**SUPPLEMENTAL MATERIAL**

**Table S1. Treatment Poolability Analysis**

| Variable                                      | No Envelope | Envelope | P-value |
|-----------------------------------------------|-------------|----------|---------|
| Length of hospitalization (days)*             | 16.5        | 21.2     | 0.3422  |
| Number of hospitalizations*                   | 1.5         | 1.9      | 0.1528  |
| HCU intensity†                                 |             |          |         |
| No system removal, had at least one inpatient hospitalization | 5           | 3        | 0.7436  |
| No system removal, no inpatient hospitalization| 2           | 1        |         |
| System removed only, no new system implanted  | 10          | 9        |         |
| System removed, new system implanted          | 27          | 13       |         |

* T-test
† Chi-squared test

**Table S2. Infection Cost Poolability Analysis**

| Cost                          | Pooled   | No Envelope | Envelope | P-value |
|-------------------------------|----------|-------------|----------|---------|
| Medicare FFS                  | $26,867  | $22,891     | $29,730  | 0.14    |
| Medicare Advantage            | $57,978  | $51,890     | $62,361  | 0.25    |
| Hospital                      | $55,547  | $51,171     | $58,697  | 0.60    |
| Patient Medicare FFS          | $2,156   | $2,013      | $2,259   | 0.70    |
| Patient Medicare Advantage    | $1,658   | $1,743      | $1,596   | 0.71    |
Table S3. Infection Diagnosis Codes

| ICD-9 | Infection due to a cardiac device (996.61), Other postoperative infection (998.59), Septicemia (38.0, 38.1, 38.11, 38.12, 38.19, 38.2, 38.3, 38.4, 38.41, 38.42, 38.43, 38.44, 38.49, 38.8, 38.9), Bacteremia (790.7), Endocarditis (421.0, 421.1, 421.9), Infection due to unspecified device (996.60), Candidiasis (112.5), Sepsis (995.91) |
| ICD-10 | Infection due to a cardiac device (T82.7XXA, T82.7XXD, T82.7XXS), Other postoperative infection (T81.4XXA), Sepsis (A40.9, A41.2, A41.01, A41.02, A41.1, A40.3, A41.4, A41.50, A41.3, A41.51, A41.52, A41.53, A41.59, A41.89, A41.9, B37.7), Bacteremia (R78.81), Endocarditis (I33.0, I33.9) |

Table S4. Quality of Life Utilities Derived From EQ-5D Health States

| EQ-5D Assessment | Questionnaires (Subjects) Completed | Mean ± SD | Adjusted Mean 95% CI* | Adjusted Mean Difference 95% CI* | P-value† |
|------------------|-------------------------------------|-----------|------------------------|---------------------------------|----------|
| Baseline         | 67 (67)                             | 0.83 ± 0.14 | 0.83 (0.79-0.87)       | --                              | --       |
| Infection Diagnosis | 31 (31)                             | 0.75 ± 0.19 | 0.75 (0.69-0.80)       | 0.09 (0.03-0.14)               | 0.004    |
| 1-Month Post-Infection | 26 (25)                             | 0.73 ± 0.20 | 0.73 (0.67-0.79)       | 0.10 (0.04-0.17)               | 0.001    |
| 3-Month Post-Infection | 30 (30)                             | 0.77 ± 0.23 | 0.76 (0.70-0.82)       | 0.07 (0.01-0.13)               | 0.02     |
| 6-Month Post-Infection | 42 (41)                             | 0.83 ± 0.15 | 0.81 (0.76-0.86)       | 0.02 (-0.03-0.07)              | 0.423    |

* Adjusted mean and adjusted mean difference from baseline and corresponding 95% confidence intervals from a repeated measures analysis of variance model.
† P-value for comparison to value at baseline.
We explored the change in quality of life using alternative covariance structures that account for the possibility of a higher correlation between quality of life measurements in closer proximity to each other. Here we provide the results using first-order autoregressive covariance structure.

**Table S5.** Quality of Life Utilities Derived From EQ-5D Health States

| EQ-5D Assessment          | Questionnaires (Subjects) Completed | Mean ± SD | Adjusted Mean 95% CI* | Adjusted Mean Difference 95% CI* | P-value† |
|---------------------------|-------------------------------------|-----------|-----------------------|----------------------------------|----------|
| Baseline                  | 67 (67)                             | 0.83 ± 0.14 | 0.84 (0.80-0.88)     | --                               | --       |
| Infection Diagnosis       | 31 (31)                             | 0.75 ± 0.19 | 0.75 (0.70-0.81)     | 0.09 (0.03-0.14)                | 0.003    |
| 1-Month Post-Infection    | 26 (25)                             | 0.73 ± 0.20 | 0.73 (0.66-0.79)     | 0.11 (0.05-0.18)                | 0.001    |
| 3-Month Post-Infection    | 30 (30)                             | 0.77 ± 0.23 | 0.75 (0.69-0.81)     | 0.09 (0.03-0.16)                | 0.006    |
| 6-Month Post-Infection    | 42 (41)                             | 0.83 ± 0.15 | 0.80 (0.75-0.86)     | 0.04 (-0.02-0.10)               | 0.239    |

* Adjusted mean and adjusted mean difference from baseline and corresponding 95% confidence intervals from a repeated measures analysis of variance model.
† P-value for comparison to value at baseline.

These results suggest the same interpretation using either methodology with a slight numeric decrease in the quality of life at the 3- and 6-month values.
Figure S1. QOL Poolability Analysis. QOL at time of infection diagnosis. Box-and-whisker plots represent distribution of data as follows: solid line = median; box = interquartile range; whiskers = minimum and maximum within 1.5 times interquartile range; dots = outliers (outside of 1.5 times interquartile range). QOL = quality of life.
**Figure S2. Patient Costs.** Total patient costs per infection in the US Cohort with Major Infections for Medicare FFS and Medicare Advantage. Box-and-whisker plots represent distribution of data as follows: solid line = median; dashed line = mean; box = interquartile range; whiskers = minimum and maximum within 1.5 times interquartile range; dots = outliers (outside of 1.5 times interquartile range). All currency reflects 2017 US dollars. FFS = fee for service, SD = standard deviation, US = United States
**List of WRAP-IT Investigators and Sites**: listed by number of enrollments (most to least)

| Site # | Site Name                                      | Country | Investigator                                      |
|-------|-----------------------------------------------|---------|---------------------------------------------------|
| 1     | The Lindner Research Center                   | US      | Edward Schloss                                   |
| 2     | Clearwater Cardiovascular & Interventional Consultants | US      | Jose Gallastegui                                 |
| 3     | Saint Thomas Research Institute, LLC          | US      | Robert Andrew (Drew) Pickett                     |
| 4     | Upper Michigan Cardiovascular Associates      | US      | Rudolph Evonich                                  |
| 5     | IUCPQ - Institut Universitaire de Cardiologie et de Pneumologie | Canada  | François Philippon                               |
| 6     | The Newcastle upon Tyne Hospitals             | UK      | Janet McComb                                     |
| 7     | Cardiology Associates of Gainesville          | US      | Steven Roark                                     |
| 8     | Iowa Heart Center, P.C. (West Des Moines)    | US      | Denise Sorrentino                                |
| 9     | Lourdes Cardiology Services Formerly (ACC)    | US      | Darius Sholevar                                  |
| 10    | Cleveland Clinic                              | US      | Khaldoun Tarakji                                 |
| 11    | Hartford Hospital                             | US      | Edmond Cronin                                    |
| 12    | Chula Vista Cardiac Center                    | US      | Brett Berman                                     |
| 13    | AZ Arrhythmia Consultants                     | US      | David Riggio                                     |
| 14    | Policlinico Sant' Orsola - Malpighi           | Italy   | Mauro Biffi / Igor Diemberger                    |
| 15    | Baylor Research Institute (Plano TX)          | US      | Hafiza Khan                                      |
| 16    | WakeMed Heart and Vascular WakeMed Health and Hospitals | US      | Marc Silver                                     |
| 17    | Oklahoma Heart Hospital                       | US      | Jack Collier                                     |
| 18    | MedStar Heart and Vascular Institute          | US      | Zayd Eldadah                                     |
| 19    | Liverpool Heart and Chest Hospital            | UK      | David Justin Wright                              |
| 20    | Minneapolis Heart Institute                   | US      | JoEllyn Moore                                    |
| 21    | Mount Carmel East                             | US      | Kamel Addo                                       |
| 22    | Centennial Heart Cardiovascular Consultants   | US      | R. Chris Jones                                   |
| 23    | University of Pennsylvania                    | US      | Robert Schaller                                  |
| 24    | Amarillo Heart Group                          | US      | Joaquin Martinez-Arraras / Ismaile Abdalla      |
| 25    | Prairie Education & Research Cooperative      | US      | Ziad Issa                                        |
| 26    | Ottawa Heart Institute                        | Canada  | Calum Redpath                                    |
| 27    | Hamot Medical Center / Medicor Associates     | US      | Jean Moubarak                                    |
| 28    | Institute Jantung Negara                      | Malaysia| Surinder Kaur Khelae                             |
| 29    | Rigshospitalet                                | Denmark | Berit Thornvig Philbert                          |
| No. | Hospital/Institution                                      | Country    | Name(s)                                    |
|-----|---------------------------------------------------------|------------|--------------------------------------------|
| 30  | Catharina Ziekenhuis                                    | Netherlands| Timothy Alexander Simmers                  |
| 31  | St. Antonius Ziekenhuis                                | Netherlands| Lucas V.A. Boersma                         |
| 32  | University Hospital of Ioannina                         | Greece     | Panagiotis Korantzopoulos                  |
| 33  | Maine Medical Center                                    | US         | John Love                                  |
| 34  | The Ohio State University                               | US         | Ralph Augustini                            |
| 35  | Haukeland Universitetssjukehus                          | Norway     | Havard Keilegavlen / Svein Faerestrand     |
| 36  | The Valley Hospital                                     | US         | Suneet Mittal                              |
| 37  | Ark-La-Tex Cardiology                                   | US         | Scott Wiggins                              |
| 38  | Hamilton General Hospital                               | Canada     | Jeff Healey                                |
| 39  | Mid America Heart Institute                             | US         | Brian Ramza                                |
| 40  | Jersey Shore University Medical Center                  | US         | Riple Hansalia                             |
| 41  | Stanford Hospital & Clinics                             | US         | Chad Brodt / Paul Wang                     |
| 42  | Universitatsklinikum Krems                              | Austria    | Attila Mihalez                             |
| 43  | Nouvelles Cliniques Nantaises                           | France     | Daniel Gras                                |
| 44  | University of California San Diego                      | US         | Ulrika Maria Birgersdotter-Green           |
| 45  | North Memorial Health Heart & Vascular Center           | US         | Ethan Fruechte / Douglas Hodgkin           |
| 46  | Fletcher Allen Health Care                              | US         | Daniel Lustgarten                          |
| 47  | Lexington Cardiac Research Foundation                  | US         | Gery Tomassoni                             |
| 48  | Central Manchester University Hospitals NHS              | UK         | Fozia Ahmed                                |
| 49  | Sjukhuset i Varberg                                     | Sweden     | Cecilia Rorsman                            |
| 50  | Geisinger Clinic                                        | US         | Pugazhendhi Vijayaraman                   |
| 51  | University Hospitals Case Medical Center                 | US         | Judith Mackall / Harish Manyam            |
| 52  | Ohio Health Corporation                                 | US         | Allan Nichols                              |
| 53  | Sheba Medical Center Tel Hashomer                       | Israel     | Serge David Bar-Lev                        |
| 54  | Wellmont CVA Heart Institute                            | US         | James Merrill                              |
| 55  | University of Minnesota                                 | US         | Wayne Adkisson                             |
| 56  | Hospital Marques de Valdecilla                          | Spain      | Juan José Olalla                          |
| 57  | Spectrum Health                                         | US         | Nagib Chalfoun                             |
| 58  | The Stern Cardiovascular Center                         | US         | Eric Johnson                               |
| 59  | Longview Regional Medical Center                        | US         | Jorge Massare                              |
| 60  | Duke University Medical Center                          | US         | Camille Frazier-Mills                      |
| 61  | Allegheny General Hospital                              | US         | John Chenarides                            |
| 62  | Bellin Health                                           | US         | Mohammad Jazayeri                         |
| 63  | Cardiovascular Consultants Heart Center                 | US         | Kevin Boran                               |
|   | Institution                                      | Location    | Contact                  |
|---|--------------------------------------------------|-------------|--------------------------|
| 64 | CentraCare Heart & Vascular Center              | US          | John Schoenhard / Simon Milstein |
| 65 | Novant Health Heart and Vascular Institute      | US          | John Bailey / Mark Kremers |
| 66 | University of Florida Health Sciences Center - Gainesville | US       | Thomas Burkart            |
| 67 | ZOL                                              | Belgium     | Wilfried Mullens          |
| 68 | Baylor Research Institute                        | US          | Jay Franklin              |
| 69 | New York Presbyterian Hospital                   | US          | Frederick Ehlert          |
| 70 | Oregon Health & Science University (OHSU)        | US          | Charles Henrikson         |
| 71 | William Beaumont Hospital                        | US          | Ilana Kutinsky            |
| 72 | Hospital Universitari Bellvitge                  | Spain       | Ignasi Anguera            |
| 73 | Norton Cardiovascular Associates                 | US          | Michael Springer          |
| 74 | Englewood Hospital & Medical Center              | US          | Grant Simons              |
| 75 | Hospital Charles Nicolle - CHU Rouen             | France      | Frederic Anselme          |
| 76 | Oklahoma Heart Institute                         | US          | David Sandler             |
| 77 | Azienda Ospedaliera Spedali Civili di Brescia    | Italy       | Luca Bontempi             |
| 78 | CHRU de Lille                                    | France      | Laurence Marie-Pierre Guedon-Moreau |
| 79 | Westchester Medical Center                       | US          | Sei Iwai                 |
| 80 | Legacy Medical Group                              | US          | John McAnulty / Eric Putz |
| 81 | Rabin Medical Center - Beilinson Hospital        | Israel      | Gregory Golovchiner       |
| 82 | University of Rochester Medical Center           | US          | David Juang               |
| 83 | Kantonsspital St.Gallen                          | Switzerland | Peter Ammann              |
| 84 | Providence Health & Services                     | US          | Randy Jones               |
| 85 | Saint Elizabeth Health Center                    | US          | Allan Katz                |
| 86 | Mayo Clinic                                      | US          | Malini Madhavan           |
| 87 | The University Kansas Medical Center Research Institute Inc. | US       | Martin Emert              |
| 88 | Centro Hospitalar do Porto                       | Portugal    | António Cândido de Freitas Fernandes Hipólito Reis |
| 89 | Sisataudit TYKS                                  | Finland     | Tina Salo                |
| 90 | Penrose Hospital                                 | US          | Christopher Cole          |
| 91 | Delmarva Heart, LLC                              | US          | Stephen Keim              |
| 92 | Cornell University                               | US          | George Thomas             |
| 93 | Saint Paul's Hospital (Vancouver BC)             | Canada      | Chanta Chakrabarti        |
| 94 | Oklahoma University Health Science Center        | US          | Christina Murray          |
| 95 | United Heart and Vascular Clinic                 | US          | Pierce Vatterott          |
|   | Institution Name                                                                 | Country  | Name                        |
|---|----------------------------------------------------------------------------------|----------|-----------------------------|
| 96| Doylestown Cardiology Associates - VIAA                                         | US       | Robert Sangrigoli           |
| 97| Massachusetts General Hospital                                                     | US       | Theofanie Mela              |
| 98| Royal Brompton & Harefield NHS Foundation Trust                                  | UK       | Mark John Mason             |
| 99| Danbury Hospital                                                                  | US       | Robert Winslow              |
|100| Mercy Hospital Springfield                                                        | US       | Shang-Chiu Lee              |
|101| Szpital Kliniczny Przemienienia Panskego                                        | Poland   | Przemyslaw Mitkowski        |
|102| Cen Hosp Univ Saint Etienne - Hopital Nord                                        | France   | Antoine Da Costa            |
|103| Saint Vincent Heart Center of Indiana                                             | US       | Girish Nair                 |
|104| NorthShore University Health System                                               | US       | Westby Fisher               |
|105| Hopital de la Timone - CHU de Marseille                                           | France   | Jean-Claude Deharo          |
|106| Sparrow Clinical Research Institute                                               | US       | Mark Castellani / David Rhine|
|107| University of Michigan Cardiovascular Center                                      | US       | Hamid Ghanbari              |
|108| Virginia Commonwealth University Medical Center                                   | US       | Gautham Kalahasty           |
|109| University of Nebraska                                                            | US       | Daniel Anderson             |
|110| Thomas Jefferson University                                                       | US       | Daniel Frisch               |
|111| NYU - Langone Medical Center                                                      | US       | Larry Chinitz / Charles Love|
|112| Eisenhower Medical Center                                                         | US       | Andrew Rubin                |
|113| Heart Clinics Northwest, P.S.                                                    | US       | Timothy Lessmeier          |
|114| Alaska Heart Institute                                                           | US       | Steven Compton              |
|115| Forsyth Medical Center                                                            | US       | Mark Mitchell               |
|116| Grantham Hospital                                                                | Hong Kong| Katherine Fan               |
|117| King Faisal Specialist Hospital                                                   | Saudi Arabia | Saeed Bandar Al Ghamdi |
|118| Stredoslovensky Ustav srdcovych a cievnych chorob (SUSCCH)                        | Slovakia | Gabriela Kaliska            |
|119| NUSCH a.s. Bratislava                                                             | Slovakia | Peter Margitfalvi           |
|120| MedStar Health Research Institute                                                 | US       | Glenn Meininger             |
|121| Saint Mary's Medical Center                                                       | US       | Aamir Cheema                |
|122| Azienda Ospedaliero Univ Pisana - Stabilimento di Cisanello                       | Italy    | Maria Grazia Bongiorni      |
|123| Pennsylvania Hospital                                                             | US       | Jeffrey Luebbert             |
|124| Northeast Ohio Cardiovascular Specialists                                         | US       | Michael Pelini              |
|125| VUSCH                                                                             | Slovakia | Silvia Misikova             |
|126| Great Lakes Heart & Vascular Institute, PC                                       | US       | Jerome Kuhnlein             |
|127| Akron General Medical Center                                                      | US       | Robert Schweikert           |
| No. | Institution                                      | Country    | Name                          |
|-----|--------------------------------------------------|------------|-------------------------------|
| 128 | CHR La Citadelle                                 | Belgium    | Jean-Manuel Herzet            |
| 129 | Presidio Ospedaliero Sant Anna                   | Italy      | Stefano Pedretti              |
| 130 | University of California San Francisco           | US         | Byron Lee                     |
| 131 | Loyola University Medical Center                | US         | Peter Santucci                |
| 132 | Karolinska Universitetssjukhuset                 | Sweden     | Jonas Hörnsten                |
| 133 | University of Pittsburgh Medical Center          | US         | Samir Saba / Evan Adelstein / Stuart Mendenhall |
| 134 | Princess Margaret Hospital                       | Hong Kong  | Ngai-Yin Chan                 |
| 135 | Sahlgrenska Universitetssjukhuset                | Sweden     | Shabbar Jamaly                |
| 136 | Hospital Universitario Ramon y Cajal             | Spain      | Javier Moreno                 |
| 137 | Cardio Centro Ticino                             | Switzerland| Tiziano Moccetti              |
| 138 | Sinai Hospital of Baltimore                      | US         | Paresh Shah                   |
| 139 | Cardiology Associates of Corpus Christi          | US         | John Douglas Pappas           |
| 140 | Universitaets-Herzzentrum Freiburg Bad Krotzingen| Germany    | Thomas Blum                   |
| 141 | CHUV - University Hospital                       | Switzerland| Etienne Pruvot                |
| 142 | The Miriam Hospital                              | US         | Anthony Chu                   |
| 143 | Temple University Hospital                       | US         | Chetan Gangireddy / Joshua Cooper |
| 144 | Saint Joseph's Medical Center                    | US         | Walter Chien                  |
| 145 | Saint Joseph's Hospital Health Center            | US         | Ali Al-Mugamgha               |
| 146 | Asheville Cardiology Associates, PA              | US         | Matthew Smelley               |
| 147 | Drexel Univ College of Medicine                  | US         | Heath Saltzman                |
| 148 | Tri-City Cardiology Consultants                  | US         | Arun Kolli                    |
| 149 | Robert Wood Johnson Medical School               | US         | William Kostis / Sluja Amardeep |
| 150 | Sahlgrenska University Hospital                  | Sweden     | Charles Kennergren            |
| 151 | Saint Anthonys Medical Center                    | US         | Rajiv Handa                   |
| 152 | University Hospital of Heraklion                 | Greece     | Emmanuel Simantirakis         |
| 153 | Wake Forest University Health System             | US         | Tony Simmons                  |
| 154 | Hattiesburg Clinic/Forrest General               | US         | Randel Smith                  |
| 155 | Washington University School of Medicine         | US         | Marye Gleva                   |
| 156 | Onassis Cardiac Surgery Center                   | Greece     | George N. Theodorakis         |
| 157 | Mount Sinai Saint Luke's Hospital                | US         | Emad Aziz                     |
| 158 | St. Marys Medical Center                         | US         | Scott Burke                   |
| 159 | National Heart Center                            | Singapore  | Kah Leng Ho                   |
| 160 | Heart Rhythm Management Centre, UZ Brussels VUB Brussel | Belgium | Carlo De Asmundis |
| 161 | Our Lady of the Lake                             | US         | Kenneth Civello               |
| 162 | Changi General Hospital                          | Singapore  | Tan Vern Hsen                 |
| 163 | Swedish Medical Center Cherry Hill               | US         | Darryl Wells                  |
| 164 | Universitatsklinikum Rostock                    | Germany    | Hüseyin Ince                  |
| 165 | Helsingin Seudun Yliopistollinen Keskussairaala | Finland | Sami Pakarinen  
| 166 | North Texas Heart Center | US | Jodie Hurwitz  
| 167 | Aurora BayCare Medical Center | US | Vinay Mehta  
| 168 | Universiti Malaya Medical Centre | Malaysia | Imra Zainal Abidin  
| 169 | Jackson Clinic | US | Michael Osayamen  
| 170 | Scott & White Hospital | US | Javier Banchs  
| 171 | SCL Physicians Heart Institute of Colo | US | Kelly Kim  
| 172 | Samodzielny Publiczny Szpital Kliniczny nr 4 w Lublinie | Poland | Andrzej Kutarski  
| 173 | Hospital de Santa Maria-Centro Hospitalar Lisboa Norte, EPE | Portugal | João Manuel Frazão Rodrigues de Sousa  
| 174 | Plaza Medical Center of Fort Worth | US | Senthil Tambidorai  
| 175 | Lehigh Valley Hospital | US | James Sandberg  
| 176 | Hospital San Juan de Dios | Chile | Rubén Aguayo  
| 177 | St. Lukes Hospital and Health Network | US | Darren Traub  
| 178 | EP Heart, LLC | US | Siddarth Mukerji / Rajesh Venaktaraman / Ramesh Hariharan  
| 179 | Hospital Sultanah Bahiyah | Malaysia | Saravanan Krishinan  
| 180 | Hospital Universitario La Paz | Spain | Jorge Silvestre  
| 181 | Florida Electrophysiology Associates | US | Vladimir Rankovic |