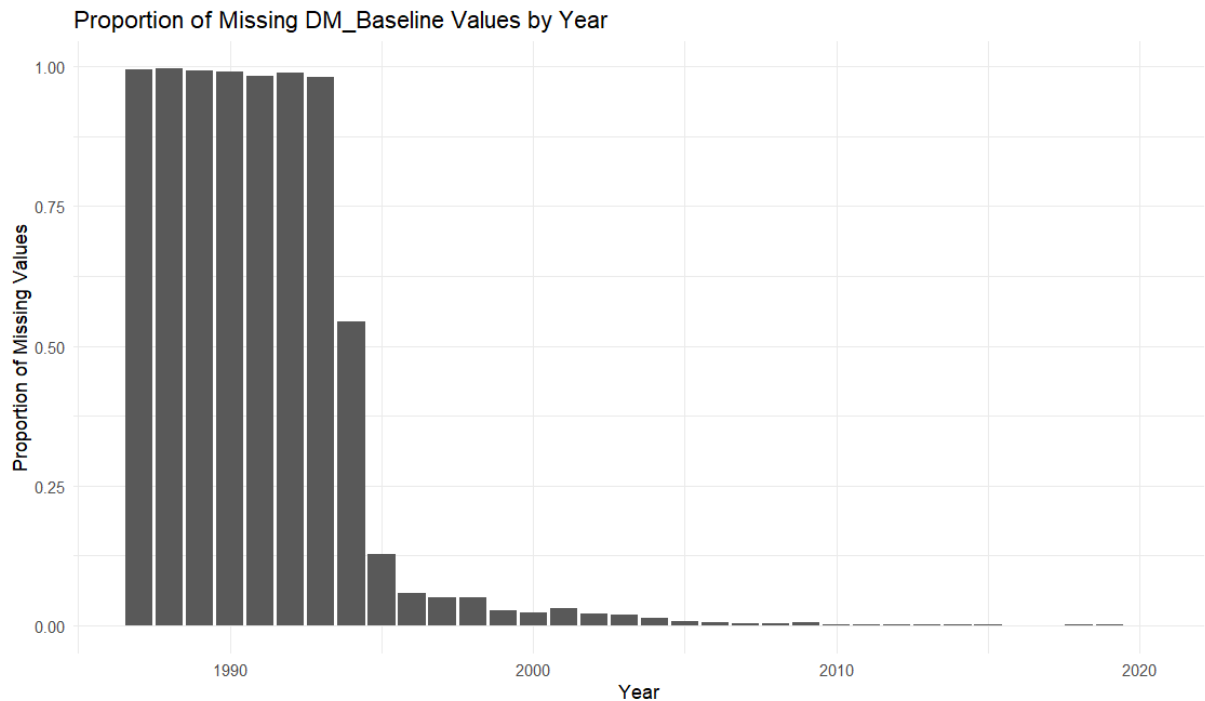
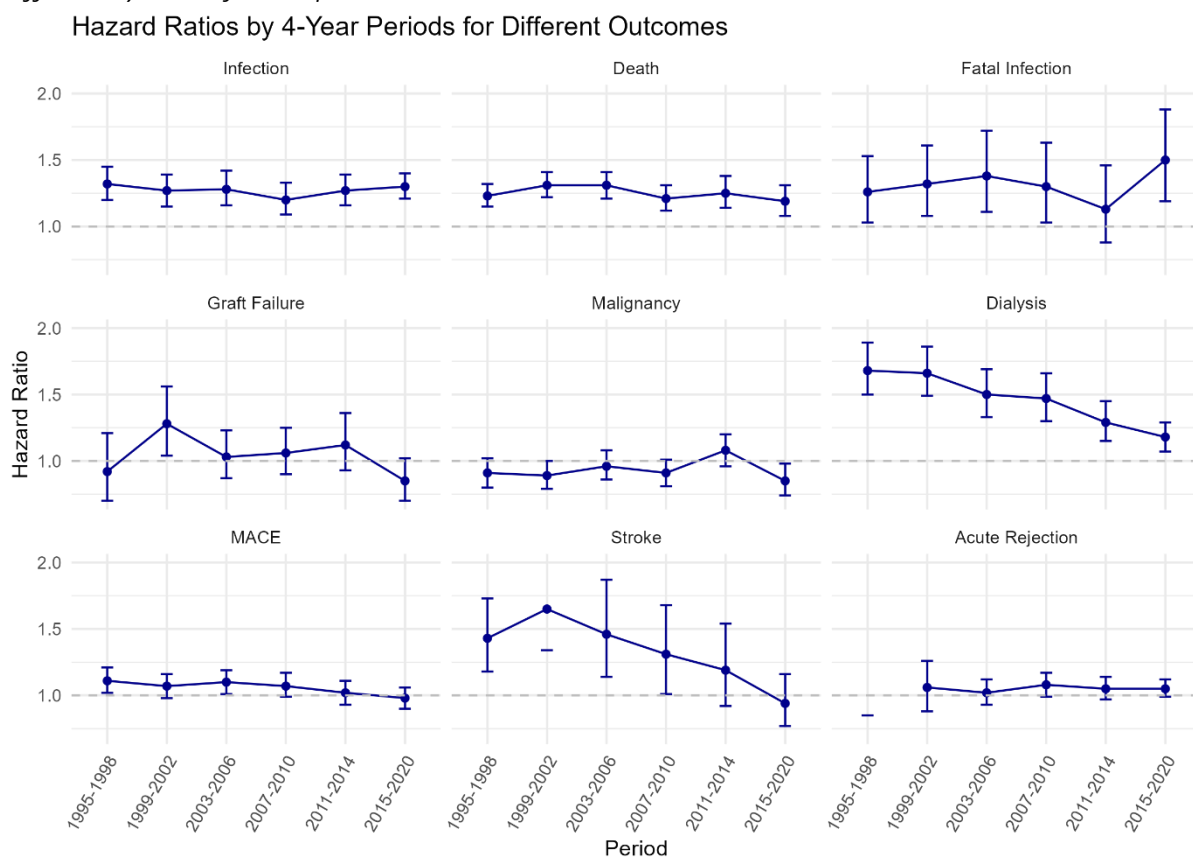


Supplemental Materials

Supplemental Figure S1: Proportion of missing values for Diabetes Mellitus in the Scientific Registry of Transplant Recipients by year

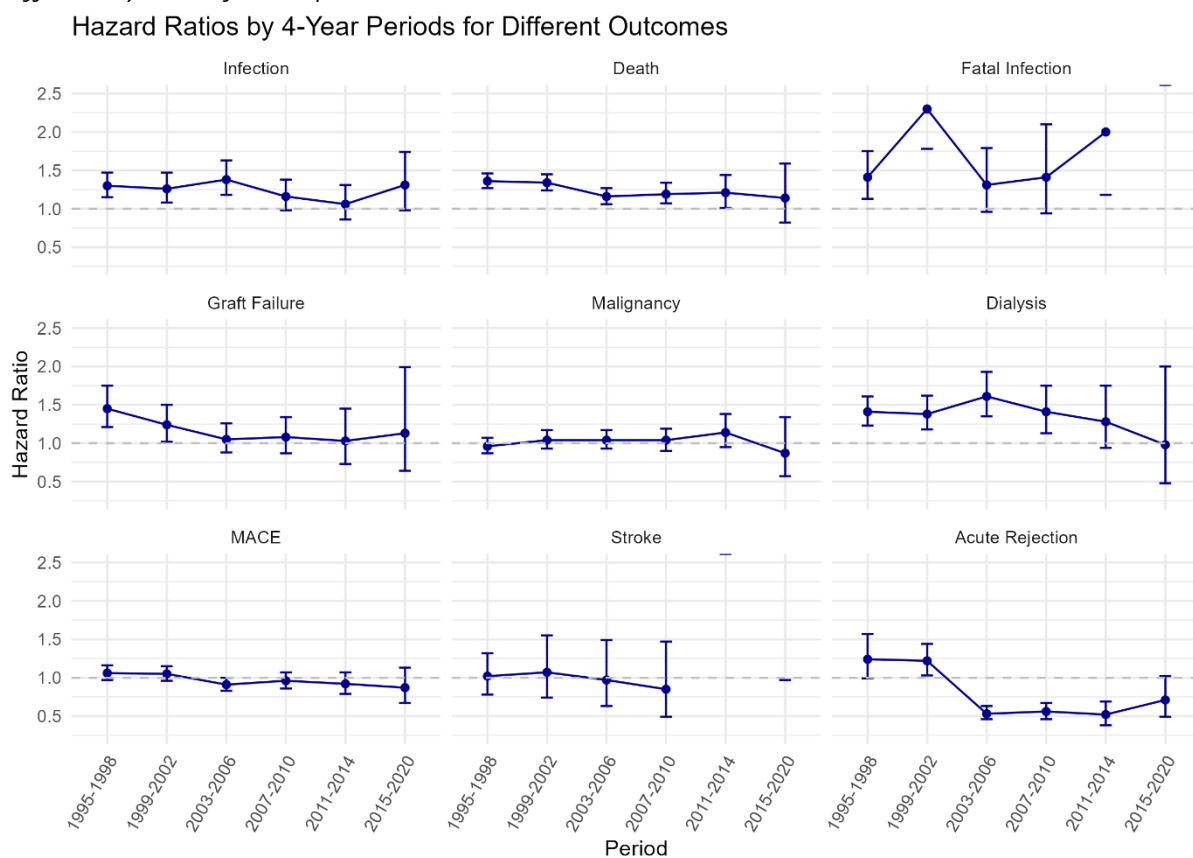


Supplemental Figure S2: Pre-transplant diabetes mellitus and various outcomes across different years of transplantation



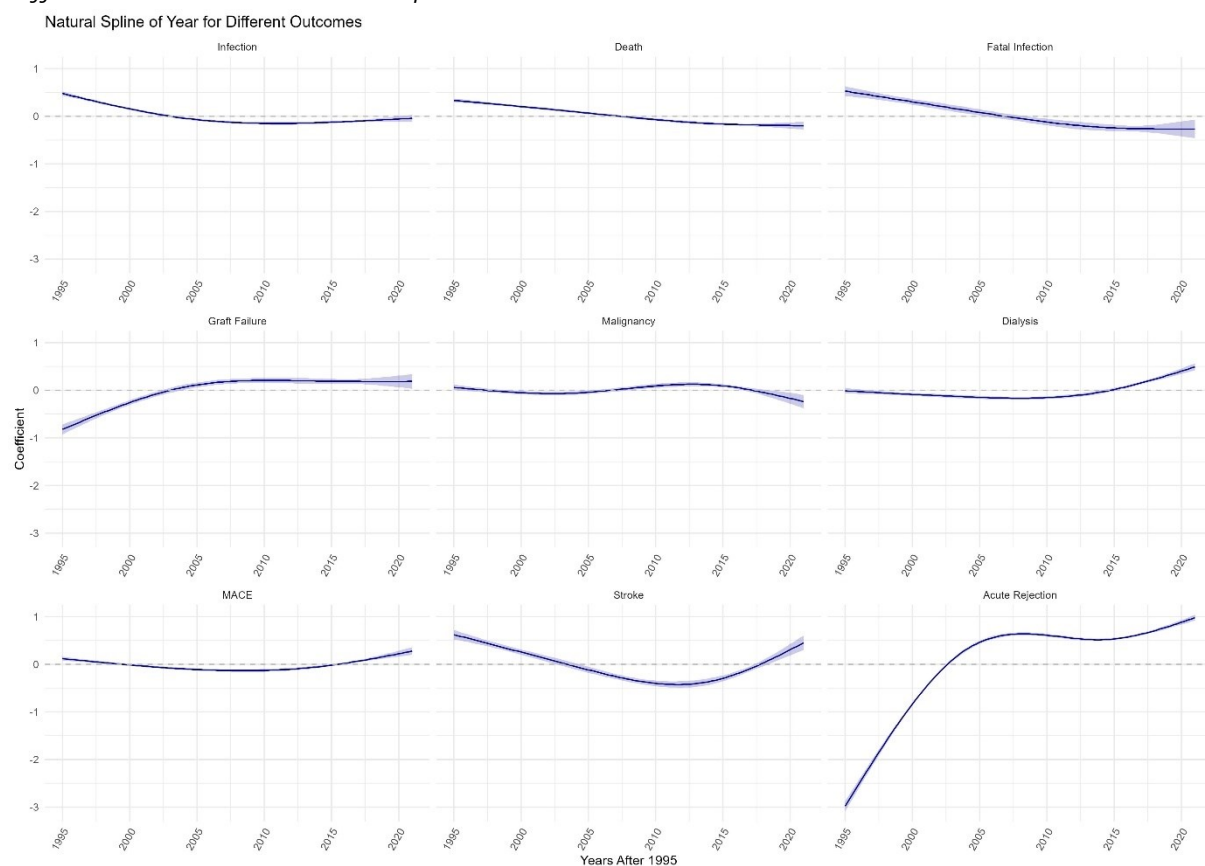
Estimates of the hazard ratios of the predictor pre-transplant diabetes mellitus in multivariable models for various outcomes across various transplant periods (models in this case not adjusted for transplant year).

Supplemental Figure S3: Post-transplant diabetes mellitus and various outcomes across different years of transplantation



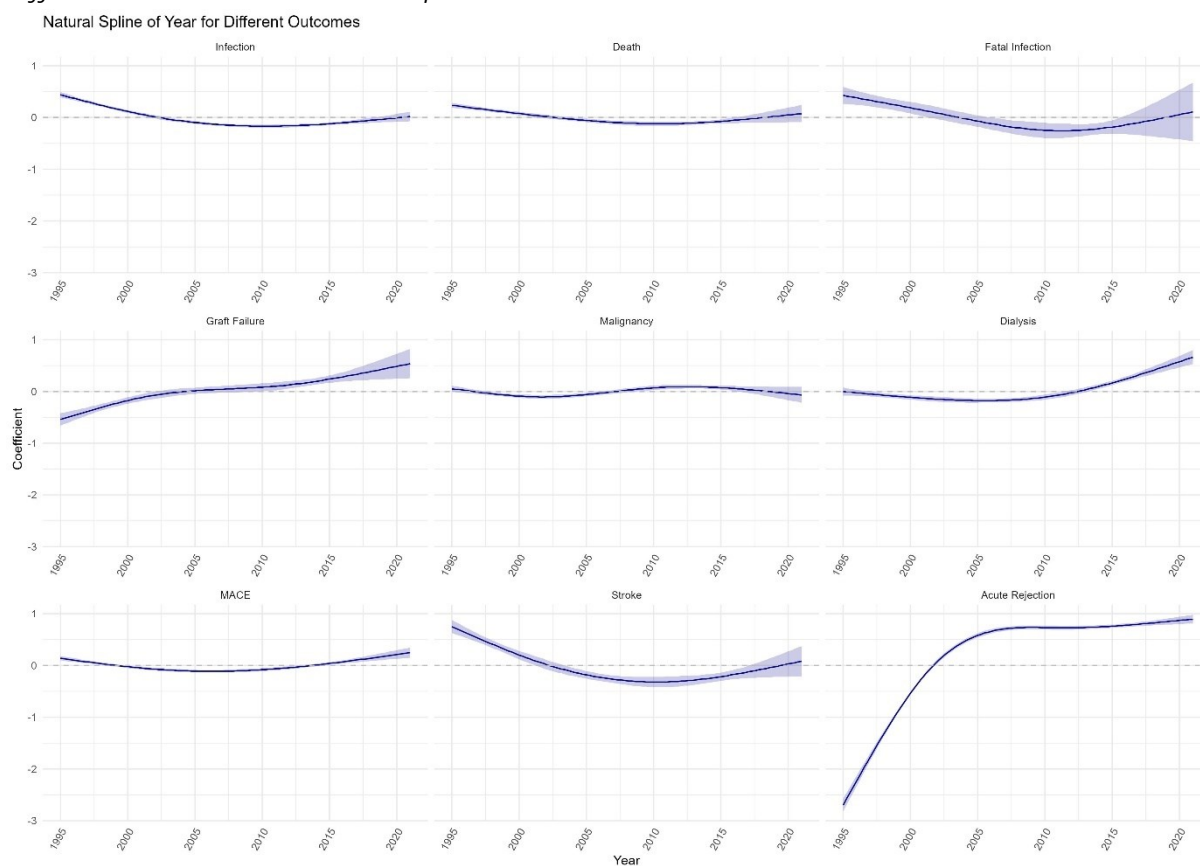
Estimates of the hazard ratios of the predictor post-transplant diabetes mellitus in multivariable models for various outcomes across various transplant periods (models in this case not adjusted for transplant year).

Supplemental Figure S4: Coefficients of transplant year in multivariable models for different outcomes: Pre-Transplant Diabetes Mellitus



Shown are the estimates of natural splines of the transplant year with three degrees of freedom in the multivariable regression Cox regression models with pre-transplant diabetes mellitus and the prespecified covariates for each respective outcome.

Supplemental Figure S5: Coefficients of transplant year in multivariable models for different outcomes: Post-Transplant Diabetes Mellitus



Shown are the estimates of natural splines of the transplant year with three degrees of freedom in the multivariable regression Cox regression models with post-transplant diabetes mellitus and the prespecified covariates for each respective outcome.

Supplemental Table 1: Patient characteristics of patients without diabetes at transplantation, with vs. without post-transplant DM, Scientific Registry of Transplant Recipients (1995-2021)

Characteristic	No DM n = 25,580¹	Post-transplant DM n = 7,491¹
Age at Tx (years)	54 [43; 61]	54 [46; 61]
Sex (male)	18,814 (74%)	5,732 (77%)
BMI (kg/m²)	25.6 [22.7; 29.1]	27.0 [23.9; 30.4]
Race		
white	18,796 (73%)	5,220 (70%)
black	4,263 (17%)	1,496 (20%)
other	2,520 (9.9%)	773 (10%)
Educational status		
grade school (0-8 years)	682 (3.1%)	245 (4.3%)
high school (9-12 years)	8,921 (41%)	2,745 (48%)
higher education	12,257 (56%)	2,749 (48%)
none	30 (0.1%)	18 (0.3%)
Donor Age (years)	29 [21; 40]	29 [21; 41]
Donor Sex (male)	17,721 (69%)	5,402 (72%)
Donor Race		
white	17,465 (68%)	5,272 (70%)
black	3,652 (14%)	1,077 (14%)
other	4,462 (17%)	1,142 (15%)
Primary diagnosis for HTx		
ICM	9,018 (35%)	3,384 (45%)
Congenital	822 (3.2%)	187 (2.5%)
DCM	13,379 (52%)	3,504 (47%)
HCM	737 (2.9%)	108 (1.4%)
other	271 (1.1%)	37 (0.5%)
Restrictive CM	804 (3.1%)	95 (1.3%)
Valvular	545 (2.1%)	176 (2.3%)

Hypertension	6,810 (39%)	2,741 (43%)
COPD	603 (3.6%)	235 (3.7%)
Cerebrovascular Disease	1,205 (4.8%)	253 (3.5%)
Peripheral Artery Disease	411 (2.4%)	182 (2.8%)

In accordance with all other analyses of post-transplant DM, only patients with a follow-up of more than 365 days were included. Median [25%; 75%]; n (%). BMI: Body Mass Index; CM: Cardiomyopathy; COPD: Chronic Obstructive Pulmonary Disease; DCM: Dilated Cardiomyopathy; DM: Diabetes Mellitus; HCM: Hypertrophic Cardiomyopathy; HTx: Heart Transplantation; ICM: Ischemic Cardiomyopathy.

Supplemental Table 2: Immunosuppressive medication and post-transplant diabetes mellitus

Immunosuppressive Medication	No DM n = 25,580¹	Post-transplant DM n = 7,491¹	p-value²
Sandimmune	1,172 (4.6%)	548 (7.3%)	<0.001
Neoral	6,175 (24%)	2,508 (33%)	<0.001
Prograf (tacrolimus)	10,469 (41%)	3,138 (42%)	0.14
Rapamune (sirolimus)	336 (1.3%)	209 (2.8%)	<0.001
Leflunomide (LFL)	3 (<0.1%)	3 (<0.1%)	0.3
Imuran (azathioprine, AZA)	4,099 (16%)	1,990 (27%)	<0.001
CellCept (MMF)	15,004 (59%)	4,650 (62%)	<0.001
Cytosan (cyclophosphamide)	86 (0.3%)	57 (0.8%)	<0.001
Methotrexate (Folex PFS, Mexate-AQ, Rheumatrex)	33 (0.1%)	28 (0.4%)	<0.001
Zortress (everolimus)	121 (0.5%)	54 (0.7%)	0.012
Myfortic (mycophenolic acid)	914 (3.6%)	191 (2.5%)	<0.001
Generic cyclosporine	110 (0.4%)	21 (0.3%)	0.087
Steroids (prednisone, methylprednisolone, Solumedrol, Medrol)	24,881 (97%)	7,288 (97%)	>0.9
Generic tacrolimus (generic Prograf)	5,666 (22%)	514 (6.9%)	<0.001
Generic MMF (generic CellCept)	4,991 (20%)	434 (5.8%)	<0.001
Generic Myfortic (generic mycophenolic acid)	98 (0.4%)	10 (0.1%)	0.001
Generic sirolimus	5 (<0.1%)	0 (0%)	0.5

Supplemental Table 3: Pre-transplant diabetes mellitus and outcomes after heart transplantation up to 3 years post-transplantation

Outcome	Univariate model					Multivariable model				
	Person -time (1000y)	HR	Lower CI	Upper CI	p	Person -time (1000y)	HR	Lower CI	Upper CI	p
Hospitalization for Infection	104	1.3	1.25	1.35	<0.001	103	1.28	1.23	1.33	<0.001
All-cause mortality	124	1.15	1.09	1.2	<0.001	122	1.14	1.08	1.2	<0.001
Fatal Infection	124	1.35	1.2	1.5	<0.001	122	1.22	1.09	1.37	0.001
Graft Failure	123	1.05	0.95	1.17	0.362	122	0.97	0.87	1.08	0.583
Any Malignancy	119	1.08	1	1.16	0.059	114	1.24	1.17	1.31	<0.001
Need for dialysis	115	1.38	1.3	1.45	<0.001	118	0.92	0.85	1	0.039
Renal Replacement Therapy	104	1.38	1.32	1.44	<0.001	102	1.36	1.3	1.42	<0.001
MACE	114	1.07	1.02	1.12	0.003	113	1.01	0.97	1.07	0.563
Stroke	121	1.24	1.13	1.37	<0.001	120	1.23	1.11	1.36	<0.001
Acute Rejection	99	1.18	1.14	1.23	<0.001	98	1.05	1.01	1.09	0.014

n=53,219; 12,708 with DM, 40,511 without DM at time of transplantation. For this sensitivity analysis, patients were censored after 1095.75 days post-transplantation. CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 4: Pre-transplant diabetes mellitus and outcomes after heart transplantation up to 5 years post-transplantation

Outcome	Univariate model					Multivariable model				
	Person -time (1000y)	HR	Lower CI	Upper CI	p	Person -time (1000y)	HR	Lower CI	Upper CI	p
Hospitalization for Infection	147	1.3	1.26	1.35	<0.001	146	1.28	1.23	1.33	<0.001
All-cause mortality	185	1.18	1.13	1.23	<0.001	183	1.17	1.12	1.22	0
Fatal Infection	185	1.35	1.21	1.5	<0.001	183	1.22	1.09	1.36	0
Graft Failure	185	1.02	0.93	1.13	0.616	183	0.99	0.9	1.1	0.864
Any Malignancy	174	1.12	1.05	1.19	<0.001	171	1.28	1.21	1.35	0
Need for dialysis	173	1.42	1.35	1.49	<0.001	172	0.95	0.89	1.01	0.115
Renal Replacement Therapy	154	1.38	1.32	1.44	<0.001	153	1.36	1.3	1.42	0
MACE	162	1.07	1.03	1.11	0.001	160	1.03	0.98	1.07	0.231
Stroke	181	1.29	1.17	1.41	<0.001	179	1.28	1.17	1.41	0
Acute Rejection	144	1.16	1.12	1.21	<0.001	142	1.05	1.01	1.09	0.019

n=53,219; 12,708 with DM, 40,511 without DM at time of transplantation. For this sensitivity analysis, patients were censored after 1826.25 days post-transplantation. CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 5: Post-transplant diabetes mellitus and outcomes after heart transplantation up to 3 years post-transplantation

Outcome	Univariate model					Multivariable model				
	Person -time (1000y)	HR	Lower CI	Upper CI	p	Person -time (1000y)	HR	Lower CI	Upper CI	p
Hospitalization for Infection	78	1.27	1.19	1.36	<0.001	77	1.21	1.12	1.29	<0.001
All-cause mortality	92	1.58	1.52	1.65	<0.001	91	1.31	1.26	1.37	<0.001
Fatal Infection	92	2.05	1.78	2.35	<0.001	91	1.67	1.44	1.92	<0.001
Graft Failure	92	1.33	1.21	1.47	<0.001	91	1.21	1.09	1.33	<0.001
Any Malignancy	89	1.17	1.1	1.24	<0.001	88	1.08	1.02	1.15	0.009
Need for dialysis	87	1.81	1.67	1.97	<0.001	86	1.67	1.53	1.82	<0.001
Renal Replacement Therapy	79	1.81	1.28	2.55	0.001	78	1.57	1.11	2.22	0.011
MACE	85	1.1	1.06	1.16	<0.001	84	1.01	0.97	1.06	0.563
Stroke	91	1.21	1	1.46	0.053	89	1.12	0.92	1.36	0.244
Acute Rejection	75	0.72	0.67	0.79	<0.001	74	0.81	0.74	0.88	<0.001

n=33,071 without DM at time of transplantation, n=5,238 developing Post-Transplant DM. For this sensitivity analysis, patients were censored after 1095.75 days post-transplantation. CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 6: Post-transplant diabetes mellitus and outcomes after heart transplantation up to 5 years post-transplantation

Outcome	Univariate model					Multivariable model				
	Person -time (1000y)	HR	Lower CI	Upper CI	p	Person -time (1000y)	HR	Lower CI	Upper CI	p
Hospitalization for Infection	113	1.26	1.18	1.35	<0.001	111	1.2	1.13	1.29	<0.001
All-cause mortality	141	1.46	1.4	1.52	<0.001	139	1.28	1.23	1.34	<0.001
Fatal Infection	141	1.88	1.65	2.15	<0.001	139	1.63	1.42	1.86	<0.001
Graft Failure	140	1.25	1.15	1.37	<0.001	138	1.18	1.08	1.3	0.001
Any Malignancy	132	1.07	1.02	1.14	0.012	130	1.06	1	1.12	0.059
Need for dialysis	132	1.64	1.52	1.78	<0.001	130	1.52	1.4	1.64	<0.001
Renal Replacement Therapy	119	1.57	1.12	2.2	0.008	117	1.39	0.99	1.94	0.058
MACE	122	1.05	1.01	1.1	0.024	121	1	0.95	1.04	0.92
Stroke	137	1.18	0.98	1.41	0.074	136	1.12	0.93	1.35	0.222
Acute Rejection	110	0.71	0.66	0.78	<0.001	108	0.8	0.74	0.87	<0.001

n=33,071 without DM at time of transplantation, n=5,238 developing Post-Transplant DM. For this sensitivity analysis, patients were censored after 1826.25 days post-transplantation. CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 7: Pre- and post-transplant DM and outcomes after heart transplantation in patients with known DM status at transplantation (n= 52295)

	Univariate model					Multivariable model				
Outcome	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>
	Pre-Transplant DM									
Hospitalization for Infection	256	1.28	1.23	1.32	<0.001	254	1.28	1.23	1.32	<0.001
All-cause mortality	350	1.35	1.31	1.39	<0.001	348	1.26	1.22	1.3	<0.001
Fatal Infection	350	1.5	1.38	1.64	<0.001	348	1.32	1.21	1.45	<0.001
Graft Failure	347	1.01	0.94	1.09	0.812	344	1.04	0.96	1.12	0.321
Any Malignancy	297	1.08	1.03	1.13	0.001	295	0.94	0.9	0.99	0.011
Need for dialysis	320	1.56	1.5	1.63	<0.001	318	1.41	1.34	1.47	<0.001
Renal Replacement Therapy	284	1.38	1.33	1.44	<0.001	283	1.36	1.3	1.43	<0.001
MACE	254	1.09	1.06	1.13	<0.001	252	1.06	1.02	1.1	0.001
Stroke	339	1.28	1.17	1.39	<0.001	336	1.3	1.18	1.42	<0.001
Acute Rejection	264	1.11	1.07	1.15	<0.001	262	1.04	1.01	1.08	0.024
	Post-Transplant DM									
Hospitalization for Infection	202	1.27	1.18	1.35	<0.001	201	1.22	1.14	1.3	<0.001
All-cause mortality	275	1.37	1.31	1.42	<0.001	273	1.28	1.23	1.33	<0.001
Fatal Infection	275	1.77	1.55	2.01	<0.001	273	1.61	1.41	1.84	<0.001
Graft Failure	272	1.19	1.09	1.3	<0.001	270	1.21	1.1	1.32	<0.001
Any Malignancy	232	0.99	0.94	1.05	0.813	230	1.04	0.98	1.1	0.222
Need for dialysis	252	1.53	1.42	1.66	<0.001	251	1.44	1.33	1.56	<0.001
Renal Replacement Therapy	227	1.72	1.26	2.35	0.001	226	1.53	1.12	2.09	0.008
MACE	197	1.02	0.98	1.07	0.361	196	0.99	0.95	1.04	0.798

Stroke	266	1.17	0.98	1.4	0.081	264	1.13	0.94	1.35	0.204
Acute Rejection	208	0.74	0.68	0.8	<0.001	207	0.82	0.76	0.89	<0.001

For pre-transplant DM: n= 52295, 12708 with DM, 39587 without DM at time of transplantation. For post-transplant DM: n= 32314 without DM at time of transplantation, n= 5144 developing Post-Transplant DM. CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 8: Pre-transplant Diabetes Mellitus and outcomes after heart transplantation stratified by transplant periods

	Univariate model					Multivariable model				
Outcome										
	<u>TRANSPLANT PERIOD 1995-2008</u>									
	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>
Hospitalization for Infection	174	1.27	1.2	1.33	<0.001	174	1.27	1.2	1.33	<0.001
All-cause mortality	247	1.37	1.32	1.42	<0.001	247	1.37	1.32	1.42	<0.001
Fatal Infection	247	1.48	1.34	1.65	<0.001	247	1.48	1.34	1.65	<0.001
Graft Failure	244	1.02	0.92	1.12	0.718	244	1.02	0.92	1.12	0.718
Any Malignancy	203	1.03	0.97	1.1	0.295	203	1.03	0.97	1.1	0.295
Need for dialysis	225	1.74	1.64	1.85	<0.001	225	1.74	1.64	1.85	<0.001
Renal Replacement Therapy	193	1.53	1.44	1.62	<0.001	193	1.53	1.44	1.62	<0.001
MACE	167	1.1	1.05	1.15	<0.001	167	1.1	1.05	1.15	<0.001
Stroke	237	1.49	1.33	1.67	<0.001	237	1.49	1.33	1.67	<0.001
Acute Rejection	200	1.16	1.09	1.23	<0.001	200	1.16	1.09	1.23	<0.001
	<u>TRANSPLANT PERIOD 2009-2021</u>									
	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>
Hospitalization for Infection	89	1.36	1.29	1.43	<0.001	89	1.28	1.21	1.35	<0.001
All-cause mortality	112	1.38	1.3	1.45	<0.001	112	1.23	1.16	1.3	<0.001
Fatal Infection	112	1.68	1.46	1.94	<0.001	112	1.4	1.2	1.63	<0.001
Graft Failure	112	0.96	0.86	1.07	0.451	112	1.01	0.9	1.13	0.915

Any Malignancy	101	1.16	1.07	1.24	<0.001	101	0.97	0.9	1.04	0.402
Need for dialysis	103	1.34	1.26	1.43	<0.001	103	1.22	1.14	1.3	<0.001
Renal Replacement Therapy	98	1.35	1.26	1.43	<0.001	98	1.22	1.14	1.3	<0.001
MACE	92	1.08	1.03	1.13	0.003	92	1.02	0.97	1.08	0.448
Stroke	110	1.12	0.97	1.28	0.119	110	1.08	0.93	1.25	0.304
Acute Rejection	72	0.98	0.94	1.03	0.413	72	1.06	1.01	1.1	0.021

CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

Supplemental Table 9: Post-transplant Diabetes Mellitus and outcomes after heart transplantation stratified by transplant periods

	Univariate model					Multivariable model				
Outcome										
	<u>TRANSPLANT PERIOD 1995-2008</u>									
	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>
Hospitalization for Infection	144	1.28	1.19	1.38	<0.001	141	1.28	1.19	1.39	<0.001
All-cause mortality	203	1.38	1.32	1.44	<0.001	199	1.3	1.25	1.36	<0.001
Fatal Infection	203	1.72	1.5	1.96	<0.001	199	1.57	1.37	1.81	<0.001
Graft Failure	200	1.3	1.18	1.43	<0.001	196	1.28	1.16	1.42	<0.001
Any Malignancy	166	0.99	0.94	1.05	0.838	163	1.03	0.97	1.09	0.369
Need for dialysis	187	1.59	1.46	1.72	<0.001	182	1.43	1.32	1.56	<0.001
Renal Replacement Therapy	162	1.56	1.12	2.17	0.008	159	1.46	1.04	2.03	0.027
MACE	137	1.04	0.99	1.09	0.085	134	1.01	0.96	1.06	0.76
Stroke	196	0.98	0.82	1.18	0.828	192	1	0.83	1.2	0.999
Acute Rejection	165	0.88	0.81	0.97	0.007	161	0.78	0.71	0.85	<0.001
	<u>TRANSPLANT PERIOD 2009-2021</u>									
	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>	<i>Person -time (1000y)</i>	<i>HR</i>	<i>Lower CI</i>	<i>Upper CI</i>	<i>p</i>
Hospitalization for Infection	64	1.18	1.03	1.36	0.017	64	1.18	1.03	1.36	0.019
All-cause mortality	81	1.2	1.07	1.35	0.001	80	1.16	1.03	1.31	0.011
Fatal Infection	81	1.61	1.09	2.4	0.018	80	1.65	1.1	2.48	0.015
Graft Failure	80	0.96	0.76	1.21	0.749	80	0.92	0.73	1.16	0.493

Any Malignancy	73	1.01	0.89	1.16	0.834	73	1.04	0.91	1.18	0.613
Need for dialysis	74	1.41	1.15	1.74	0.001	74	1.37	1.11	1.68	0.003
Renal Replacement Therapy	72	2.48	1.09	5.65	0.031	72	2.22	0.98	5.06	0.057
MACE	66	0.92	0.83	1.02	0.118	66	0.91	0.82	1.01	0.067
Stroke	79	1.22	0.63	2.38	0.551	79	1.12	0.58	2.19	0.731
Acute Rejection	51	0.57	0.48	0.69	<0.001	51	0.56	0.46	0.67	<0.001

CI = Confidence Interval, DM = Diabetes Mellitus, HR = Hazard Ratio, MACE = Major Adverse Cardiovascular Events. Multivariable regression models included the following covariates, chosen *a priori*: age, gender, race, BMI of the recipient at transplantation; donor age, gender, and race; and the primary diagnosis for HTx.

