

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

	Questionnaires (Subjects) Completed
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

Change in EQ-5D Utility Following Major CIED Infection within 12-Months					
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

Change in EQ-5D Utility Following Major CIED Infection within 12-Months					
EQ-5D Assessment	Questionnaires (Subjects) Completed	Mean \pm SD	Adjusted Mean 95% CI*	Adjusted Mean Difference 95% CI*	P-value[†]
Baseline	67 (67)	0.83 \pm 0.14	0.84 (0.80-0.88)	--	--
Infection Diagnosis	31 (31)	0.75 \pm 0.19	0.75 (0.70-0.81)	0.09 (0.03-0.14)	0.003
1-Month Post-Infection	26 (25)	0.73 \pm 0.20	0.73 (0.66-0.79)	0.11 (0.05-0.18)	0.001
3-Month Post-Infection	30 (30)	0.77 \pm 0.23	0.75 (0.69-0.81)	0.09 (0.03-0.16)	0.006
6-Month Post-Infection	42 (41)	0.83 \pm 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

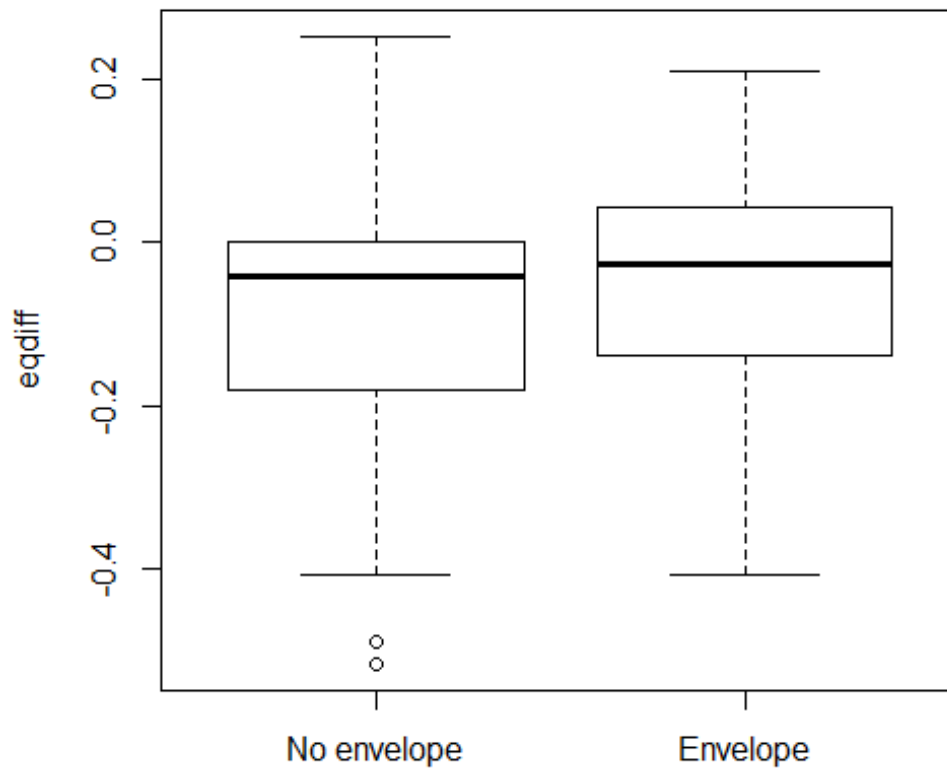
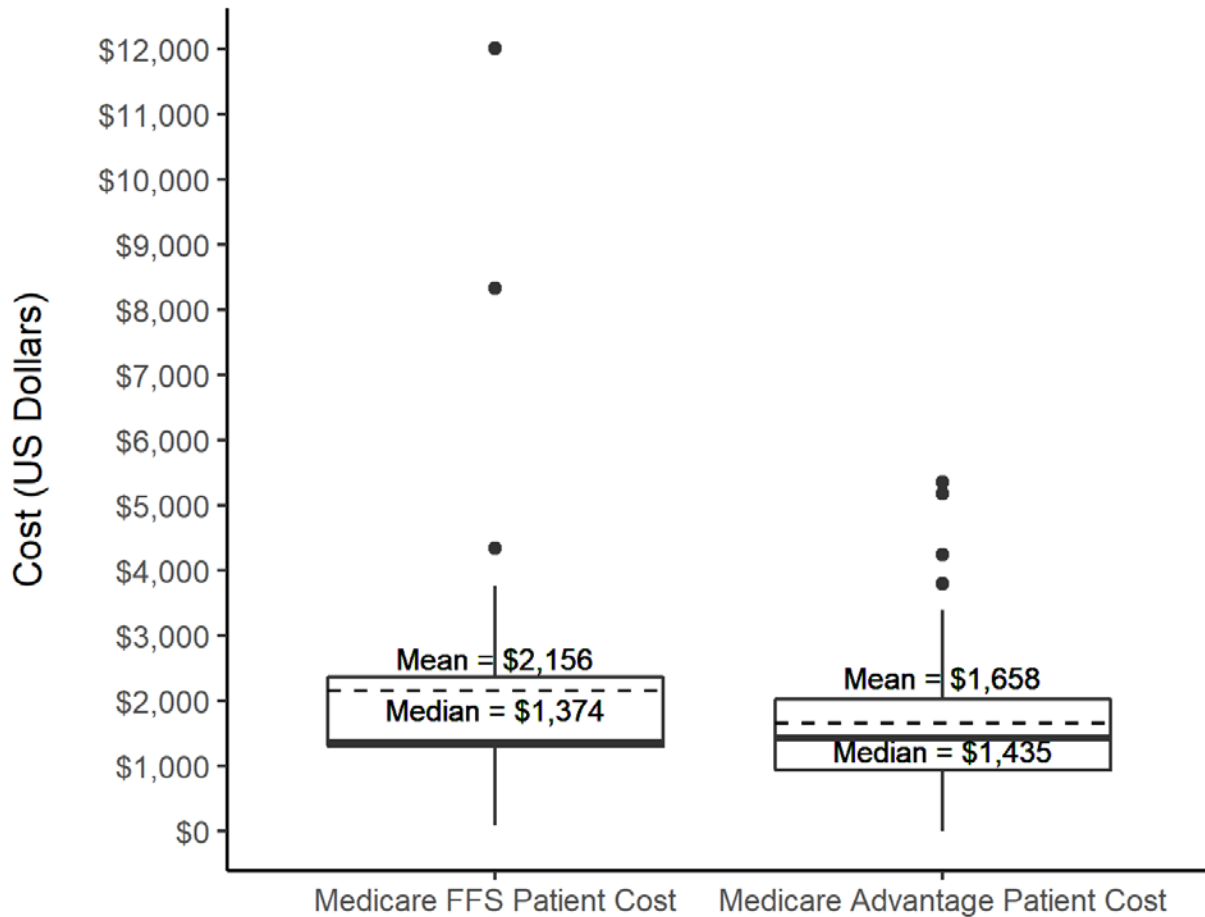


Figure S2. Patient Costs. Total patient costs per infection in the US Cohort with Major Infections for Medicare FFS and Medicare Advantage. Box-and-whisker plots represent distribution of data as follows: solid line = median; dashed line = mean; box = interquartile range; whiskers = minimum and maximum 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

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 Augostini
35	Haukeland Universitetssjukehus	Norway	Havard Keilegavlen / Svein Faerestrland
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	Universitätsklinikum Krems	Austria	Attila Mihalcz
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

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 Ehler
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	Hopital 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

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-Chiun Lee
101	Szpital Kliniczny Przemienienia Panskiego	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 Bongiorno
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

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 Krozingen	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	Universitätsklinikum 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