

Appendix I: Author Affiliations

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Appendix II: Detailed Description of Main Models

Of central interest in the paper is the characterization of risk of incident microvascular disease at any given point in time post-surgery, as a function of a patient's current and prior type 2 diabetes mellitus (T2DM) state. Towards this, we specified two key covariates. The first indicates which state the patient is currently in at any given point in time:

1. The patient is in the initial state (i.e. active T2DM), labeled 'no remission'.
2. The patient is in the state of 'remission', having transitioned from the initial 'no remission' state.
3. The patient is in the state of 'relapse', having transitioned from the state of 'remission'.

The second key covariate is an indicator, at any given point in time, of the cumulative time spent in the state of remission to that time point. At the outset (i.e. time of surgery), this variable is equal to zero (since all patients have active T2DM at the time of surgery). If a patient transitions into a state of 'remission', they accrue person-time in this state until they experience a relapse. If a patient experiences a relapse, person-time no longer accrues.

Towards building a model, we formalize these covariates with the following notation:

$X_1(t) = 1$ if the subject is in the state of *remission* at time t and 0 otherwise

$X_2(t) = 1$ if the subject is in the state of *relapse* at time t and 0 otherwise

$A(t)$ is a continuous time-varying measure of the cumulative time spent in remission at time t

In addition, we let Z denote a vector of time-variant adjustment variables (i.e. adjustment variables measured at baseline). Based on this notation, the "main effects only model" that is the basis for results in Table 2 of the manuscript can be succinctly written as:

$$h(t) = h_0(t) \exp\{\beta_1 X_1(t) + \beta_2 X_2(t) + \beta_z Z\}$$

Notice that patients in the initial state of active T2DM or no remission, $X_1(t)=0$ and $X_2(t)=0$. Hence, this group is the referent group. Consequently, the hazard ratio (HR) $\exp(\beta_1)$ quantifies the relative difference in risk between patients who are in the state of remission compared to those who have not transitioned out of their initial state. Similarly, the HR $\exp(\beta_2)$ quantifies the relative difference in risk between patients who are in the state of relapse compared to those who have not transitioned out of their initial state.

Again using the notation outlined above, the "interaction model" in Table 2 can be succinctly written as:

$$h(t) = h_0(t) \exp\{\beta_1 X_1(t) + \beta_2 X_2(t) + \beta_3 X_2(t)A(t) + \beta_z Z\}.$$

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The addition of the interaction between $X_2(t)$ and $A(t)$ permits the HR for patients who have relapsed, compared to those who have not remitted, to depend on the cumulative time spent in remission (prior to relapse). This legacy HR can be written as:

$$HR(t) = \exp\{\beta_2 + \beta_3 A(t)\}.$$

Hence, if a patient accrued 0.5 years of time in remission, their HR relative to those who have not remitted is $\exp(\beta_2 + 0.5\beta_3)$. If a patient has accrued 2 years of time in remission, their HR relative to those who have not remitted is $\exp(\beta_2 + 2\beta_3)$.

Appendix III: Complete Results from Adjusted Models

	Main effects only model			Interaction model		
	Unadjusted		Adjusted	Unadjusted		Adjusted
	HR (95% CI)		HR (95% CI)	HR (95% CI)		HR (95% CI)
T2DM status						
Remission	0.49 (0.41, 0.57)		0.71 (0.60, 0.85)	0.48 (0.41, 0.57)		0.70 (0.59, 0.84)
Relapse	0.73 (0.55, 0.98)		0.87 (0.65, 1.16)	1.02 (0.71, 1.47)		1.14 (0.79, 1.65)
Legacy effect				0.79 (0.65, 0.95)		0.81 (0.67, 0.99)
Year of surgery						
2001-2			1.00			1.00
2003-4			1.10 (0.75, 1.6)			1.12 (0.77, 1.63)
2005-6			0.74 (0.50, 1.09)			0.75 (0.51, 1.10)
2007-8			0.82 (0.56, 1.21)			0.83 (0.56, 1.23)
2009-10			0.83 (0.56, 1.24)			0.84 (0.57, 1.26)
2011			0.96 (0.63, 1.48)			0.98 (0.63, 1.5)
Type of surgery						
RYGB			1.00			1.00
AGB			1.31 (0.99, 1.73)			1.3 (0.98, 1.73)
SG			1.15 (0.91, 1.45)			1.14 (0.91, 1.44)
Race/Ethnicity						
Nonhispanic white			1.00			1.00
Hispanic			0.87 (0.71, 1.06)			0.86 (0.7, 1.06)
Nonhispanic black			0.88 (0.71, 1.09)			0.88 (0.71, 1.09)
Other			0.90 (0.67, 1.2)			0.90 (0.67, 1.2)
Unknown/missing			0.56 (0.41, 0.77)			0.56 (0.41, 0.77)

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Age (years)					
20-29			1.00		1.00
30-44			2.67 (0.84, 8.54)		2.75 (0.86, 8.83)
45-54			6.33 (1.99, 20.12)		6.48 (2.03, 20.68)
	Main effects only model			Interaction model	
	Unadjusted		Adjusted	Unadjusted	Adjusted
	HR (95% CI)		HR (95% CI)	HR (95% CI)	HR (95% CI)
Age (years)					
55-65			16.00 (5.04, 50.83)		16.38 (5.13, 52.30)
65-79			33.56 (10.3, 108.94)		34.26 (10.5, 111.75)
Insurance Type					
Commercial			1.00		1.00
Medicaid			1.37 (0.85, 2.21)		1.36 (0.84, 2.19)
Medicare			1.29 (0.95, 1.75)		1.29 (0.95, 1.76)
Other			1.07 (0.62, 1.83)		1.07 (0.62, 1.83)
Gender					
Female			1.00		1.00
Male			0.92 (0.78, 1.07)		0.92 (0.78, 1.07)
Smoking status					
Never			1.00		1.00
Current			1.01 (0.8, 1.28)		1.00 (0.79, 1.27)
Former			1.02 (0.88, 1.19)		1.02 (0.88, 1.18)
Co-morbidity in prior two years					
Hypertension Diagnosis			1.07 (0.88, 1.31)		1.07 (0.88, 1.31)
High Blood Pressures			0.96 (0.74, 1.25)		0.96 (0.74, 1.25)
Dyslipidemia			1.19 (0.96, 1.48)		1.21 (0.97, 1.5)
LDL (mg/dL)					
< 100			1.00		1.00
≥ 100			0.87 (0.75, 1.01)		0.87 (0.75, 1.02)
Triglycerides (mg/DL)					
< 150			1.00		1.00
≥ 150			0.96		0.95

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			(0.83, 1.1)				(0.83, 1.1)
Medication use							
Statins			1.09 (0.93, 1.28)				1.09 (0.93, 1.27)
	Main effects only model			Interaction model			
	Unadjusted		Adjusted		Unadjusted		Adjusted
	HR (95% CI)		HR (95% CI)		HR (95% CI)		HR (95% CI)
Medication use							
Lipid-lowering			0.91 (0.68, 1.22)				0.9 (0.67, 1.21)
Anticoagulants			1.19 (0.75, 1.89)				1.21 (0.76, 1.93)
Insulin			1.41 (1.19, 1.68)				1.41 (1.18, 1.67)
Oral diabetes			1.05 (0.89, 1.25)				1.05 (0.88, 1.24)
ACE inhibitors or ARB			0.93 (0.80, 1.08)				0.93 (0.80, 1.09)
Other antihypertensives			1.16 (1.00, 1.35)				1.17 (1.01, 1.35)
Duration of diabetes prior to surgery (years)							
< 1			1.00				1.00
1-2			0.99 (0.73, 1.35)				0.99 (0.73, 1.35)
2-5			1.04 (0.80, 1.35)				1.04 (0.80, 1.36)
≥ 5			1.46 (1.13, 1.89)				1.45 (1.12, 1.89)
HbA1c (%)							
< 6.0			1.00				1.00
6.0-6.5			1.17 (0.89, 1.56)				1.17 (0.88, 1.55)
6.5-7.0			1.38 (1.05, 1.8)				1.37 (1.04, 1.79)
7.0-8.0			1.32 (1.01, 1.73)				1.31 (1.00, 1.72)
≥ 8.0			1.57 (1.18, 2.09)				1.55 (1.17, 2.07)
BMI (kg/m²)							
35.0-39.9			1.00				1.00
40.0-49.9			1.06 (0.89, 1.25)				1.06 (0.90, 1.25)
≥ 50.0			1.13 (0.92, 1.39)				1.13 (0.92, 1.39)
Cardiovascular disease							
≥ 1 cardiac event			1.31 (0.88, 1.95)				1.31 (0.88, 1.94)

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	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Cardiovascular disease				
≥ 1 cerebrovascular event		1.2 (0.7, 2.03)		1.2 (0.71, 2.03)
≥ 1 peripheral arterial event		1.12 (0.75, 1.68)		1.12 (0.74, 1.67)

Appendix IV: Results from Sensitivity Analyses

Primary analyses				
	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
T2DM status				
Remission	0.49 (0.41, 0.57)	0.71 (0.60, 0.85)	0.48 (0.41, 0.57)	0.70 (0.59, 0.84)
Relapse	0.73 (0.55, 0.98)	0.87 (0.65, 1.16)	1.02 (0.71, 1.47)	1.14 (0.79, 1.65)
Legacy effect			0.79 (0.65, 0.95)	0.81 (0.67, 0.99)
Sensitivity analysis #1: Removal of the largest healthcare site to determine if effects were due to only one site.				
	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
T2DM status				
Remission	0.54 (0.42, 0.68)	0.71 (0.55, 0.91)	0.53 (0.42, 0.67)	0.70 (0.55, 0.90)
Relapse	0.81 (0.55, 1.19)	0.86 (0.58, 1.27)	1.28 (0.78, 2.09)	1.28 (0.77, 2.13)
Legacy effect			0.75 (0.60, 0.94)	0.78 (0.61, 0.98)
Sensitivity analysis #2: Addition of urine protein to eGFR to define nephropathy.				

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	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
T2DM status				
Remission	0.52 (0.39, 0.68)	0.69 (0.51, 0.93)	0.52 (0.39, 0.68)	0.69 (0.51, 0.92)
Relapse	0.81 (0.52, 1.27)	0.79 (0.49, 1.25)	1.13 (0.62, 2.04)	1.07 (0.58, 1.98)
	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Legacy effect			0.82 (0.62, 1.07)	0.83 (0.62, 1.09)
Sensitivity analysis #3: Multiple imputation for missing BMI, HbA1c, serum creatinine and race/ethnicity.				
	Main effects only model		Interaction model	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
T2DM status				
Remission	0.47 (0.40, 0.54)	0.69 (0.59, 0.81)	0.46 (0.40, 0.54)	0.69 (0.59, 0.81)
Relapse	0.73 (0.56, 0.94)	0.83 (0.64, 1.07)	0.95 (0.69, 1.32)	1.00 (0.72, 1.38)
Legacy effect			0.84 (0.72, 0.97)	0.88 (0.76, 1.02)