393 | -0.091 | 0.91 | 0.227 |
| NYHA I | -0.81 | 0.44 | 0.052 | **-0.755** | **0.47** | 0.035 |  | -0.767 | 0.46 | 0.08 | -0.644 | 0.53 | 0.648 |  | **-0.832** | **0.44** | **0.004** | **-0.79** | **0.45** | **0.041** |
| NYHA III | 1.049 | 2.85 | 0.768 | 0.957 | 2.6 | 0.009 |  | **0.851** | **2.34** | **<.0001** | 0.769 | 2.16 | 0.319 |  | **1.16** | **3.19** | **<.0001** | **1.072** | **2.92** | **0.011** |
| Age (per year) | **-0.003** | **1** | 0.063 | -0.002 | 1 | 0.958 |  | 0.001 | 1 | 0.908 | 0.002 | 1 | 0.269 |  | **-0.003** | **1** | 0.613 | -0.003 | 1 | 0.625 |
| Male gender | **0.211** | **1.23** | 0.639 | 0.188 | 1.21 | 0.415 |  | 0.069 | 1.07 | 0.813 | 0.07 | 1.07 | 0.731 |  | **0.267** | **1.31** | 0.113 | **0.244** | **1.28** | 0.427 |
| 2nd Degree AV block | **-0.015** | **0.98** | **0.038** | 0.015 | 1.01 | 0.379 |  | -0.223 | 0.8 | 0.339 | -0.126 | 0.88 | 0.856 |  | 0.166 | 1.18 | 0.431 | 0.161 | 1.17 | 0.23 |
| 3rd Degree AV block | **-0.251** | **0.78** | **0.074** | -0.179 | 0.84 | 0.215 |  | **-0.568** | **0.57** | **0.022** | **-0.438** | **0.65** | **0.486** |  | -0.032 | 0.97 | 0.879 | **0.014** | **1.01** | 0.126 |
| LVEF >35% | -0.147 | 0.86 | 0.717 | -0.136 | 0.87 | 0.433 |  | 0.008 | 1.01 | 0.973 | -0.031 | 0.97 | 0.557 |  | -0.273 | 0.76 | 0.165 | -0.21 | 0.81 | 0.287 |
| Previous HF Hosp. | N/A | N/A | N/A | **1.386** | **4** | **<.0001** |  | N/A | N/A | N/A | **1.57** | **4.81** | **<.0001** |  | N/A | N/A | N/A | **1.254** | **3.5** | **<.0001** |

Model 1: excluding previous HF hospitalization as a predictor variable; Model 2; Including previous HF hospitalization as a predictor variable; Bold values indicate statistically significant coefficients (p<0.05).

**Supplementary Table S6**: Statistical Models Used for Emergency Department (ED) and Clinic Visit Rates

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All Patients** | | |  | **Defibrillator Patients** | | |  | **Non-Defibrillator Patients** | | |
| **Event** | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** |  | **Coefficient** | **RRR** | ***p*-Value** |
| *ED Visits* | | | | | | | | | | | |
| **Intercept** | **-3.923** | **N/A** | **<.0001** |  | **-4.951** | **N/A** | **<0.001** |  | **-3.613** | **N/A** | **<0.001** |
| BiV Usage | **-0.368** | **0.69** | **0.022** |  | -0.175 | 0.84 | 0.528 |  | **-0.434** | **0.65** | **0.025** |
| **NYHA I** | **-1.153** | **0.32** | **<0.001** |  | **-2.418** | **0.09** | **0.019** |  | **-0.886** | **0.41** | **0.004** |
| NYHA III | **0.837** | **2.31** | **<.0001** |  | 0.454 | 1.57 | 0.11 |  | **1.05** | **2.86** | **<0.001** |
| Age (per year) | 0.012 | 1.01 | 0.146 |  | 0.028 | 1.03 | 0.111 |  | 0.007 | 1.01 | 0.461 |
| Male gender | 0.127 | 1.14 | 0.508 |  | 0.133 | 1.14 | 0.739 |  | 0.189 | 1.21 | 0.172 |
| 2nd degree AV block | 0.169 | 1.18 | 0.435 |  | 0.2 | 1.22 | 0.539 |  | 0.177 | 1.19 | 0.938 |
| 3rd Degree AV block | -0.153 | 0.86 | 0.482 |  | -0.389 | 0.68 | 0.281 |  | -0.064 | 0.94 | 0.512 |
| LVEF >35% | -0.278 | 0.76 | 0.097 |  | -0.29 | 0.75 | 0.389 |  | -0.404 | 0.67 | 0.229 |
| *Clinic Visits* | | | | | | | | | | | |
| **Intercept** | **-3.309** | **N/A** | **0.001** |  | **-5.719** | **N/A** | **0.002** |  | **-3.882** | **N/A** | **0.005** |
| BiV Usage | -0.297 | 0.74 | 0.264 |  | -0.665 | 0.51 | 0.111 |  | -0.184 | 0.83 | 0.601 |
| NYHA I | -0.711 | 0.49 | 0.106 |  | -1.165 | 0.31 | 0.156 |  | -0.388 | 0.68 | 0.468 |
| **NYHA III** | **1.092** | **2.98** | **<0.001** |  | 0.562 | 1.75 | 0.186 |  | **1.451** | **4.27** | **<0.001** |
| Age (per year) | -0.018 | 0.98 | 0.14 |  | 0.022 | 1.02 | 0.345 |  | -0.025 | 0.97 | 0.088 |
| Male gender | **1.077** | **2.94** | **0.003** |  | 1.398 | 4.05 | 0.092 |  | **0.865** | **2.37** | **0.045** |
| 2nd degree AV block | -0.507 | 0.6 | 0.17 |  | **-1.189** | **0.3** | **0.027** |  | 0.403 | 1.5 | 0.514 |
| 3rd Degree AV block | -0.065 | 0.94 | 0.846 |  | -0.541 | 0.58 | 0.251 |  | 0.715 | 2.04 | 0.217 |
| LVEF >35% | -0.329 | 0.72 | 0.235 |  | 0.006 | 1.01 | 0.989 |  | -0.089 | 0.92 | 0.864 |

\* Included as a time varying covariate rather than baseline value; Bold values indicate statistically significant coefficients (p<0.05).