

Type 2 Diabetes and Cancer

Is there a Connection?

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UNIVERSITY OF HAWAI'I

CANCER CENTER

Support for MEC-related research

R37 CA54281 (Kolonel)

U01 CA164973 (Le Marchand/Wilkens/Haiman)

P01 CA138338 (Le Marchand/Lim)

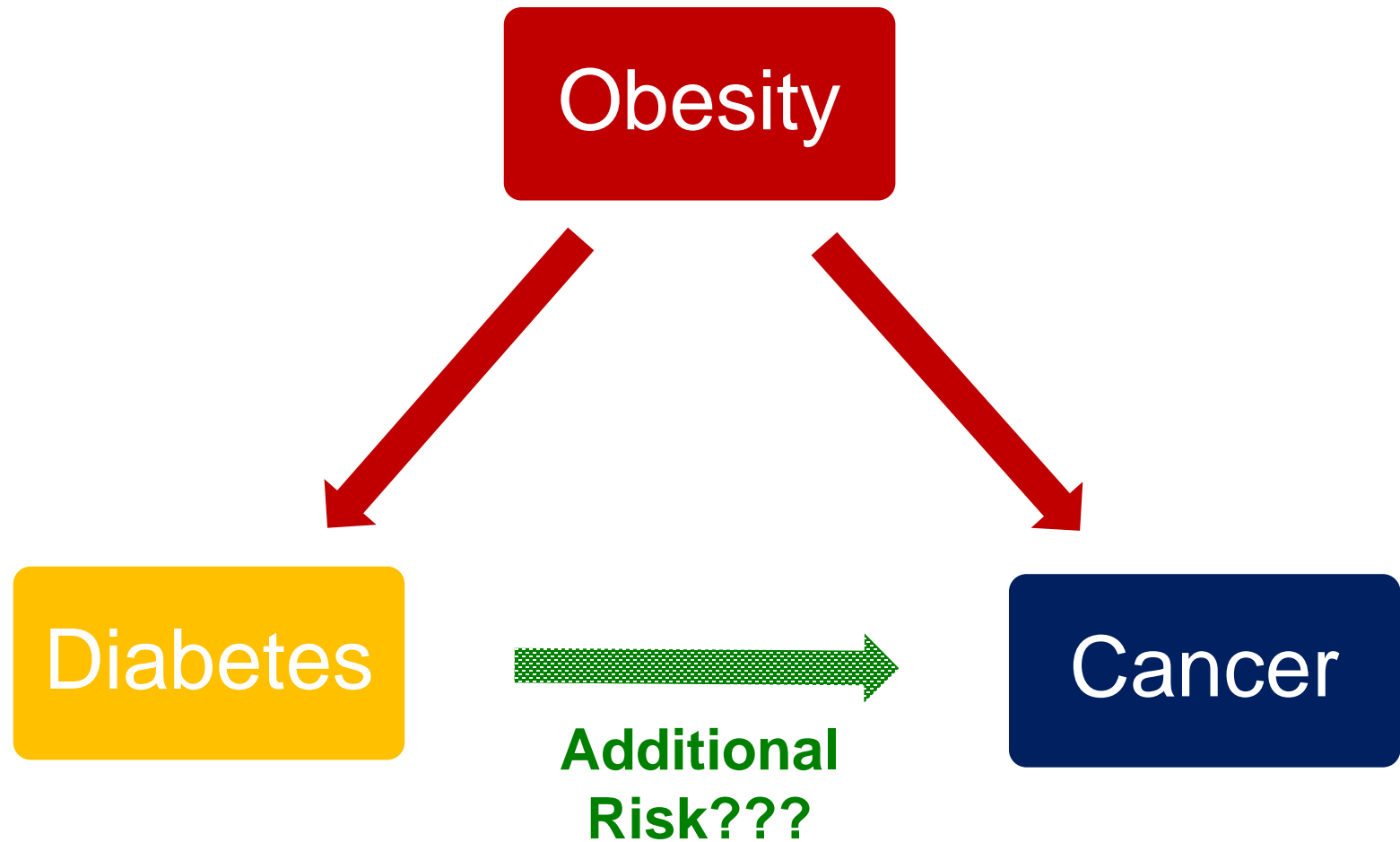
R21 DK073816 (Maskarinec)

Objectives

At the conclusion of this program, the participant will be able to:

- 1) Describe the burden of type 2 diabetes in Hawai'i's population.
- 2) Explain the role of obesity in the development of type 2 diabetes and cancer.
- 3) Identify cancer sites (breast, colon/rectum, and pancreas) that appear to be affected by the presence of type 2 diabetes.
- 4) Discuss the adverse influence of obesity and type 2 diabetes on cancer survival.

Underlying Etiologic Model

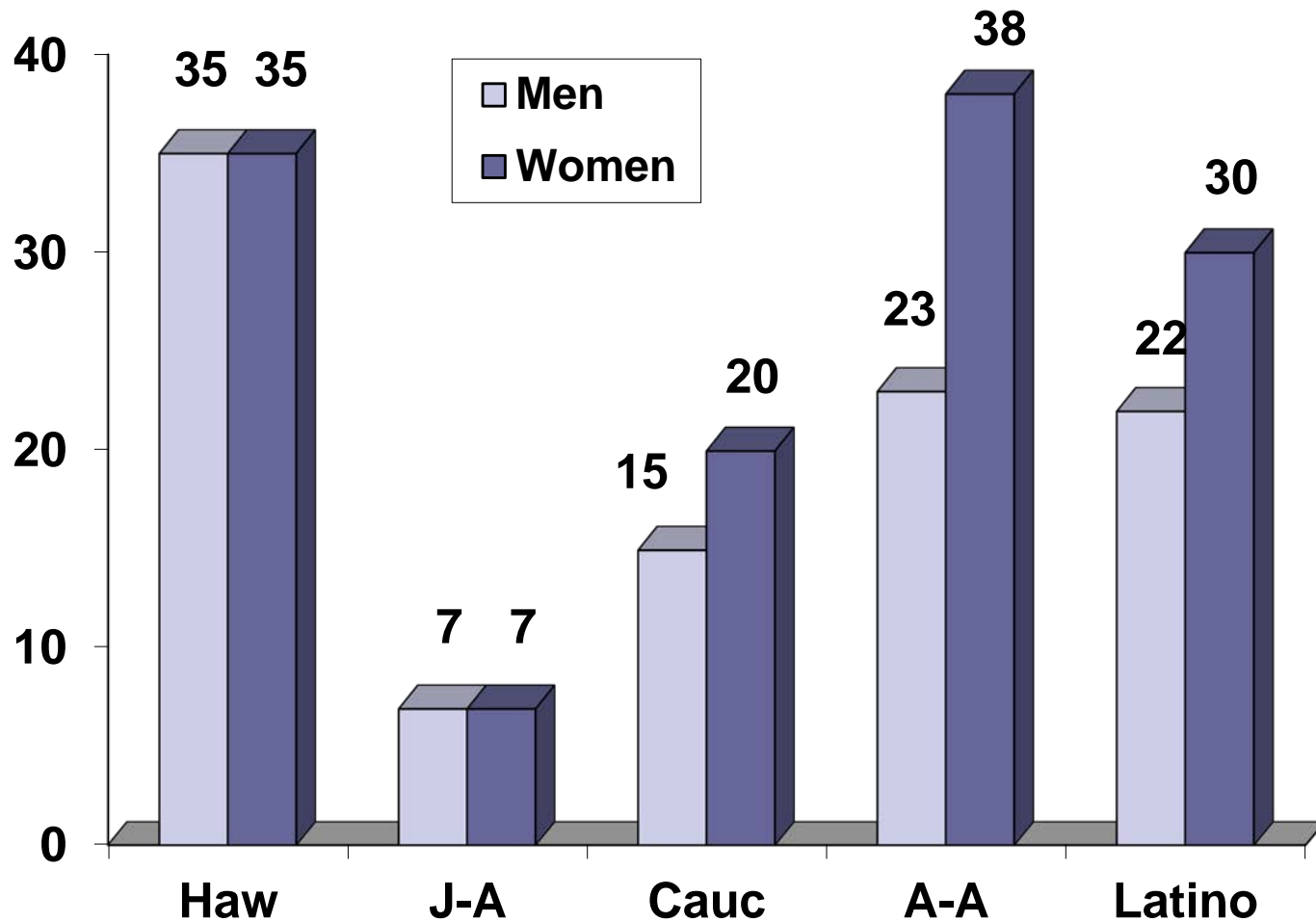


The Multiethnic Cohort Study

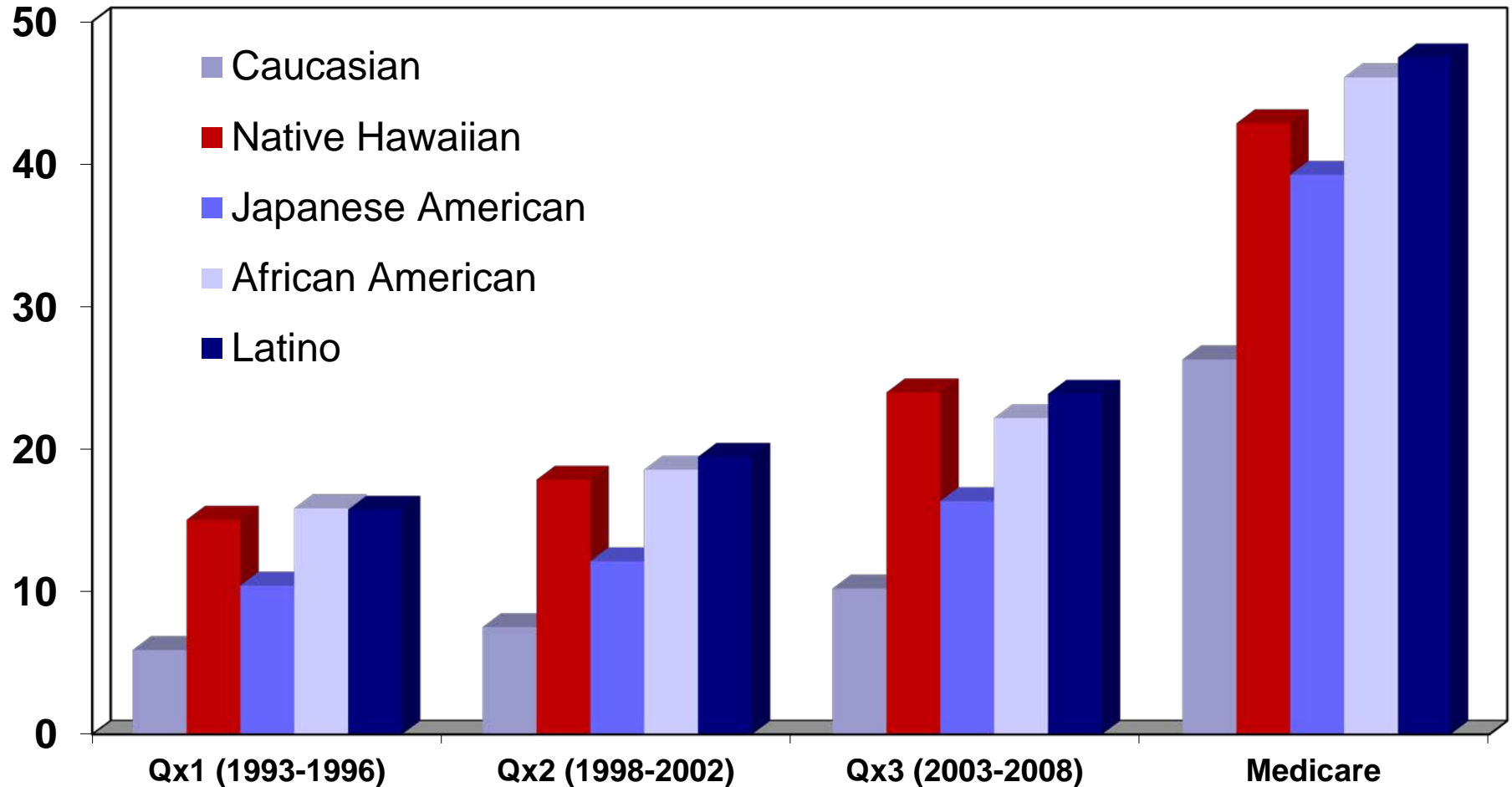


- Baseline, 26 page self-administered questionnaire in 1993-1996
- Validated food frequency questionnaire
- Sent to residents of Hawaii and Los Angeles County
- Names were obtained through drivers' license records, voter registration records and Medicare files
- Follow-up questionnaires every 5 years with updated body weight
- In 2001-2006, 67,594 cohort members (49.7% of eligible) contributed blood and urine samples to biospecimen repository
- 215,251 adult men & women ages 45-75 years were recruited
 - Japanese American (26.4%)
 - White (22.9%)
 - Latino (22.0%)
 - African American (16.3%)
 - Native Hawaiian (6.5%)
 - Other ancestry (5.8%)

Obesity in the Multiethnic Cohort



Diabetes Prevalence over Time by Ethnicity



Diabetes Incidence-Focus on Asians

Ethnicity	N	Cases	Incidence*
White	31564	2231	9.9
Japanese	36712	5522	21.1
Filipino	3871	634	21.3
Chinese/Korean	1632	201	17.9
Part-Asian	694	103	16.3
Mixed Asian	8480	1529	24.9
Native Hawaiian	4772	799	22.8
Other	1473	199	19.2
Total	89198	11218	10.6

*per 1,000 person-years

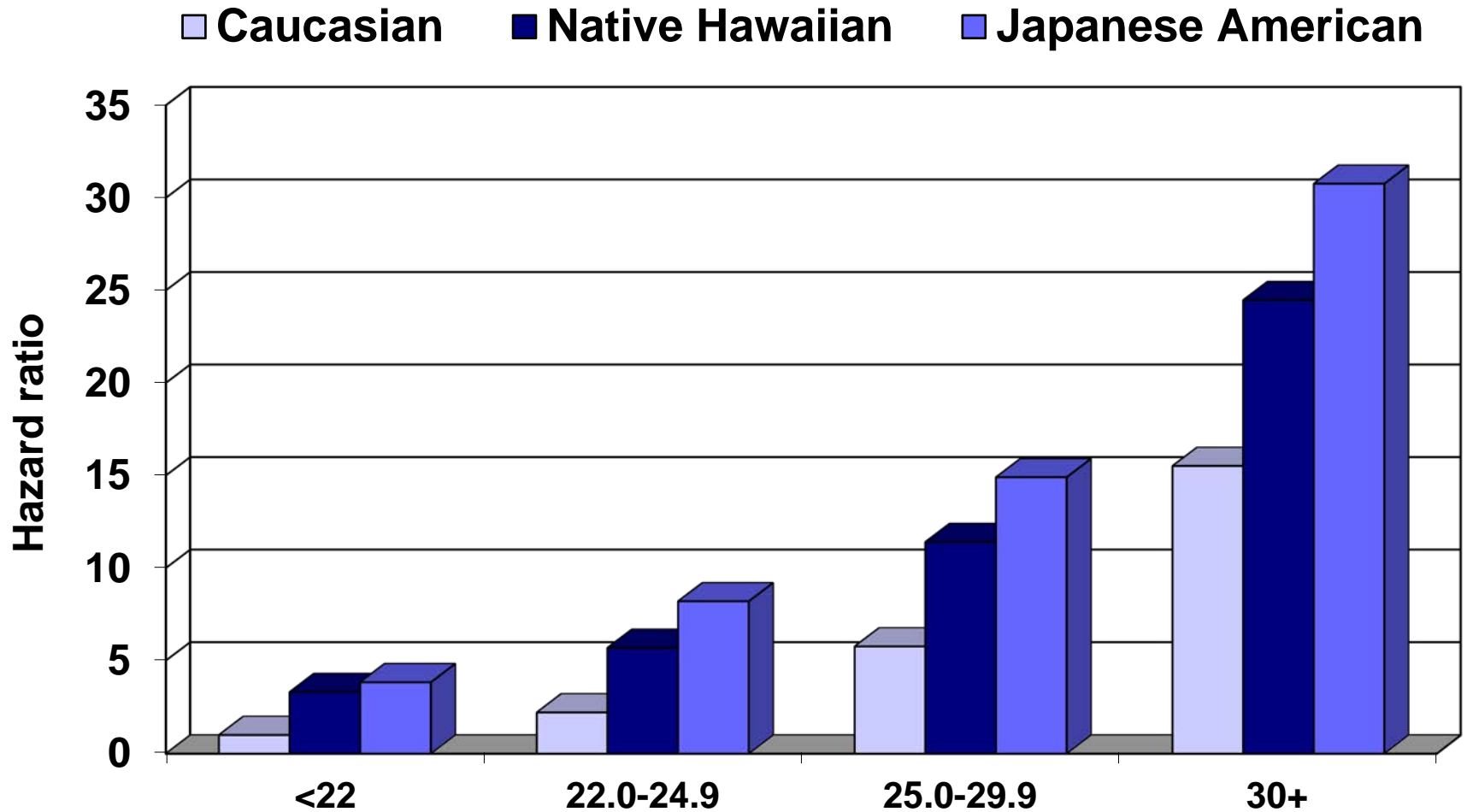
Diabetes Incidence by Hawaiian Admixture

Ethnicity	N	Cases	Incidence*
White only	32,641	2,321	5.8
Hawaiian & White	2,712	410	13.4
Hawaiian only	1,974	366	17.4
Hawaiian & Other	4,385	774	15.3
Hawaiian & Asian	2,916	597	18.4
Asian	44,634	6,738	12.7
Total	89,262	11,206	10.5

*per 1,000 person-years

Diabetes Risk by Body Mass Index

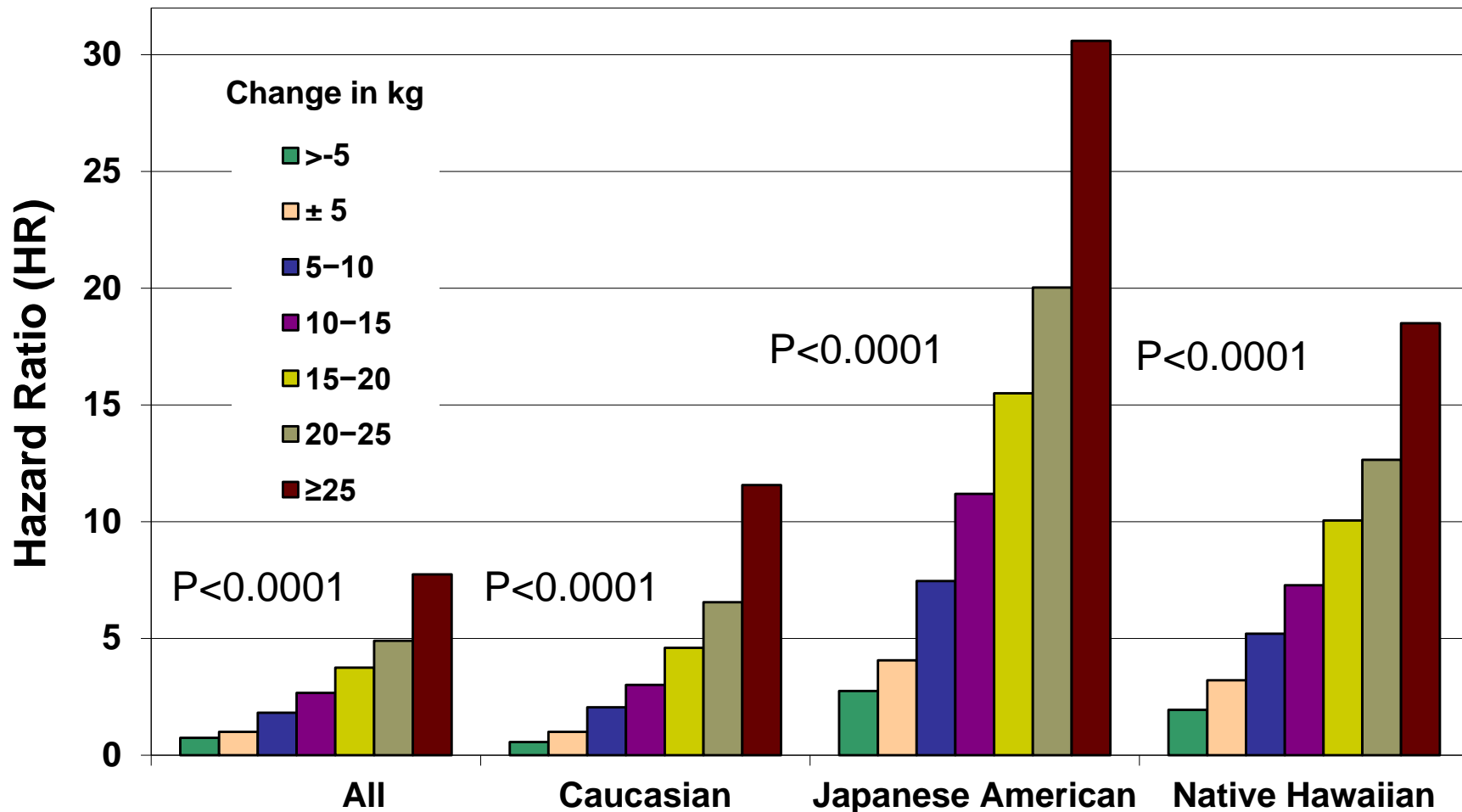
Maskarinec et al. Diabetes 2009



Weight Change and Diabetes Risk: Age 21 to Qx1

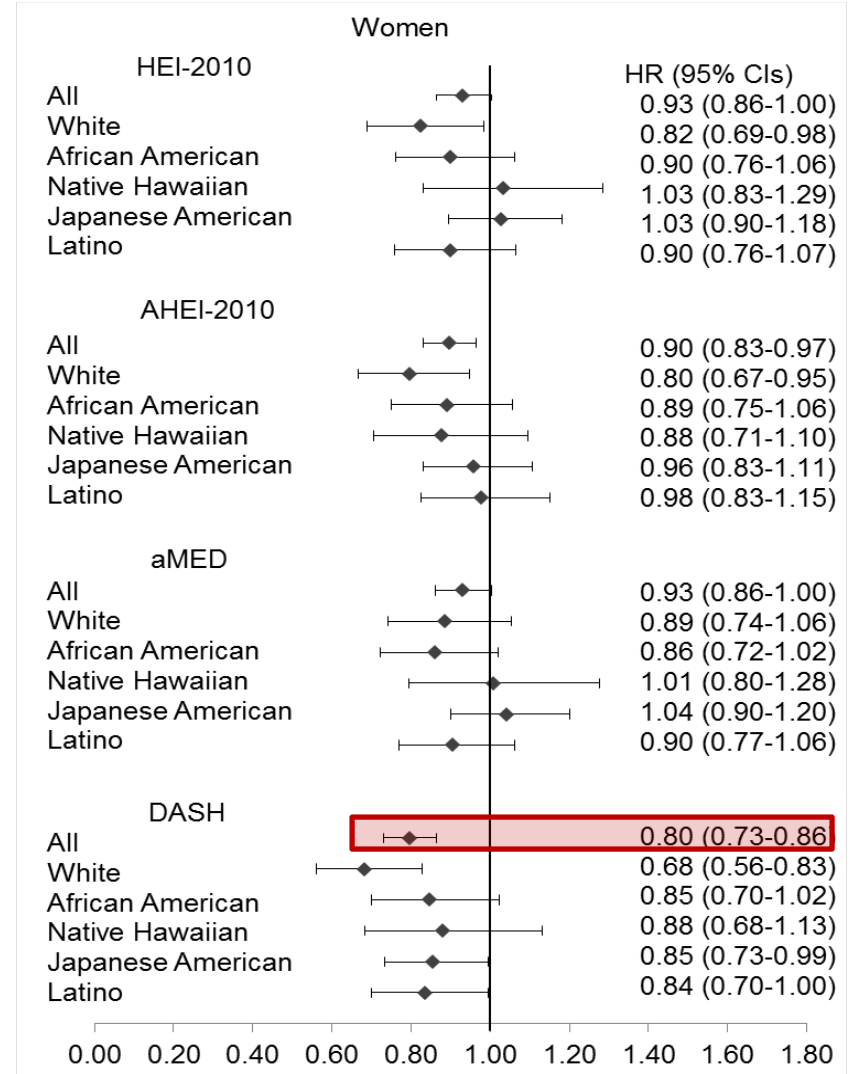
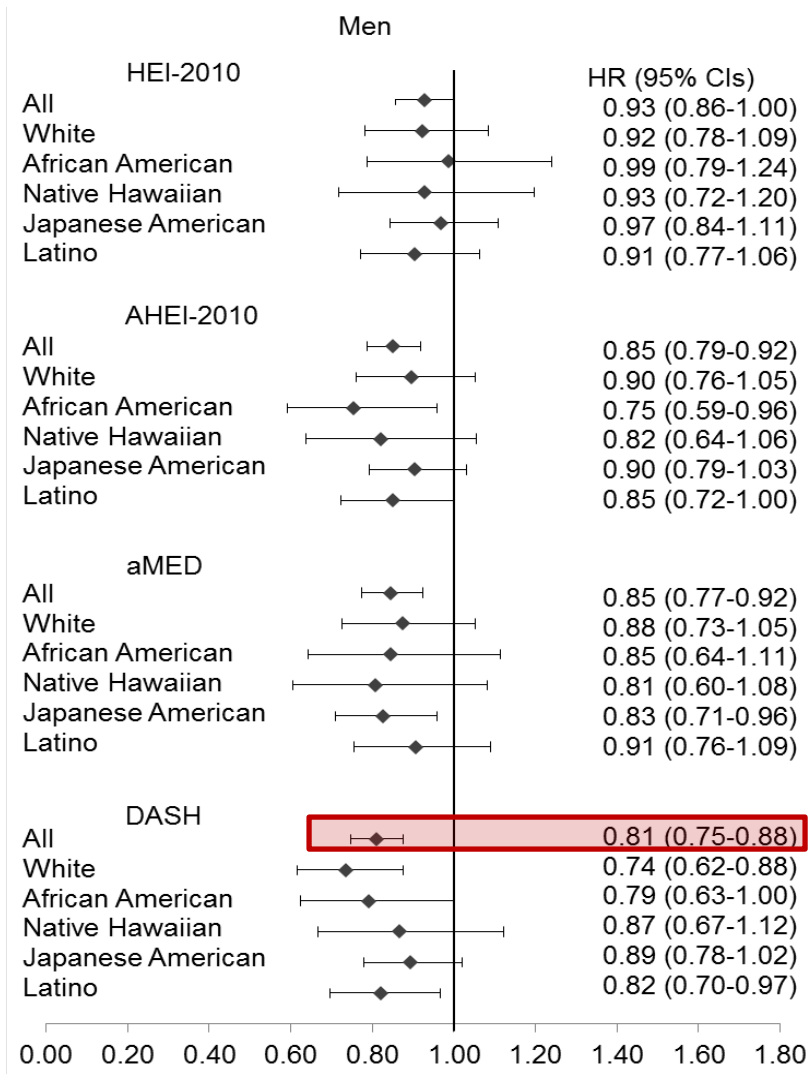
(Caucasians with stable weight as reference)

Morimoto et al. Diabetes & Metabolism 2011



Association of Diet Quality with Diabetes Risk

Jacobs et al. Br J Nutrition 2017



Visceral vs. Subcutaneous Fat

Lim et al. Nutrition and Diabetes 2011

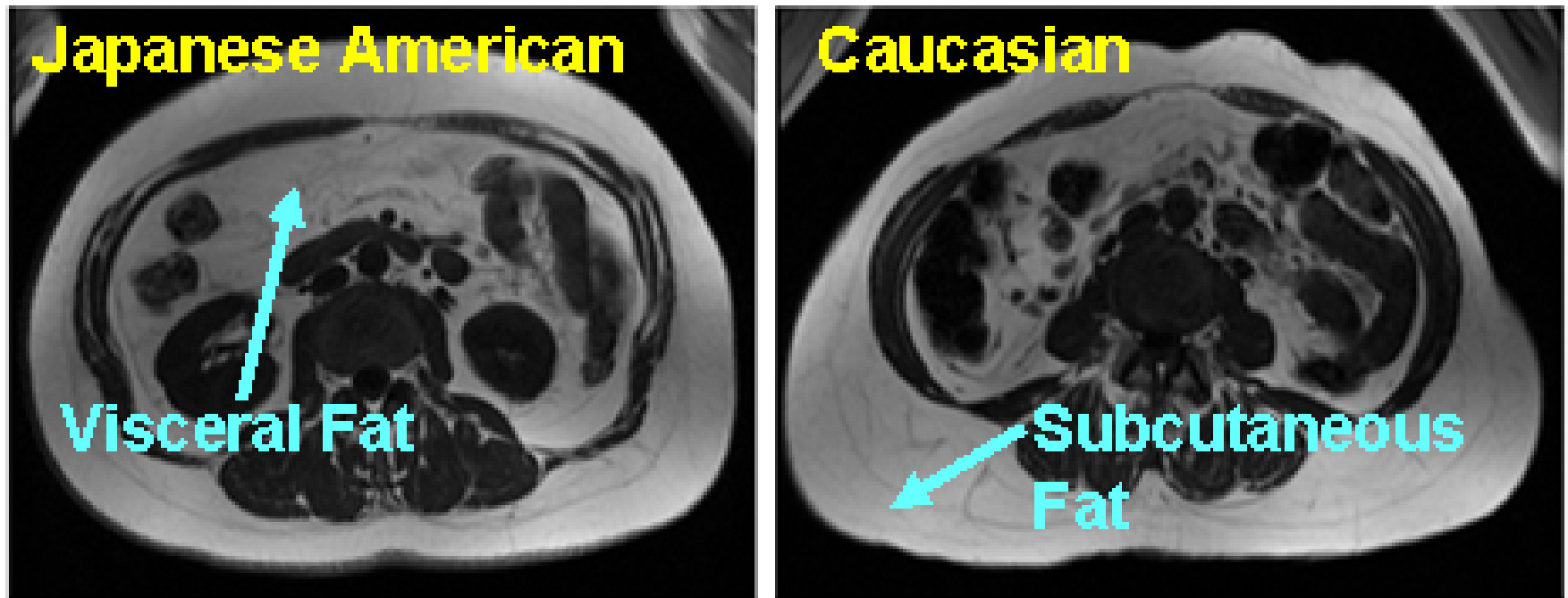
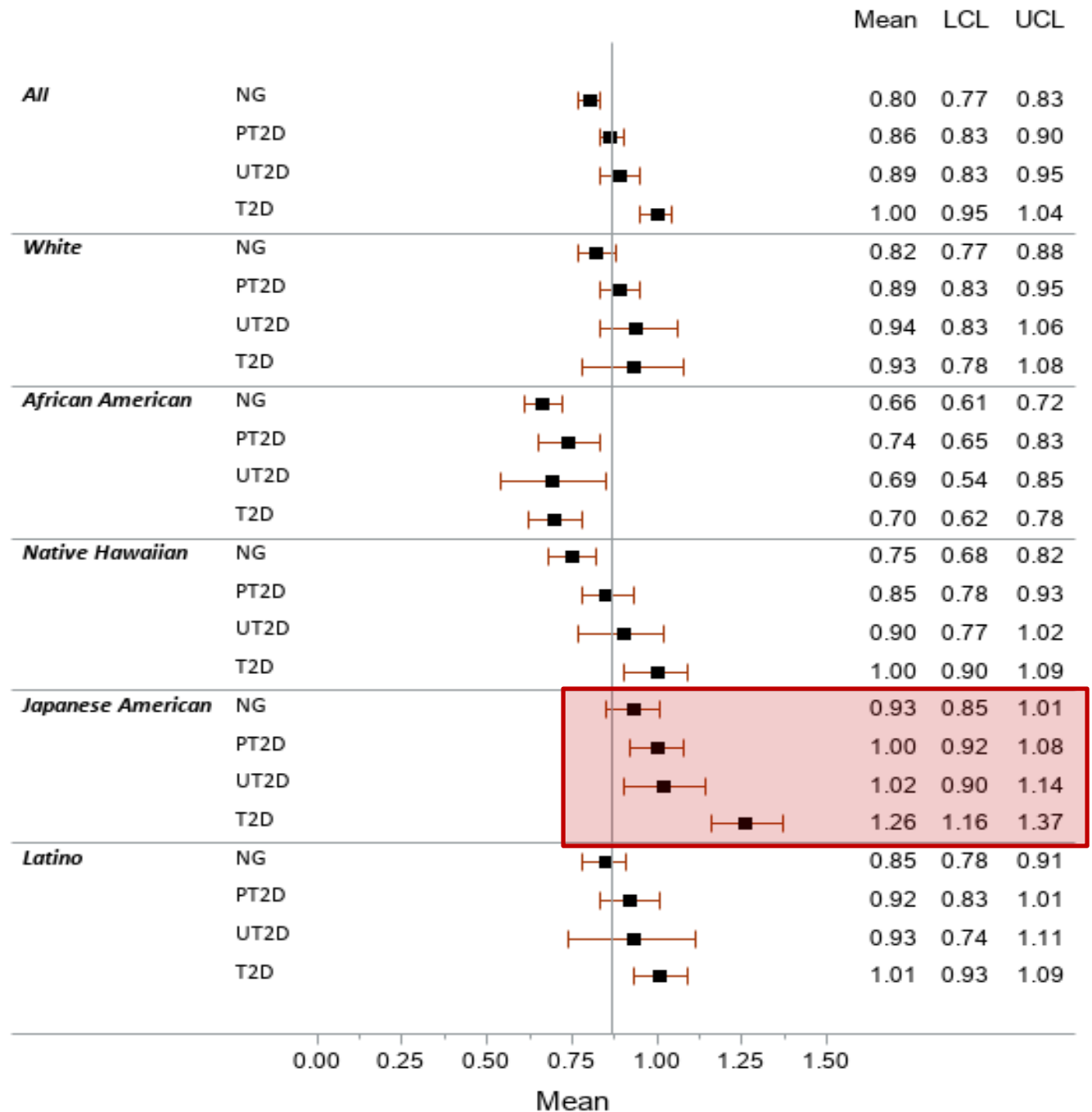


Figure 2. An example MRI scan of L4/L5 vertebral inter-space for visceral and subcutaneous fat

VAT/SAT and Diabetes Status

($p_{\text{trend}} < 0.0001$)

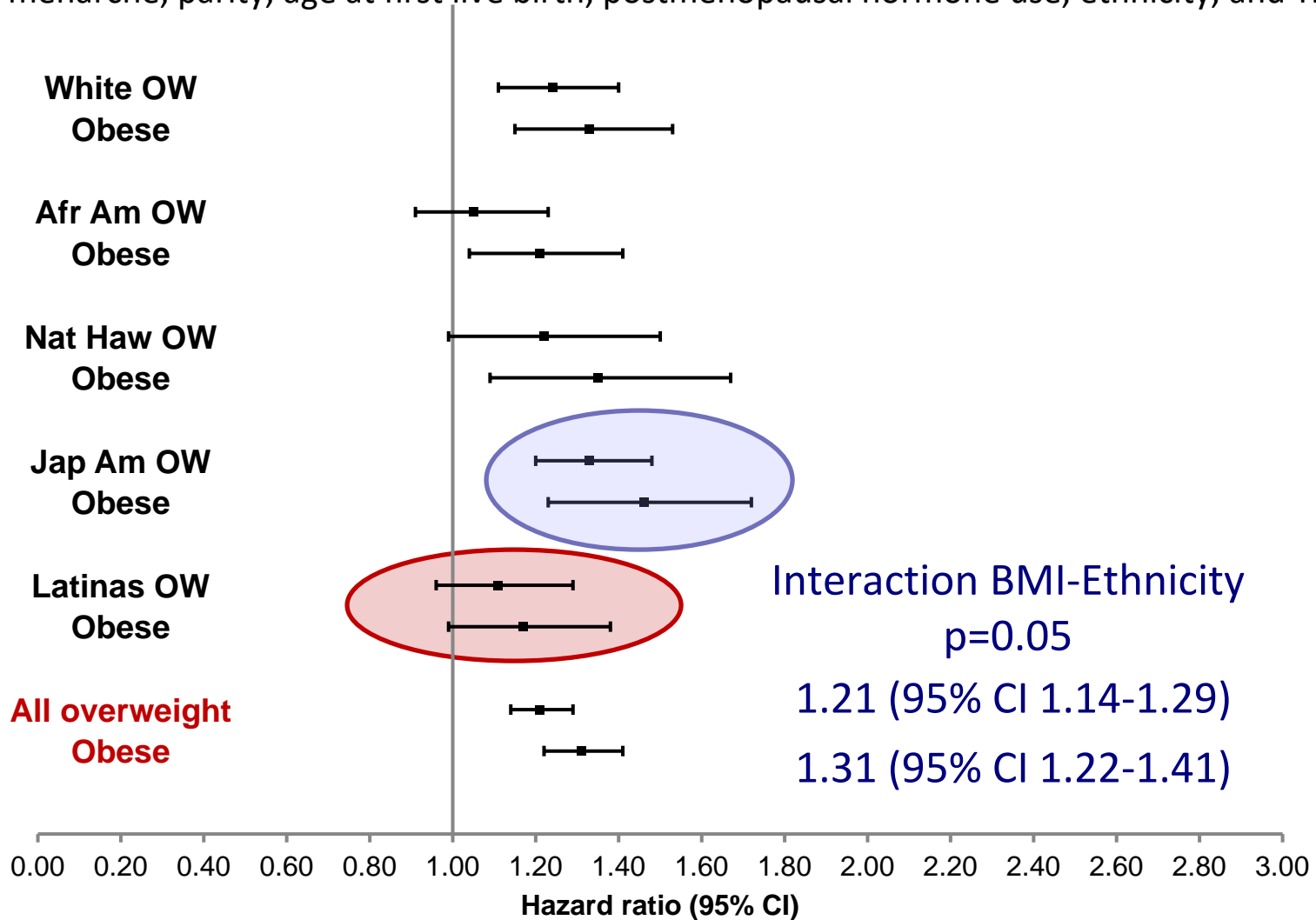
NG=No diabetes
PT2D=Prediabetes
UT2D=Undiagnosed
T2D=Diabetes



BMI and Breast Cancer Risk by Ethnicity

Maskarinec et al. Cancer Epidemiol Biomarkers & Prev 2017

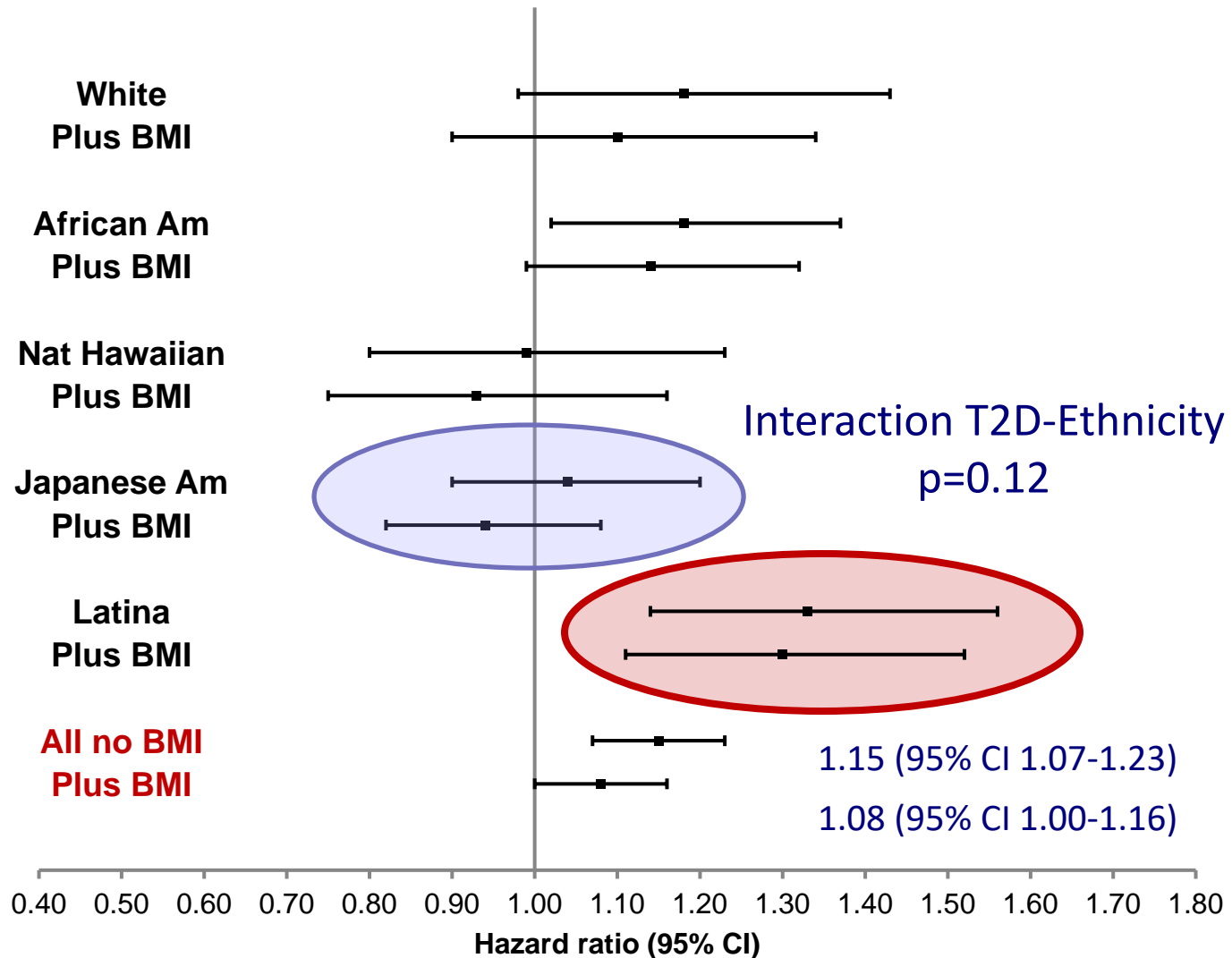
Adjusted for age at cohort entry, education, family history, alcohol intake, physical activity, age at menarche, parity, age at first live birth, postmenopausal hormone use, ethnicity, and T2D



T2D and Breast Cancer Risk by Ethnicity

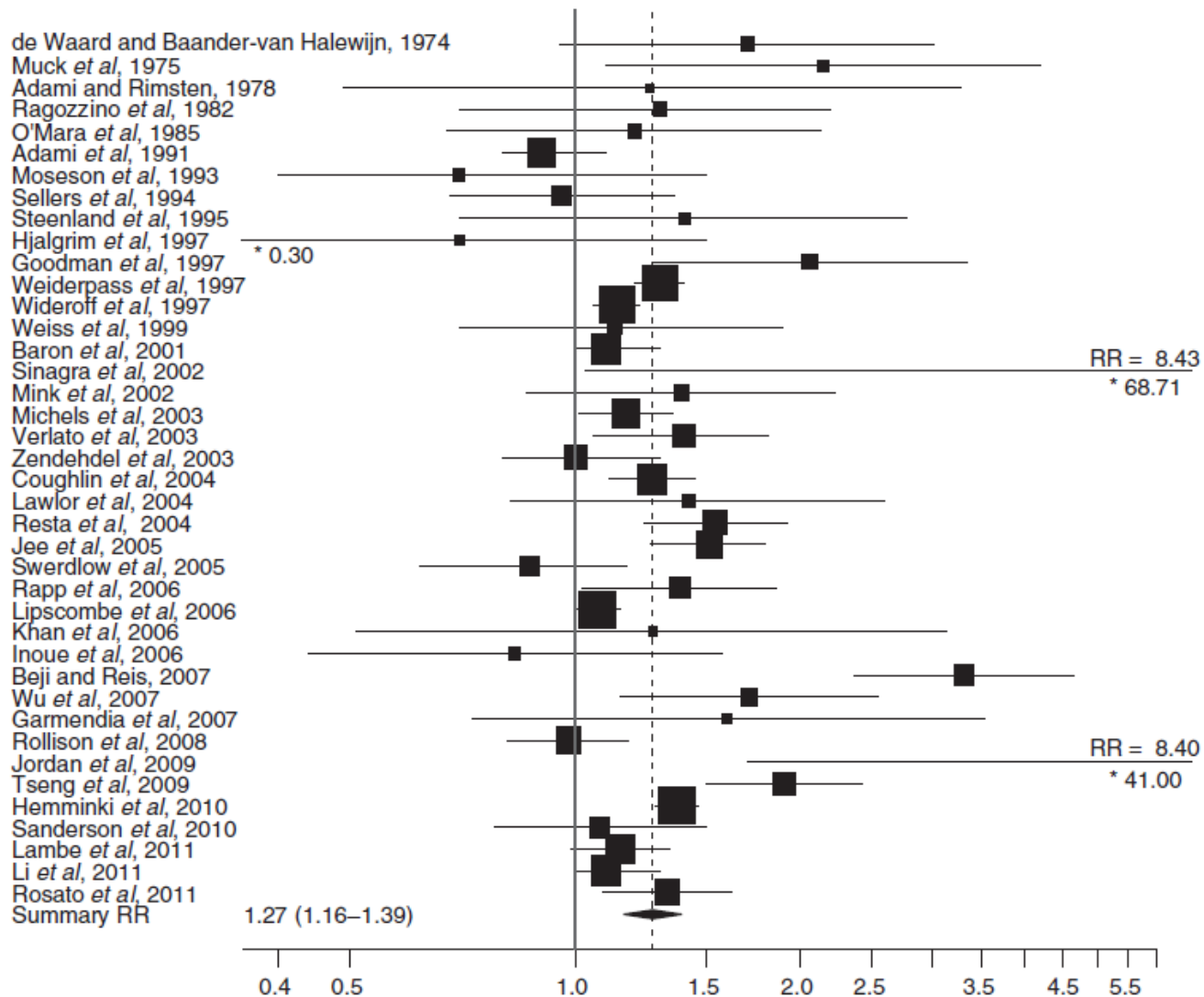
Maskarinec et al. Cancer Epidemiol Biomarkers & Prev 2017

Adjusted for age at cohort entry, education, family history, alcohol intake, physical activity, age at menarche, parity, age at first live birth, postmenopausal hormone use, ethnicity, and BMI



T2D and Breast Cancer Risk – Meta-analysis

Boyle et al. British J Cancer 2012



**Summary
RR
1.27 (1.16-1.39)**

The Association of Diabetes with Colorectal Cancer Risk: The Multiethnic Cohort

He et al. BJC 2010

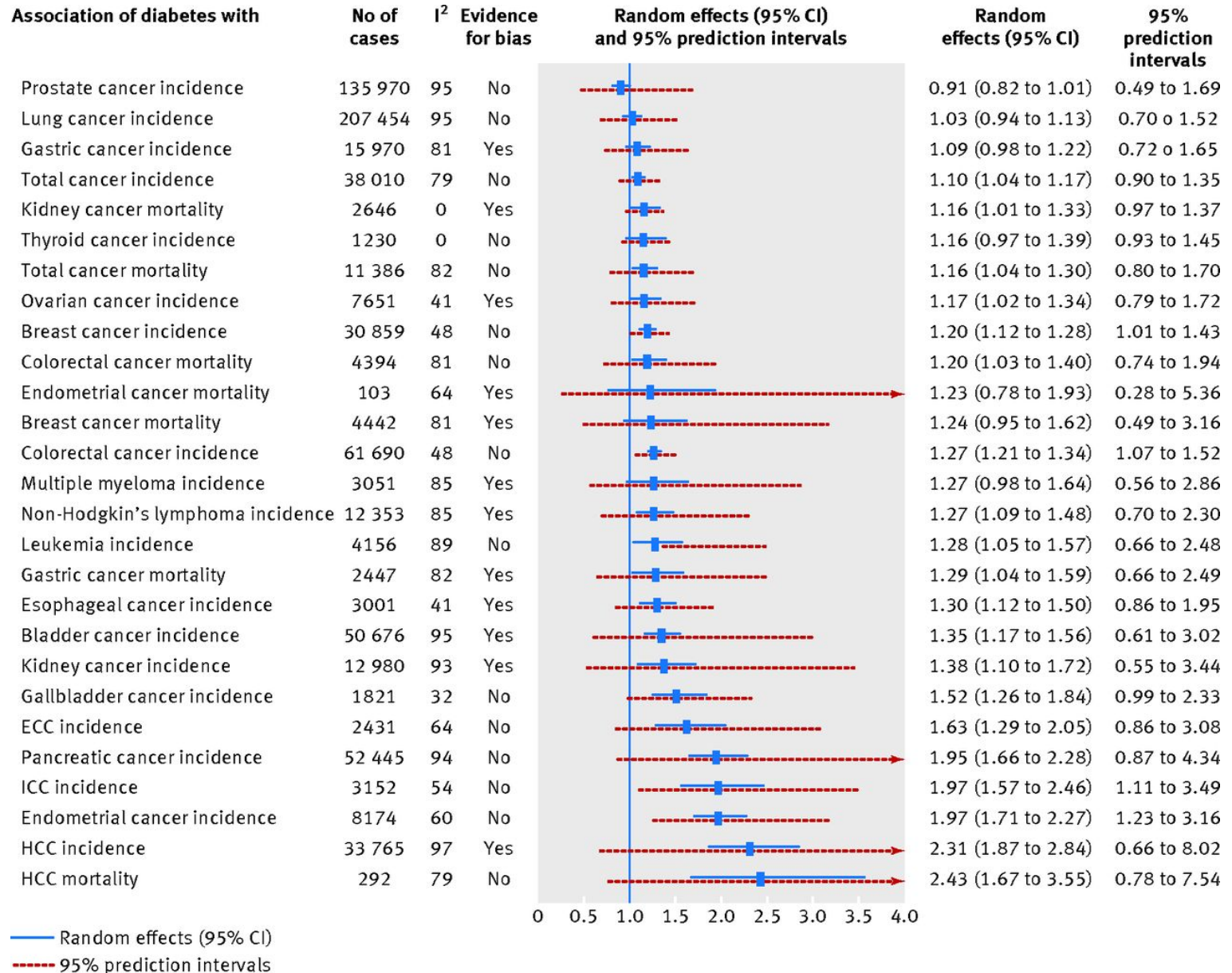
	N	RR	95% CI		P Value
All	3549	1.19	1.09	1.29	<0.001
Men	1921	1.12	0.99	1.26	0.063
Women	1628	1.28	1.12	1.46	<0.001
White	664	1.16	0.91	1.48	0.24
African American	791	1.16	0.97	1.38	0.10
Native Hawaiian	205	0.89	0.62	1.27	0.52
Japanese American	1197	1.27	1.09	1.47	0.002
Latino	692	1.21	1.02	1.46	0.03

Diabetes and Pancreatic/Liver Cancer

Group	Pancreatic cancer	Liver cancer
	Setiawan et al. JNCI 2019	Setiawan et al. JNCI 2014
All	2.39 (1.91-2.98)	
≤3 yrs	3.71 (2.83-4.88)	
>3 yrs	1.61 (1.18-2.21)	
White	NA	2.15 (0.95-4.90)
African Am.	2.03 (1.47-2.82)	2.02 (1.17-3.48)
Native Hawaiian	NA	2.50 (1.11-5.46)
Japanese Am.	NA	2.34 (1.60-3.41)
Latino	2.76 (2.03-3.76)	3.36 (2.41-4.70)

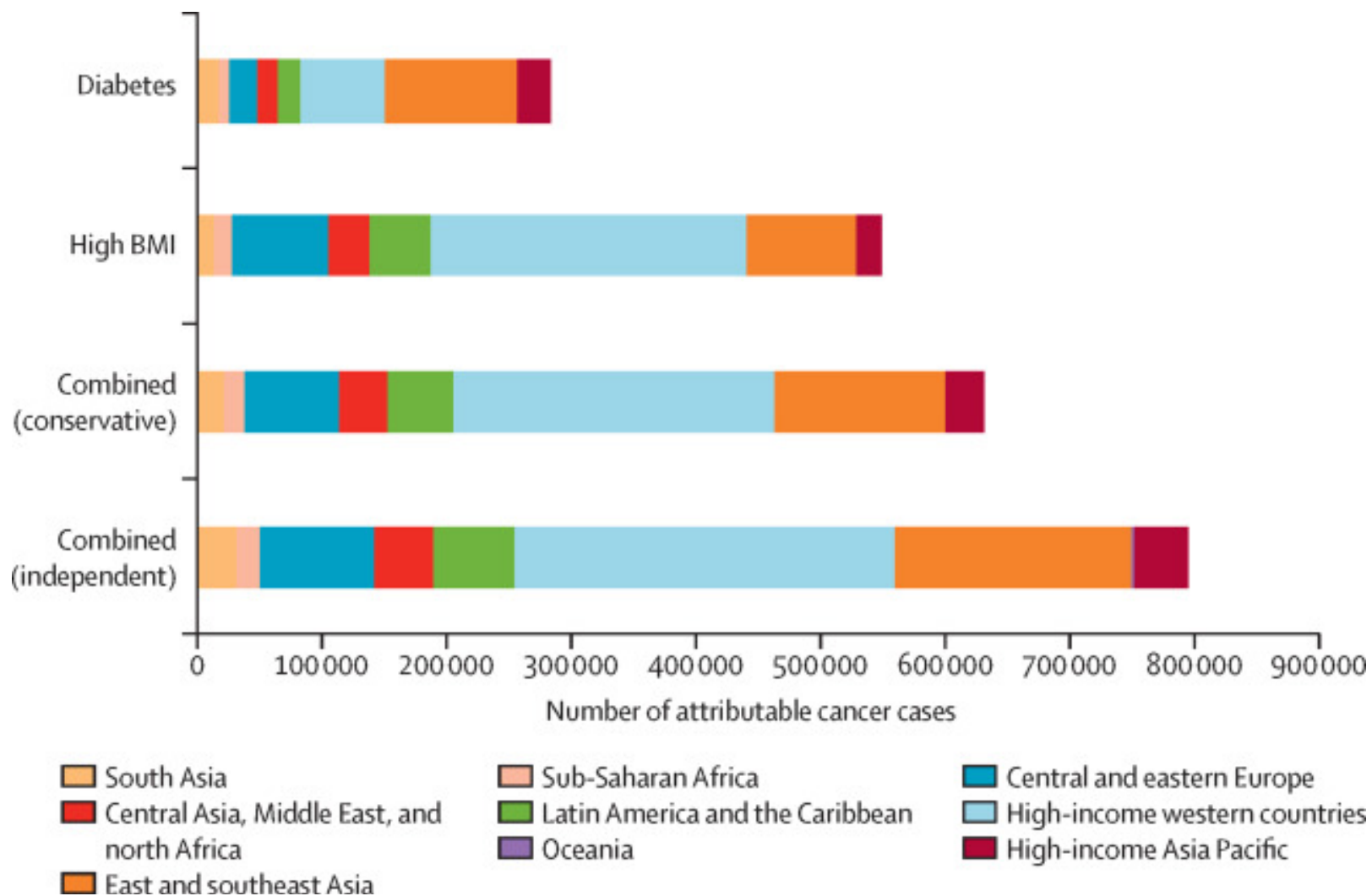
Meta-Analyses of Type 2 Diabetes and Cancer

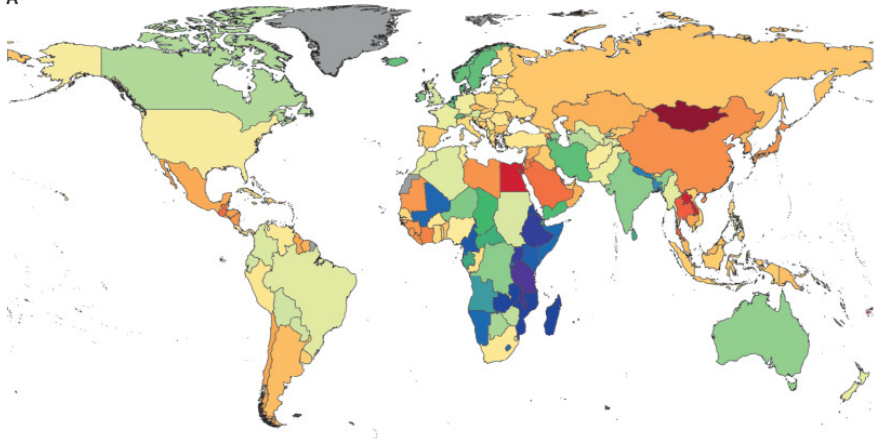
Tsilidis et al. BMJ 2015



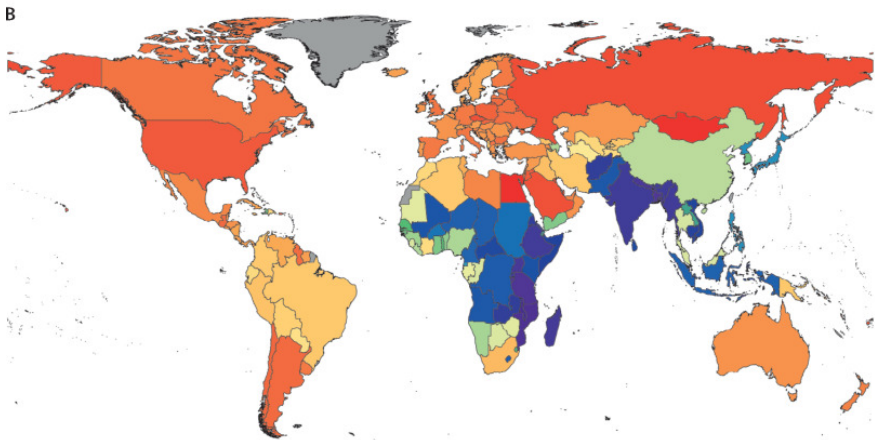
Worldwide Burden of Cancer Attributable to Diabetes and High BMI: A Comparative Risk Assessment

Pearson-Stuttard et al. Lancet Diabetes Endocrinol 2018

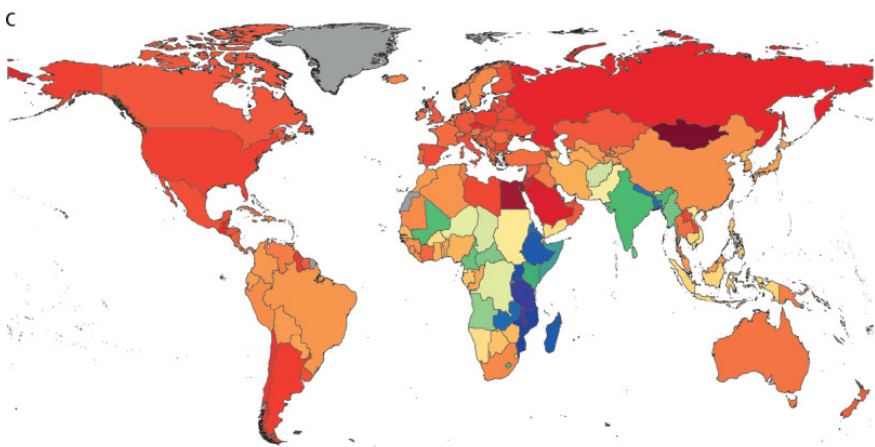




Diabetes



High BMI



Both

**Diabetes
and high BMI
responsible for
5.7% of all
cancers**

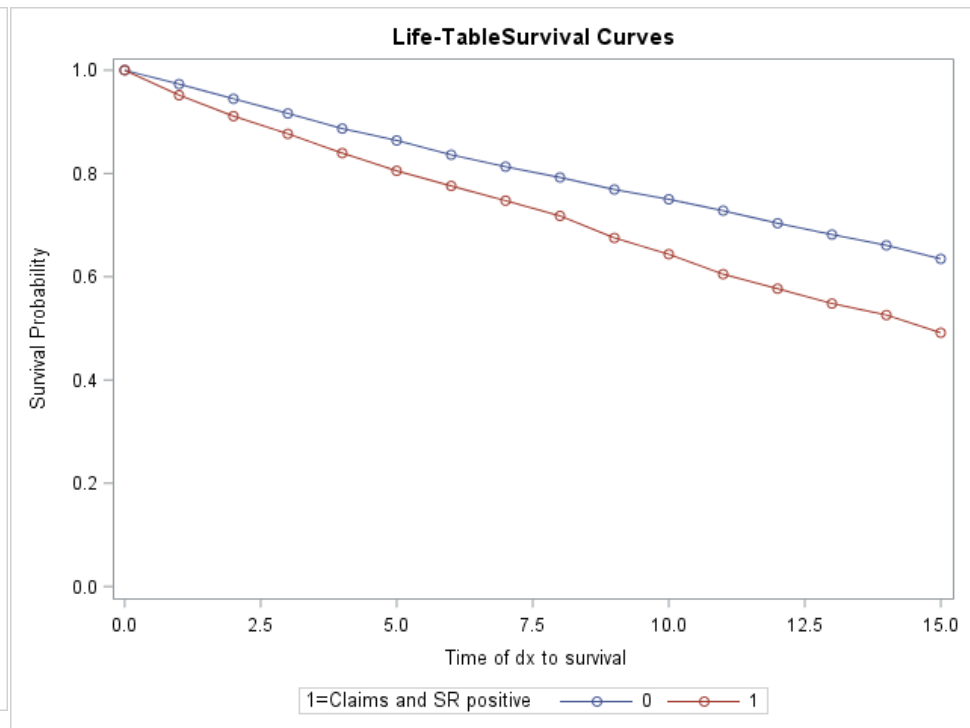
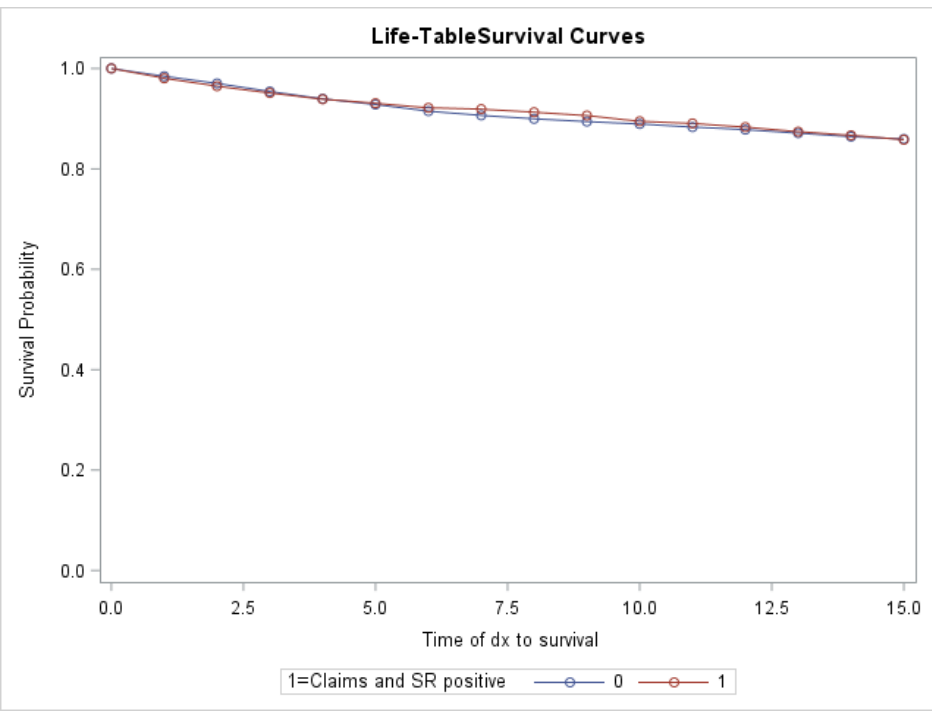
Worldwide Burden of
Cancer Attributable to
Diabetes & High BMI
Pearson-Stuttard et al.
Lancet Diabetes
Endocrinol 2018

Survival among Women with Breast Cancer

Maskarinec et al. Breast Ca Research and Treatment 2018

Breast Cancer Deaths

All Cause Deaths



Survival among Colorectal Cancer Patients

Amshoff et al. Int J Cancer 2018

Characteristic	Category	CRC-specific			All causes		
		HR	95% CI		HR	95% CI	
All	Diabetes	0.84	0.67	1.07	1.11	0.98	1.27
T2D duration	<10 years	0.61	0.46	0.82	0.95	0.82	1.11
	≥10 years	1.48	1.06	2.07	1.49	1.22	1.82
Comorbidity	None	0.49	0.25	0.96	0.90	0.65	1.26
	1+	1.08	0.85	1.38	1.36	1.19	1.56
	P _{Interaction}	0.03			0.03		

Conclusions

- Overweight is the most important risk factor for type 2 diabetes
- The prevalence of diabetes is high in persons of Asian ancestry despite their lower obesity rates
- Obesity increases the risk for breast & colorectal cancer
- Having diabetes for many years appears to make it more likely to develop certain types of cancer
- Cancer survivors with type 2 diabetes experience a shorter life expectancy than those without a diabetes diagnosis
- Diabetes prevention involves weight control, physical activity, and a high quality diet