Risks and Prevention Across the Lifespan

UCI MIND

30th SoCal Alzheimer's Disease Research Conference

JOHNS HOPKINS MEDICINE

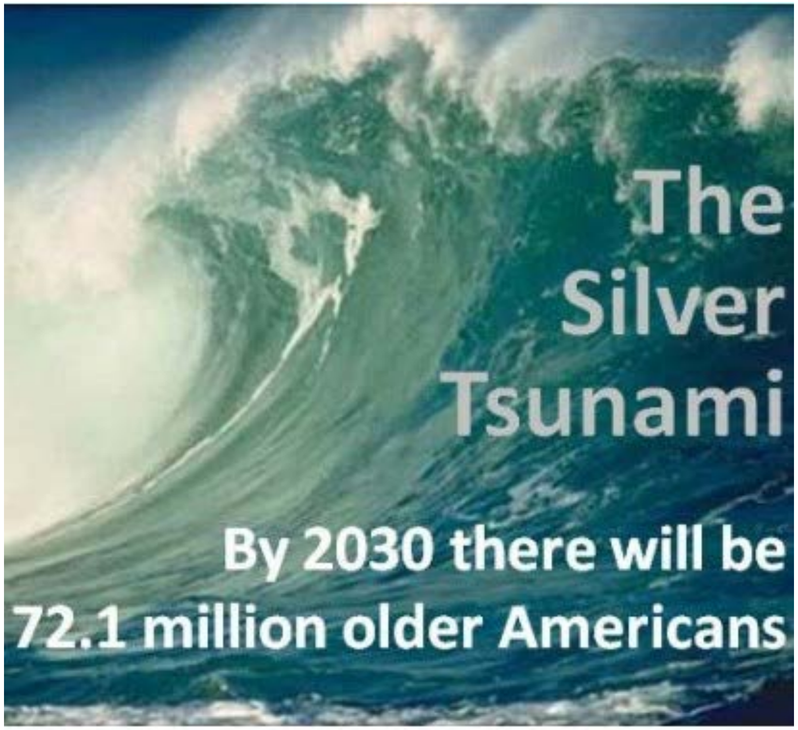
Presented by: Rebecca Gottesman, MD PhD

October 25, 2019

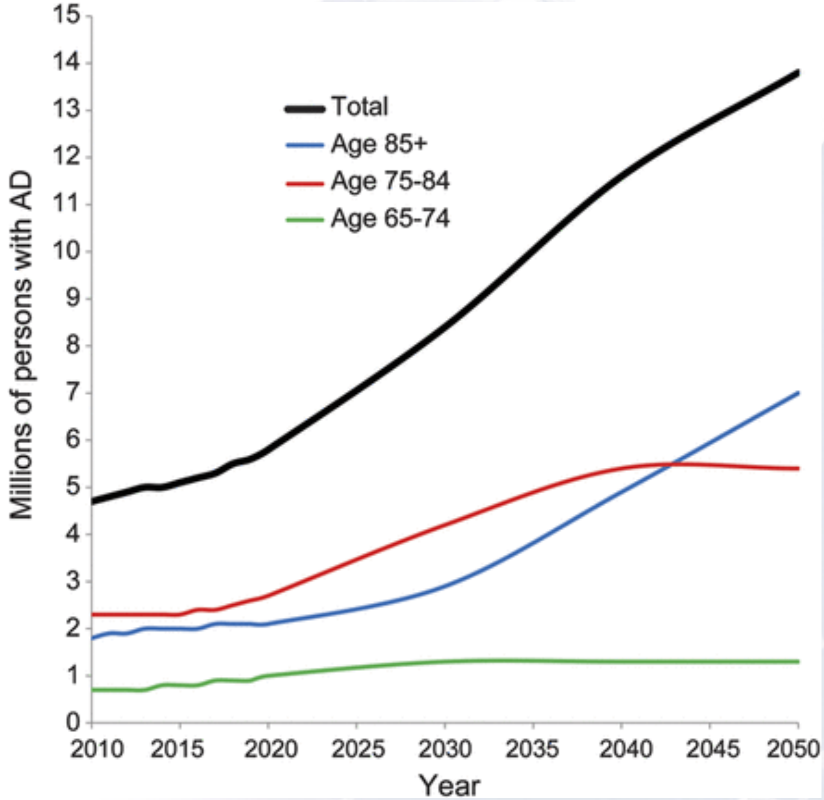
Disclosures

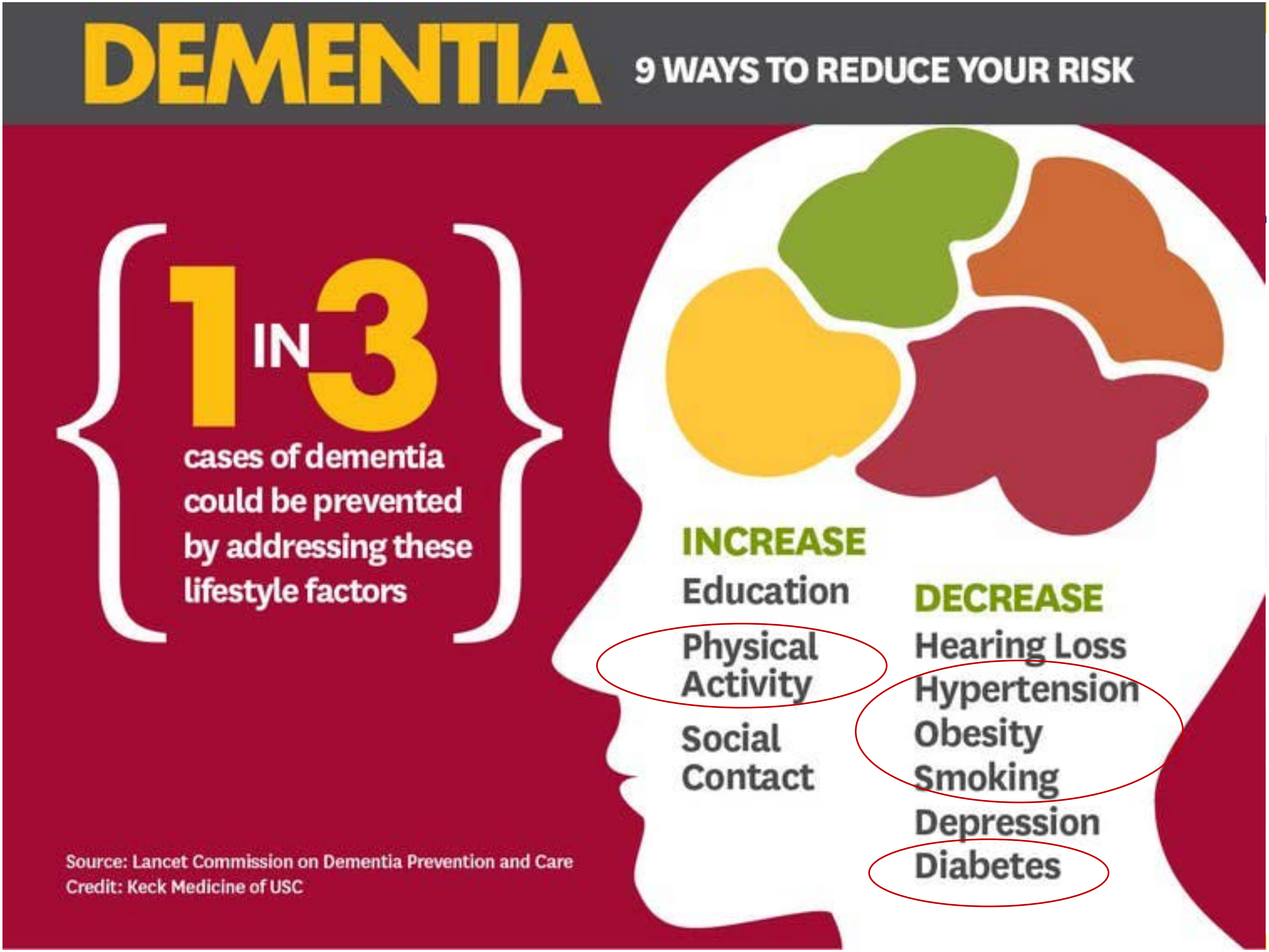
- I am an Associate Editor for the journal *Neurology.*

Alzheimer's disease is on the rise



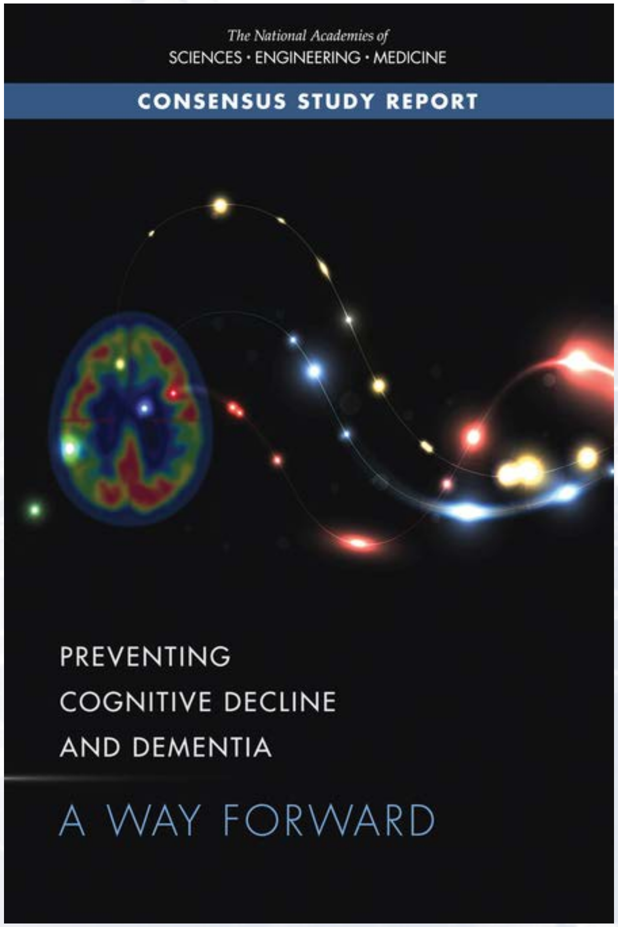
From Hebert et al., Neurology 2013



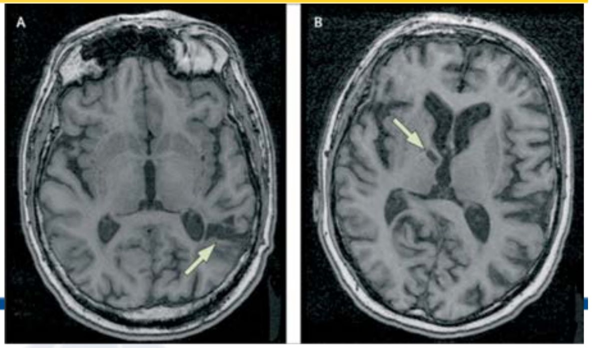

DEMENTIA
9 WAYS TO REDUCE YOUR RISK
1 IN 3
cases of dementia could be prevented by addressing these lifestyle factors
INCREASE
Education
Physical Activity
Social Contact
DECREASE
Hearing Loss
Hypertension
Obesity
Smoking
Depression
Diabetes
Source: Lancet Commission on Dementia Prevention and Care
Credit: Keck Medicine of USC

National Academy of Medicine: Preventing Dementia

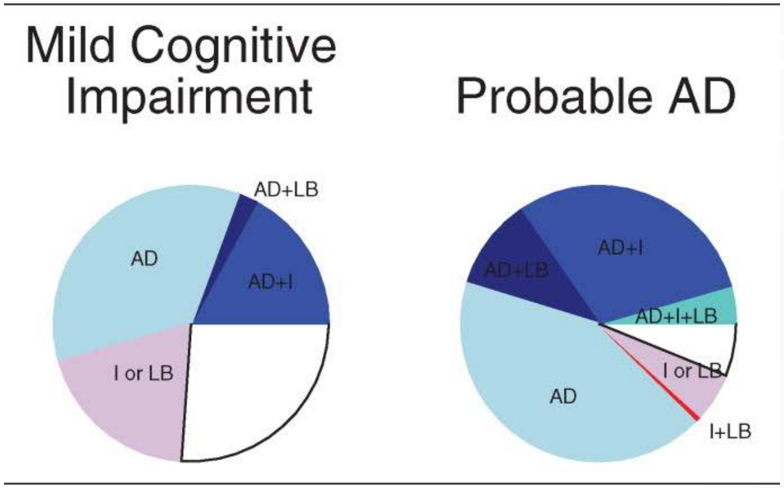
- Recommendations from this systematic review:
  - Cognitive training
  - **Control of high BP (especially during ages 35-65)**
  - **Increasing physical activity**



Vascular contribution to Alzheimer's Disease



- In autopsy studies of patients who were diagnosed with Alzheimer's disease, >50% had evidence of strokes ("silent strokes")
  - Fewer Alzheimer's-type changes are seen in people with higher levels of vascular changes in the brain (for an equivalent level of dementia)



AD=Alzheimer's Disease
I=Infarcts
LB=Lewy Bodies

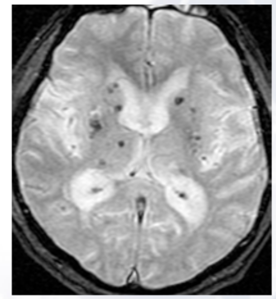
Schneider et al., *Annals of Neurology* 2009

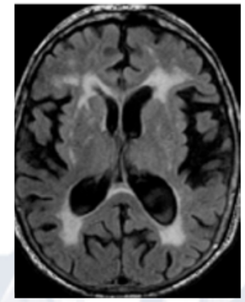
Heart disease risk factors (vascular risk factors) that may also affect brain health

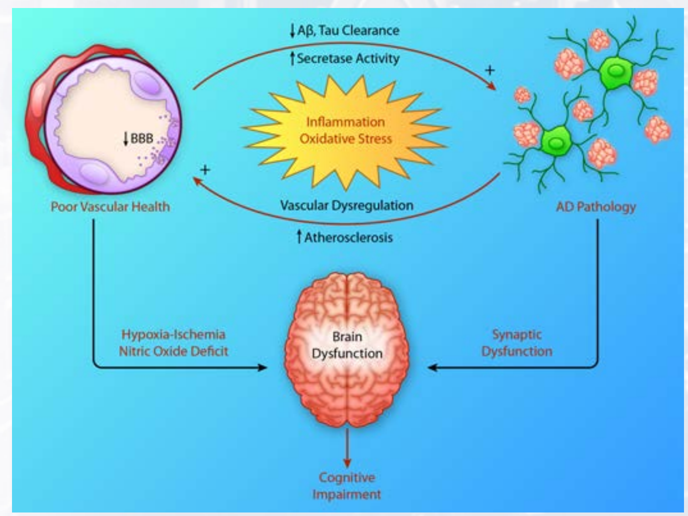
- High blood pressure
- Diabetes
- Smoking
- High cholesterol
- Obesity
- Physically inactive lifestyle
- Poor diet
- Inflammation

How do heart disease risk factors lead to problems with memory and thinking?

- Strokes
- “Silent” strokes or related brain changes
- Not enough flow/ oxygen to brain through diseased blood vessels
- Changes in ability to clear brain toxins or block access to the brain



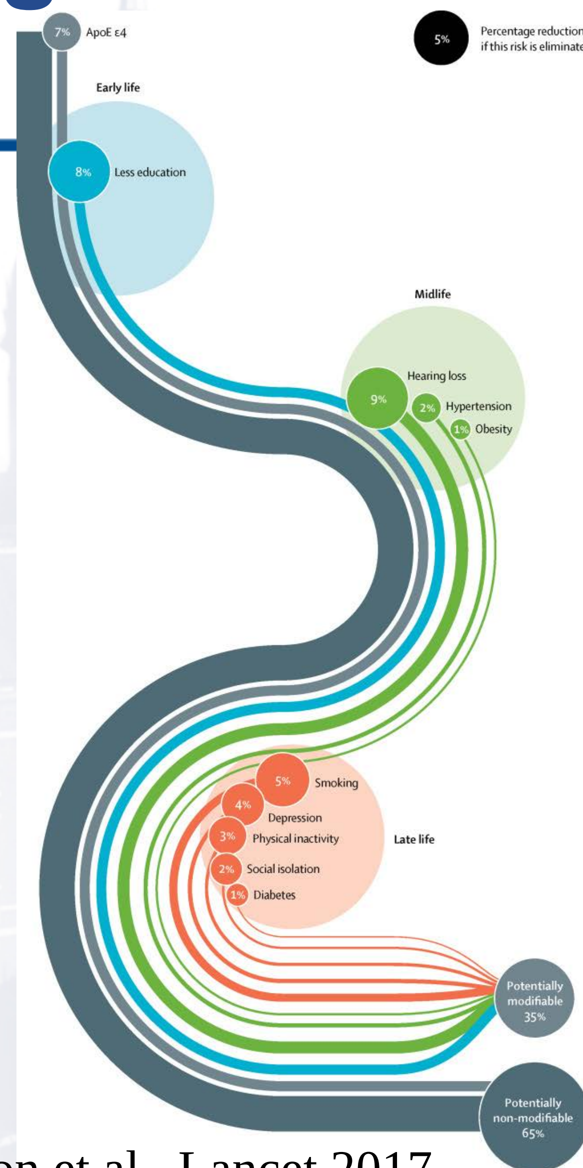




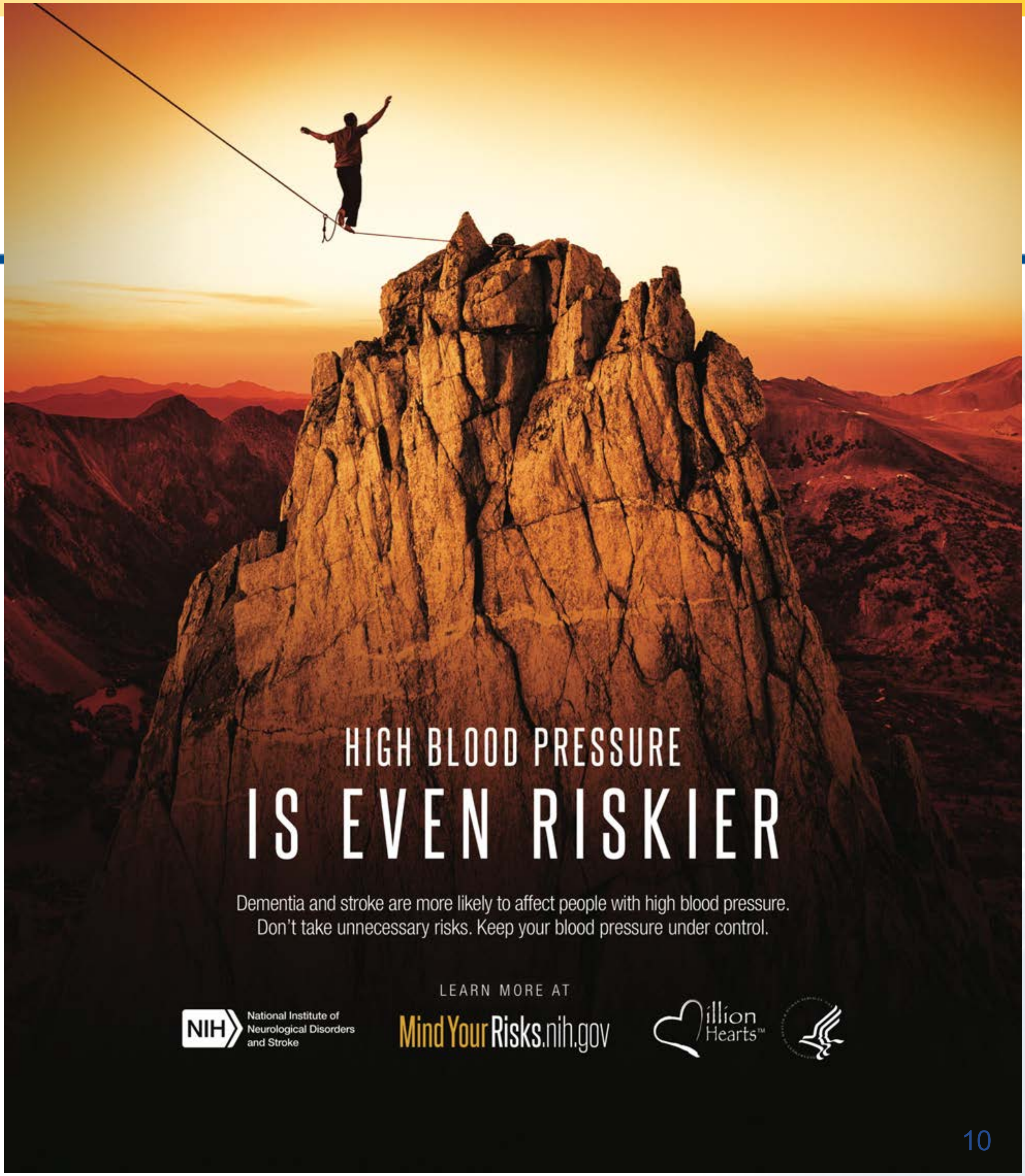
Iadecola & Gottesman, Circulation Research 2019 (124(7): 1025-1044

Importance of considering the whole life course

- Vascular factors have strongest relationships with cognitive decline and dementia when considered in middle age
- Changes in vascular risk factor status over the life course may change the way a risk factor affects an individual person



From Livingston et al., Lancet 2017


HIGH BLOOD PRESSURE
IS EVEN RISKIER
Dementia and stroke are more likely to affect people with high blood pressure.
Don't take unnecessary risks. Keep your blood pressure under control.
LEARN MORE AT
MindYourRisks.nih.gov
NIH National Institute of Neurological Disorders and Stroke
Million Hearts

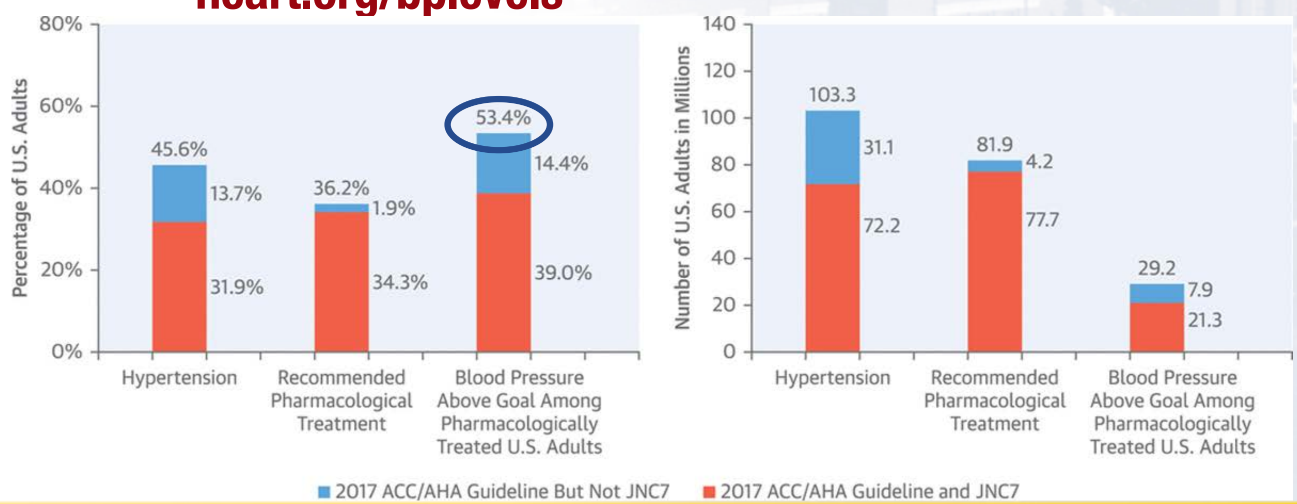
High Blood Pressure:
New AHA/ ACC definitions in 2017

Blood Pressure Categories

American Heart Association | American Stroke Association

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

heart.org/bplevels

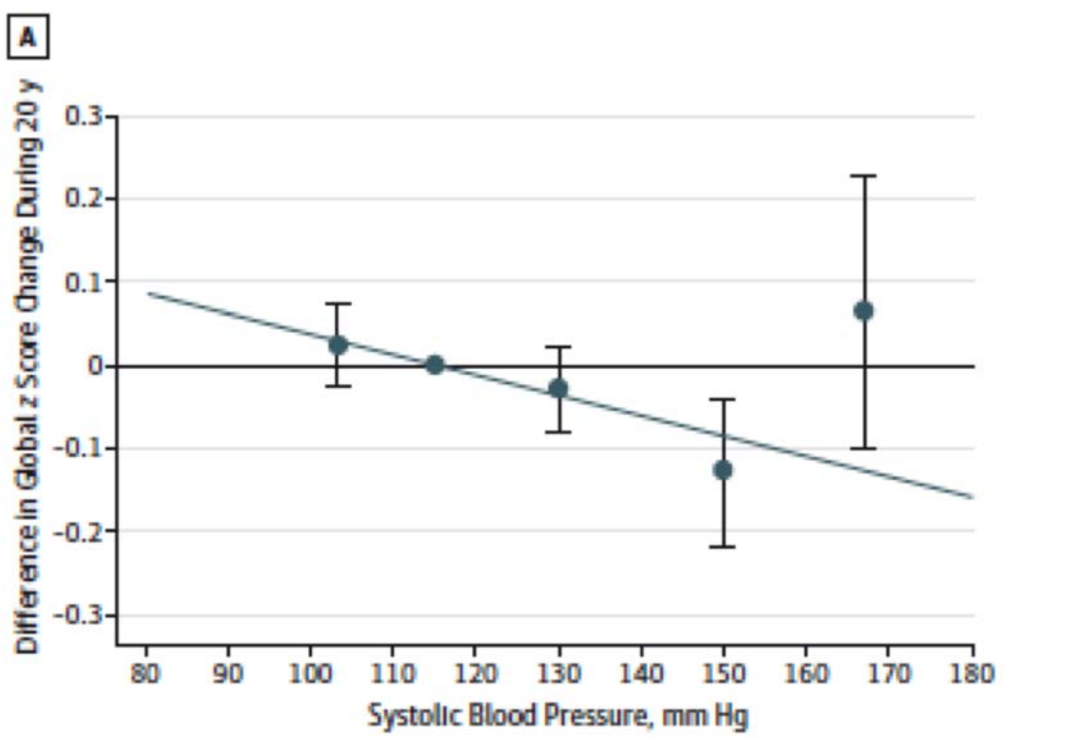


Muntner et al., Circulation 2017

October 25, 2019

Higher BP, especially in middle age, is associated with worse cognition

Figure 2. Adjusted Association of Visit 2 (1990-1992) Systolic Blood Pressure Change Among Whites



Adapted from Gottesman et al., JAMA Neurology 2014

Table 2. Cox Proportional Hazards Regression Model of Time to Incident Dementia Overall and Stratified by Race

Variable	Hazard Ratio (95% CI) Full Eligible Cohort (n = 15 407)[a]	Black (n = 4004)	White (n = 11 403)
Female	0.89 (0.79-0.99)	0.87 (0.72-1.06)	0.92 (0.80-1.05)
Black	1.36 (1.21-1.54)	NA	NA
Visit 1 age, y[b]			
44-49	1 [Reference]	1 [Reference]	1 [Reference]
50-54	2.04 (1.66-2.49)	2.22 (1.66-2.98)	1.98 (1.49-2.62)
55-59	3.97 (3.28-4.81)	3.53 (2.63-4.73)	4.37 (3.37-5.65)
60-66	8.06 (6.69-9.72)	6.20 (4.64-8.28)	9.54 (7.41-12.27)
Educational attainment			
<High school	1.37 (1.20-1.57)	1.61 (1.28-2.03)	1.29 (1.09-1.53)
High school graduate or GED	1.05 (0.93-1.20)	1.17 (0.90-1.53)	1.02 (0.88-1.18)
>High school	1 [Reference]	1 [Reference]	1 [Reference]
Visit 1 BMI			
Underweight	0.99 (0.53-1.87)	1.15 (0.36-3.66)	0.92 (0.43-1.97)
Normal	1 [Reference]	1 [Reference]	1 [Reference]
Overweight	1.05 (0.92-1.19)	0.95 (0.73-1.22)	1.08 (0.93-1.26)
Obese	1.14 (0.99-1.31)	0.92 (0.71-1.20)	1.22 (1.03-1.45)
Visit 1 smoking[b]			
Current	1.41 (1.23-1.61)	1.07 (0.85-1.35)	1.62 (1.37-1.92)
Former	1.00 (0.89-1.13)	0.77 (0.61-0.98)	1.13 (0.97-1.31)
Never	1 [Reference]	1 [Reference]	1 [Reference]
APOE ε4 genotype[b]			
0 Alleles	1 [Reference]	1 [Reference]	1 [Reference]
≥1 Alleles	1.98 (1.78-2.21)	1.61 (1.34-1.92)	2.23 (1.96-2.54)
Visit 1 hypertension			
Normal	1 [Reference]		
Prehypertension	1.31 (1.14-1.51)		
Hypertension	1.39 (1.22-1.59)		
200 to <240	0.87 (0.77-0.98)	0.91 (0.74-1.13)	0.86 (0.74-1.00)
≥240	0.91 (0.80-1.04)	0.78 (0.62-0.98)	0.99 (0.84-1.16)

Hypertension in middle age is associated with a ***39% higher chance*** of dementia

Prehypertension in middle age is associated with a ***31% higher chance*** of dementia…

compared to people with normal BP's

From Gottesman et al., JAMA Neurology 2017

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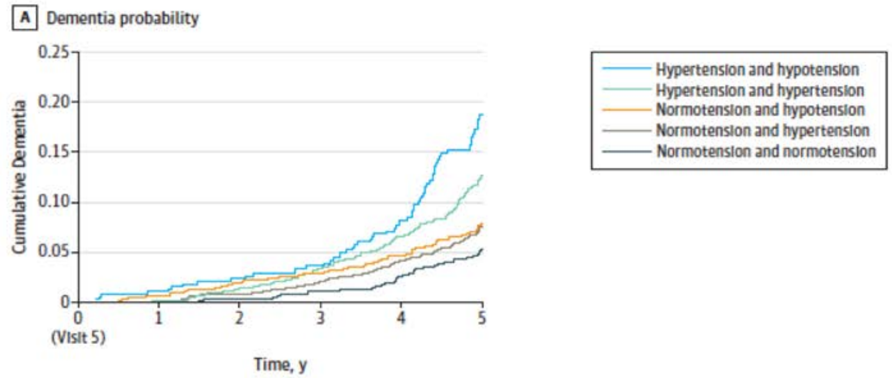
Life course and hypertension

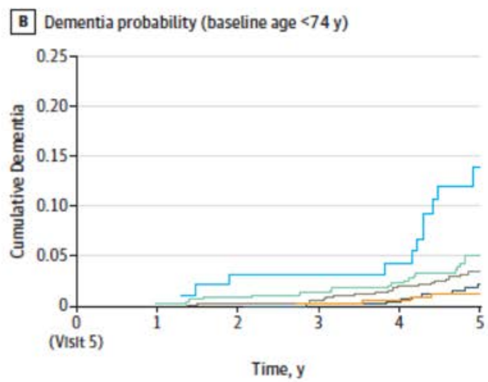
- In our studies, similar associations are *not* found for high blood pressure in later life
  - Risk of cognitive decline and dementia is most pronounced for people with midlife (aged 45-64 in our study) high blood pressure

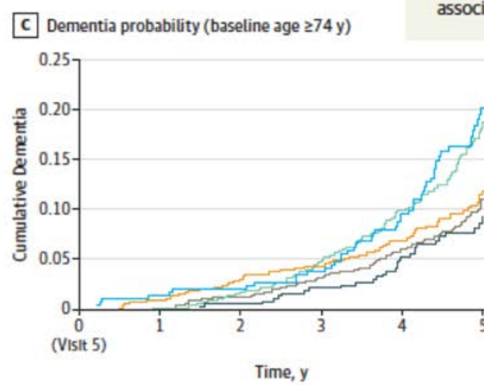
Low blood pressure in late life may not be as well tolerated for people with midlife hypertension

Figure 2. Kaplan-Meier Curves for Time to Dementia Onset for Standard Hypertension Definition Blood Pressure Groups



No. at risk, midlife and late life	0	1	2	3	4	5
Normotension and normotension	833	833	831	819	751	377
Normotension and hypertension	1559	1558	1545	1521	1353	709
Normotension and hypotension	927	922	910	892	800	413
Hypertension and hypertension	1030	1028	1015	988	874	439
Hypertension and hypotension	389	385	380	368	320	165





No. at risk, midlife and late life	B: 0	B: 1	B: 2	B: 3	B: 4	B: 5	C: 0	C: 1	C: 2	C: 3	C: 4	C: 5
Normotension and normotension	459	459	459	457	431	227	374	374	372	362	320	150
Normotension and hypertension	715	715	711	708	647	335	844	843	834	813	706	374
Normotension and hypotension	339	339	339	338	315	177	588	583	571	554	485	236
Hypertension and hypertension	446	445	442	439	411	206	584	583	573	549	463	233
Hypertension and hypotension	94	94	91	91	81	40	295	291	289	277	239	125

Key Points

Question Are specific midlife to late-life longitudinal blood pressure patterns associated with increased risk of dementia among older adults?

Finding In this prospective cohort study that included 4761 participants with 24-year follow-up and blood pressure measurements at midlife and at late life, those with midlife and late-life hypertension (hazard ratio, 1.49) and those with midlife hypertension and late-life hypotension (hazard ratio, 1.62) had higher risk for incident dementia compared with those who remained normotensive.

Meaning Patterns of blood pressure in midlife and late life may be associated with differing risks for incident dementia.

Walker et al, JAMA 2019

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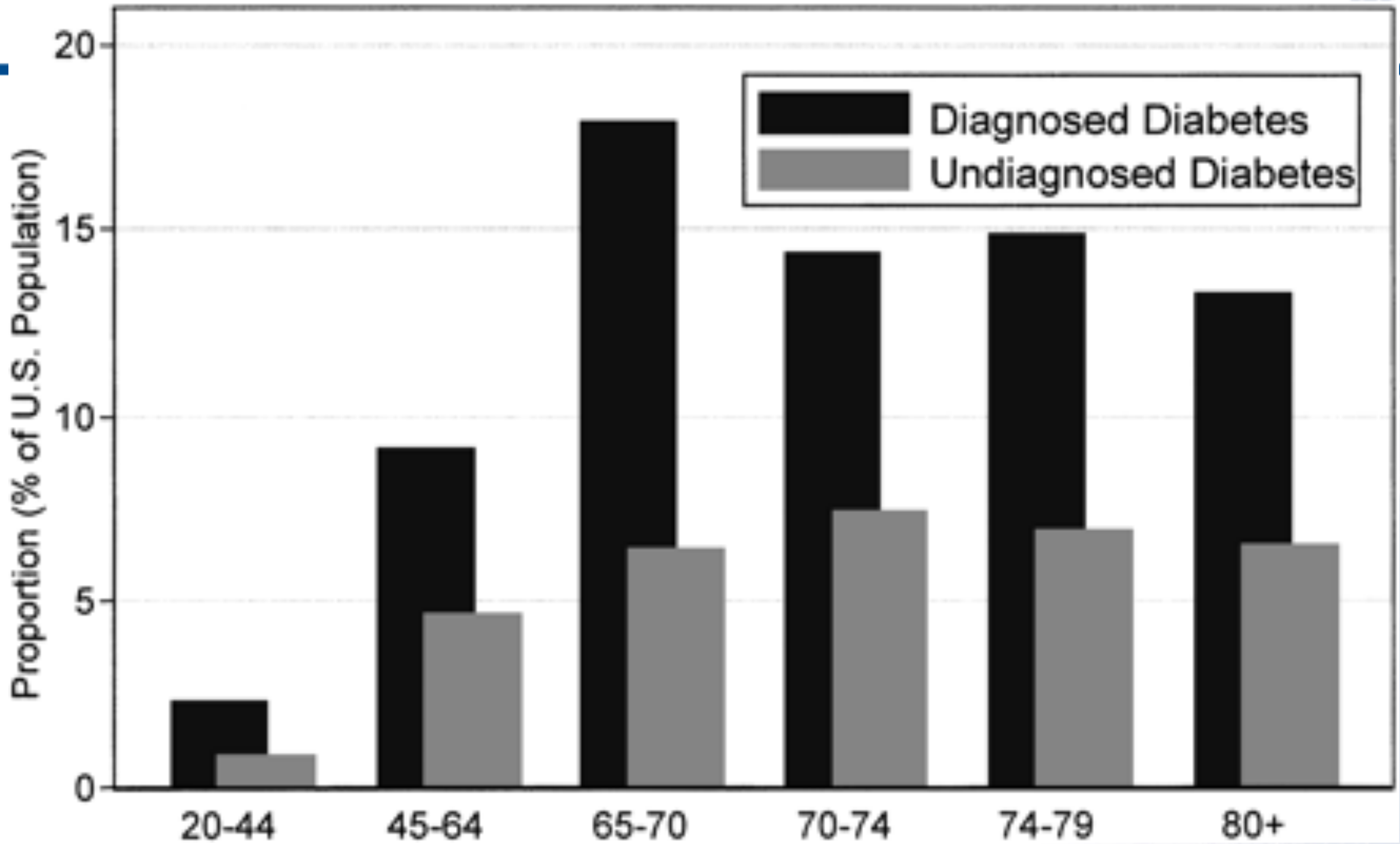
Life course blood pressure trajectories may need to consider earlier exposures than midlife

Associations between blood pressure across adulthood and late-life brain structure and pathology in the neuroscience substudy of the 1946 British birth cohort (Insight 46): an epidemiological study

Lancet Neurol 2019

Interpretation High and increasing blood pressure from early adulthood into midlife seems to be associated with increased WMHV and smaller brain volumes at 69–71 years of age. We found no evidence that blood pressure affected cognition or cerebral amyloid-β load at this age. Blood pressure monitoring and interventions might need to start around 40 years of age to maximise late-life brain health.

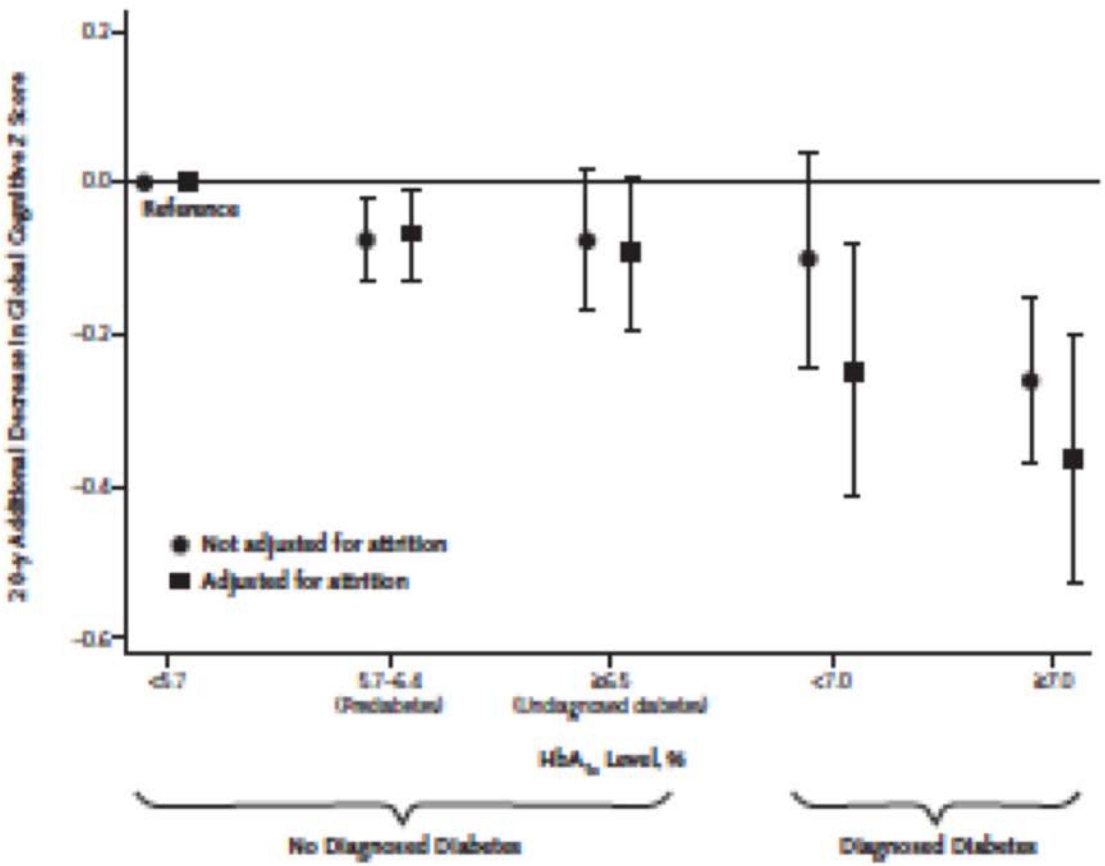
Diabetes



From Selvin et al., Diabetes Care 2006

Diabetes as a risk factor for cognitive decline

Figure 2. Difference in global cognitive *Z* score decline by clinical category of HbA_{1c} level compared with decline in persons without diabetes and HbA_{1c} level <5.7%.



from Rawlings et al., Annals of Internal Medicine 2014

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Current	1.41 (1.23-1.61)	1.07 (0.85-1.35)	1.62 (1.37-1.92)

APOE ε4 genotype[b]	
0 Alleles	1 [Reference]
≥1 Alleles	1.98 (1.78-2.21)
Visit 1 diabetes	1.77 (1.53-2.04)

Normal	1 [Reference]	1 [Reference]	1 [Reference]
Prehypertension	1.31 (1.14-1.51)	1.17 (0.86-1.59)	1.35 (1.14-1.59)
Hypertension	1.39 (1.22-1.59)	1.36 (1.04-1.77)	1.37 (1.17-1.60)
Visit 1 total cholesterol, mg/dL			
<200	1 [Reference]	1 [Reference]	1 [Reference]
200 to <240	0.87 (0.77-0.98)	0.91 (0.74-1.13)	0.86 (0.74-1.00)
≥240	0.91 (0.80-1.04)	0.78 (0.62-0.98)	0.99 (0.84-1.16)

Diabetes in middle age is associated with a ***77% higher chance*** of dementia.

This near-doubling is almost as high as the risk from the APOE e4 genotype, the strongest genetic risk factor for Alzheimer's disease.

From Gottesman et al., JAMA Neurology 2017

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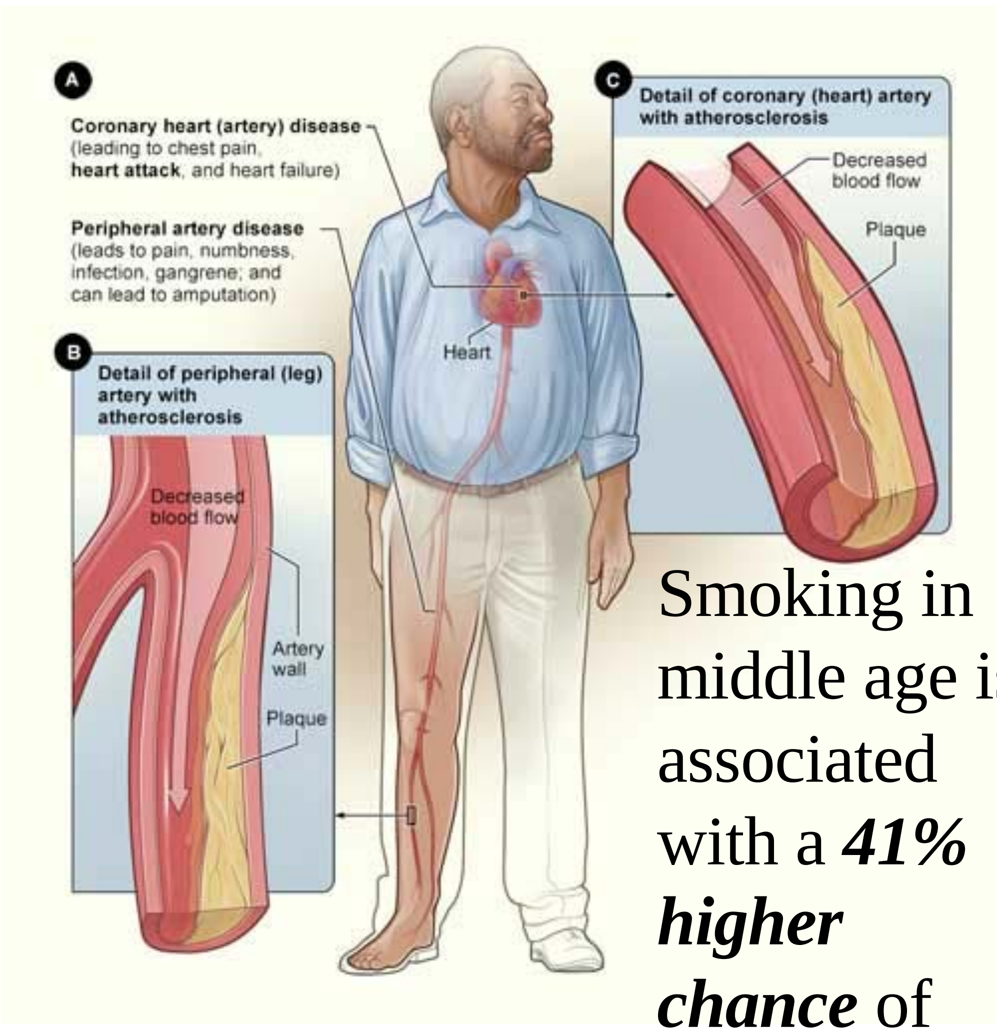
Smoking, Heart Disease, and Dementia



Smoking in middle age is associated with a ***41% higher chance*** of dementia.

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Normal	1 [Reference]	1 [Reference]	1 [Reference]
0 Alleles	1 [Reference]	1 [Reference]	1 [Reference]
≥1 Alleles	1.98 (1.78-2.21)	1.61 (1.34-1.92)	2.23 (1.96-2.54)
Unknown APOE	1.18 (0.89-1.56)	1.84 (0.97-3.47)	1.11 (0.81-1.52)
Visit 1 diabetes	1.77 (1.53-2.04)	1.85 (1.50-2.29)	1.69 (1.39-2.07)
Visit 1 hypertension			
Normal	1 [Reference]	1 [Reference]	1 [Reference]
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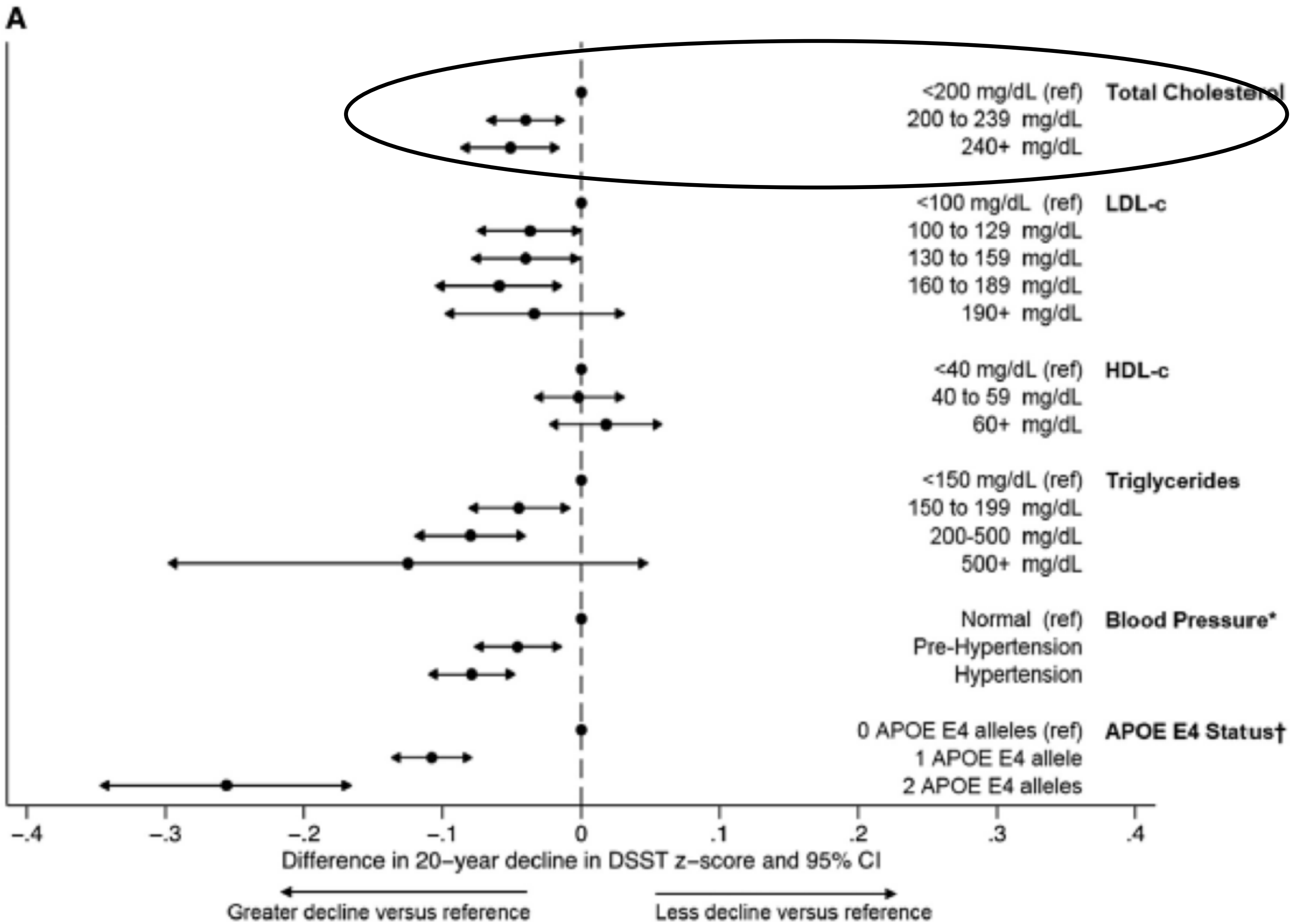
≥240	0.91 (0.80-1.04)	0.78 (0.62-0.98)	0.99 (0.84-1.16)

Visit 1 smoking[b]	
Current	1.41 (1.23-1.61)
Former	1.00 (0.89-1.13)
Never	1 [Reference]

From Gottesman et al., JAMA Neurology 2017

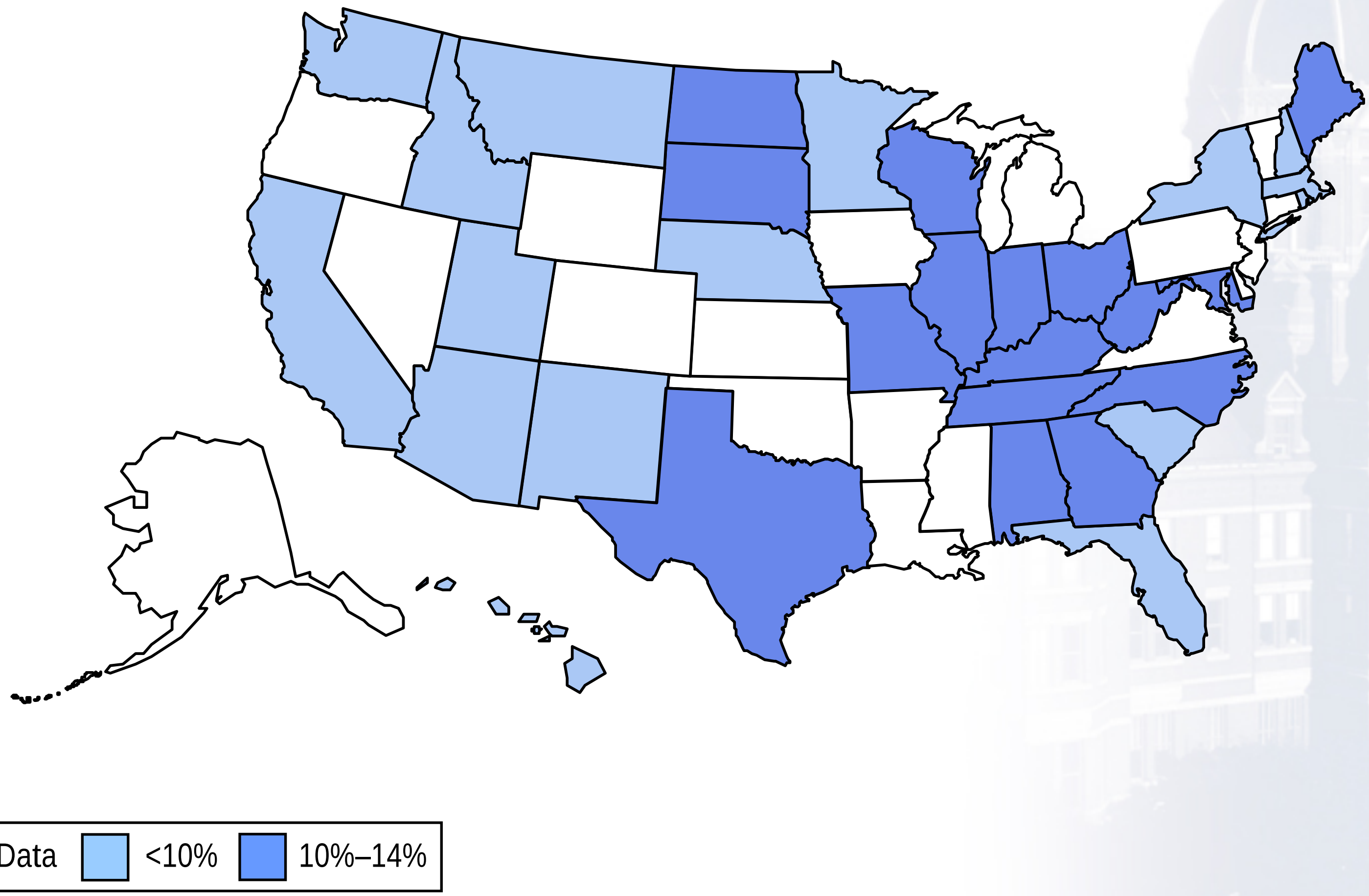
High cholesterol:
Risk factor for cognitive decline



From Power et al., Alzheimer's and Dementia 2017

Obesity Trends* Among U.S. Adults
BRFSS, 1987

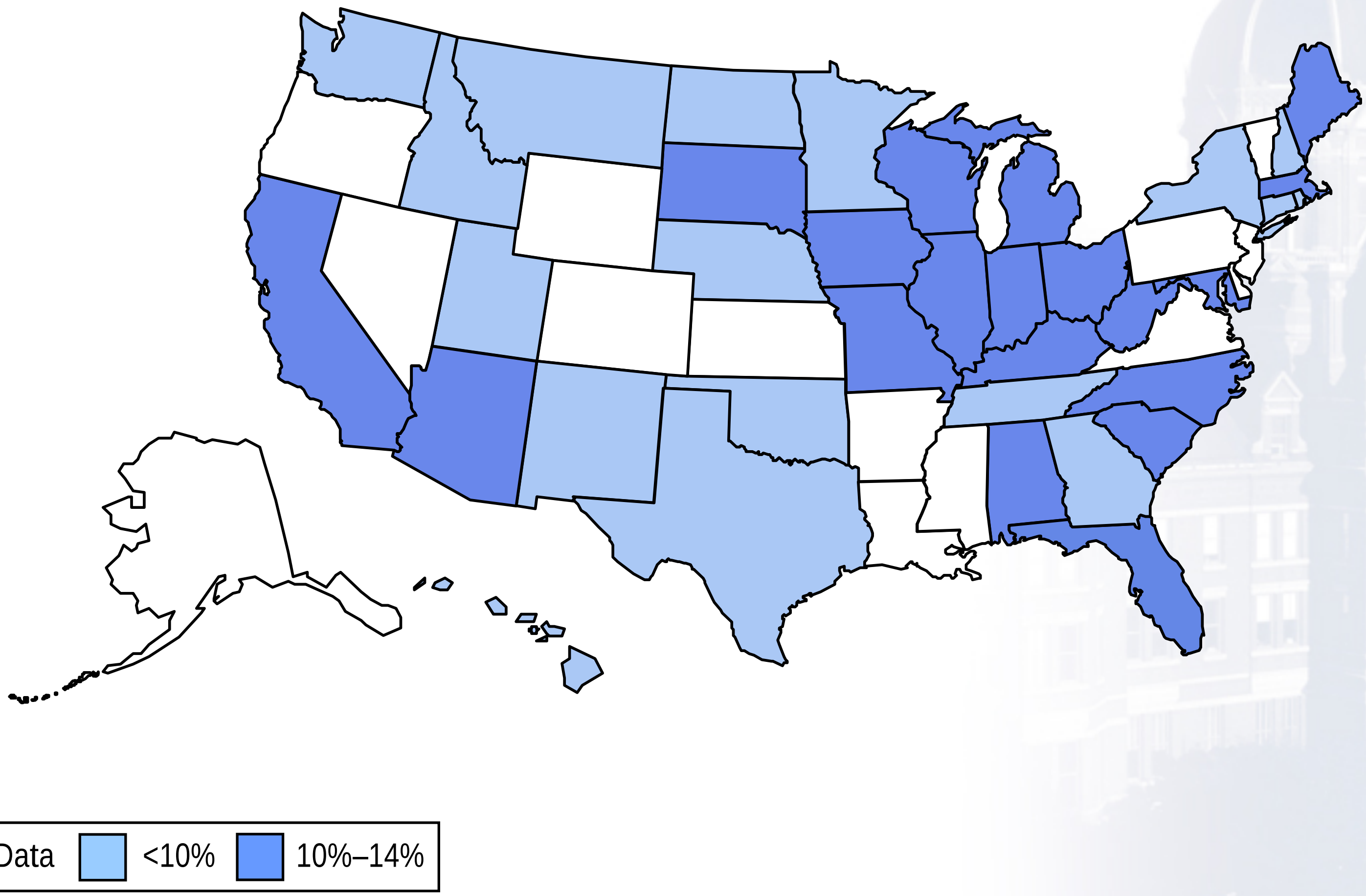
(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 1988

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



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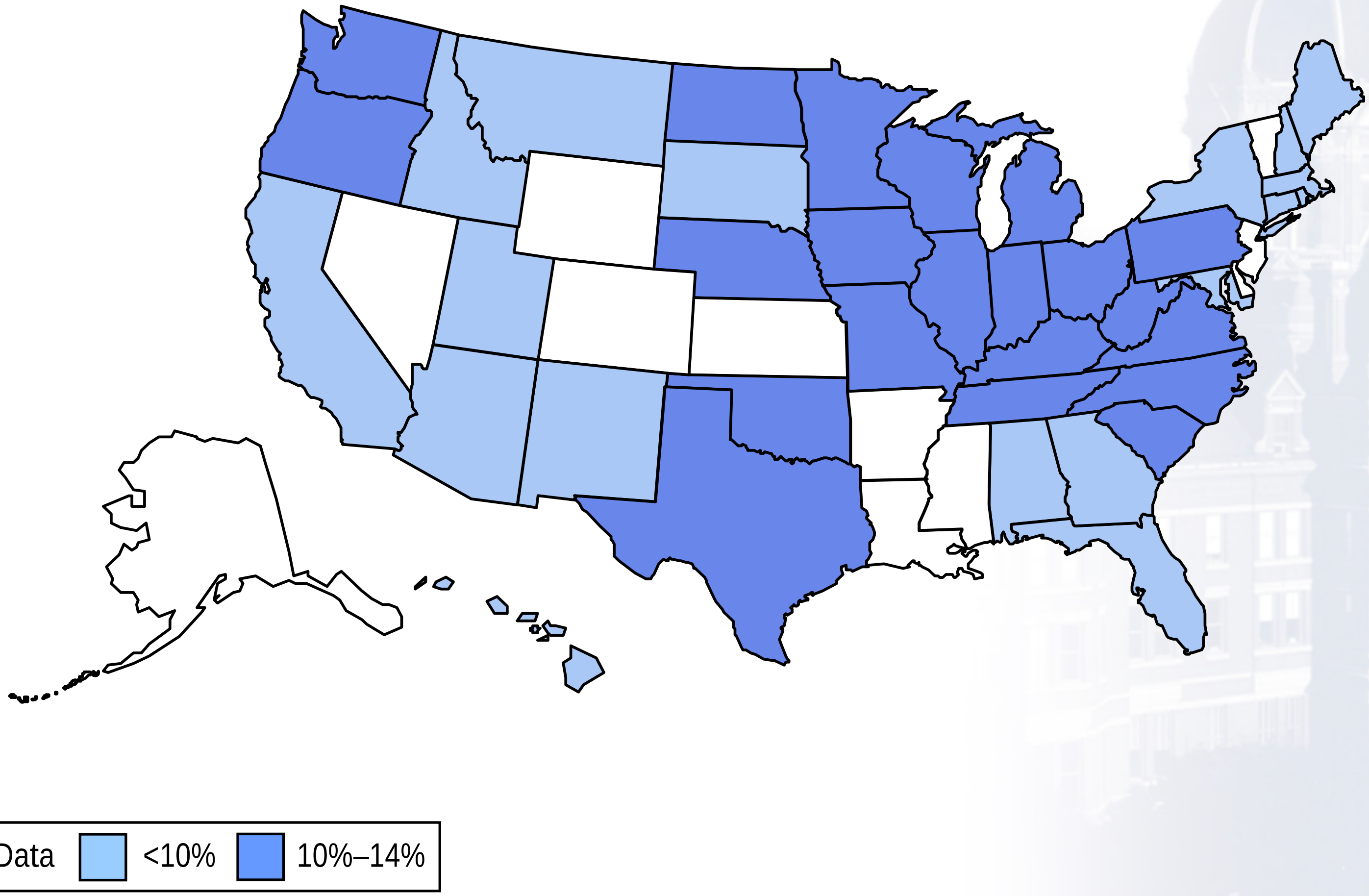

Obesity Trends* Among U.S. Adults

BRFSS, 1990

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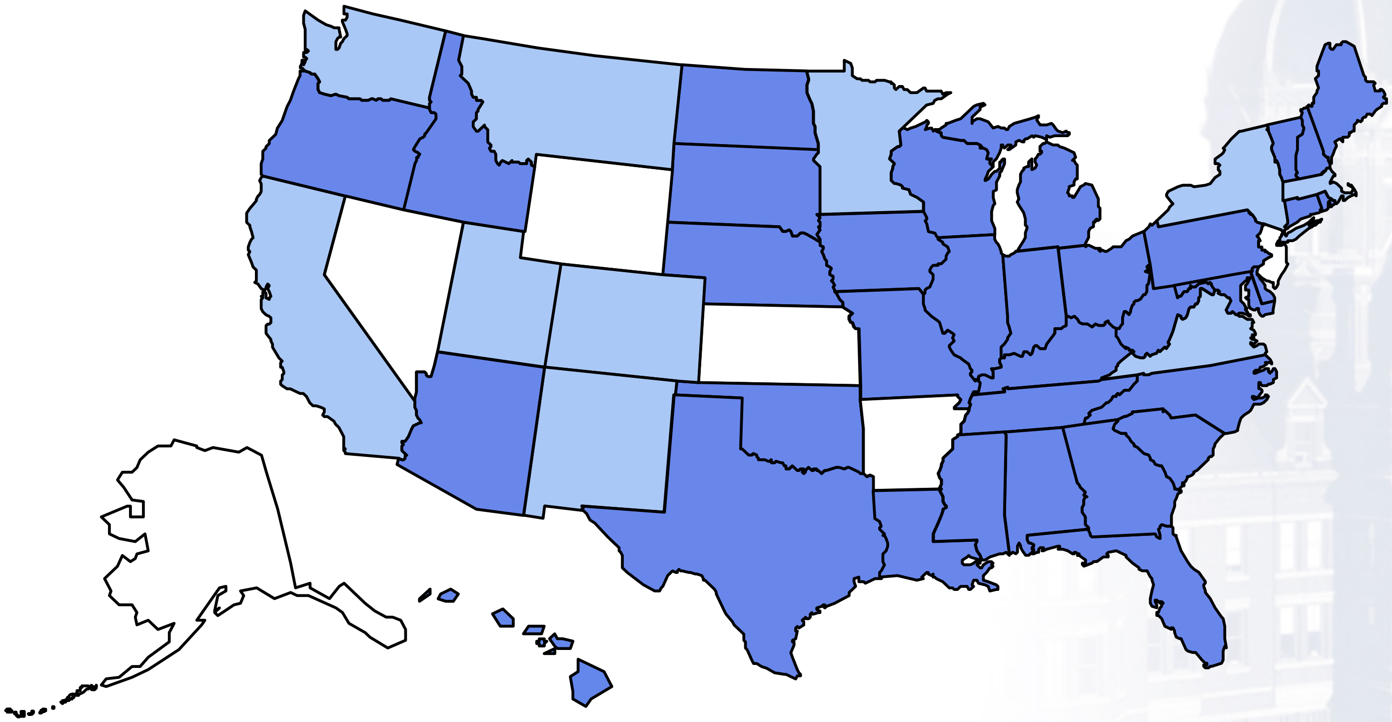

No Data	<10%	10%–14%

Obesity Trends* Among U.S. Adults

BRFSS, 1991

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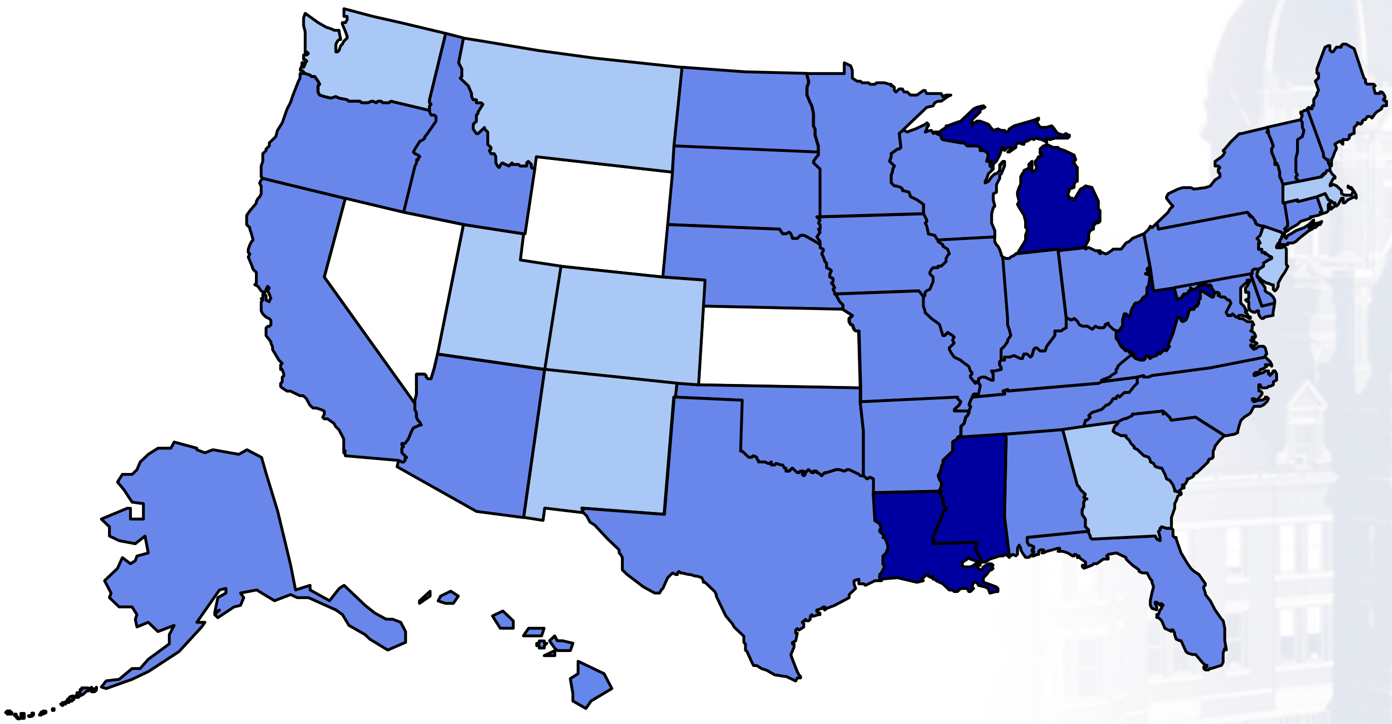

No Data	
<10%	
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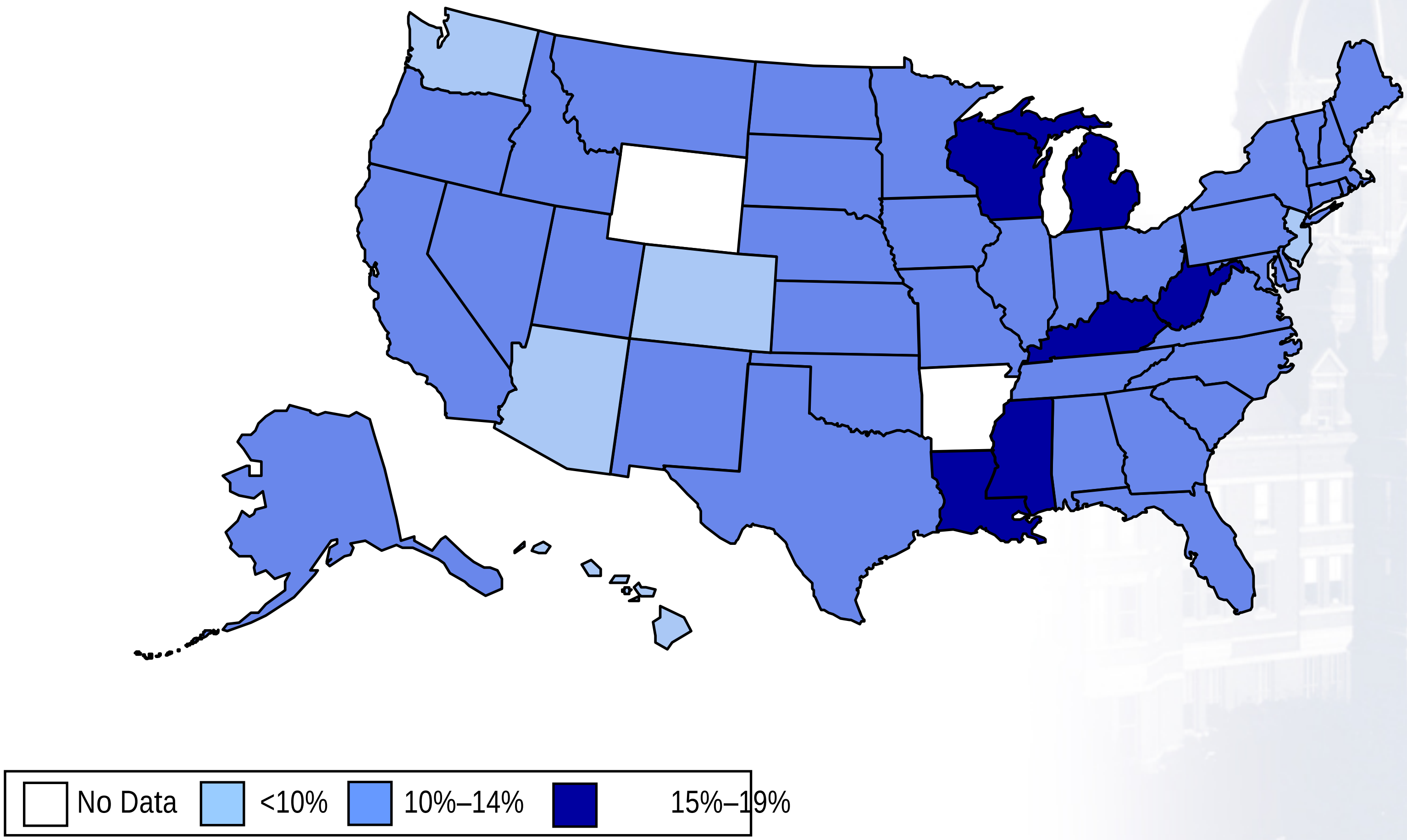

Obesity Trends* Among U.S. Adults
BRFSS, 1993

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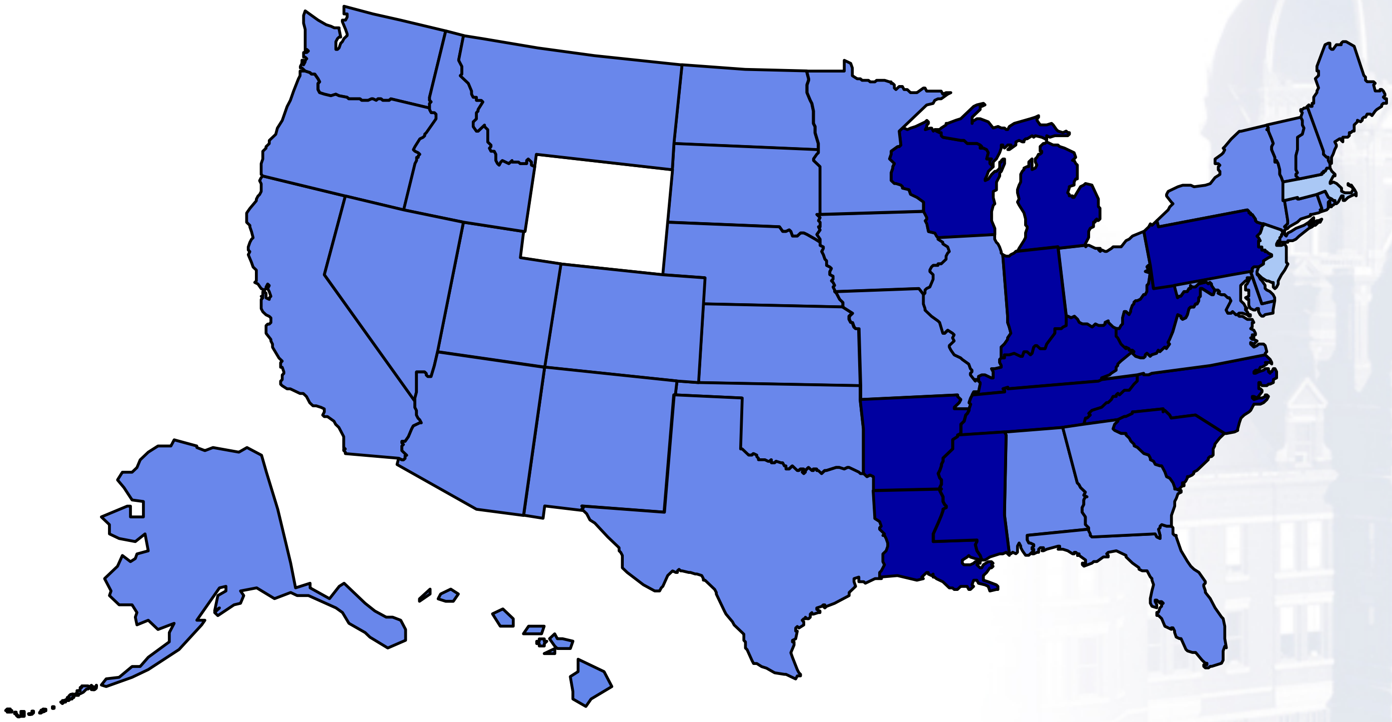
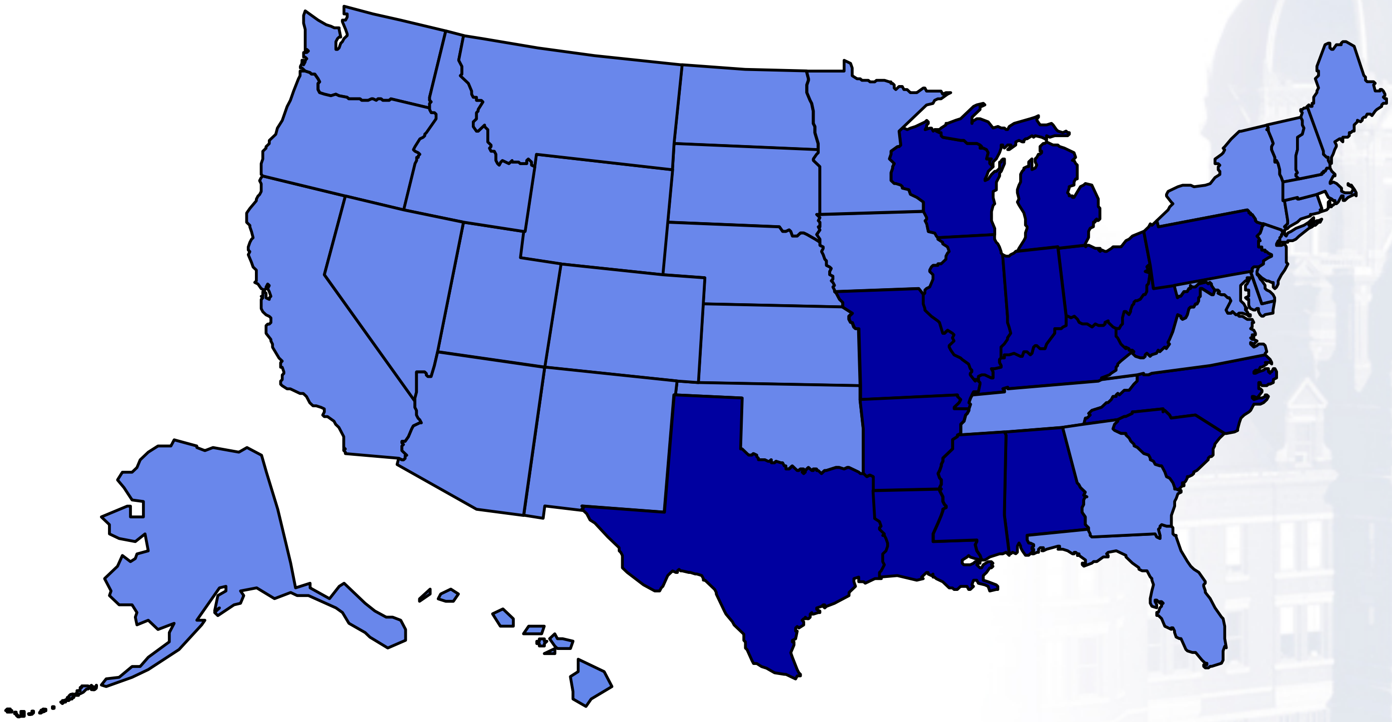


No Data | <10% | 10%–14% | 15%–19%

Obesity Trends* Among U.S. Adults

BRFSS, 1994

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



No Data	
<10%	
10%–14%	
15%–19%	

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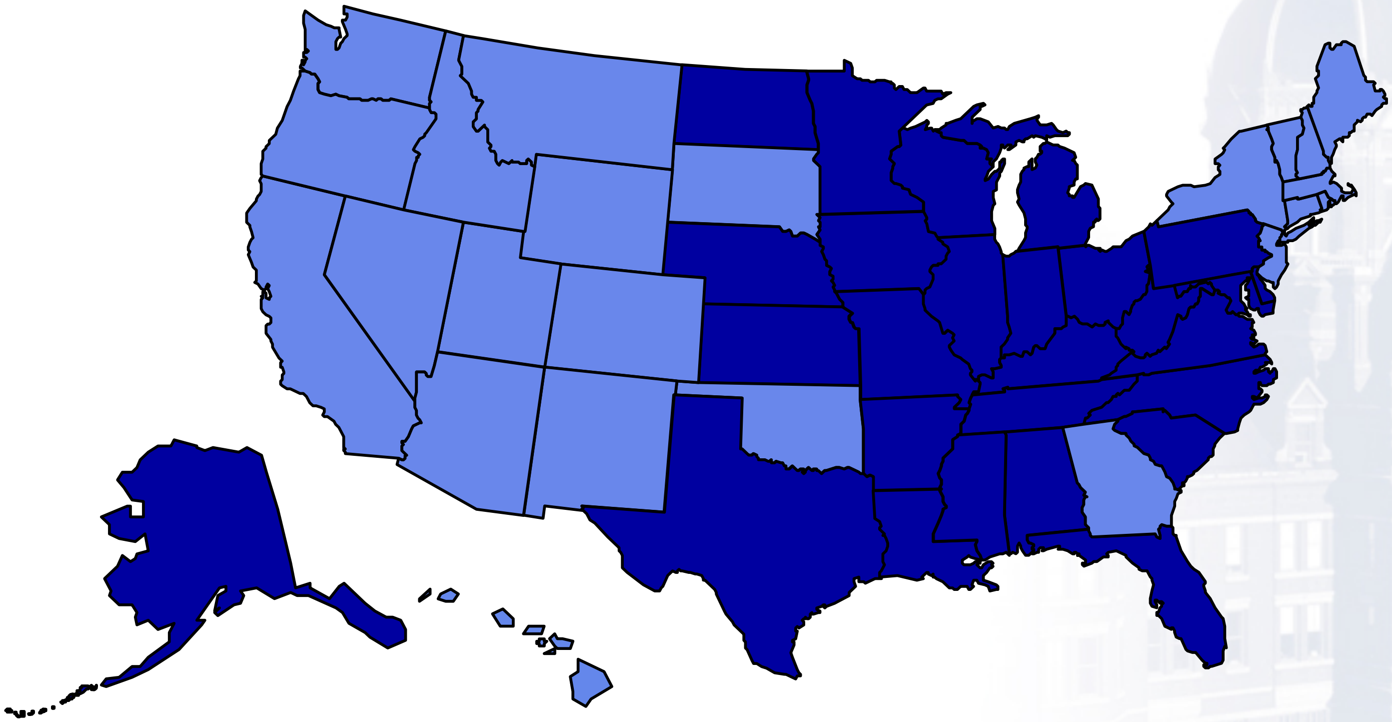
Obesity Trends* Among U.S. Adults
BRFSS, 1995

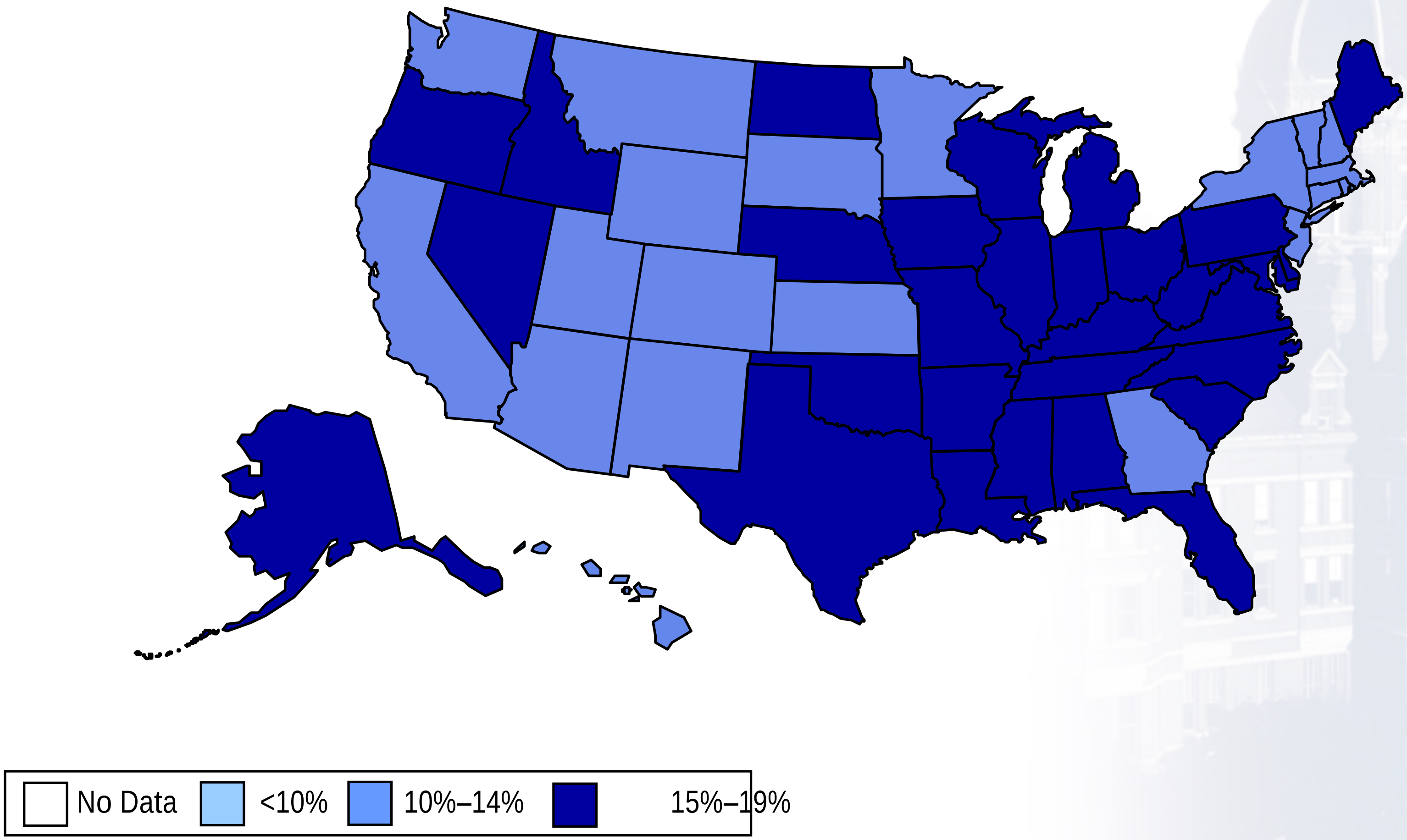
(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



No Data | <10% | 10%–14% | 15%–19%

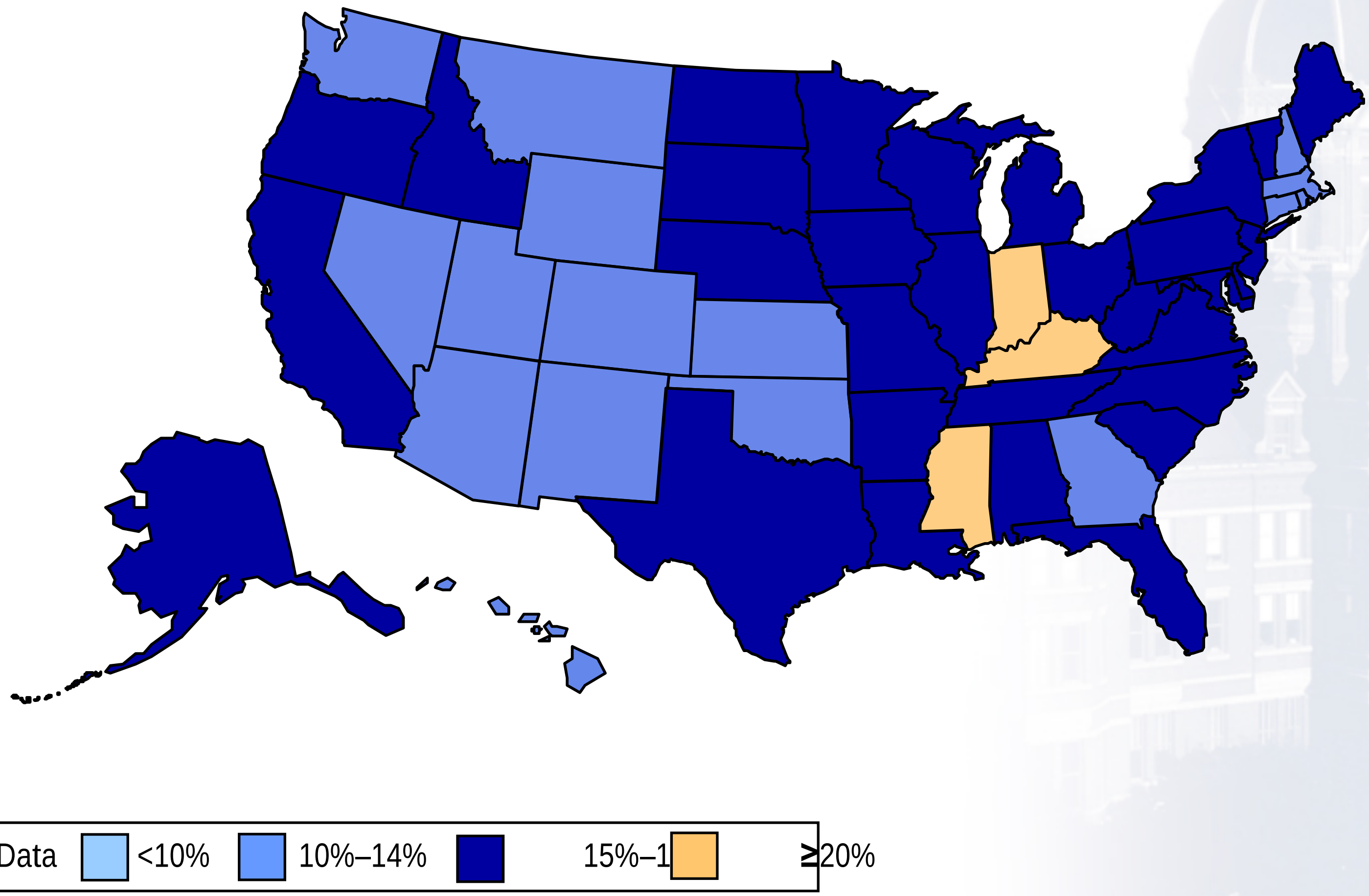
Obesity Trends* Among U.S. Adults
BRFSS, 1996

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



Obesity Trends* Among U.S. Adults
BRFSS, 1997

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



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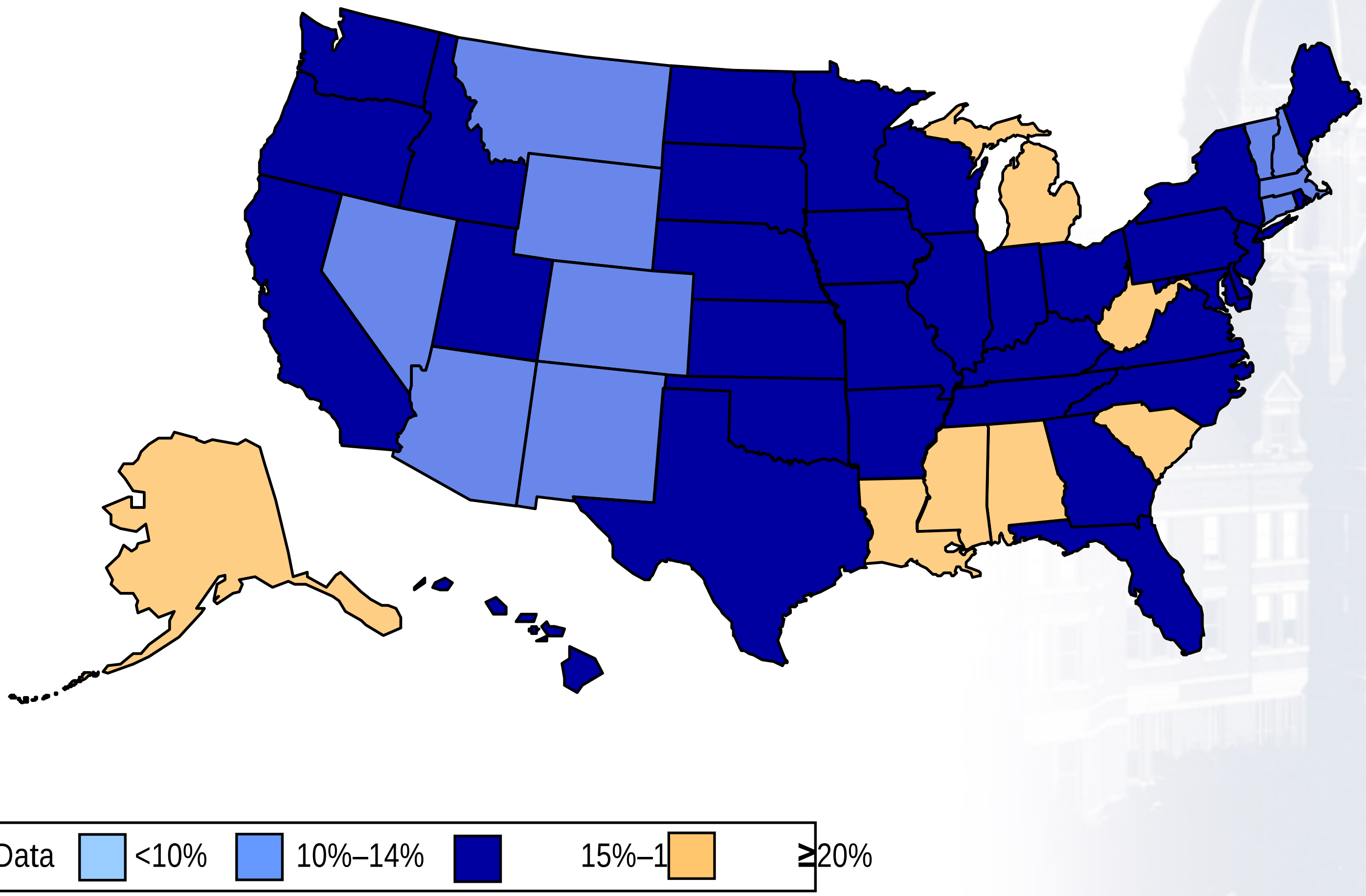
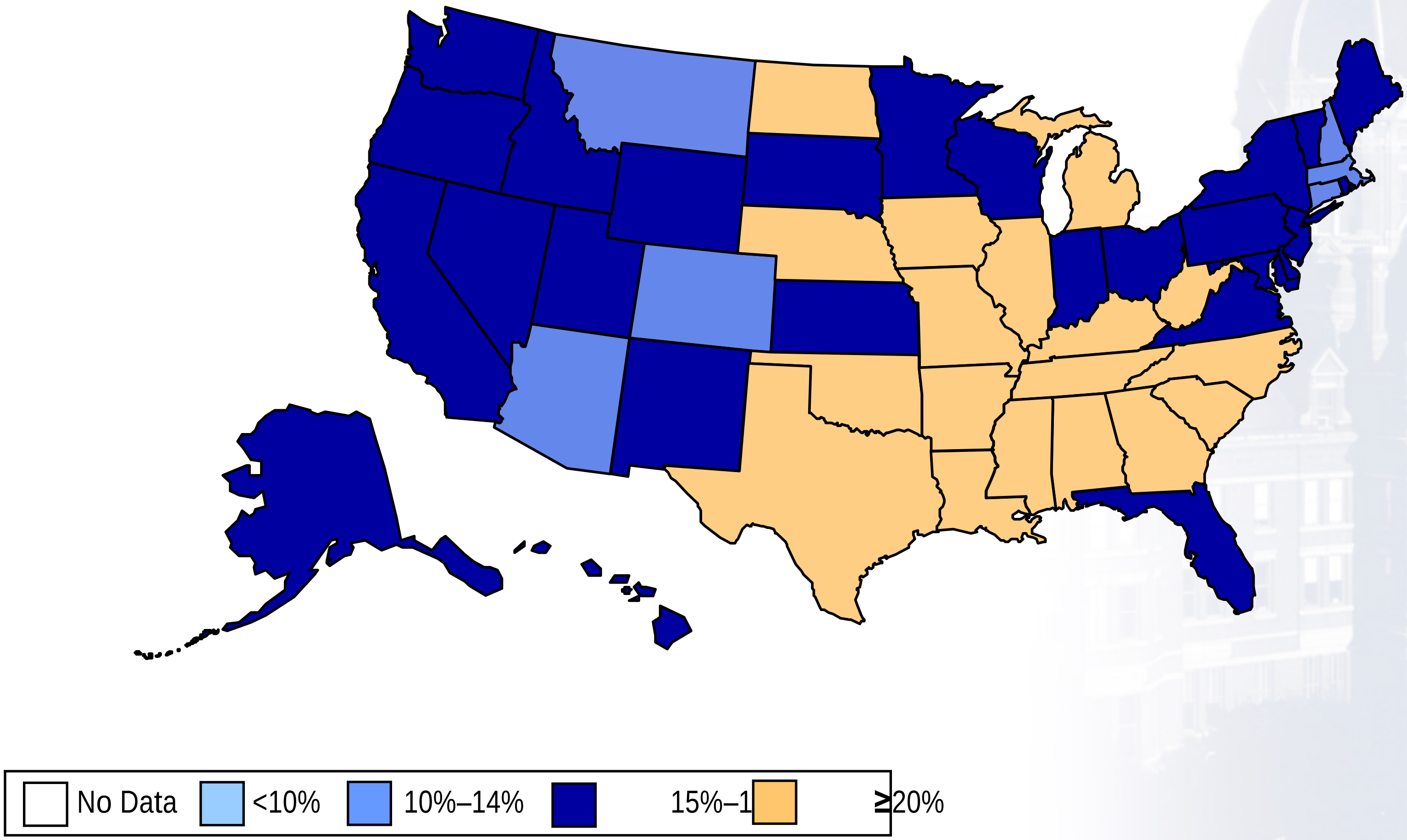
Obesity Trends* Among U.S. Adults
BRFSS, 1998

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



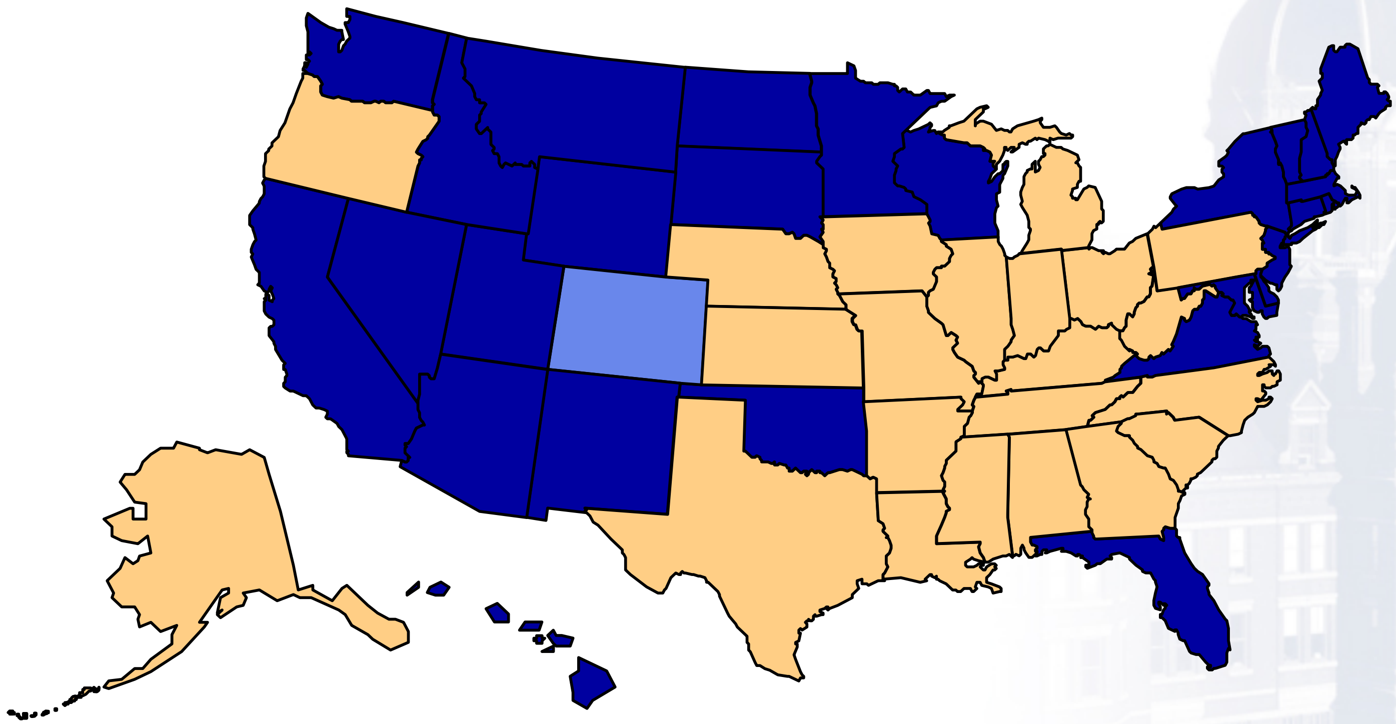
Obesity Trends* Among U.S. Adults
BRFSS, 1999

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults
BRFSS, 2000

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



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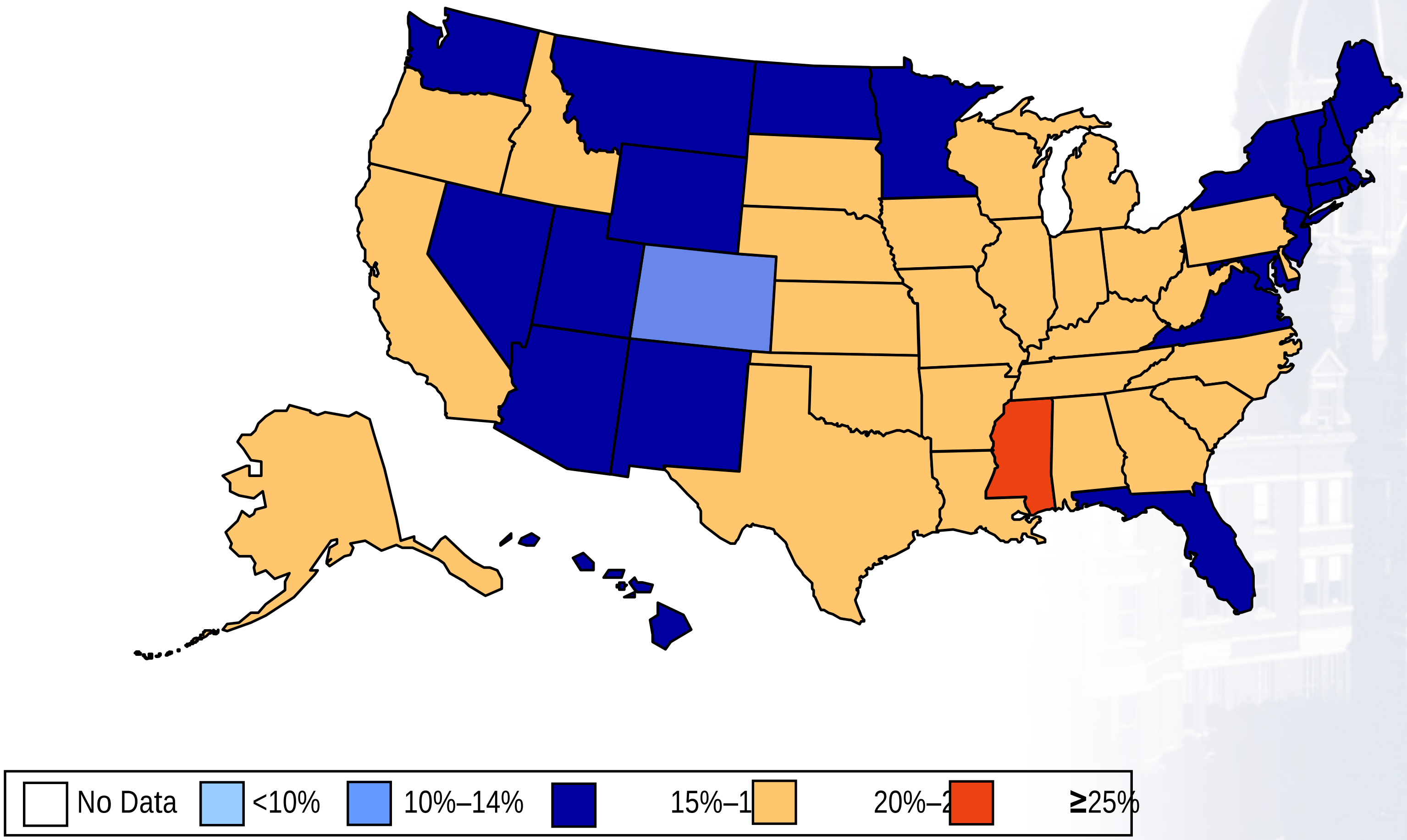
Obesity Trends* Among U.S. Adults

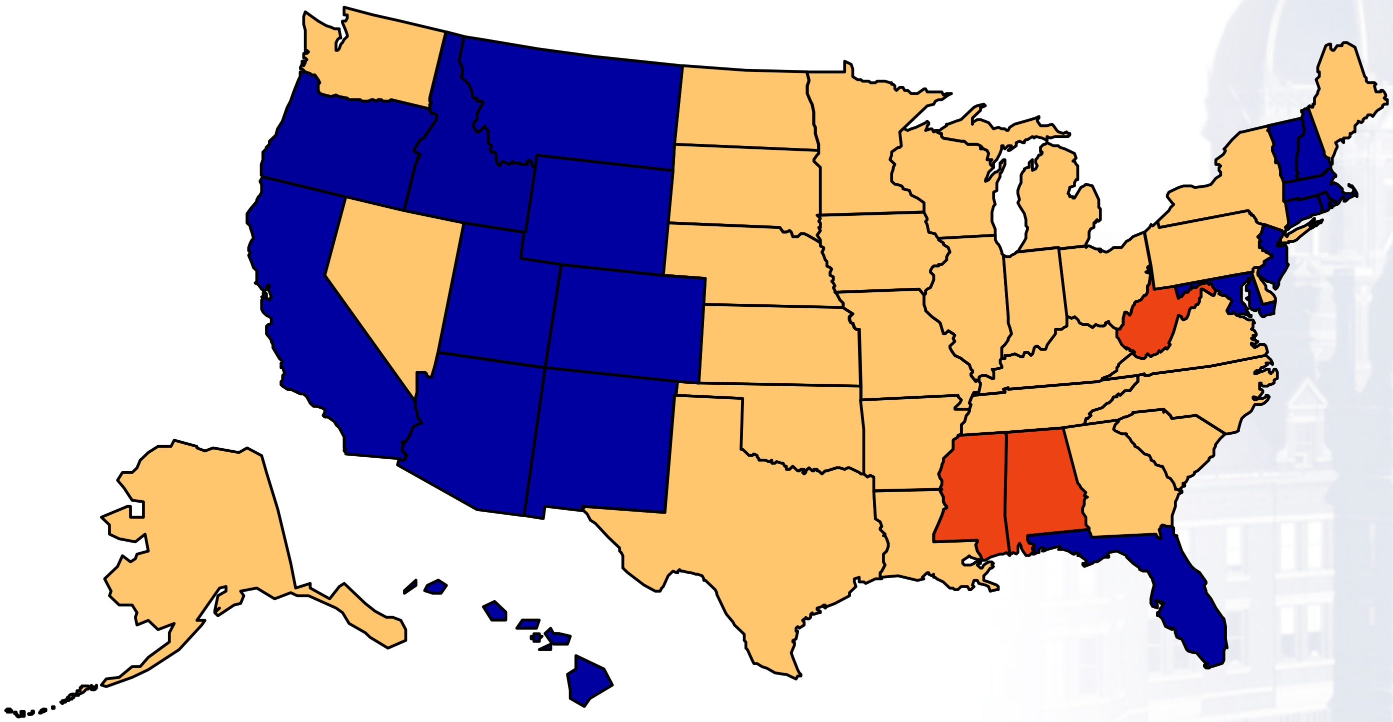
BRFSS, 2001

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



Obesity Trends* Among U.S. Adults
BRFSS, 2002

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



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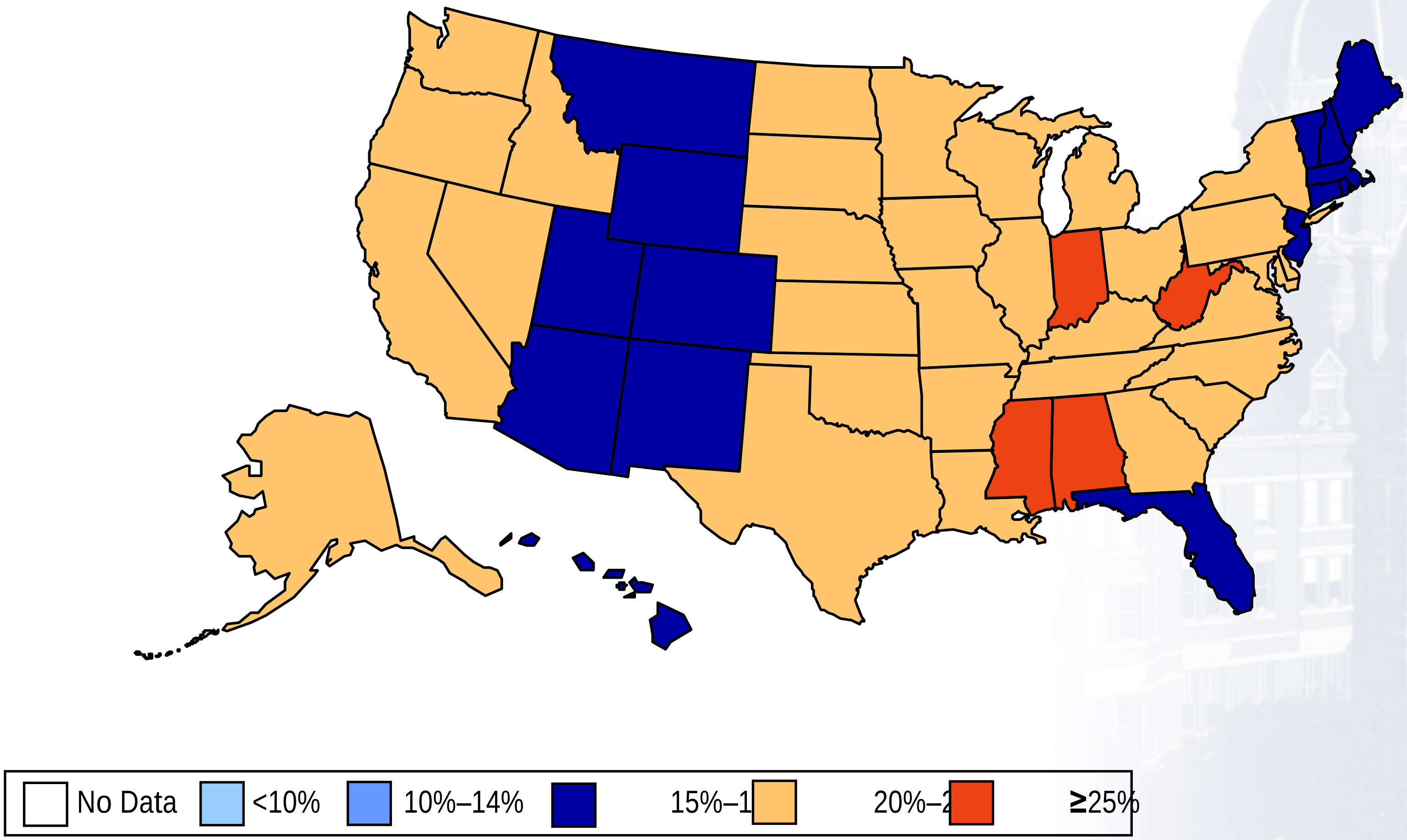
Obesity Trends* Among U.S. Adults
BRFSS, 2003

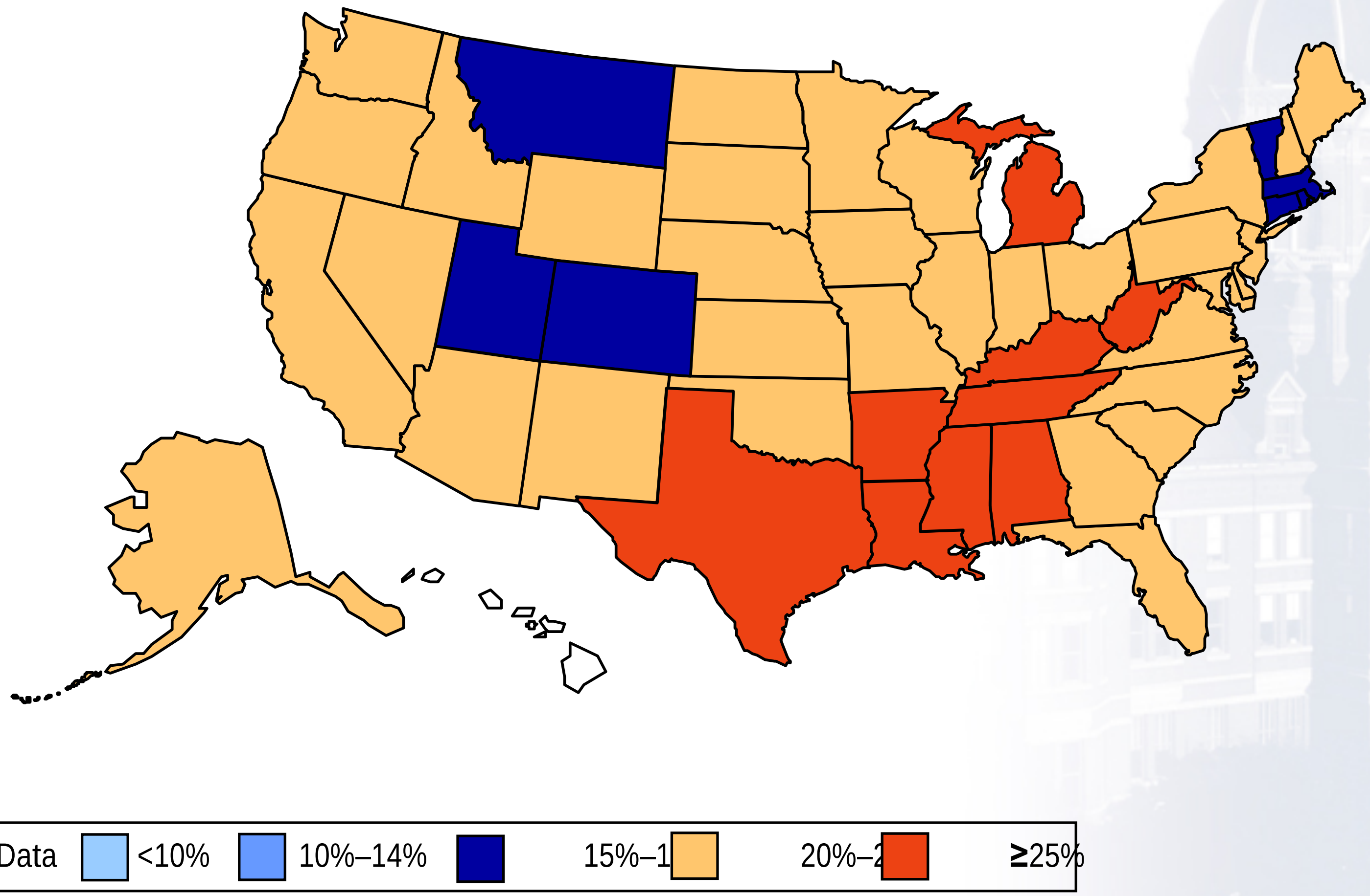
(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

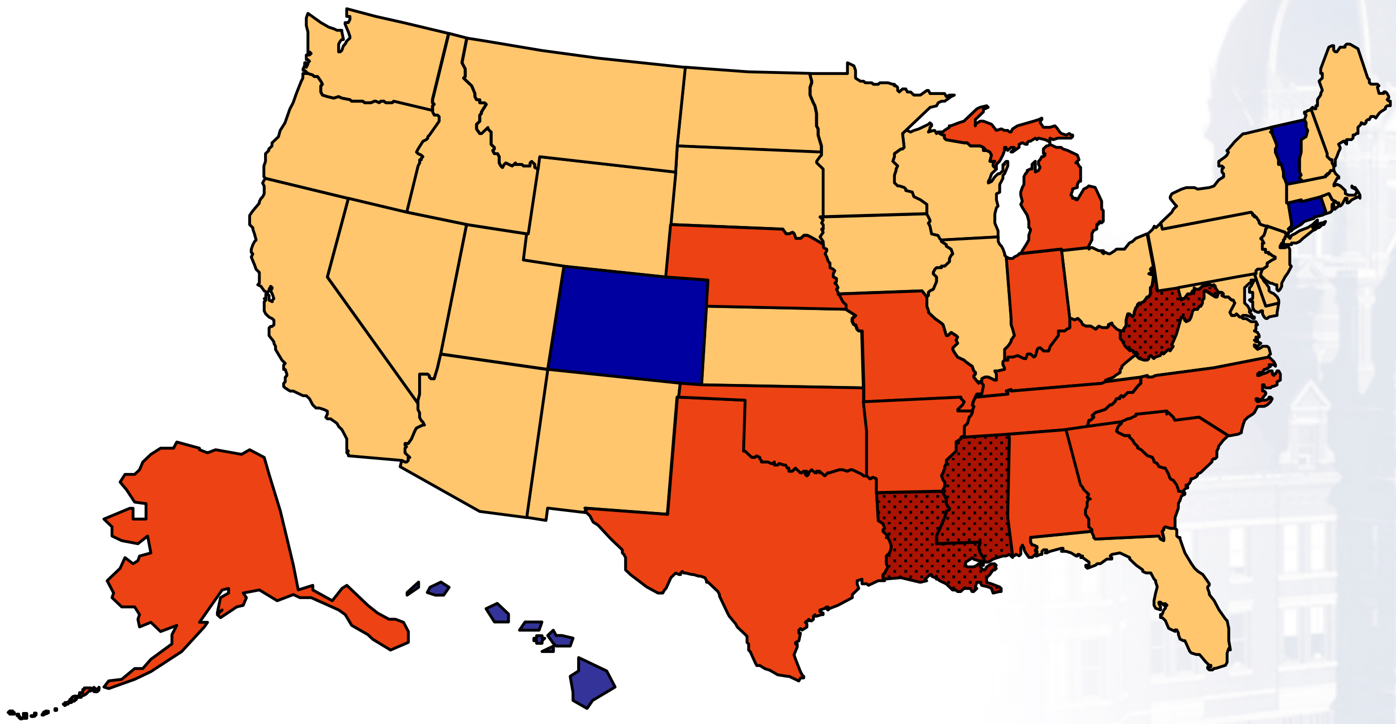
BRFSS, 2004

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults
BRFSS, 2005

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



No Data | <10% | 10%–14% | 15%–19% | 20%–24% | 25%–29% | ≥30%

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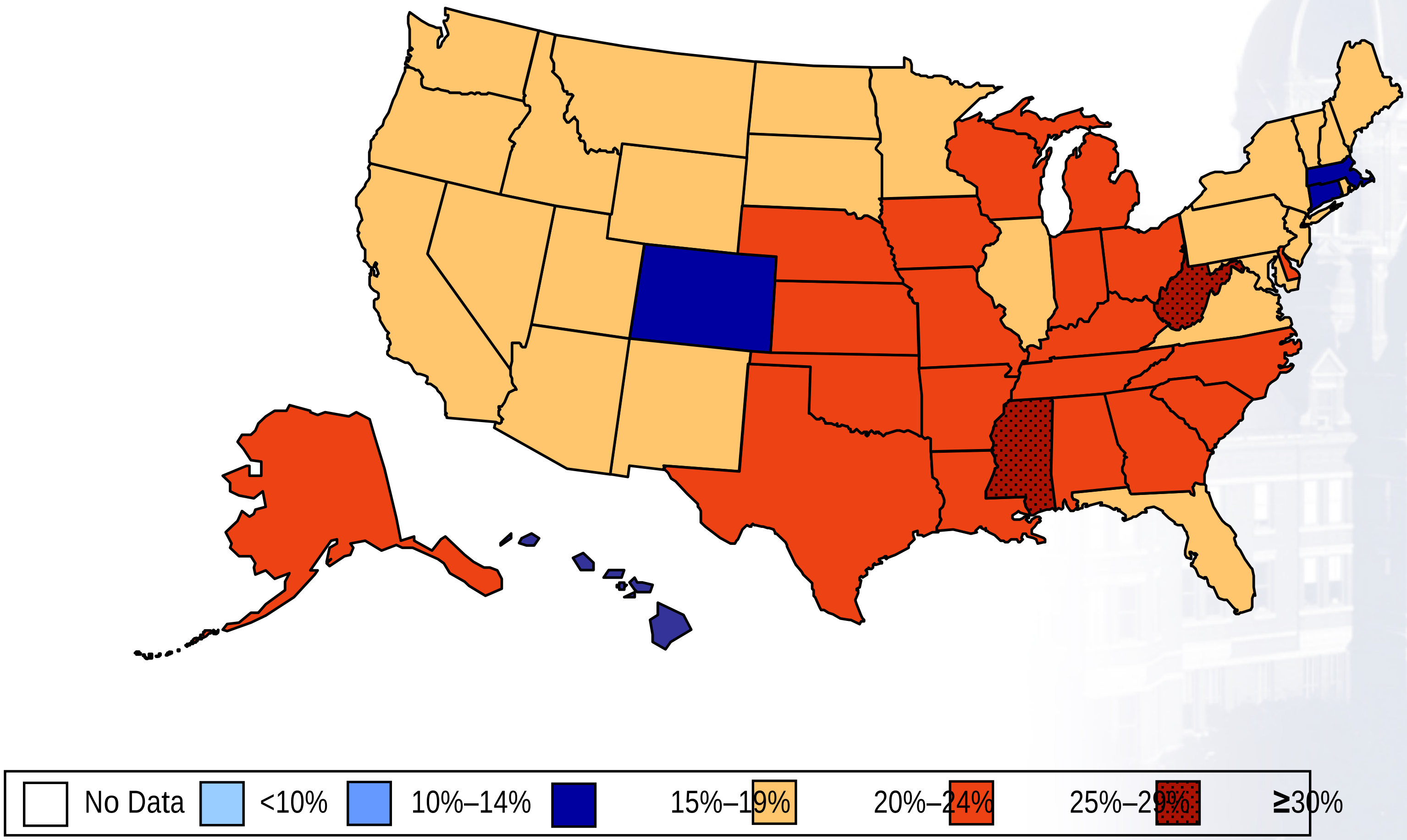
Obesity Trends* Among U.S. Adults

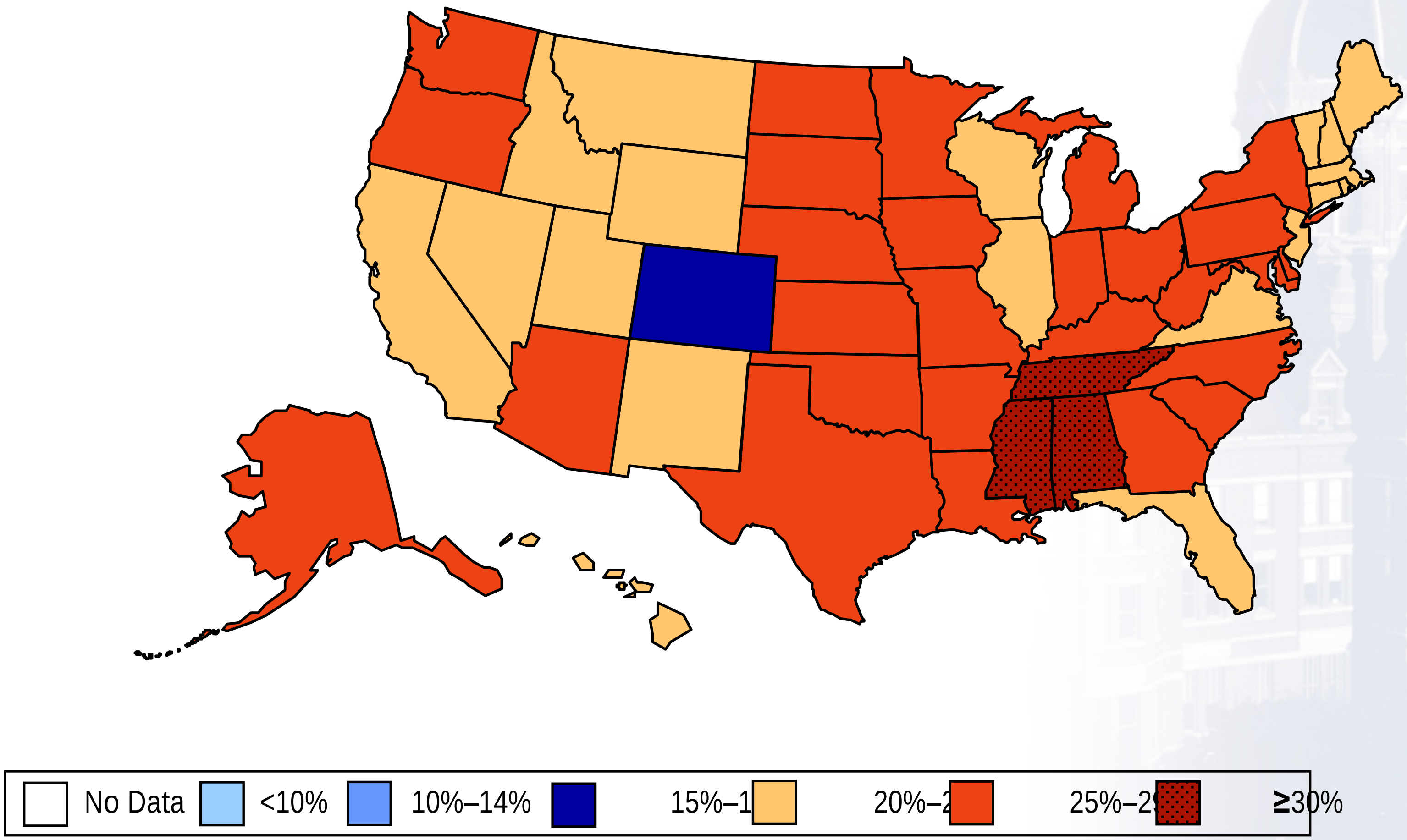
BRFSS, 2006

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



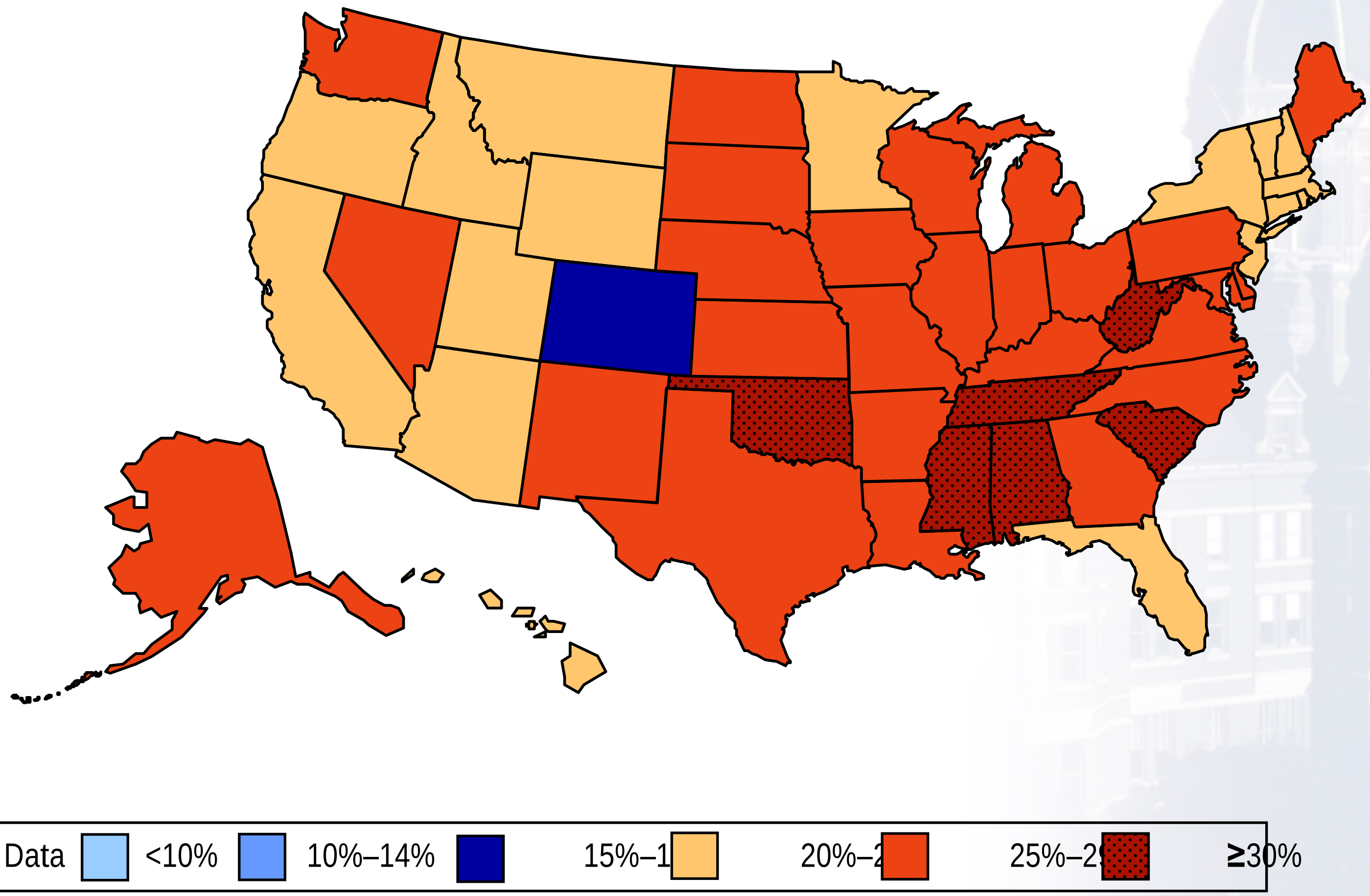
Obesity Trends* Among U.S. Adults
BRFSS, 2007

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



Obesity Trends* Among U.S. Adults
BRFSS, 2008

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



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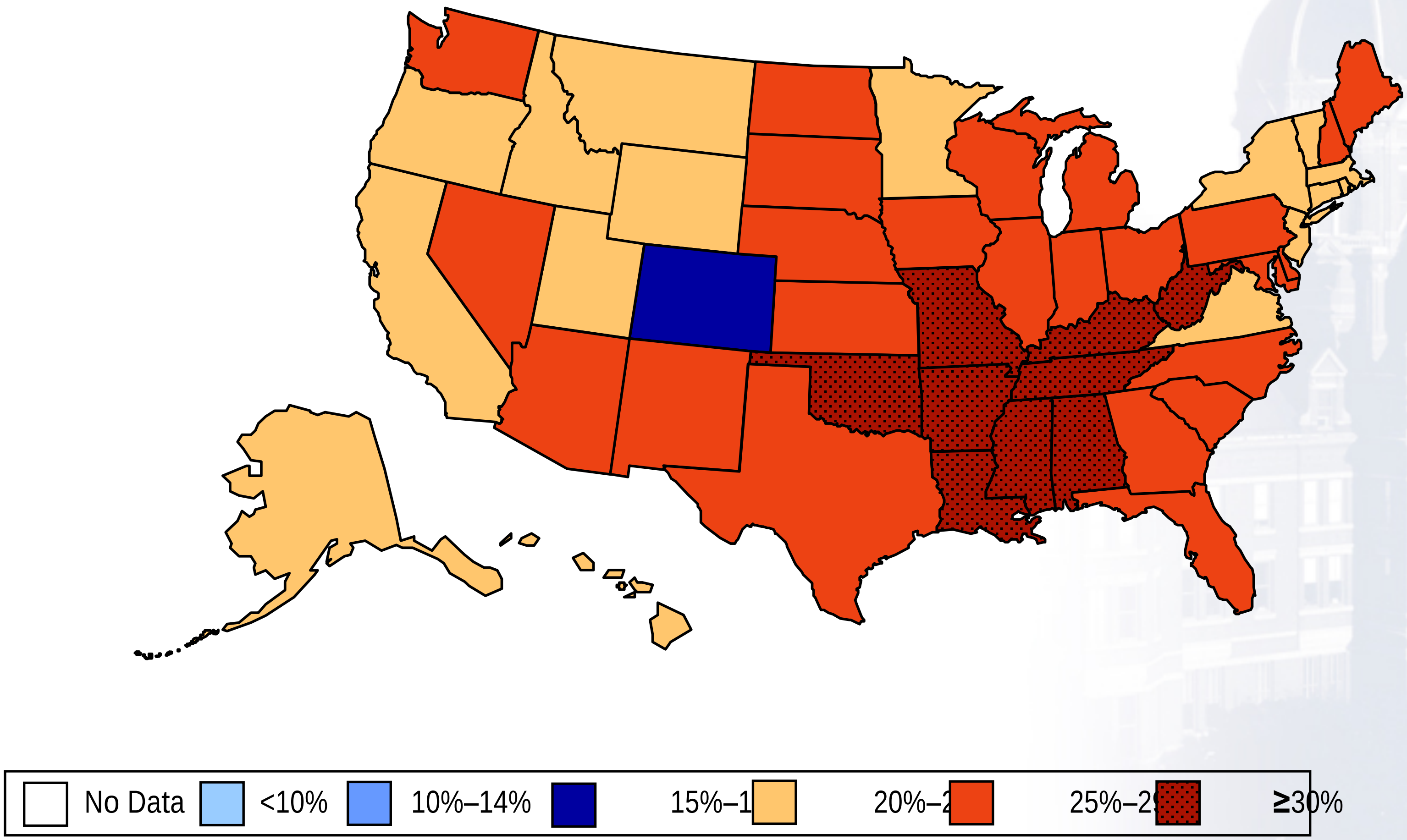
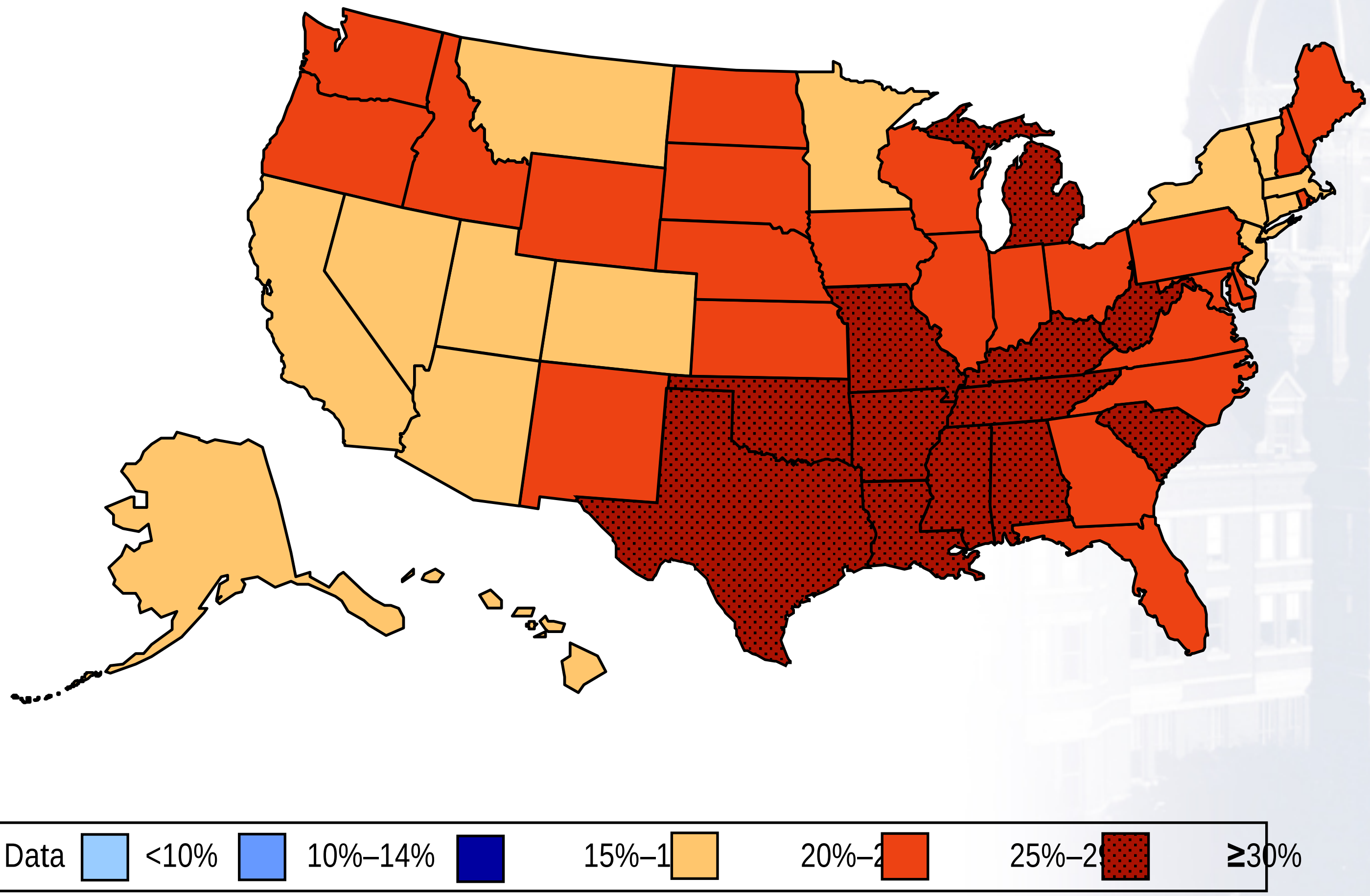
Obesity Trends* Among U.S. Adults
BRFSS, 2009

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



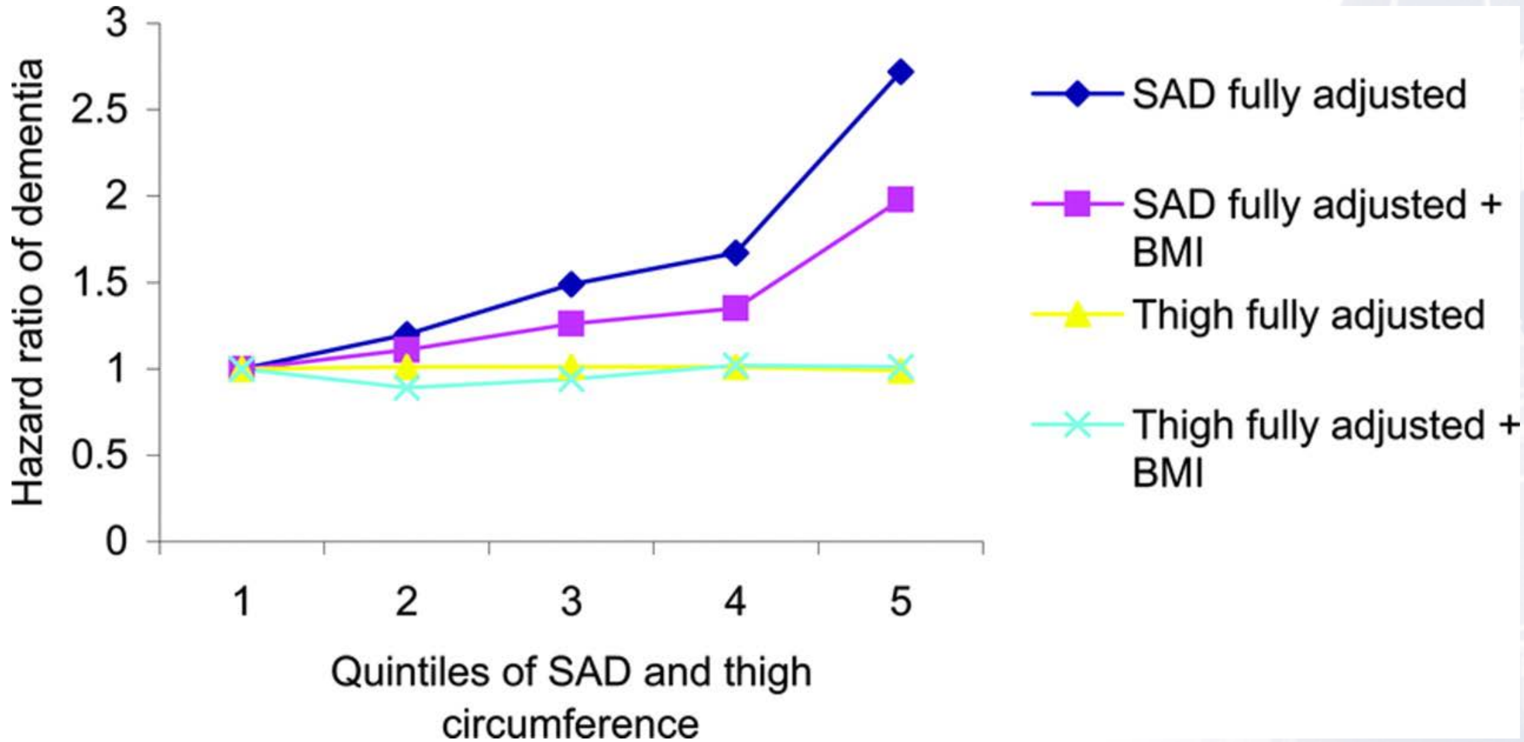
Obesity Trends* Among U.S. Adults
BRFSS, 2010

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



JOHNS HOPKINS MEDICINE

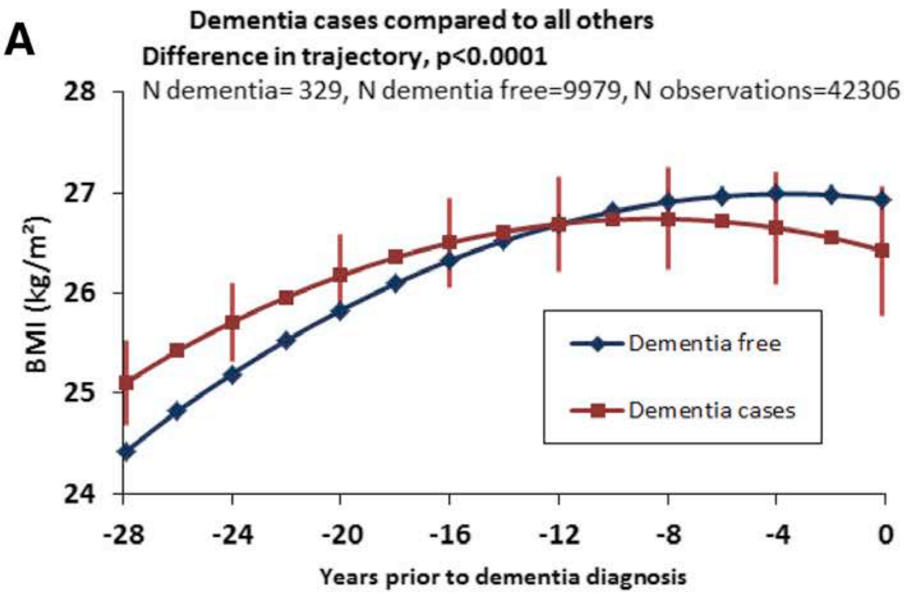
Obesity *in midlife* is associated with higher risk of dementia

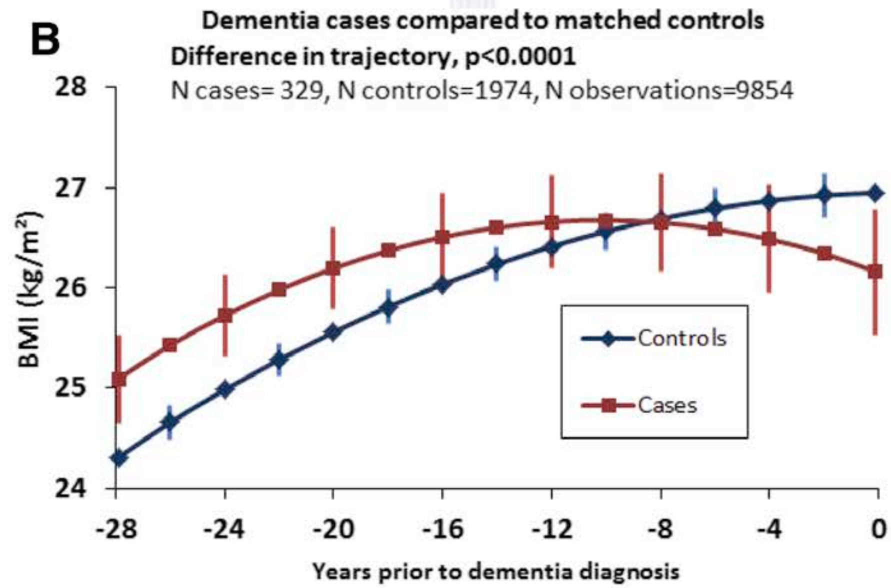


SAD: sagittal abdominal diameter

Whitmer et al, Neurology 2008

Obesity and Dementia



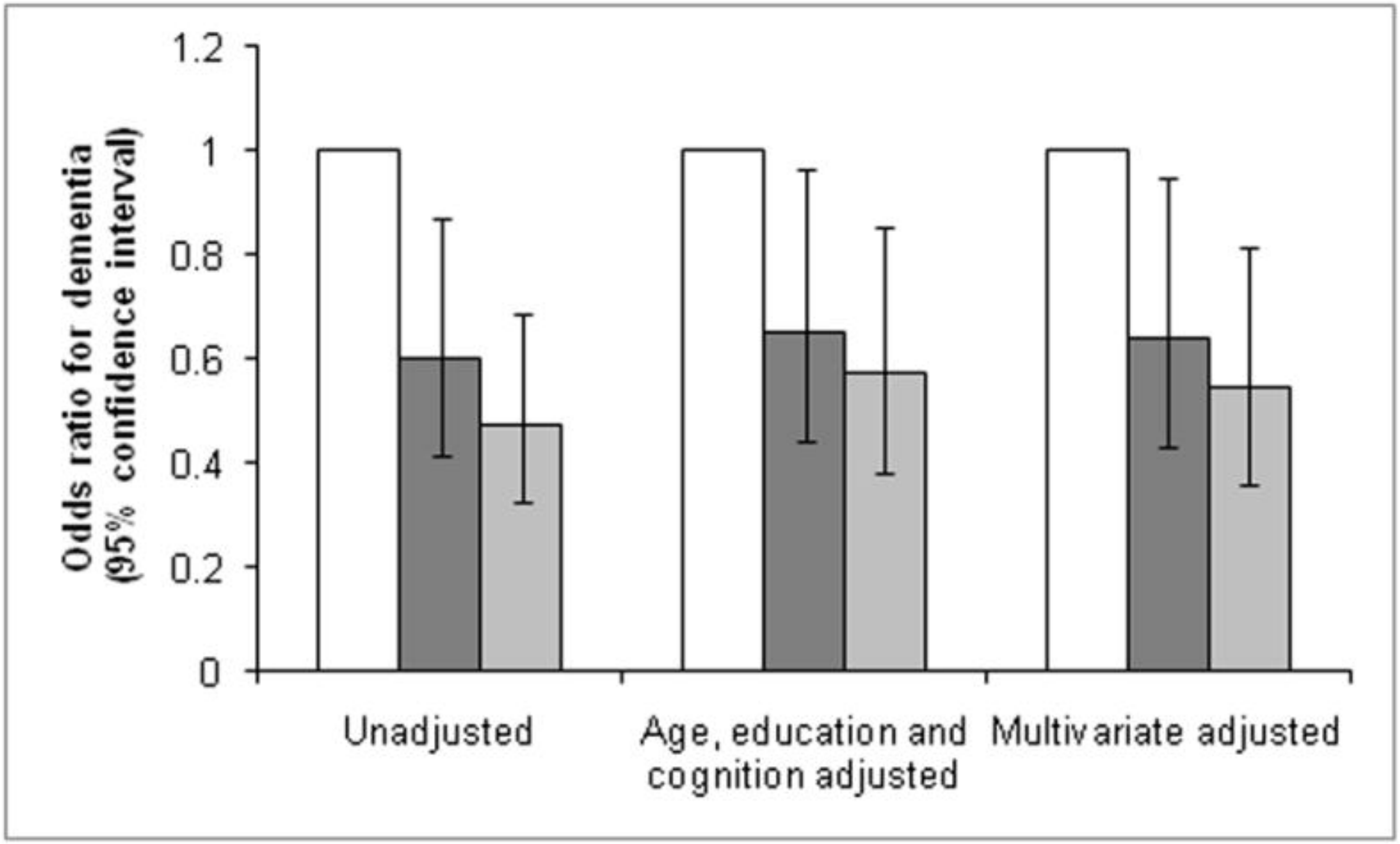


	Number of observations in the analysis						
Years	-28 to -24	-24 to -20	-20 to -16	-16 to -12	-12 to -8	-8 to -4	-4 to 0
Dementia free	9135	7161	5513	2944	4086	6353	6040
Dementia cases	219	196	141	126	147	133	112

	Number of observations in the analysis						
Years	-28 to -24	-24 to -20	-20 to -16	-16 to -12	-12 to -8	-8 to -4	-4 to 0
Controls	1460	1381	1044	1003	1245	1135	1512
Cases	219	196	141	126	147	133	112

Singh-Manoux et al., Alzheimer's and Dementia 2017

Physical activity in midlife and risk of dementia



Wang et al., Am J Geriatr Psychiatry, 2014

ELSEVIER

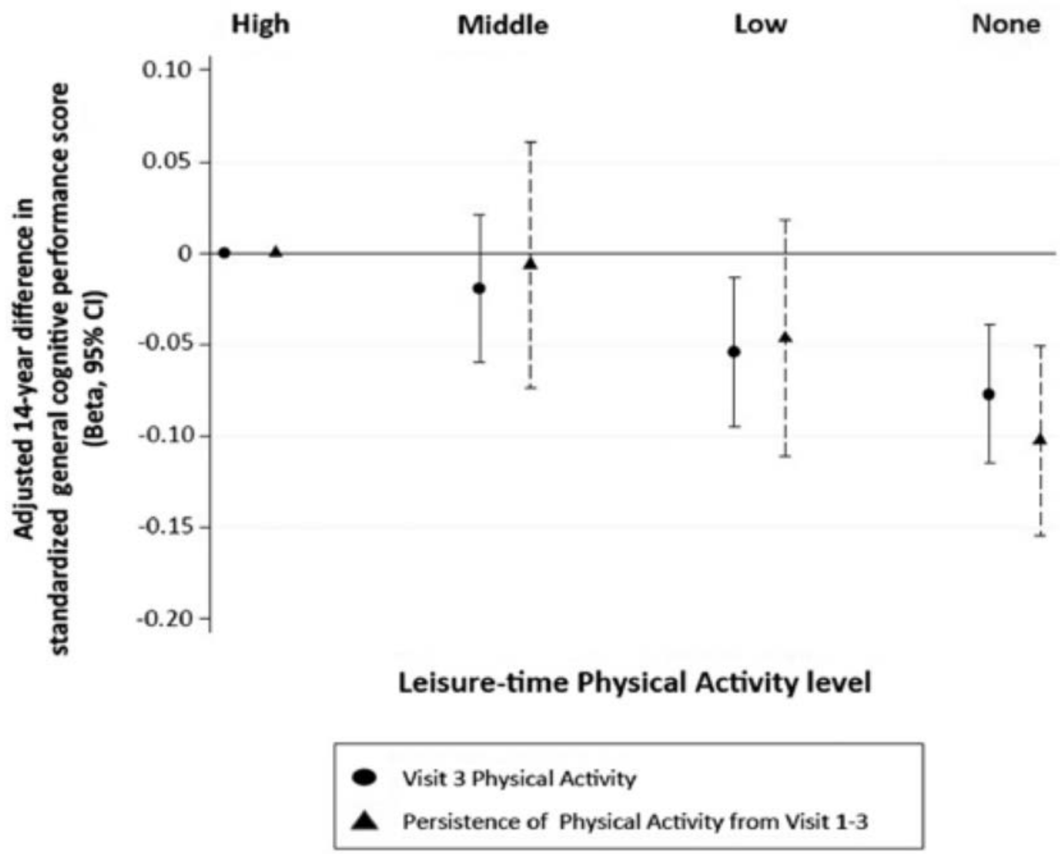
Alzheimer's & Dementia ■ (2018) 1-9

Alzheimer's & Dementia

Research Article

Leisure-time physical activity sustained since midlife and preservation of cognitive function: The Atherosclerosis Risk in Communities Study

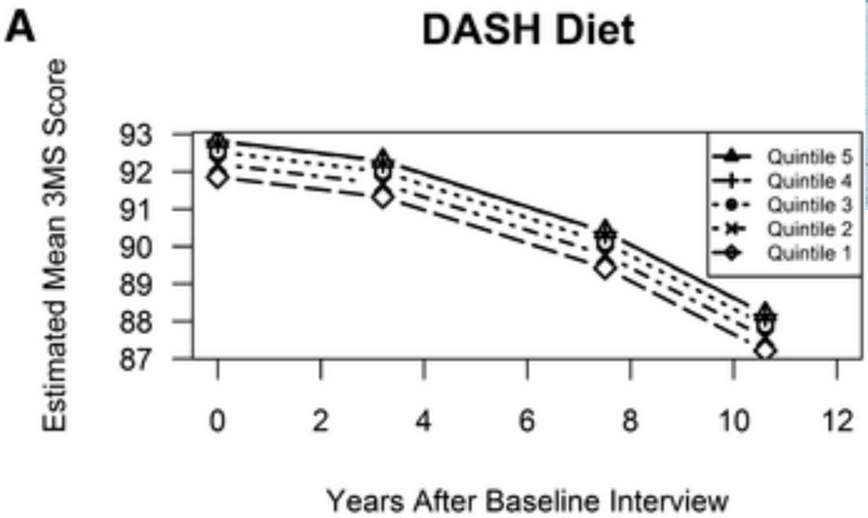
Priya Palta[a,*], A. Richey Sharrett[b], Jennifer A. Deal[b], Kelly R. Evenson[a], Kelley Pettee Gabriel[c,d], Aaron R. Folsom[e], Alden L. Gross[b], B. Gwen Windham[f], David Knopman[g], Thomas H. Mosley[f], Gerardo Heiss[a]

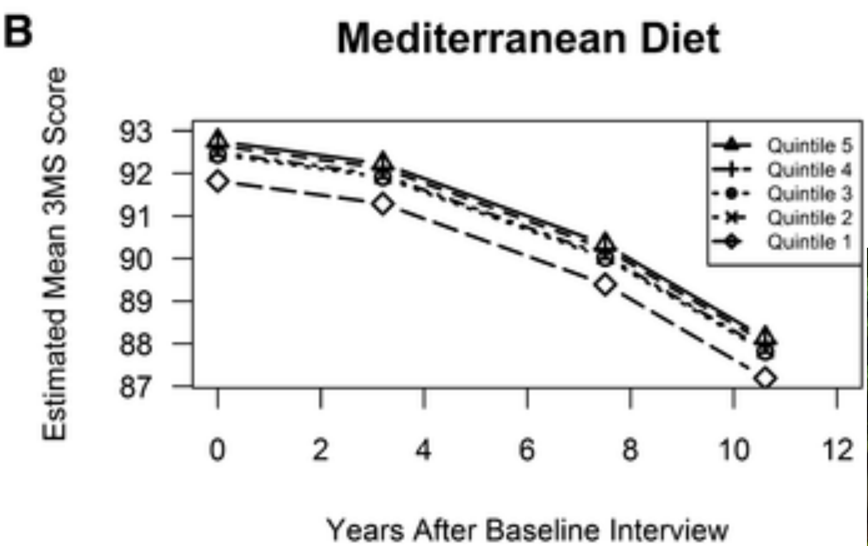


Reference: High physical activity

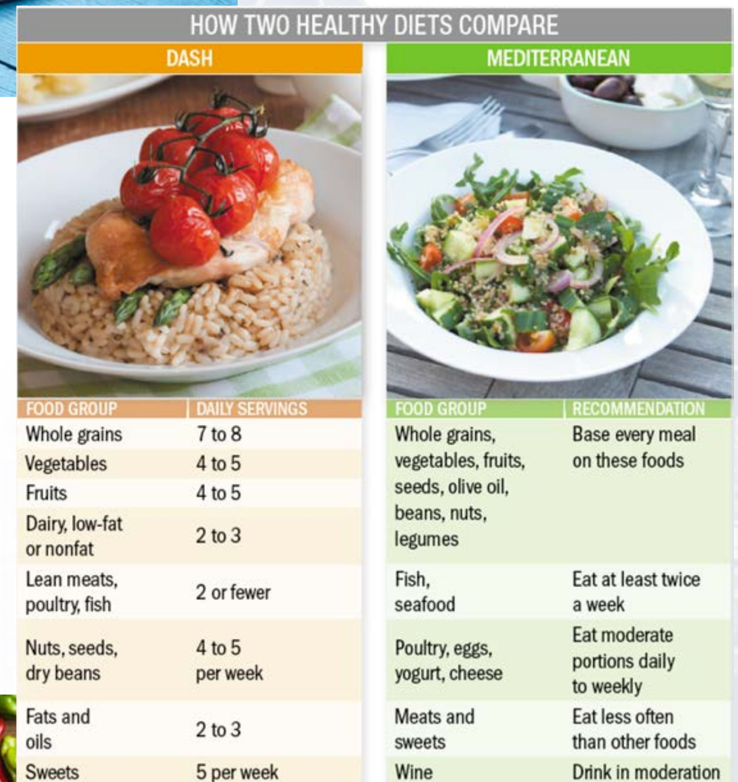
Adjusted for age, sex, education, race-center, ApoE4, smoking, household income, neighborhood SES

Diet and nutrition





from Wengreen et al., Amer J Clin Nutrition 2013



HOW TWO HEALTHY DIETS COMPARE

DASH

FOOD GROUP	DAILY SERVINGS
Whole grains	7 to 8
Vegetables	4 to 5
Fruits	4 to 5
Dairy, low-fat or nonfat	2 to 3
Lean meats, poultry, fish	2 or fewer
Nuts, seeds, dry beans	4 to 5 per week
Fats and oils	2 to 3
Sweets	5 per week

MEDITERRANEAN

FOOD GROUP	RECOMMENDATION
Whole grains, vegetables, fruits, seeds, olive oil, beans, nuts, legumes	Base every meal on these foods
Fish, seafood	Eat at least twice a week
Poultry, eggs, yogurt, cheese	Eat moderate portions daily to weekly
Meats and sweets	Eat less often than other foods
Wine	Drink in moderation

From www.health.harvard.edu

From www.cnn.com

JAMA | Original Investigation

Association Between Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition

Rebecca F. Gottesman, MD, PhD; Andrea L. C. Schneider, MD, PhD; Yun Zhou, PhD; Josef Coresh, MD, PhD; Edward Green, MD; Naresh Gupta, MD; David S. Knopman, MD; Akiva Mintz, MD; Arman Rahmim, PhD; A. Richey Sharrett, MD, DrPH; Lynne E. Wagenknecht, DrPH; Dean F. Wong, MD, PhD; Thomas H. Mosley, PhD

JAMA. 2017;317(14):1443-1450.

Table 3. Adjusted Odds Ratios for the Association of Midlife and Late-Life Number of Vascular Risk Factors With Global Cortex SUVR >1.2 Overall and Stratified by *APOE* ε4 Genotype (N = 322)

	Overall (n = 322)		0 *APOE* ε4 Alleles (n = 220)		1 or 2 *APOE* ε4 Alleles (n = 100)	
Risk Factors[a]	No. With SUVR >1.2/Total No. (%)	Adjusted OR (95% CI)[b]	No. With SUVR >1.2/Total No. (%)	Adjusted OR (95% CI)[b]	No. With SUVR >1.2/Total No. (%)	Adjusted OR (95% CI)[b]
Midlife (Study Visit 1, 1987-1989)						
Vascular risk factors						
0	20/65 (30.8)	1 [Reference]	14/47 (29.8)	1 [Reference]	6/18 (33.3)	1 [Reference]
1	62/123 (50.4)	1.88 (0.95-3.73)	37/85 (43.5)	1.36 (0.61-3.05)	25/38 (65.8)	3.10 (0.84-11.50)
≥2	82/134 (61.2)	2.88 (1.46-5.69)	45/90 (50.0)	1.86 (0.83-4.14)	37/44 (84.1)	9.15 (2.27-36.89)
Late life (Study Visit 5, 2011-2013)						
Vascular risk factors						
0	13/35 (37.1)	1 [Reference]	6/23 (26.1)	1 [Reference]	7/12 (58.3)	1 [Reference]
1	37/82 (45.1)	1.02 (0.43-2.43)	16/50 (32.0)	1.38 (0.43-4.39)	21/32 (65.6)	0.56 (0.12-2.67)
≥2	114/205 (55.6)	1.66 (0.75-3.69)	74/149 (49.7)	2.21 (0.78-6.26)	40/56 (71.4)	1.03 (0.25-4.29)

Abbreviations: OR, odds ratio; SUVR, standardized uptake value ratio.

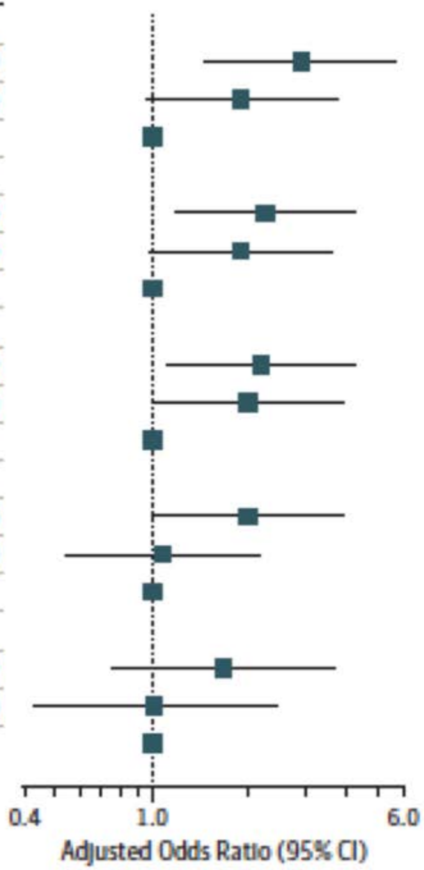
[a] Vascular risk factors included body mass index ≥30, current smoking, hypertension, diabetes, and total cholesterol ≥200 mg/dL.

[b] Models are adjusted for age (at visit 5, 2011-2013), sex, race, education level, and *APOE* ε4 genotype.

Association between number of risk factors and brain amyloid is reduced when later-life risk factors are considered

Figure 1. Adjusted Odds Ratios for Global Cortex Florbetapir SUVRs >1.2 by Number of Vascular Risk Factors, Midlife Through Late Life

No. of Risk Factors by Study Visit	No. With Elevated SUVR/Total No. (%)	Adjusted Odds Ratio (95% CI)
Visit 1 (1987-1989)		
≥2	82/134 (61.2)	2.88 (1.46-5.69)
1	62/123 (50.4)	1.88 (0.95-3.73)
0	20/65 (30.8)	1 [Reference]
Visit 2 (1990-1992)		
≥2	80/137 (58.4)	2.24 (1.19-4.23)
1	57/108 (52.8)	1.88 (0.97-3.62)
0	27/77 (35.1)	1 [Reference]
Visit 3 (1993-1995)		
≥2	83/146 (56.9)	2.18 (1.12-4.26)
1	60/111 (54.1)	1.98 (1.00-3.92)
0	21/65 (32.3)	1 [Reference]
Visit 4 (1996-1998)		
≥2	93/153 (60.8)	1.98 (1.01-3.89)
1	47/111 (42.3)	1.07 (0.53-2.14)
0	24/58 (41.4)	1 [Reference]
Visit 5 (2011-2013)		
≥2	114/205 (55.6)	1.66 (0.75-3.69)
1	37/82 (45.1)	1.02 (0.43-2.43)
0	13/35 (37.1)	1 [Reference]



Is there evidence that treatment of vascular risk prevents dementia?

- Previously, few studies had shown a benefit from treatment of risk factors to prevent dementia
- The recent "SPRINT-MIND" trial showed that tight control of blood pressure (to a goal of Systolic BP<120 mm Hg) was associated with 15% fewer cases of a combined outcome of MCI and dementia (and fewer MCI cases, but no difference in dementia alone)

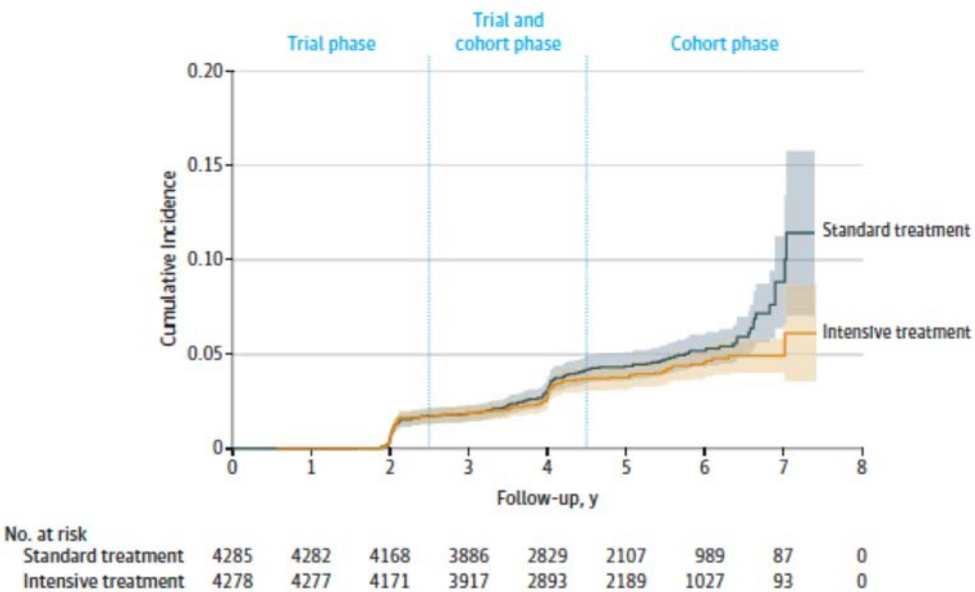
JAMA | Original Investigation

Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia
A Randomized Clinical Trial

The SPRINT MIND Investigators for the SPRINT Research Group

SPRINT-MIND:
Williamson et al, JAMA 2019

Figure 2. Probable Dementia by Treatment Group



Key Points

Question Does intensive blood pressure control reduce the occurrence of dementia?

Findings In this randomized clinical trial that included 9361 adults with hypertension, randomization to a systolic blood pressure target of less than 120 mm Hg compared with less than 140 mm Hg resulted in a rate of probable dementia of 7.2 vs 8.6 cases per 1000 person-years, a difference that was not statistically significant.

Meaning Among adults with hypertension, intensive blood pressure control did not significantly reduce the risk of probable dementia.

Table 2. Incidence of Probable Dementia and Mild Cognitive Impairment by Treatment Group

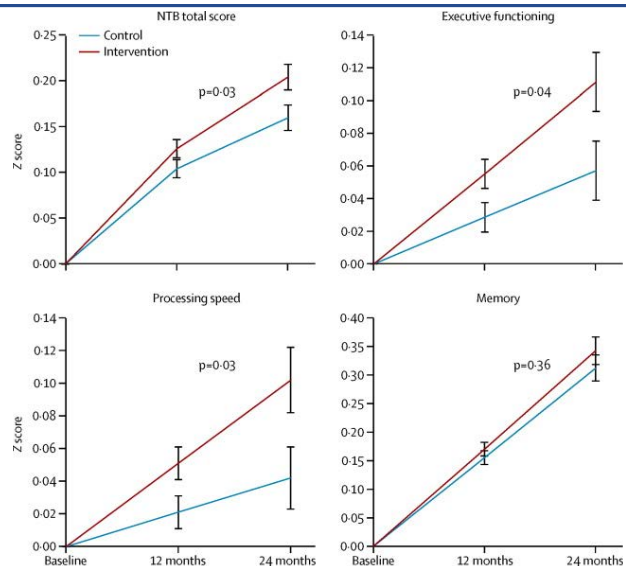
	Treatment Group					
	Intensive		Standard			
Outcomes	No. With Outcome/Person-Years	Cases per 1000 Person-Years	No. With Outcome/Person-Years	Cases per 1000 Person-Years	Hazard Ratio (95% CI)[a]	P Value
Probable dementia	149/20 569	7.2	176/20 378	8.6	0.83 (0.67-1.04)	.10
Mild cognitive impairment[b]	287/19 690	14.6	353/19 281	18.3	0.81 (0.69-0.95)	.007
Composite of mild cognitive impairment or probable dementia	402/19 873	20.2	469/19 488	24.1	0.85 (0.74-0.97)	.01

[a] Intensive treatment group vs standard treatment group based on Cox proportional hazards regression.

[b] Participants adjudicated as having probable dementia at the first follow-up visit (year 2) do not contribute to the analyses of mild cognitive impairment.

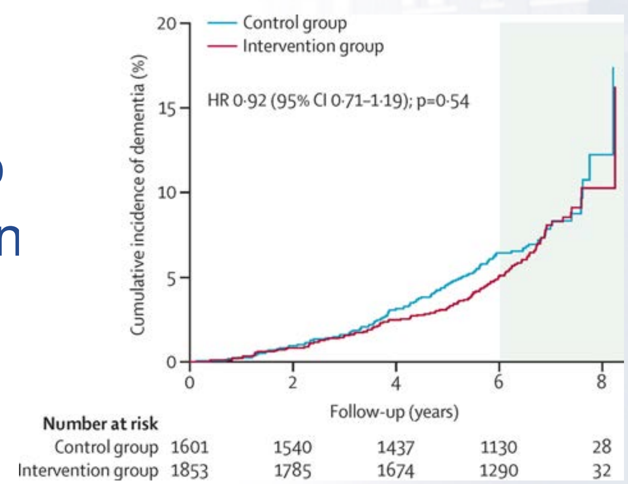
JOHNS HOPKINS MEDICINE

Multi-modal approaches to treatment & prevention: Mixed results



- FINGER trial (Ngandu et al., Lancet 2015): randomized Finnish participants to 2-year multidomain intervention (diet, exercise, cognitive training, vascular risk factor monitoring) vs control
- 2-year followup was better in the intervention group, for *cognitive change*

- PreDIVA Trial: Evaluated new dementia cases, and found no difference in people randomized to a multidomain vascular intervention over 6 years compared to those with standard care (Moll van Charante et al., Lancet 2016)



Take Home Messages

- Risk factors for heart disease and stroke are also risk factors for cognitive decline and dementia, and **many of these are modifiable**
- These vascular risk factors may directly contribute to changes in the brain that cause Alzheimer's disease
- Focusing on vascular health in *middle age* is especially important for the maintenance of brain health
- Aggressive treatment of high blood pressure reduces risk of mild cognitive impairment or dementia
- Treatment aimed at overall health: lifestyle, diet/ exercise, and vascular risk, may plan an important role in preserving brain health

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- Arman Rahmim
- Marilyn Albert
- SCAN Lab

University of Minnesota

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University of Mississippi Medical Center

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- Edward Green

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- Cliff Jack

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