

## **ONLINE SUPPLEMENTARY MATERIALS**

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**Supplemental table 1: Baseline characteristics of study cohort, by race/ethnicity**

Characteristic	Total (N=1,499,627)		Asian (N=166,395)		Black (N=160,228)		Hispanic (N=487,185)		White (N=685,819)	
	N	%	N	%	N	%	N	%	N	%
Pancreatic cancer cases	2,002	0.1	174	0.1	270	0.2	461	0.1	1,097	0.2
Person-years, total	7,462,072.5		829,641.2		859,927.9		2,254,357.7		3,518,145.7	
Follow-up time (years), mean (SD)	5.0 (3.0)		5.0 (3.0)		5.4 (3.0)		4.6 (3.0)		5.1 (2.9)	
Time to pancreatic cancer (years), mean (SD)	3.8 (2.5)		4.0 (2.6)		3.8 (2.4)		4.0 (2.6)		3.7 (2.5)	
Incidence rate, unadjusted	26.8		21.0		31.4		20.4		31.2	
Incidence rate, age-adjusted <sup>1</sup>	30.7		27.5		36.2		29.0		31.2	
Age, mean (SD)	57.9 (10.9)		57.0 (10.2)		57.4 (10.9)		55.2 (10.0)		60.1 (11.3)	
Age group										
45-50	433,225	28.9	49,638	29.8	49,542	30.9	187,708	38.5	146,337	21.3
50-54	249,754	16.7	28,156	16.9	26,612	16.6	89,481	18.4	105,505	15.4
55-59	227,267	15.2	27,130	16.3	23,779	14.8	69,596	14.3	106,762	15.6
60-64	191,088	12.7	22,710	13.7	18,827	11.8	48,295	9.9	101,256	14.8
65-69	153,534	10.2	17,265	10.4	15,718	9.8	39,832	8.2	80,719	11.8
≥70	244,759	16.3	21,496	12.9	25,750	16.1	52,273	10.7	145,240	21.2
Gender										
F	827,460	55.2	95,415	57.3	95,918	59.9	268,168	55.0	367,959	53.7
M	672,167	44.8	70,980	42.7	64,310	40.1	219,017	45.0	317,860	46.4
BMI, mean (SD)	29.2 (6.2)		25.7 (4.4)		31.0 (6.9)		30.1 (5.8)		28.9 (6.2)	
BMI category										
<25	379,339	25.3	81,059	48.7	27,579	17.2	80,396	16.5	190,305	27.8
25-30	555,925	37.1	62,532	37.6	52,919	33.0	192,659	39.6	247,815	36.1
≥30	564,363	37.6	22,804	13.7	79,730	49.8	214,130	44.0	247,699	36.1
Smoking status										
Never/Passive	967,251	64.5	126,775	76.2	97,111	60.6	346,421	71.1	396,944	57.9

Past	392,214	26.2	29,402	17.7	42,757	26.7	103,415	21.2	216,640	31.6
Current	140,162	9.4	10,218	6.1	20,360	12.7	37,349	7.7	72,235	10.5
Alcohol user										
No	864,634	57.7	122,172	73.4	96,485	60.2	304,266	62.5	341,711	49.8
Yes	634,993	42.3	44,223	26.6	63,743	39.8	182,919	37.6	344,108	50.2
Education <sup>2</sup>										
High school or less	586,579	39.1	9,856	5.9	3,670	2.3	24,690	5.1	33,033	4.8
Some college	523,205	34.9	53,529	32.2	72,130	45.0	285,010	58.5	175,910	25.7
College graduate	318,594	21.2	47,225	28.4	64,266	40.1	127,466	26.2	284,248	41.5
Missing	71,249	4.8	55,785	33.5	20,162	12.6	50,019	10.3	192,628	28.1
Family history of pancreatic cancer	16,066	1.1	1,706	1.0	1,487	0.9	4,518	0.9	8,355	1.2
Pancreatitis	18,418	1.2	1,304	0.8	2,866	1.8	5,956	1.2	8,292	1.2
Diabetes status										
None	1,055,996	70.4	110,579	66.5	103,112	64.4	327,726	67.3	514,579	75.0
Incident	110,699	7.4	14,836	8.9	14,730	9.2	36,892	7.6	44,241	6.5
Prevalent	332,932	22.2	40,980	24.6	42,386	26.5	122,567	25.2	126,999	18.5

<sup>1</sup>Incidence rate per 100,000 person-years, age-standardized to US Census 2000 standard population, truncated to ages 45+.

<sup>2</sup>Based on population geocoding files and not specific to individual patient.

All tests comparing distribution of risk factors across race/ethnicity had p-values <0.0001.

**Supplemental table 2: Association between diabetes status and pancreatic cancer, among specific subgroups**

Subgroup	No diabetes			Incident diabetes <sup>1</sup>			Prevalent diabetes			p <sup>3</sup>
	N Cases	Person-years	RR (95% CI) <sup>2</sup>	N Cases	Person-years	RR (95% CI) <sup>2</sup>	N Cases	Person-years	RR (95% CI) <sup>2</sup>	
Gender										0.75
Females	521	2,993,149.9	1 (ref)	171	396,488.0	3.27 (2.70-3.96)	355	2,067,194.6	1.85 (1.61-2.14)	
Males	416	2,067,194.6	1 (ref)	135	329,567.0	3.05 (2.48-3.76)	404	849,473.1	1.85 (1.60-2.14)	
BMI (kg/m <sup>2</sup> )										0.40
<25	303	1,516,627.4	1 (ref)	55	108,002.9	2.89 (2.10-3.99)	142	262,633.0	1.76 (1.42-2.17)	
25-30	373	1,985,713.6	1 (ref)	125	241,533.6	3.62 (2.91-4.51)	284	554,451.0	1.96 (1.66-2.30)	
≥30	261	1,558,003.5	1 (ref)	126	376,518.5	2.88 (2.29-3.61)	333	858,589.1	1.79 (1.51-2.11)	
Smoking status										0.02
Never	501	3,377,796.1	1 (ref)	172	447,694.9	3.35 (2.77-4.06)	428	992,526.0	2.13 (1.86-2.44)	
Past	313	1,232,906.0	1 (ref)	97	200,397.7	3.02 (2.36-3.85)	251	546,545.1	1.50 (1.26-1.79)	
Current	123	449,642.3	1 (ref)	37	77,962.4	2.81 (1.87-4.22)	80	136,602.0	1.75 (1.29-2.36)	
Alcohol user										0.86
No	509	2,745,676.0	1 (ref)	185	444,507.4	3.11 (2.59-3.73)	534	1,146,417.6	1.85 (1.63-2.11)	
Yes	428	2,314,668.5	1 (ref)	121	281,547.6	3.30 (2.63-4.13)	225	529,255.4	1.85 (1.56-2.19)	
Pancreatitis										0.10
No	912	5,017,861.9	1 (ref)	295	717,016.4	3.20 (2.77-3.69)	728	1,633,082.8	1.89 (1.70-2.09)	
Yes	25	42,482.6	1 (ref)	11	9,038.6	2.06 (0.83-5.09)	31	42,590.3	1.03 (0.61-1.74)	

<sup>1</sup>Incident diabetes treated as a time-varying exposure.

<sup>2</sup>From a Cox proportional hazards regression with age at cohort entry, gender, race, smoking, BMI, alcohol, pancreatitis, family history of pancreatic cancer and education as covariates.

<sup>3</sup>P-values for heterogeneity across particular subgroup.

**Supplemental table 3: Association between incident diabetes duration and pancreatic cancer, among specific subgroups**

Subgroup	No diabetes			Incident diabetes ≤1 year <sup>1</sup>			Incident diabetes >1 year <sup>1</sup>			p <sup>3</sup>
	N Cases	Person-years	RR (95% CI) <sup>2</sup>	N Cases	Person-years	RR (95% CI) <sup>2</sup>	N Cases	Person-years	RR (95% CI) <sup>2</sup>	
Gender										0.09
Female	521	2,993,149.9	1 (ref)	91	54,946.7	6.42 (4.94-8.33)	80	341,541.2	2.29 (1.79-2.93)	
Male	416	2,067,194.6	1 (ref)	84	47,764.8	7.42 (5.74-9.58)	51	281,802.2	1.60 (1.18-2.17)	
BMI (kg/m <sup>2</sup> )										0.35
<25	303	1,516,627.4	1 (ref)	36	18,627.6	6.51 (4.34-9.76)	19	89,375.3	1.61 (1.00-2.59)	
25-30	373	1,985,713.6	1 (ref)	73	35,958.6	8.32 (6.29-11.00)	52	205,575.0	2.15 (1.60-2.91)	
≥30	261	1,558,003.5	1 (ref)	66	48,125.3	5.91 (4.39-7.97)	60	328,393.2	1.97 (1.46-2.65)	
Smoking status										0.63
Never	501	3,377,796.1	1 (ref)	101	62,999.4	7.67 (5.99-9.81)	71	384,695.5	2.02 (1.55-2.62)	
Past	313	1,232,906.0	1 (ref)	52	27,922.0	6.07 (4.39-8.38)	45	172,475.7	2.03 (1.47-2.81)	
Current	123	449,642.3	1 (ref)	22	11,790.2	6.33 (3.83-10.46)	15	66,172.2	1.57 (0.88-2.81)	
Alcohol user										0.52
No	509	2,745,676.0	1 (ref)	101	61,959.7	6.46 (5.08-8.21)	84	382,547.7	2.03 (1.59-2.59)	
Yes	428	2,314,668.5	1 (ref)	74	40,751.8	7.67 (5.79-10.16)	47	240,795.8	1.85 (1.35-2.54)	

<sup>1</sup>Incident diabetes duration treated as a time-varying exposure.

<sup>2</sup>From a Cox proportional hazards regression with age at cohort entry, gender, race, smoking, BMI, alcohol, pancreatitis, family history of pancreatic cancer and education as covariates.

<sup>3</sup>P-values for heterogeneity across particular subgroup.

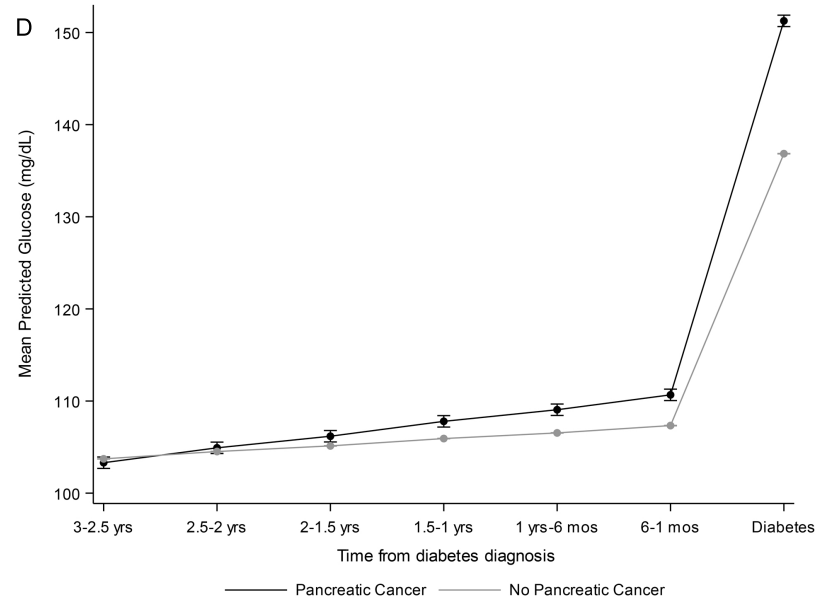
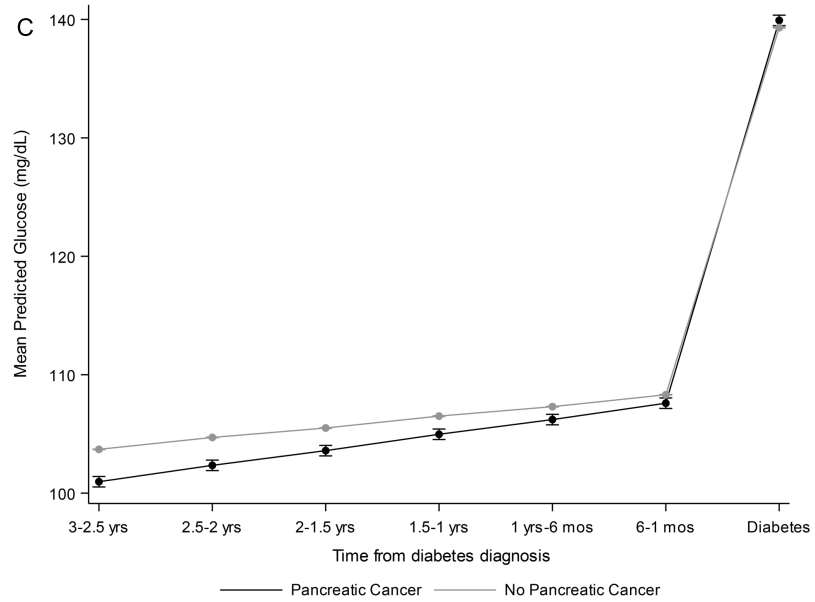
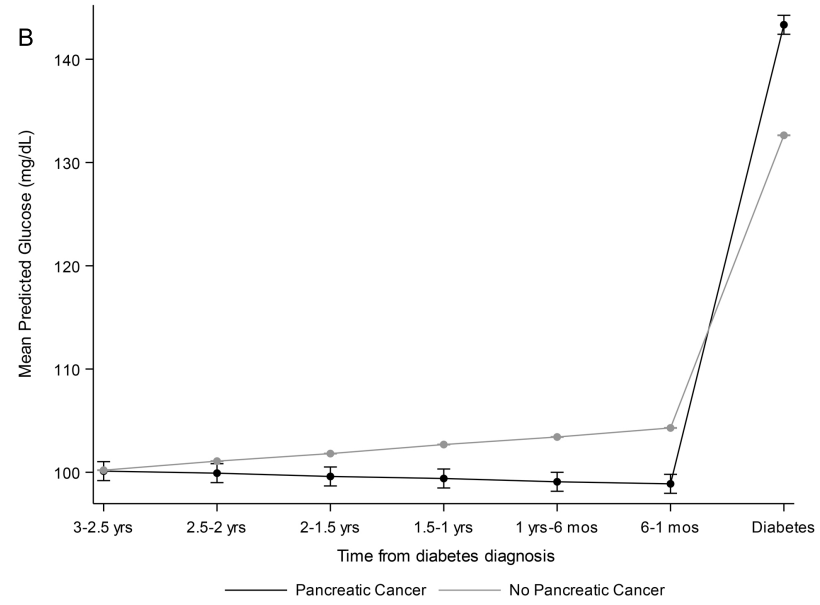
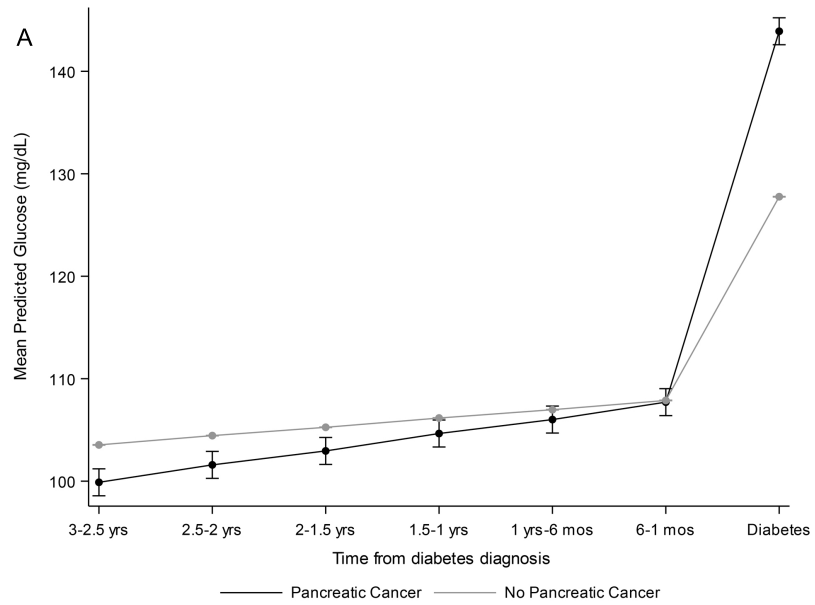
**Supplemental table 4: Predicted trends for longitudinal measurements of fasting glucose, HbA1c and weight among incident diabetes patients who developed pancreatic cancer**

Parameter <sup>1</sup>	Estimate (CI) <sup>2</sup>
Glucose (mg/dL)	
Slope 5 yrs-1.5 yrs	0.49 (-0.31–1.29)
Change in slope at 1.5 yrs	10.17 (7.36–12.98)
HbA1c (%)	
Slope 5 yrs-1.5 yrs	0.09 (0.05–0.12)
Change in slope at 1.5 yrs	0.17 (0.08–0.27)
Weight (kg)	
Slope 5 yrs-1.5 yrs	0.27 (0.00–0.55)
Change in slope at 1.5 yrs	-2.50 (-2.94–2.05)

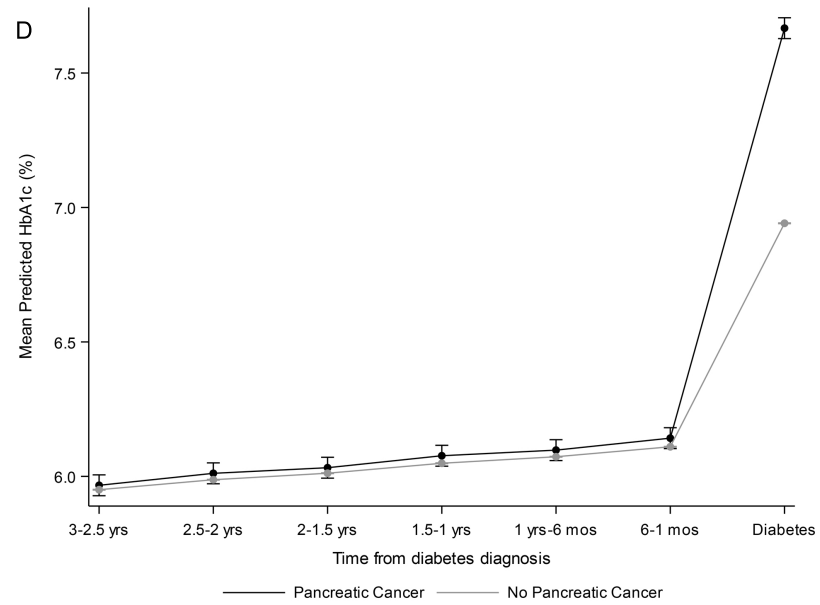
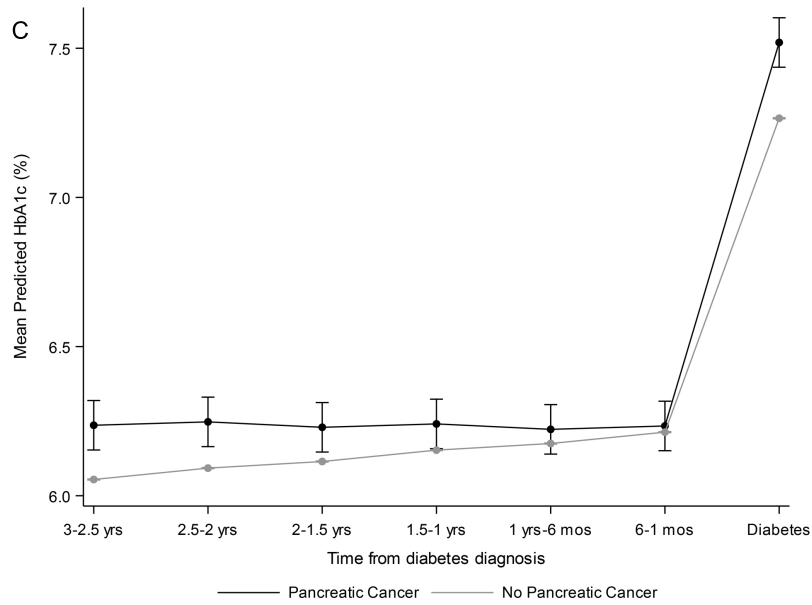
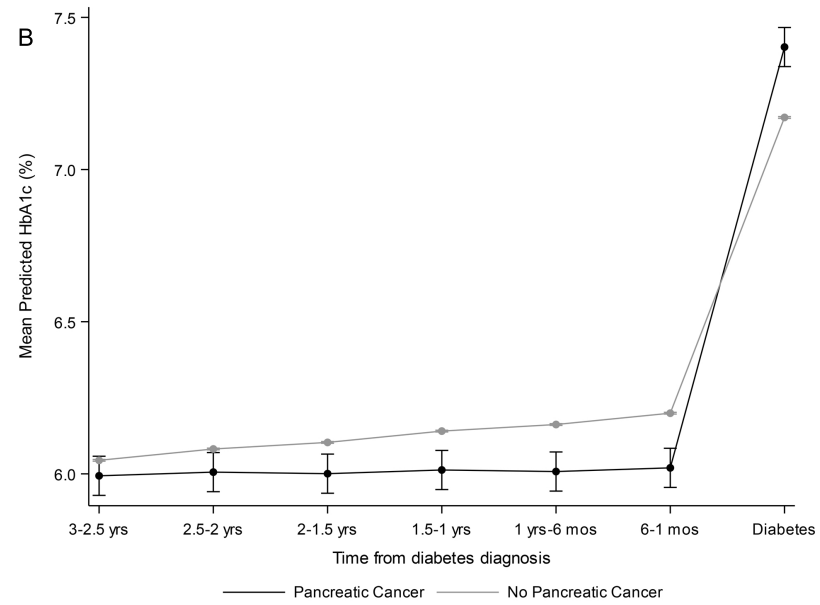
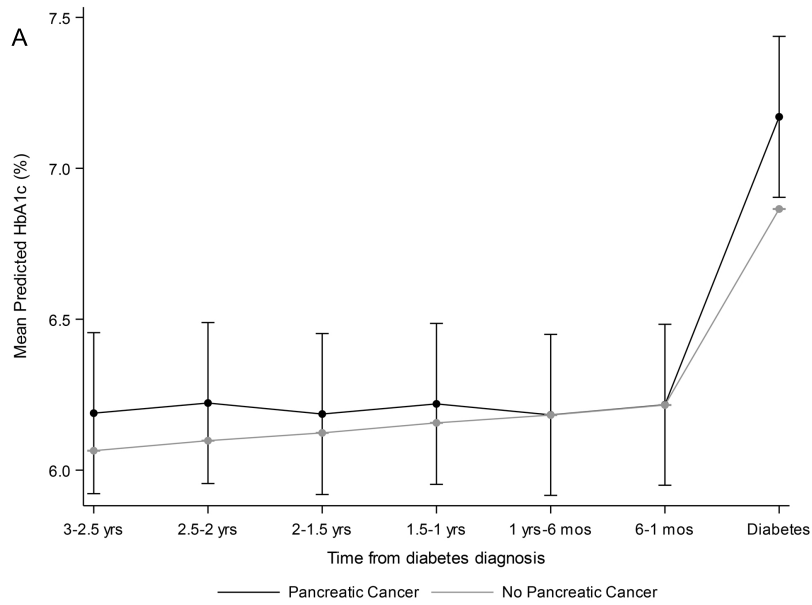
<sup>1</sup>Metabolic markers were evaluated from pancreatic cancer diagnosis up to five years prior in six month intervals.

<sup>2</sup>From a GEE model with the metabolic characteristic as a continuous outcome variable (identity link), time period as the main exposure, age, gender and race as covariates, and patient as the clustering variable. All models included a spline term at the 2-1.5 yr time interval to model the change in slope.

**Supplemental figure 1: Predicted mean values of fasting glucose during the three years prior to diabetes for (a) Asians, (b) blacks, (c) Hispanics and (d) whites, across pancreatic cancer status**

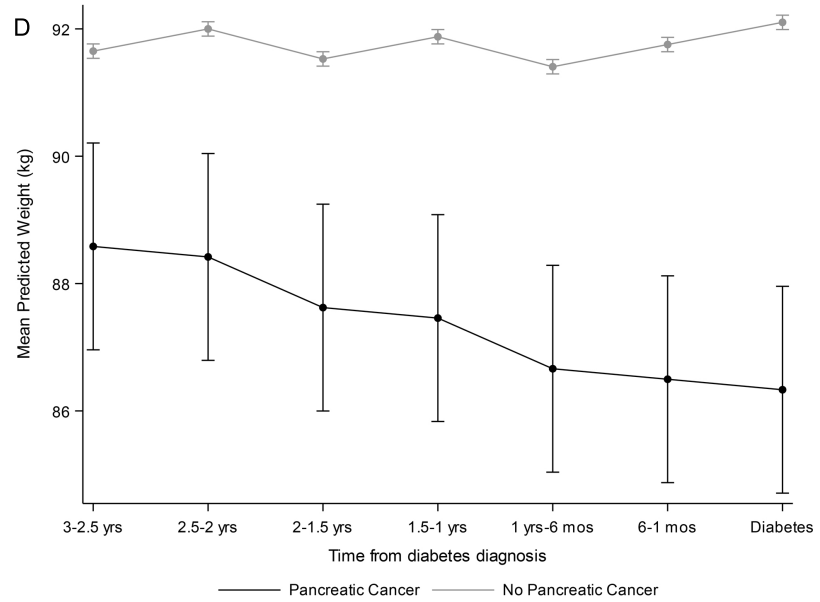
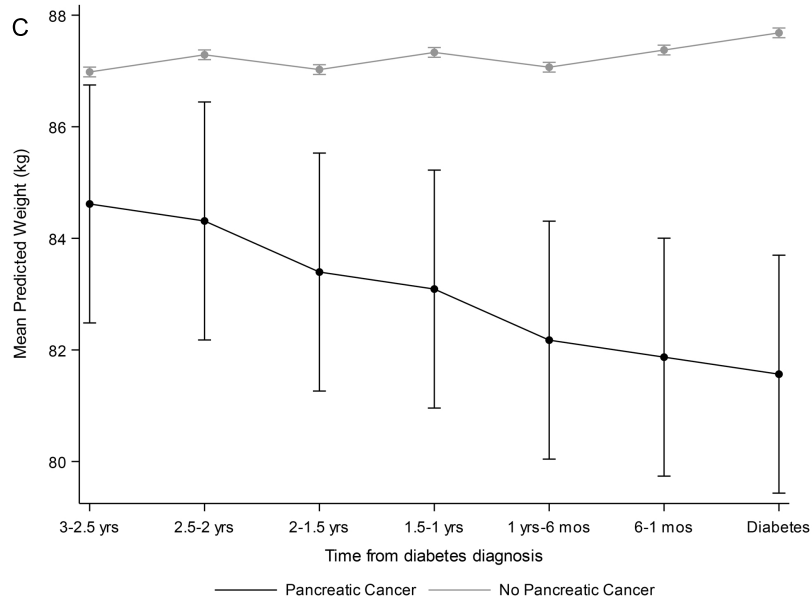
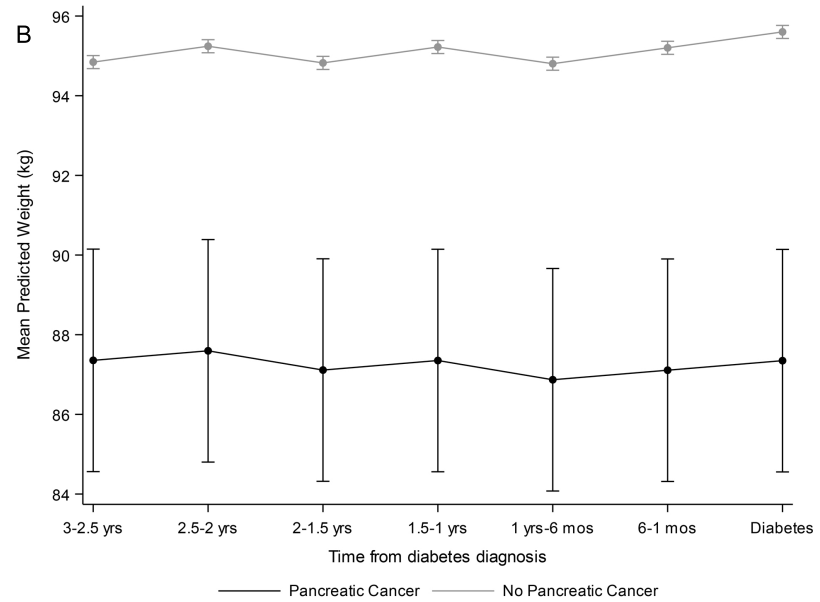
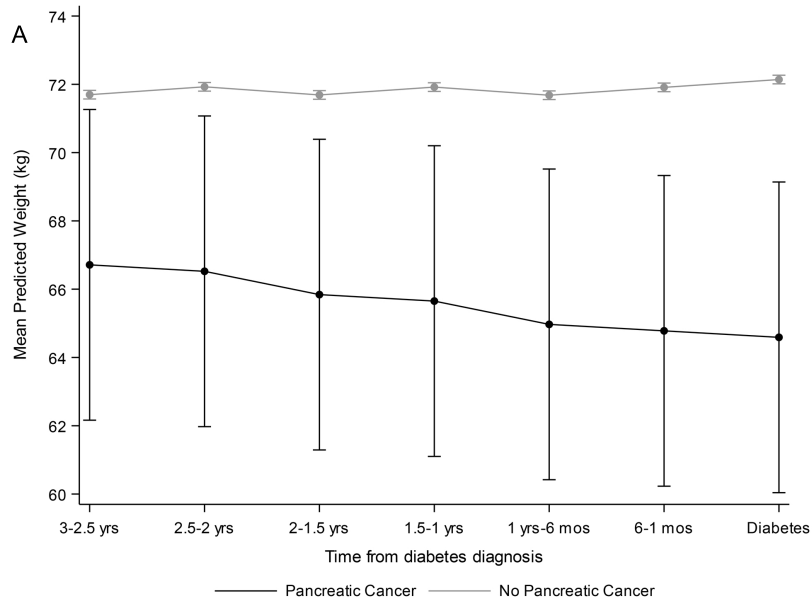


**Supplemental figure 2: Predicted mean values of HbA1c during the three years prior to diabetes for (a) Asians, (b) blacks, (c) Hispanics and (d) whites, across pancreatic cancer status**





**Supplemental figure 3: Predicted mean values of weight during the three years prior to diabetes for (a) Asians, (b) blacks, (c) Hispanics and (d) whites, across pancreatic cancer status**



**Supplemental figure 4: Predicted mean values of (a) fasting glucose, (b) HbA1c and (c) weight during the five years prior to pancreatic cancer diagnosis, among incident diabetes patients who developed pancreatic cancer**

