June 25, 2009

WHI BAA Study #16: Identifying Biomarkers for Early Detection of Pancreatic Cancer

Study population: WHI Observational Study (OS)

Case sample:

As of March 26, 2009, 217 cases of pancreatic cancer were centrally adjudicated and confirmed among OS participants. One in situ case was excluded, leaving 216 invasive pancreatic cancer cases with the following time and blood availability distribution:

      A. 59 cases 0-3 years after baseline with baseline blood
      B. 20 cases 0-3 years after Y3 with only baseline blood
      C. 9 cases more than 3 years after Y3 with only baseline blood
      D. 51 cases 0-3 years after Y3 with baseline and Y3 blood
      E. 77 cases more than 3 years after Y3 with Y3 blood

Number of Controls to be selected:

158 of the 216 invasive pancreatic cancers were also part of the PanScan study and will use the matched controls from that study. These 158 PanScan case-control pairs were checked for exact matching using the current BAA16 matching criteria (age, enrollment year, follow-up duration, alcohol, race/ethnicity, smoking, diabetes, HT use at baseline and Y3, and blood availability). Seven of the 158 case-control pairs match exactly (2 from category A, 1 from category B, 1 from category D, and 3 from category E above). For these 7 cases, the case-control matching is complete. The remaining 151 PanScan cases are matched to an additional control along with the 58 non-PanScan cases, for a total of 367 controls.

Control selection was done in a time-forward manner, selecting one control for each case from the risk set at the time of the case's event. The matching algorithm was allowed to select the closest match based on a criteria to minimize an overall distance measure (Bergstralh EJ, Kosanke JL. Computerized matching of cases to controls. Technical Report #56, Department of Health Sciences Research, Mayo Clinic, Rochester MN. April 1995). Each matching factor was given the same weight.

Part A - Case-Control Selection Summary for <u>Cases 0-3 Years After the Year 3</u> Blood Draw

Number of cases needing newly matched controls = 50

Control sample:

Eligible controls are all OS participants without pancreatic cancer as of March 26, 2009 (N= 93,459).

Exclusions:

a) Already a PanScan control (n=158)
b) Insufficient EDTA (< 275 µl) at baseline and Y3 (n=21,617)
c) Less than 3 years of follow-up in WHI or follow-up time < time to Y3 blood draw (n=2714)

Eligible controls = 71,589

Case-control matching (1:1):

Matching criteria:
a) Age at screening
b) Enrollment year
c) Baseline alcohol intake (Non/past drinker, <1drink per week, 1-<7 drinks per week, 7+ drinks per week)
d) Race/ethnicity (White, Black, Hispanic, American Indian, Asian/PI, Unknown)
e) Smoking (never, past, current)
f) Diabetes history (yes, no)
g) Hormone therapy use at time of baseline and Y3 blood draws (None, E-alone only, E+P)
h) Blood draw visit (baseline only, baseline+Y3, Y3 only)
i) Follow-up duration (controls must have been alive and followed for at least as long as the interval between enrollment and pacreas cancer diagnosis)

Matching results/summary:

Step 1) One control meeting the matching criteria *exactly* was matched to each of 41 cases.

Step 2) Dropping the match to HT use at baseline (still matching on HT use at Y3), allowed for 4 more matches.

Step 3) Dropping the match to HT use at Y3 (still matching on HT use at baseline), allowed for 4 more matches.

Step 4) The race/ethnicity of the 1 remaining case was Hispanic. After collapsing race/ethnicity to White versus non-White and allowing for a 1 year difference in year of enrollment, the remaining case was matched with all other factors matching exactly.

Part B - Case-Control Selection Summary for <u>Cases >3 Years After the Year 3</u> Blood Draw

Number of cases needing newly matched controls = 74

Control sample:

Eligible controls are all OS participants without pancreatic cancer as of March 26, 2009 (N= 93,459).

Exclusions:

a) Already a PanScan control (n=158)
b) Insufficient EDTA (< 275 µl) at Y3 (n=20,370)
c) Less than 6 years of follow-up in WHI (n=7688)
d) Used as a control in Part A (n=50)

Eligible controls = 70,147

Case-control matching (1:1):

Matching criteria:
a) Age at screening
b) Enrollment year
c) Baseline alcohol intake (Non/past drinker, <1drink per week, 1-<7 drinks per week, 7+ drinks per week)
d) Race/ethnicity (White, Black, Hispanic, American Indian, Asian/PI, Unknown)

e) Smoking (never, past, current)
f) Diabetes history (yes, no)
g) Hormone therapy use at time of Y3 blood draw (None, E-alone only, E+P)
h) Blood draw visit (Y3)
i) Follow-up duration (controls must have been alive and followed for at least as long as the interval between enrollment and pacreas cancer diagnosis)

Matching results/summary:

Step 1) One control meeting the matching criteria *exactly* was matched to each of 64 cases.

Step 2) Allowing for a 1 year difference in enrollment year resulted in 5 more matches.

Step 3) After collapsing race/ethnicity to White versus non-White and allowing for a 5 year difference in age and a 2 year difference in year of enrollment, the remaining 5 cases were matched with all other factors matching exactly. Of these 5 cases, one differed in age by 5 years and year of enrollment by 1 year; two differed in age by 1 year; one differed in age by 1 year and year of enrollment by 2 years; and one differed in age by 3 years.

Part C - Case-Control Selection Summary for <u>Cases 0-3 Years After Baseline</u>

Number of cases needing newly matched controls = 85

<u>Control sample:</u>

Eligible controls are all OS participants without pancreatic cancer as of March 26, 2009 (N= 93,459).

Exclusions:

a) Already a PanScan control (n=158)
b) Insufficient EDTA (< 275 μl) at baseline (n=3593)
c) No follow-up in WHI (n=498)
d) Used as a control in Part A or Part B (n=124)

Eligible controls = 89,098

Case-control matching (1:1):

Matching criteria:
a) Age at screening
b) Enrollment year
c) Baseline alcohol intake (Non/past drinker, <1drink per week, 1-<7 drinks per week, 7+ drinks per week)
d) Race/ethnicity (White, Black, Hispanic, American Indian, Asian/PI, Unknown)
e) Smoking (never, past, current)
f) Diabetes history (yes, no)
g) Hormone therapy use at time of baseline blood draw (None, E-alone only, E+P)
h) Blood draw visit (baseline only)
i) Follow-up duration (controls must have been alive and followed for at least as long as the interval between enrollment and pacreas cancer diagnosis)

Matching results/summary:

Step 1) One control meeting the matching criteria *exactly* was matched to each of 76 cases.

Step 2) After collapsing race/ethnicity to White versus non-White and allowing for a 1 year difference in age and 1 year difference in year of enrollment, the remaining 9 cases were matched with all other factors matching exactly. Two case-control pairs differed in age by 1 year; 4 differed in age of enrollment by 1 year; and 3 matched exactly after collapsing race/ethnicity categories.

Final number of matched cases = 216

Match exactly to PanScan control	7
PanScan cases with a new match	151 (also have an additional 151 PanScan controls)
Non-PanScan cases with a new match	58

Matching summary for 216 case/control sets:

Matching Factor	Cases (n=216)		Matched Controls (n=216)		All Controls (n=367)	
Age (years), mean	66.6		66.5		66.9	
	N	%	N	%	N	%
Race/ethnicity						
White	184	85.2	184	85.2	313	85.3
Black	16	7.4	18	8.3	28	7.6
Hispanic	3	1.4	2	0.9	4	1.1
American Indian	1	0.5	1	0.5	2	0.5
Asian/Pacific Islander	9	4.2	8	3.7	14	3.8
Unknown	3	1.4	3	1.4	6	1.6
Smoking status						
Missing	4	1.9	4	1.9	5	1.4
Never	99	45.8	99	45.8	187	51.0
Past	96	44.4	96	44.4	152	41.4
Current	17	7.9	17	7.9	23	6.3
Diabetes ever						
No	201	93.1	201	93.1	344	93.7
Yes	15	6.9	15	6.9	23	6.3
Alcohol intake						
Missing	3	1.4	3	1.4	4	1.1
Non or past drinker	70	32.4	70	32.4	108	29.4
<1 drink/week	62	28.7	62	28.7	117	31.9
1 - <7 drinks/week	52	24.1	52	24.1	86	23.4
7+ drinks/week	29	13.4	29	13.4	52	14.2
Prior hormone use at baseline						
Never/Past	140	64.8	139	64.4	242	65.9
Current E-alone	38	17.6	41	19.0	65	17.7
Current E+P	38	17.6	36	16.7	60	16.3
F44 hormone use at Y3						
Missing	1	0.8	1	0.8	27	7.4
None	81	63.3	81	63.3	210	57.2
E-alone only	24	18.8	24	18.8	70	19.1
Any E+P	22	17.2	22	17.2	60	16.3
OS enrollment year						
1994	1	0.5	0	0.0	0	0.0
1995	57	26.4	62	28.7	104	28.3
1996	66	30.6	63	29.2	112	30.5
1997	50	23.1	52	24.1	85	23.2
1998	42	19.4	39	18.1	66	18.0
Blood draw group						
Baseline only	88	40.7	88	40.7	165	45.0
Baseline and Y3	54	25.0	54	25.0	128	34.9
Y3 only	74	34.3	74	34.3	74	20.2