

Il Cancro Colorettale

Prof. Luigi Ricciardiello

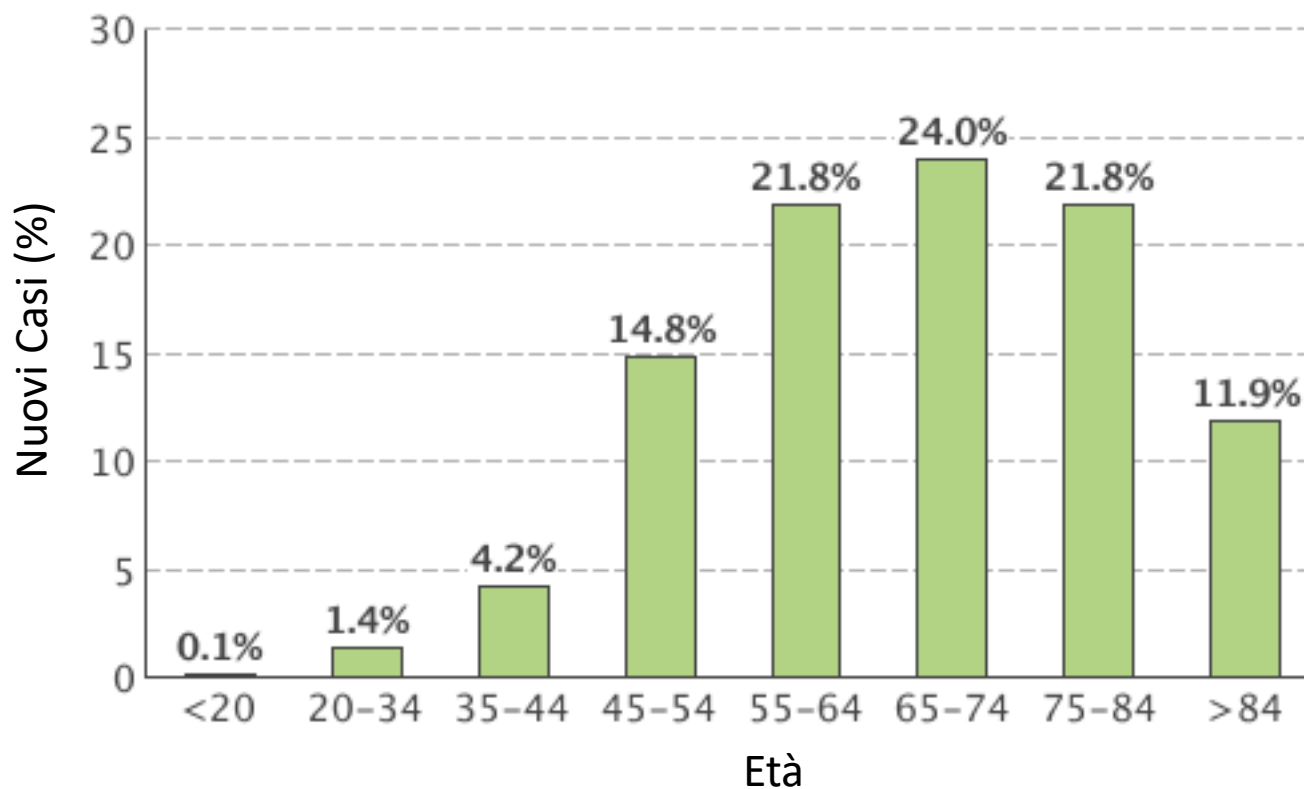
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Dipartimento di Scienze Mediche e Chirurgiche - Università di Bologna

Epidemiologia del cancro colorettales

	Nuovi casi per anno		Morti per anno	
	Maschi	Femmine	Maschi	Femmine
Mondo	663,600	570,100	320,600	288,100
Paesi occidentali	389,700	337,700	166,200	153,900
Paesi in via di sviluppo	274,000	232,400	154,400	134,100

2008 data

Percentuali di CRC in base all'età alla diagnosi

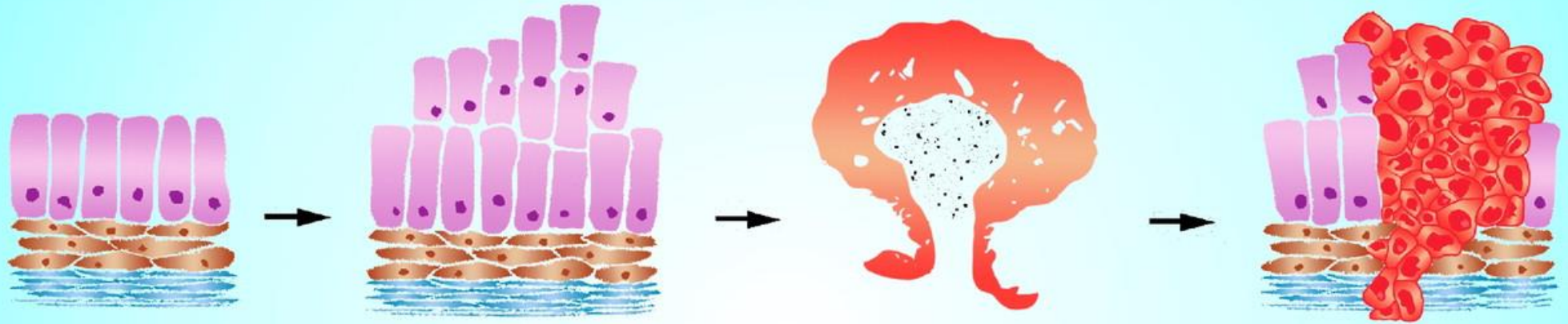


Trends di incidenza nella popolazione di età fra i 20 e i 49 anni negli USA: 1992-2005

Razze	Sex	APC
Tutte le razze	Maschi	1.5
	Femmine	1.6
Bianchi non ispanici	Maschi	2.0
	Femmine	2.2
Neri non ispanici	Maschi	-0.2
	Femmine	-0.6
Ispanici	Maschi	2.7
	Femmine	1.1
Hawaiiiani	Maschi	1.2
	Femmine	0.6

APC = Annual Percent Change

Sequenza Adenoma-Carcinoma



Mucosa
Normale

Aumento
Proliferazione

Adenoma

Cancro

10-15 anni

Prevenzione del cancro coloretta

PRIMARIA: Identificazione e modificazione di fattori ambientali e genetici → **Età giovanile**

SECONDARIA: Identificazione e rimozione delle lesioni premaligne → **Adulti/Anziani**

Fattori di rischio per CCR

Età
Familiarità
Sindromi genetiche
MICI



Fattori che influenzano la
prevenzione secondaria

Fattori che influenzano la
prevenzione primaria



Fumo
Alcool
Dieta
Obesità

Obesità

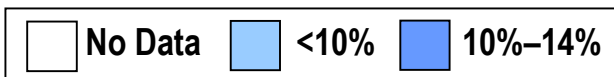
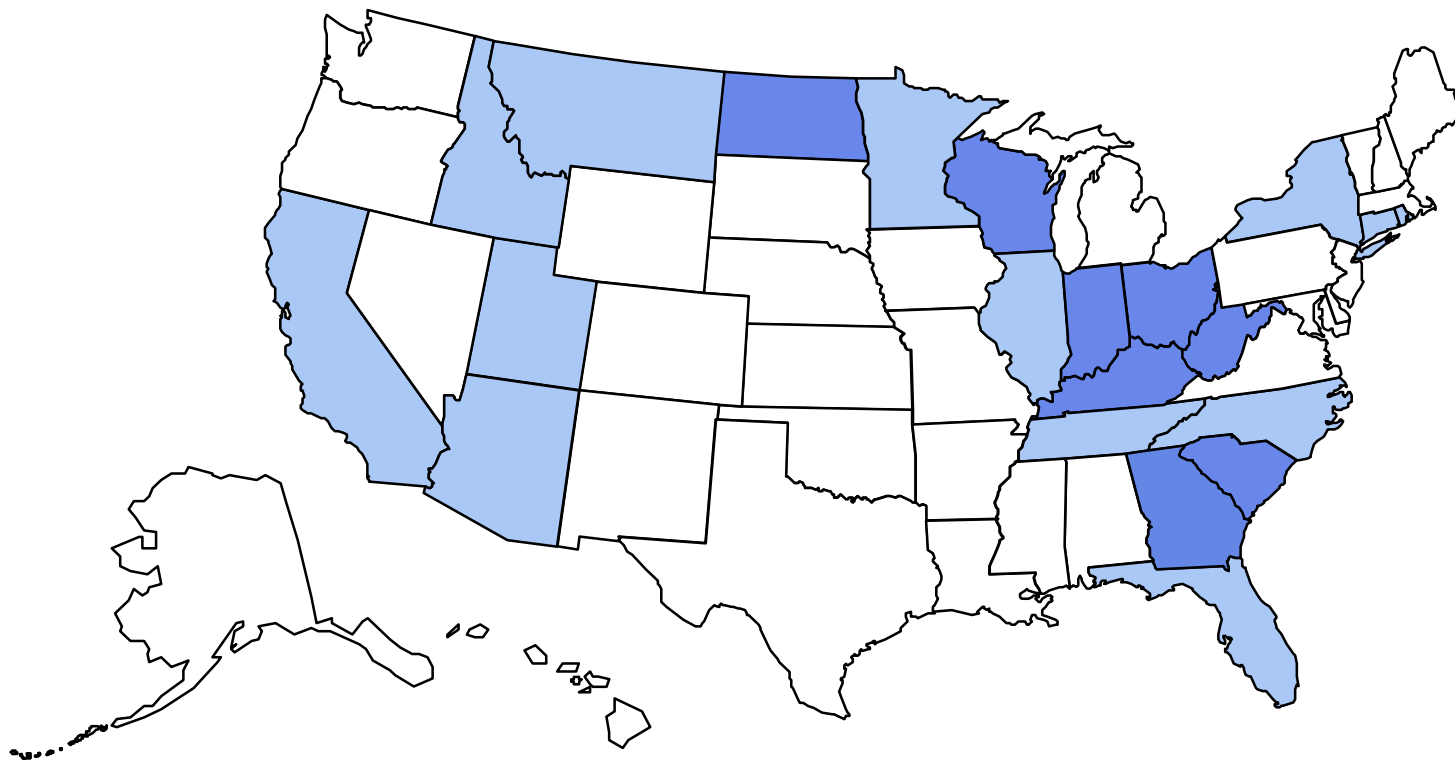
Trends Mondiali 1980-2008

- 1980-2008 l'indice di massa corporea (BMI) è aumentato di 0.4 kg/m^2 per decade
- Nel 2008 1.5 miliardi di adulti con BMI > 25 (sovrappeso)
- Nel 2008, 600 milioni di persone con BMI > 30 (Obesi)

Obesity Trends* Among U.S. Adults

BRFSS, 1985

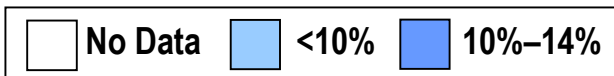
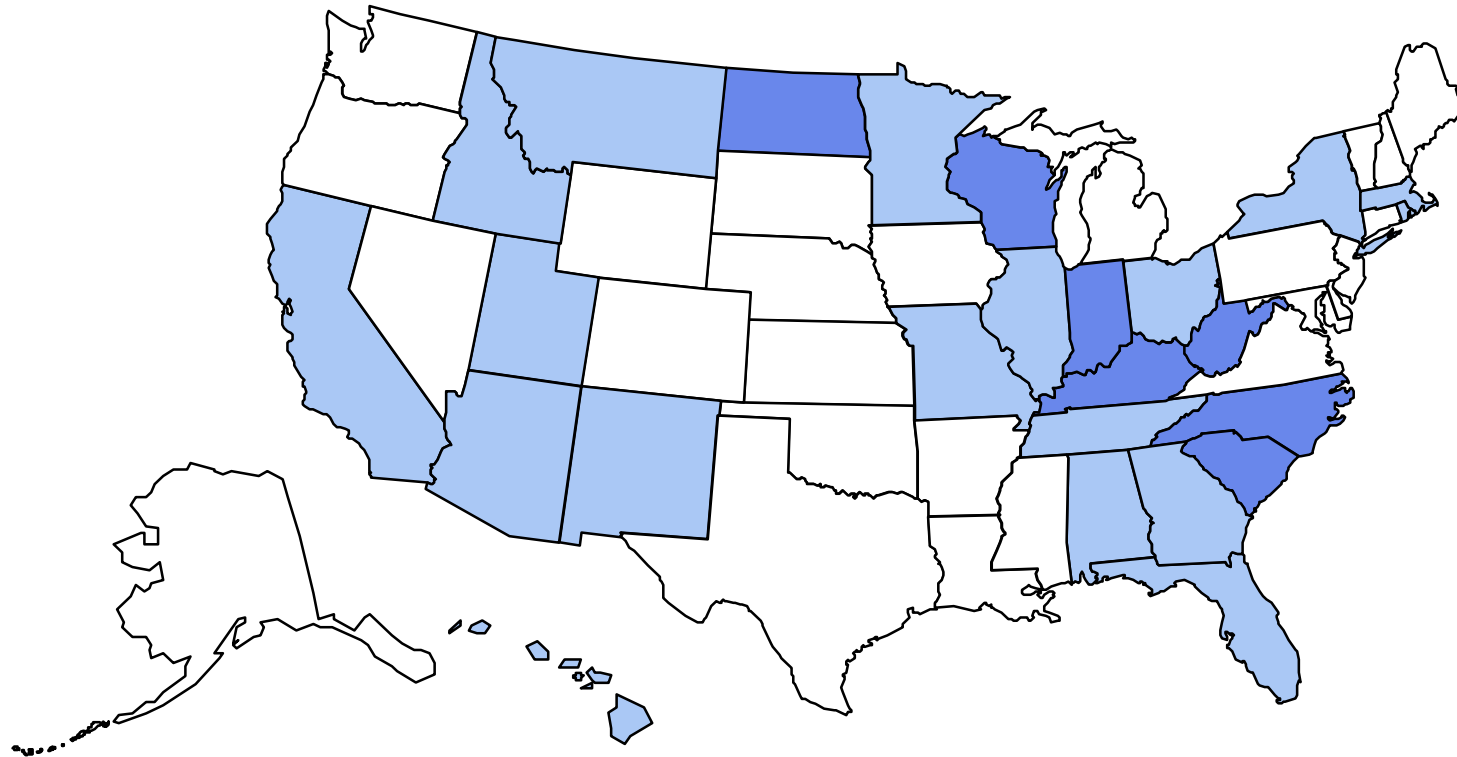
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 1986

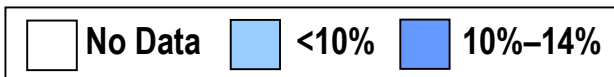
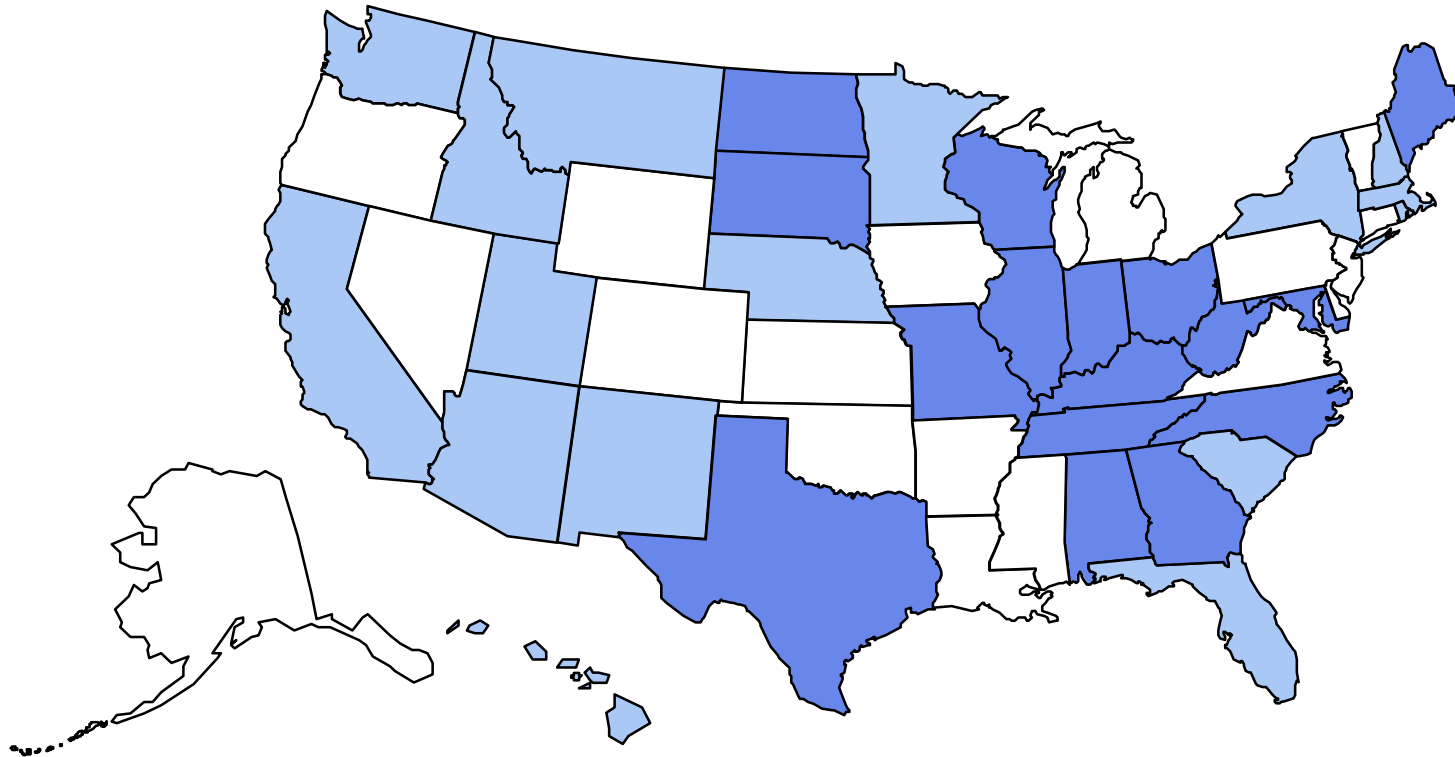
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Obesity Trends* Among U.S. Adults

BRFSS, 1987

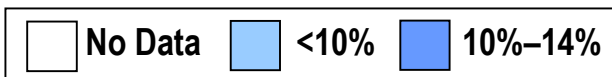
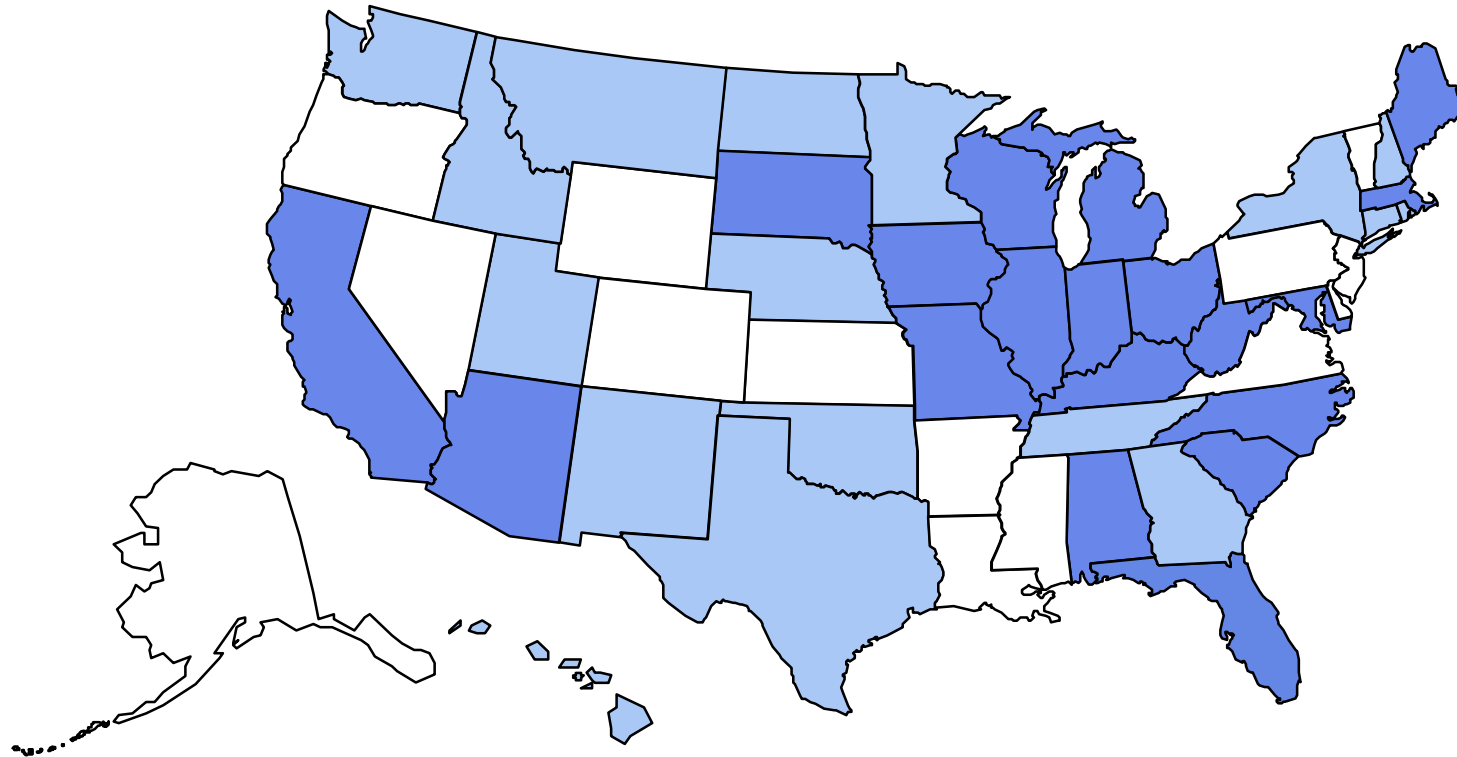
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Obesity Trends* Among U.S. Adults

BRFSS, 1988

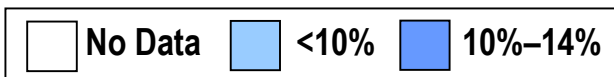
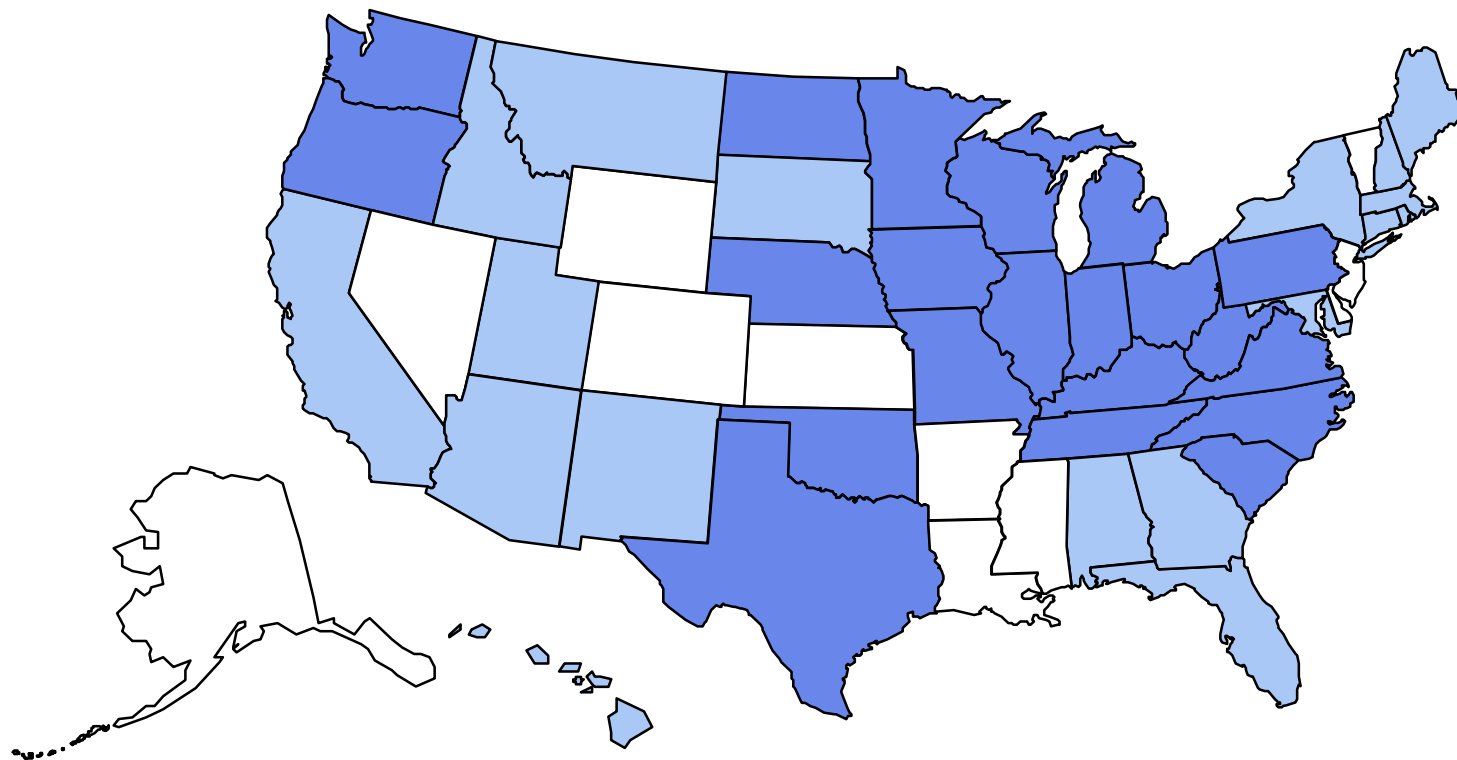
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Obesity Trends* Among U.S. Adults

BRFSS, 1989

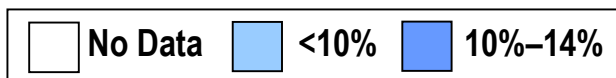
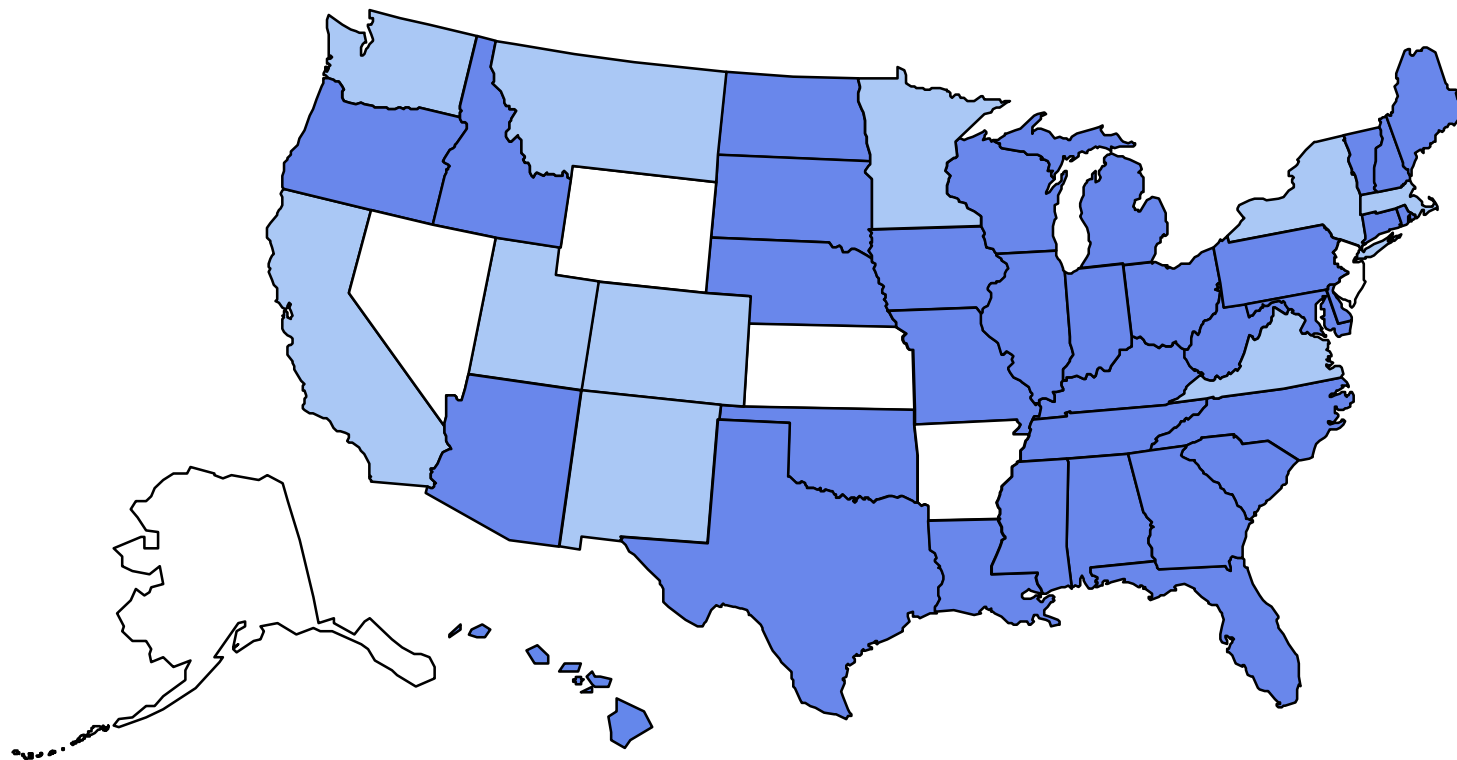
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Obesity Trends* Among U.S. Adults

BRFSS, 1990

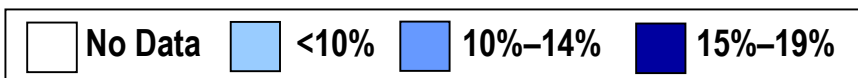
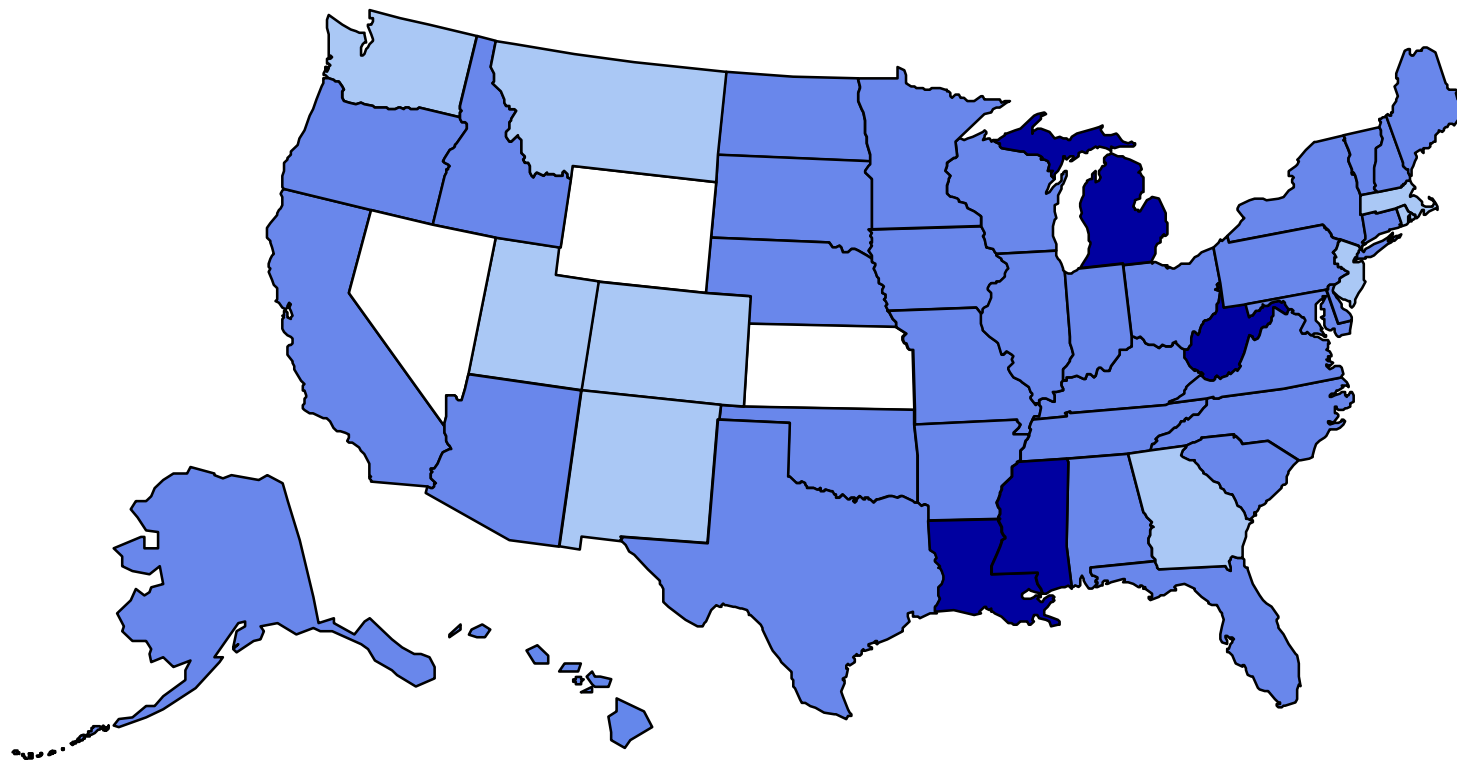
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Obesity Trends* Among U.S. Adults

BRFSS, 1991

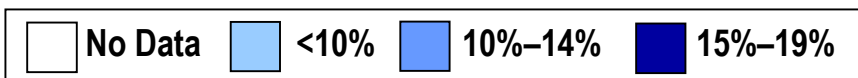
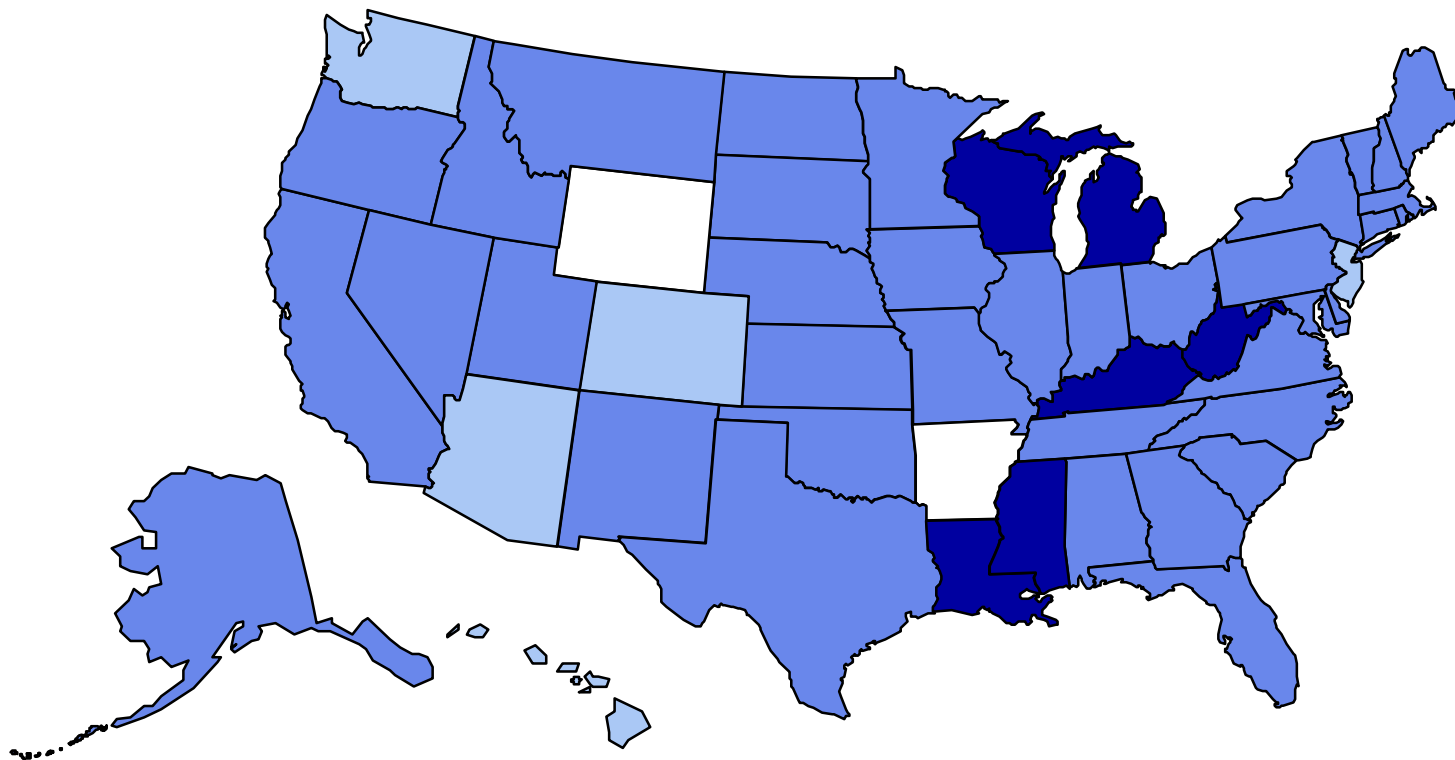
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Obesity Trends* Among U.S. Adults

BRFSS, 1992

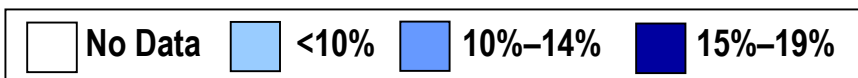
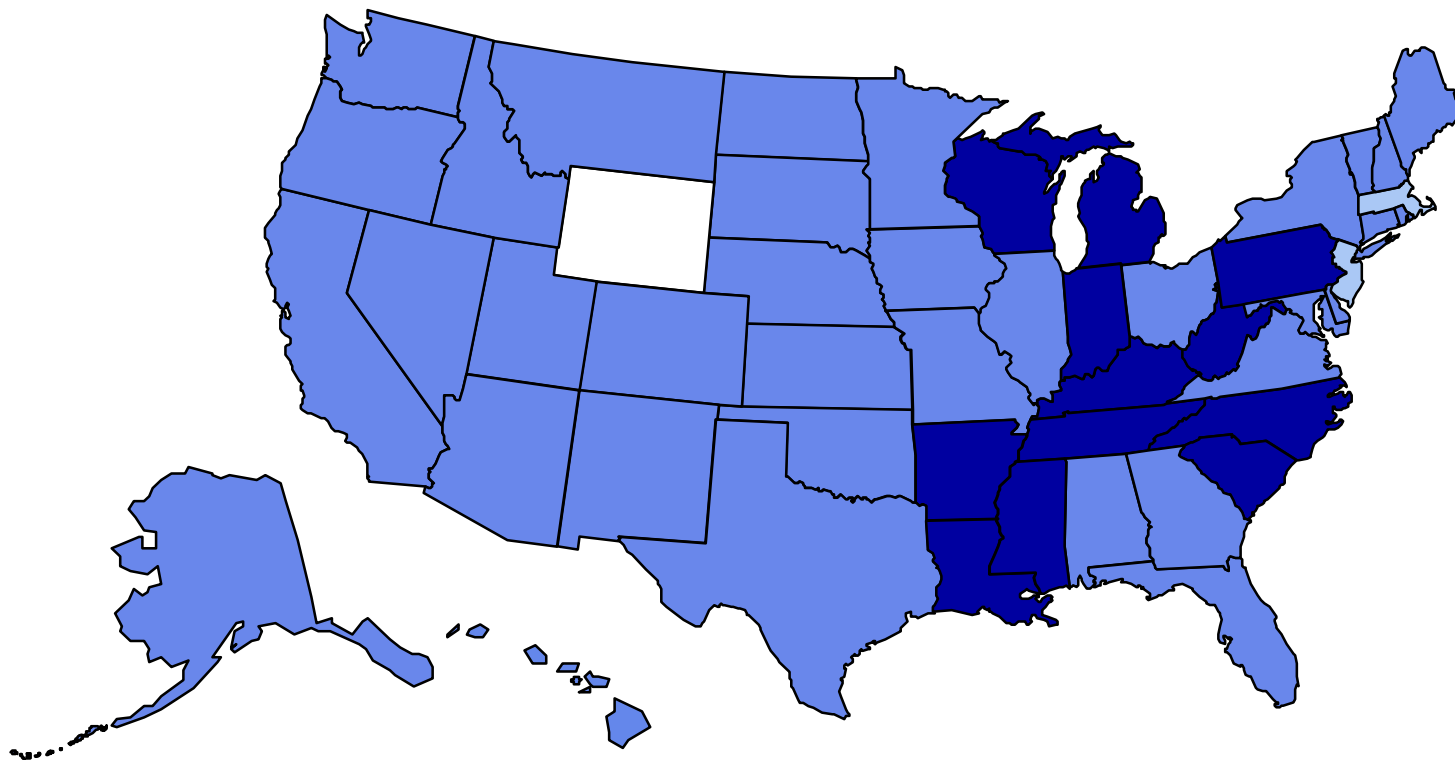
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Obesity Trends* Among U.S. Adults

BRFSS, 1993

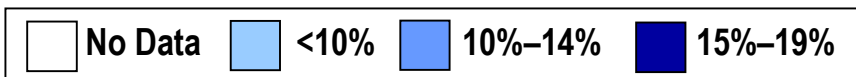
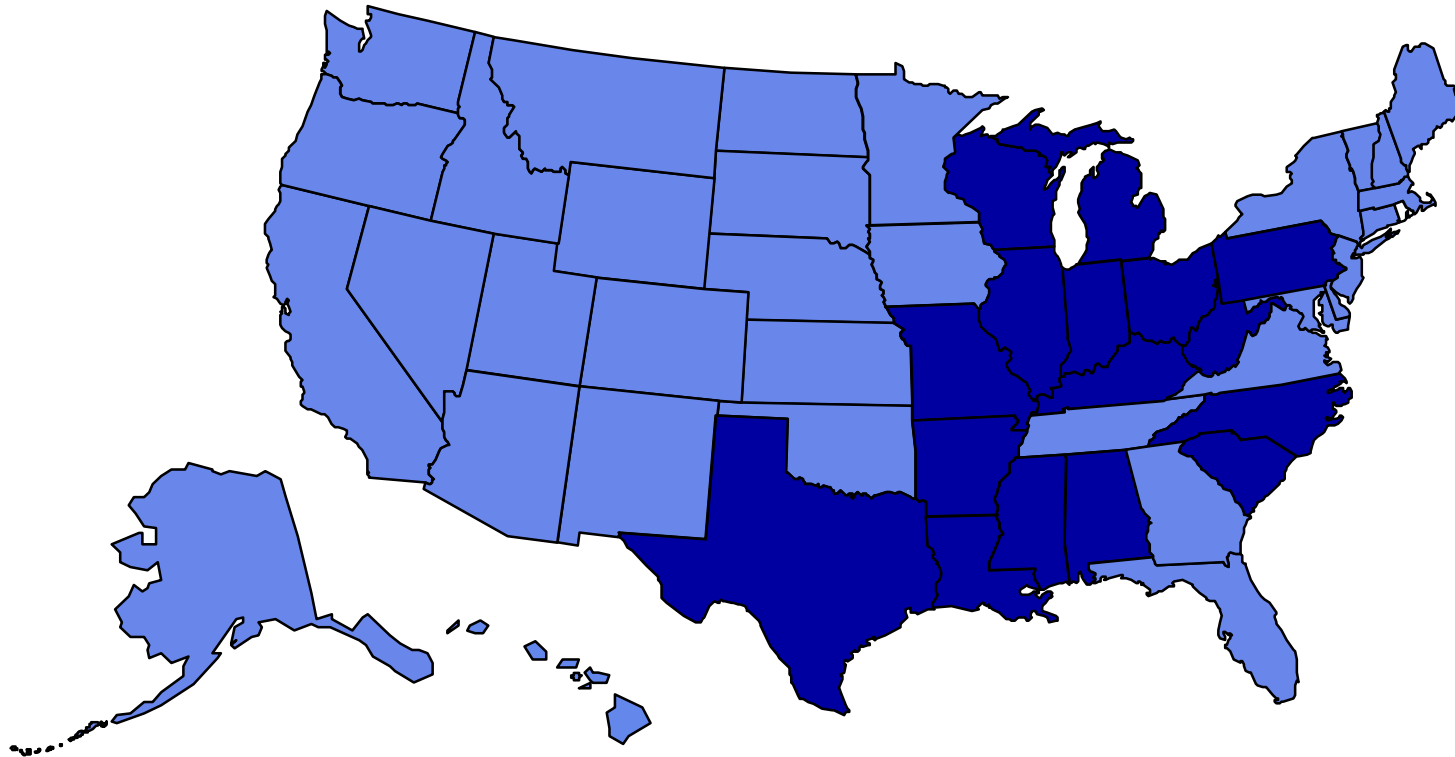
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 1994

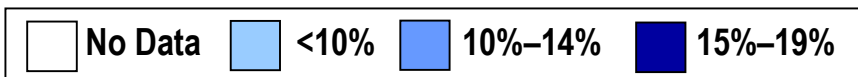
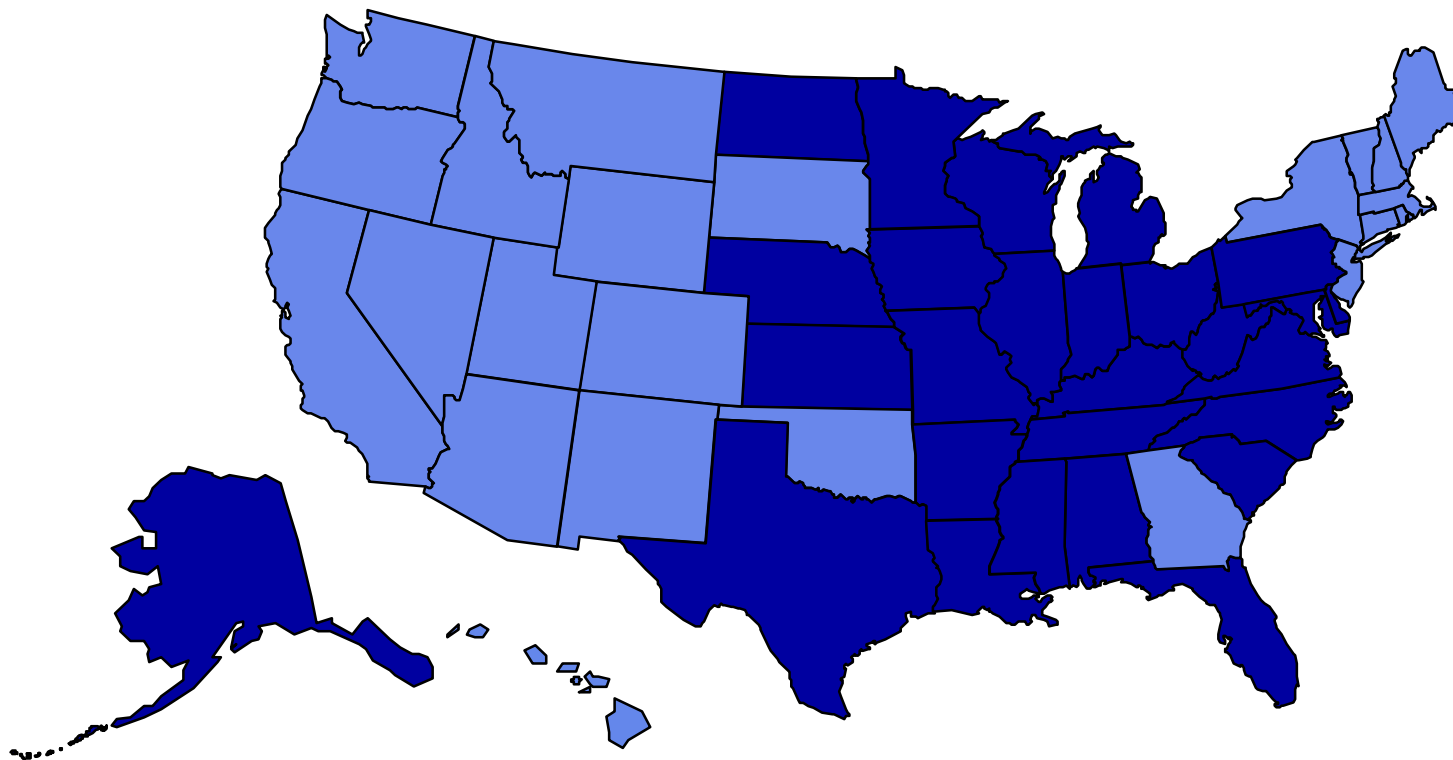
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Obesity Trends* Among U.S. Adults

BRFSS, 1995

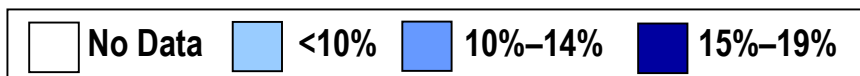
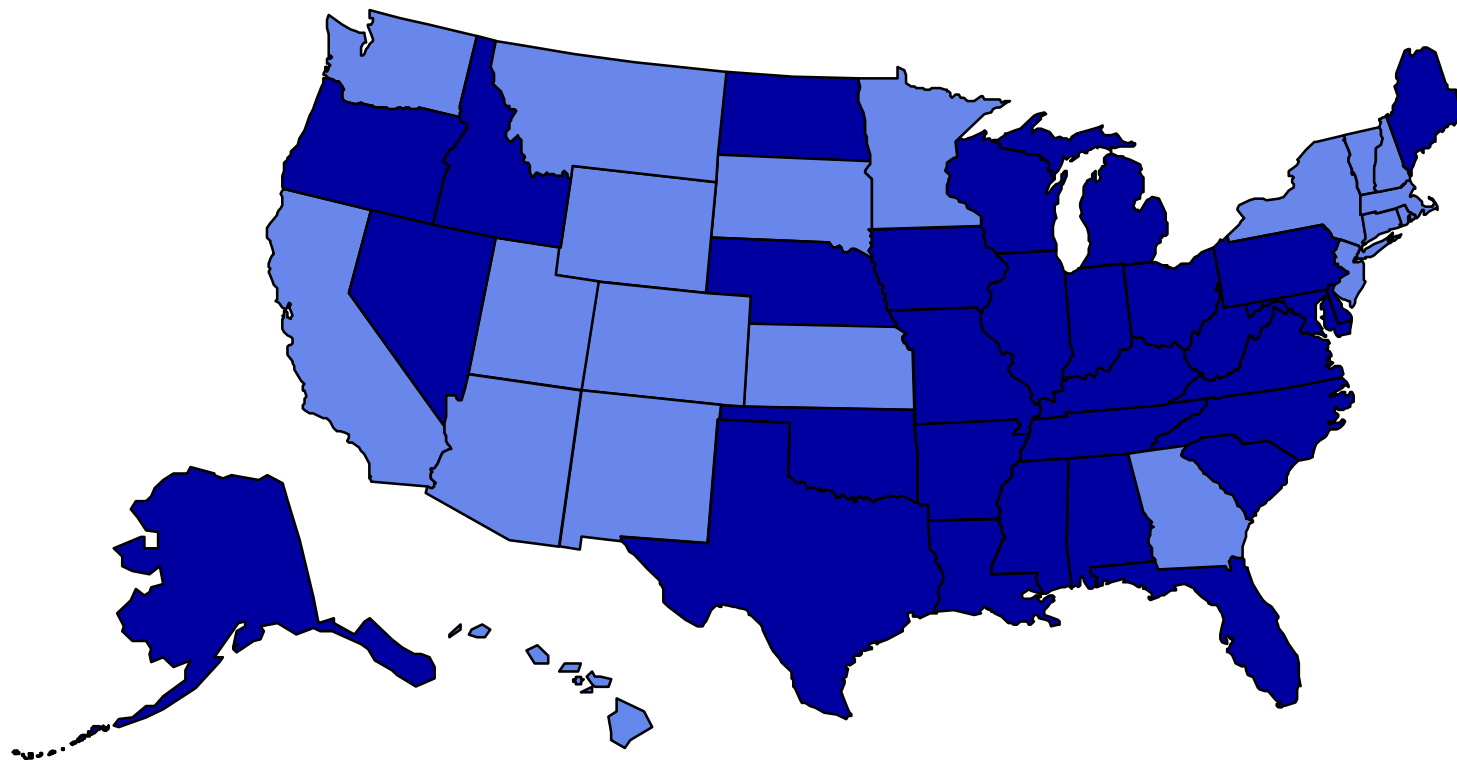
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Obesity Trends* Among U.S. Adults

BRFSS, 1996

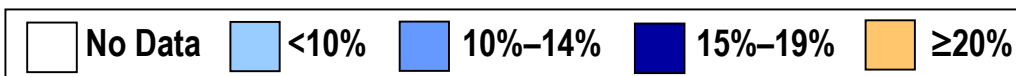
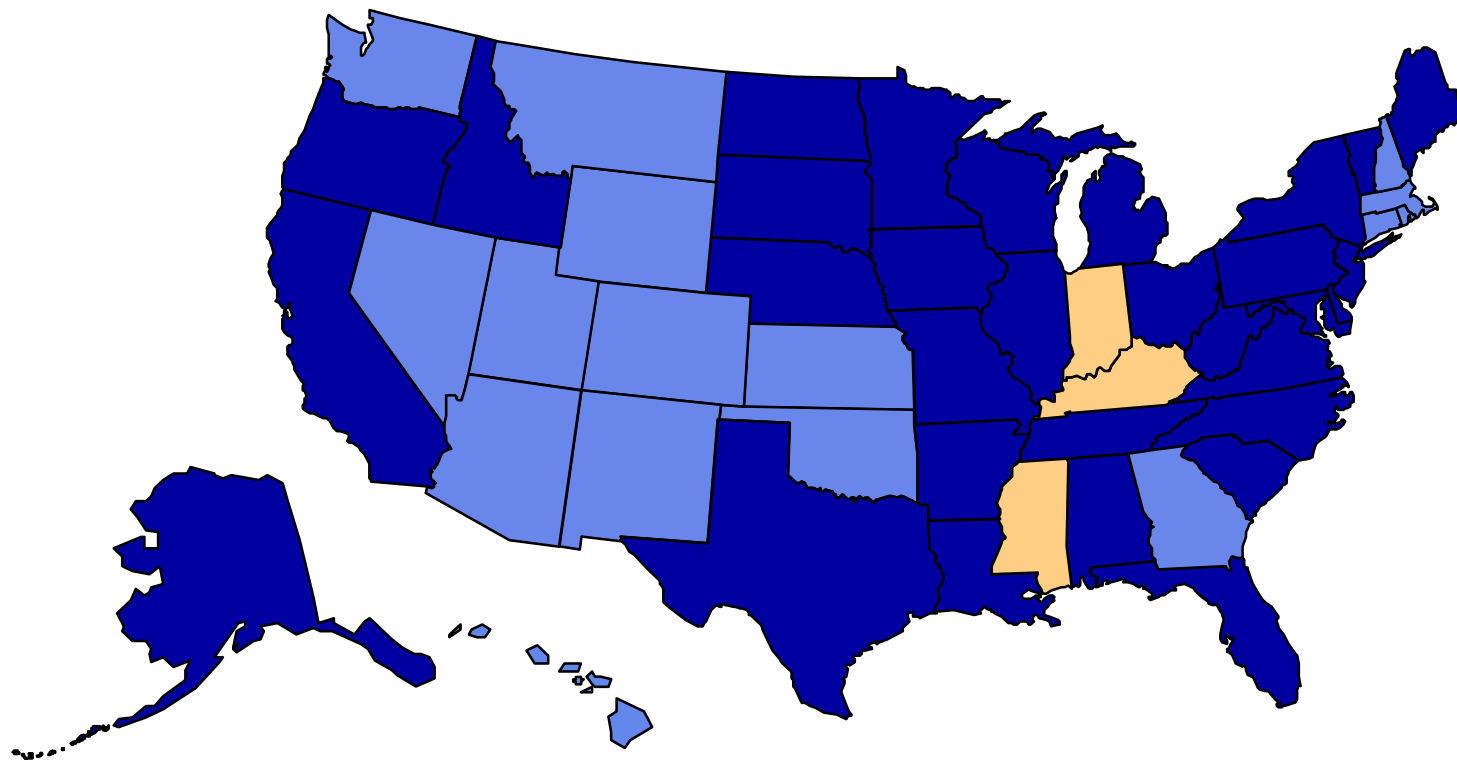
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 1997

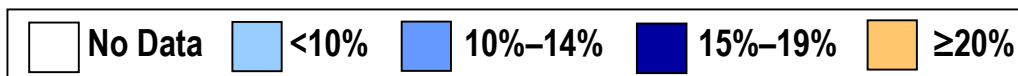
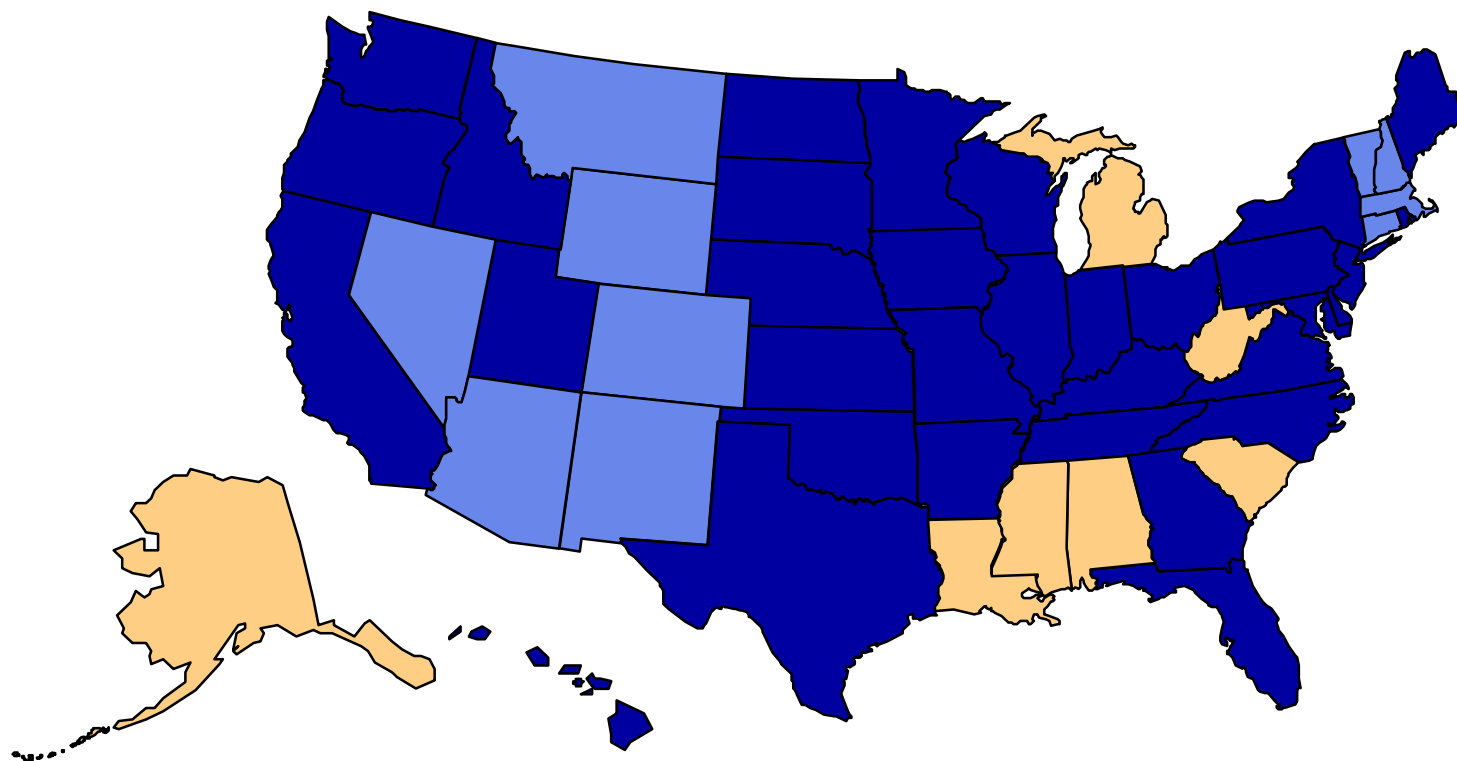
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Obesity Trends* Among U.S. Adults

BRFSS, 1998

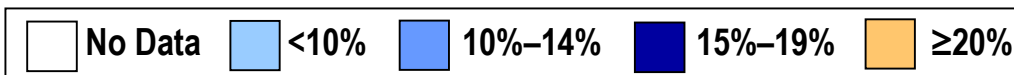
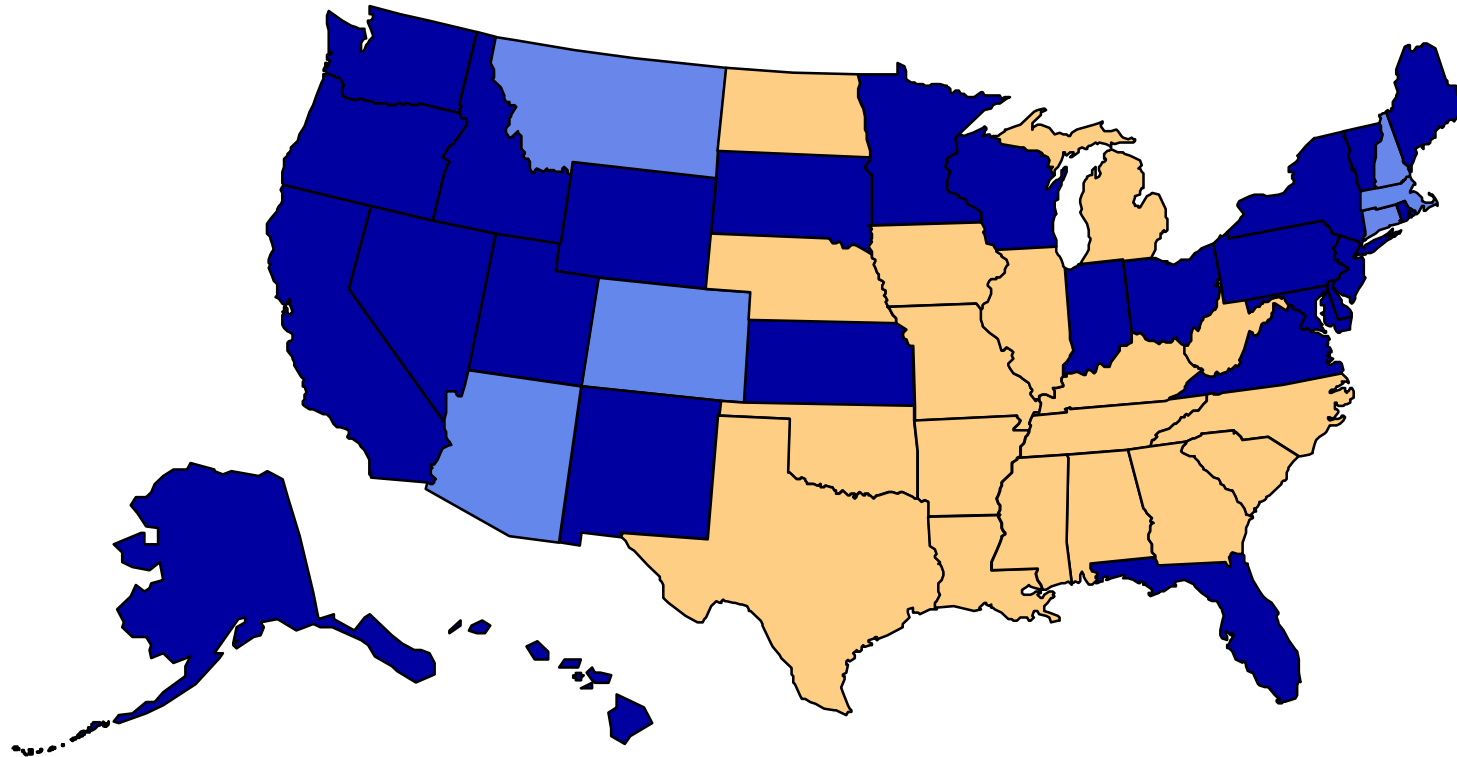
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Obesity Trends* Among U.S. Adults

BRFSS, 1999

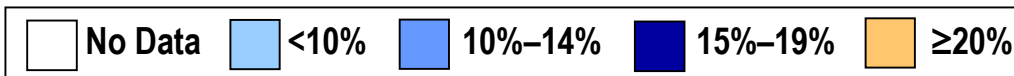
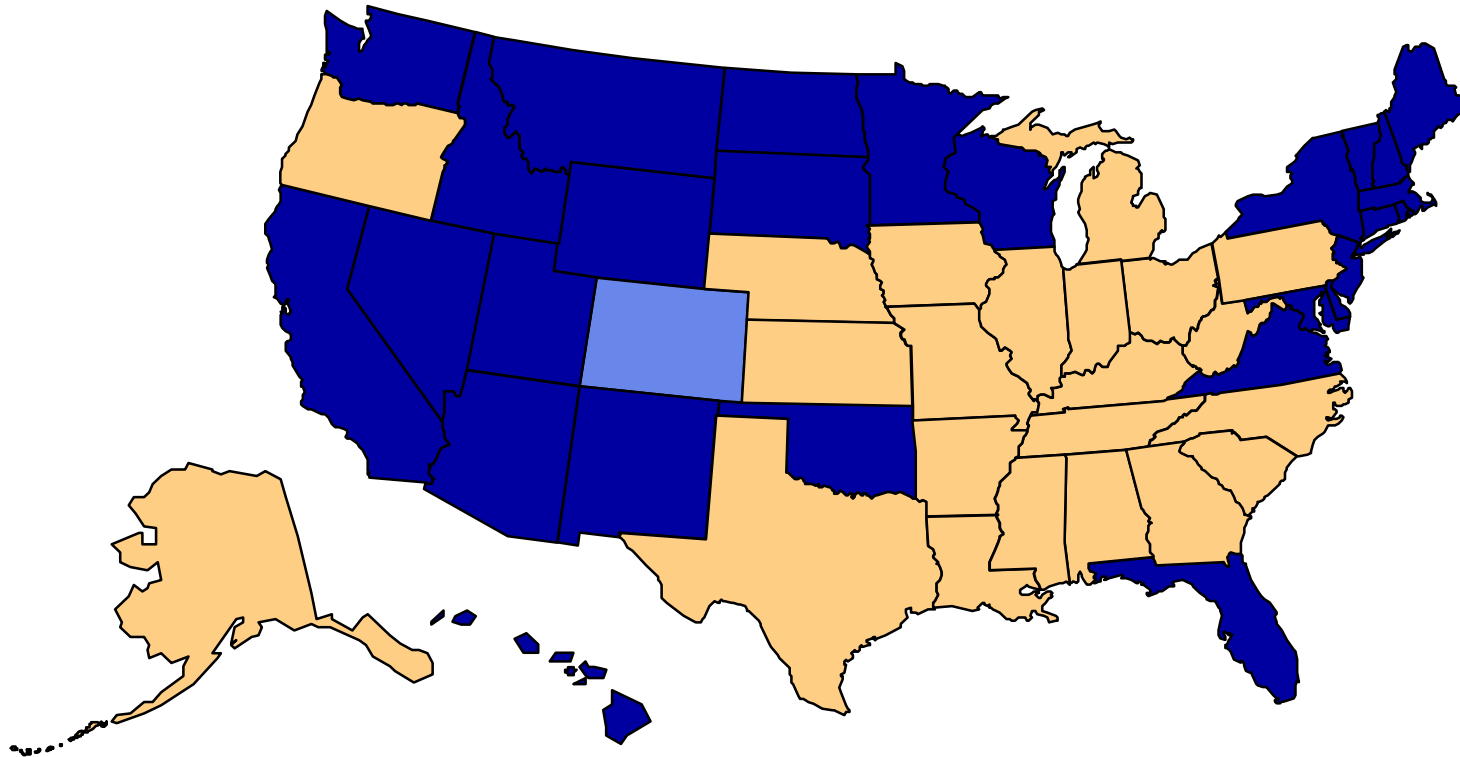
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 2000

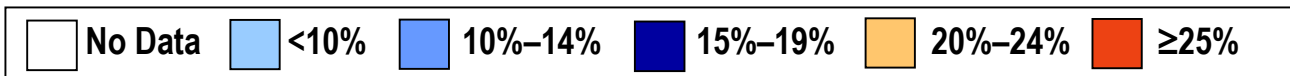
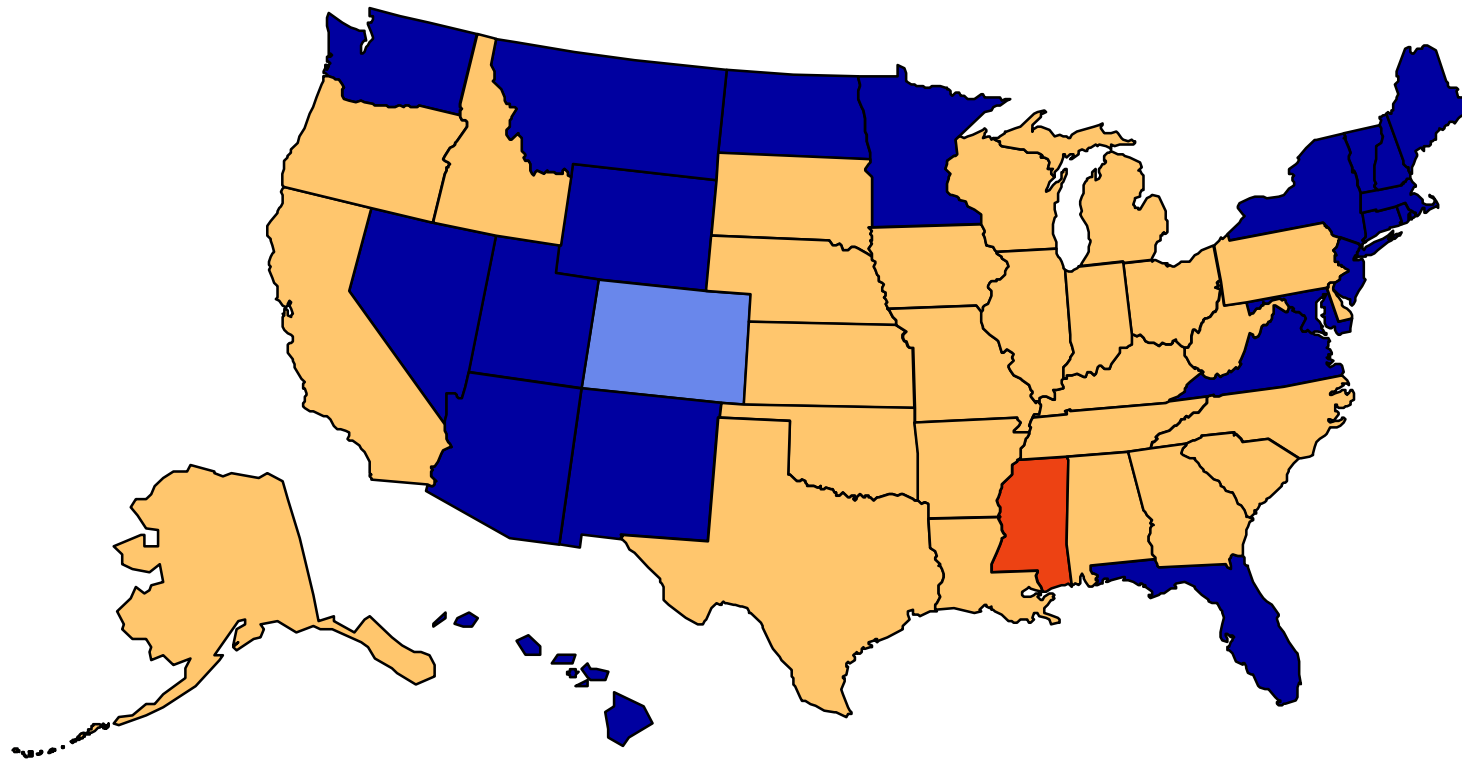
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 2001

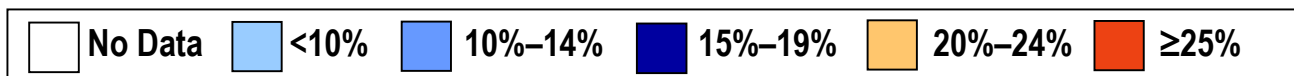
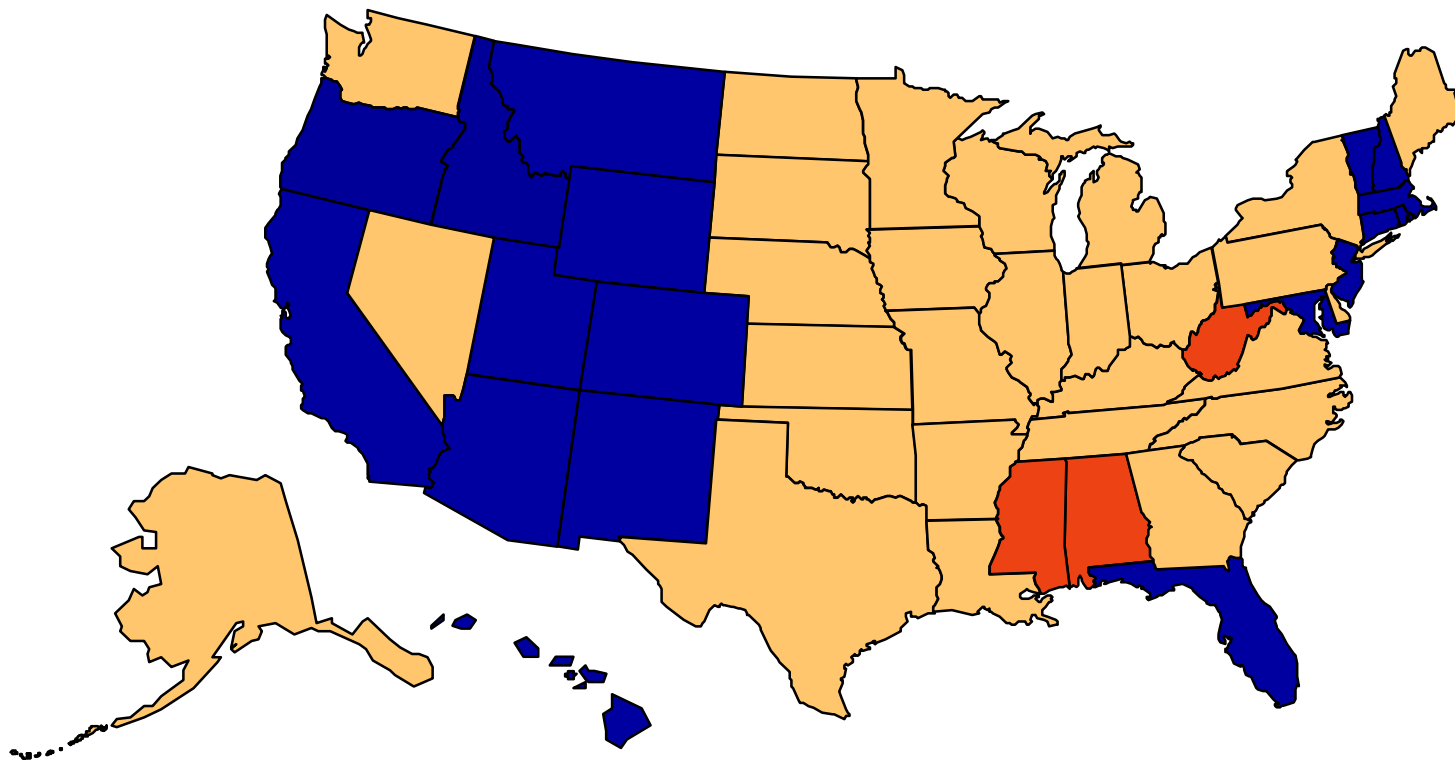
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Obesity Trends* Among U.S. Adults

BRFSS, 2002

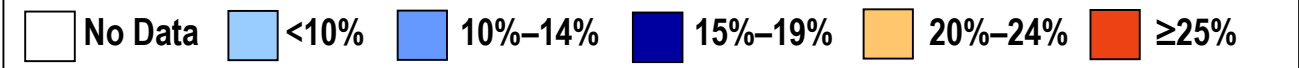
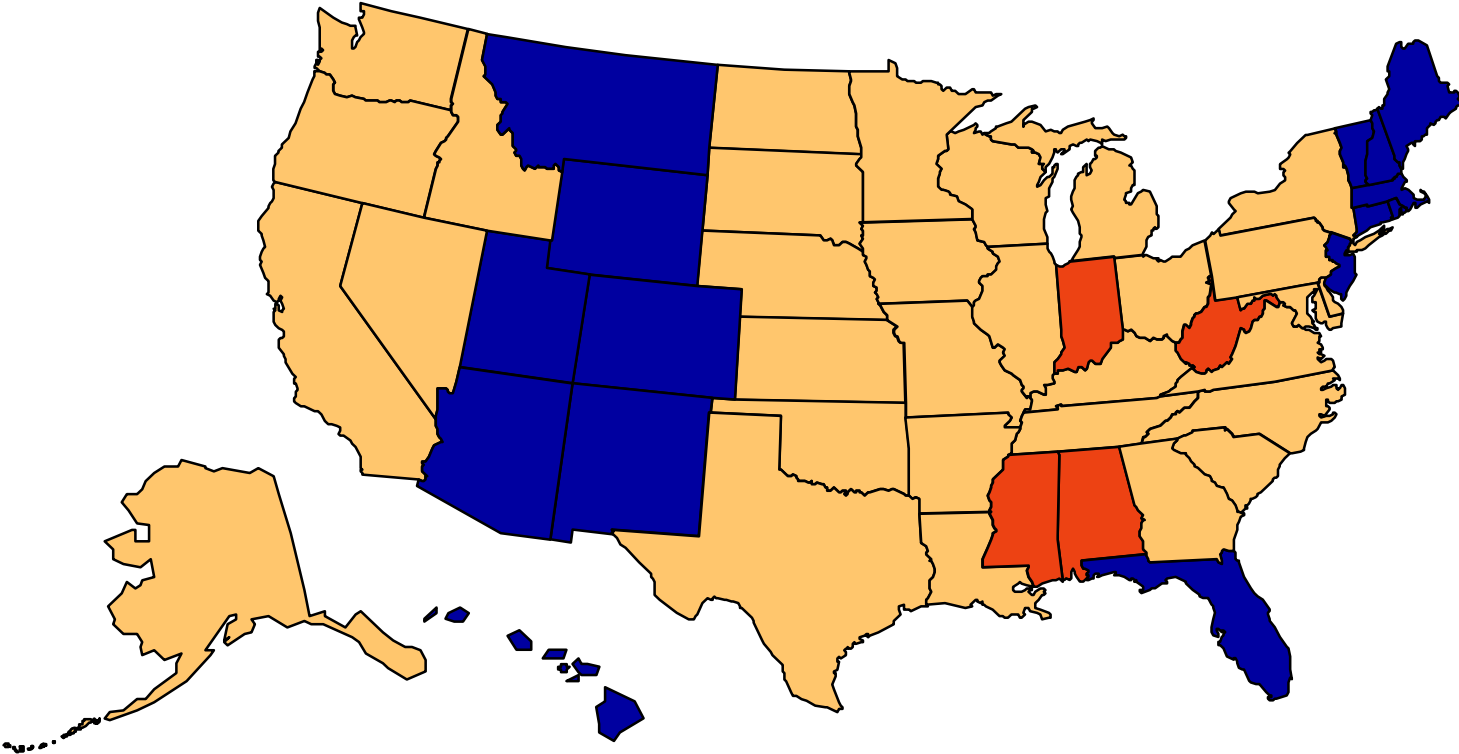
(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Obesity Trends* Among U.S. Adults

BRFSS, 2003

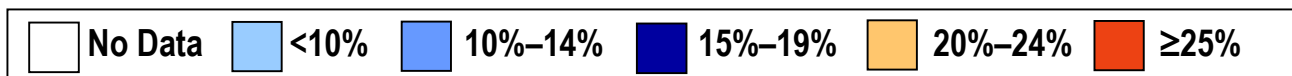
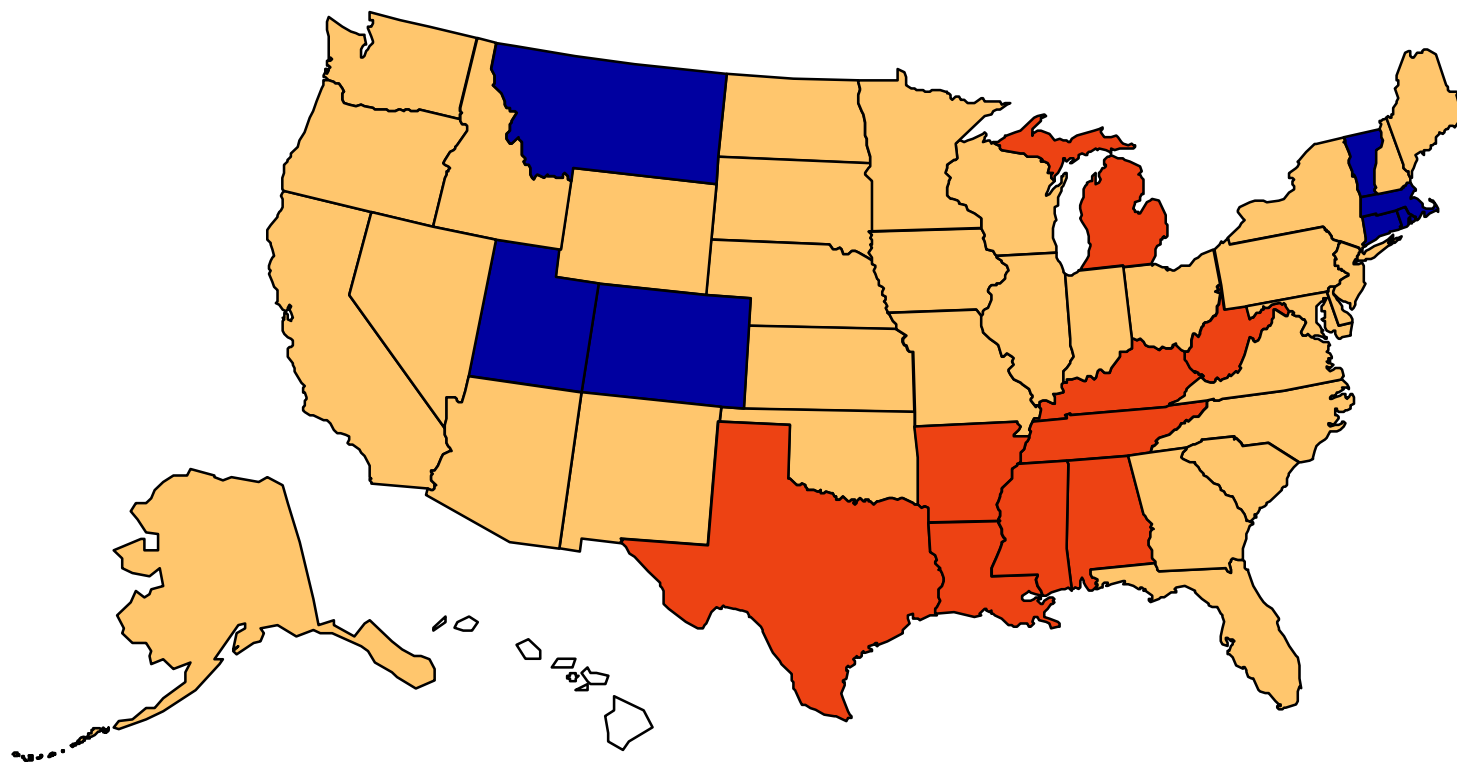
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Obesity Trends* Among U.S. Adults

BRFSS, 2004

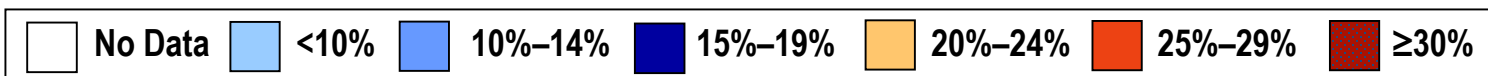
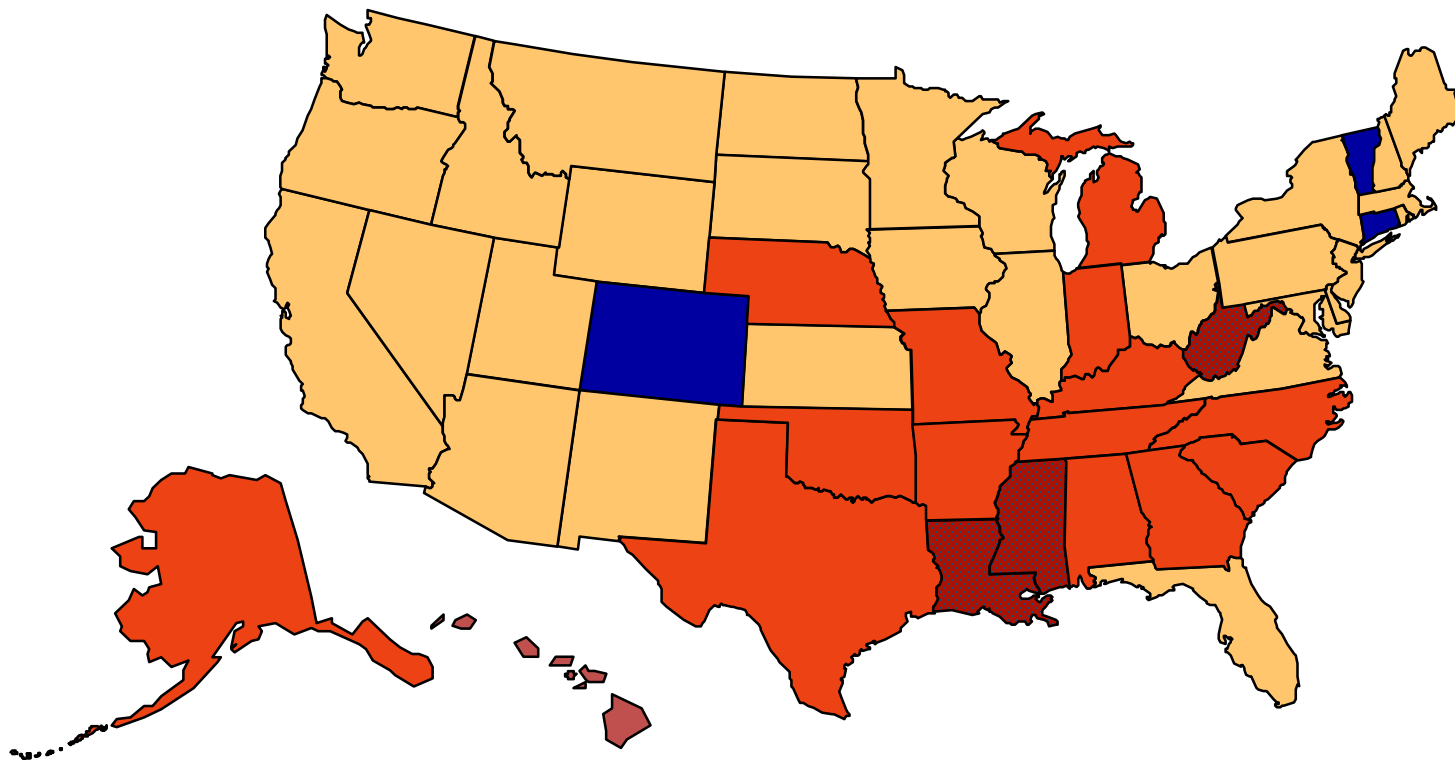
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Obesity Trends* Among U.S. Adults

BRFSS, 2005

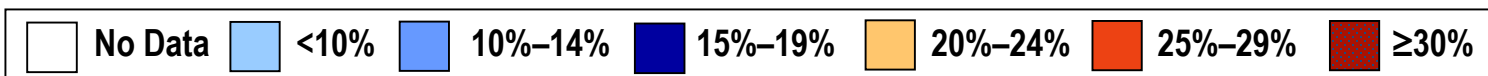
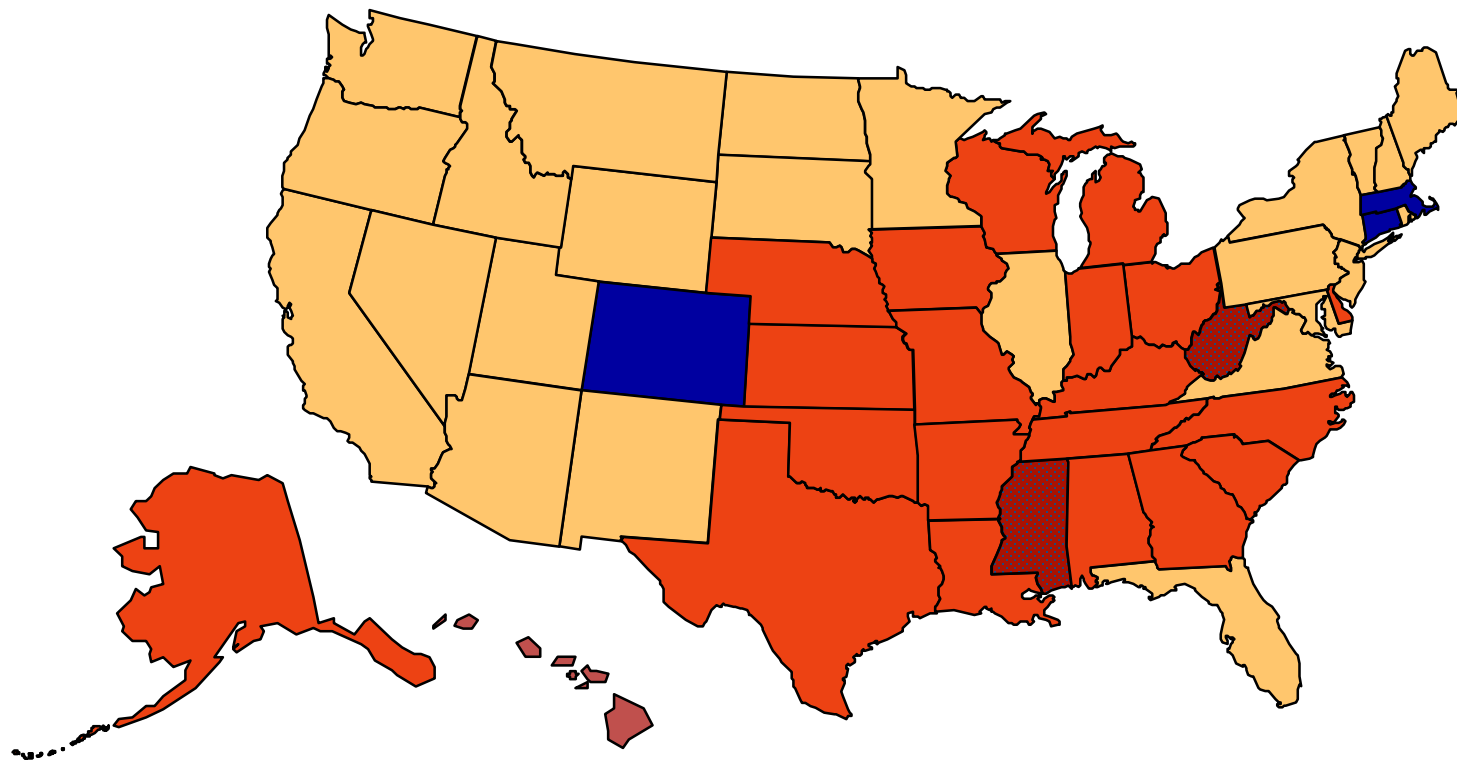
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Obesity Trends* Among U.S. Adults

BRFSS, 2006

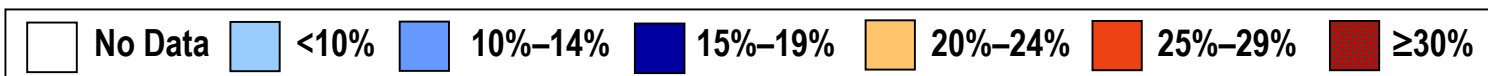
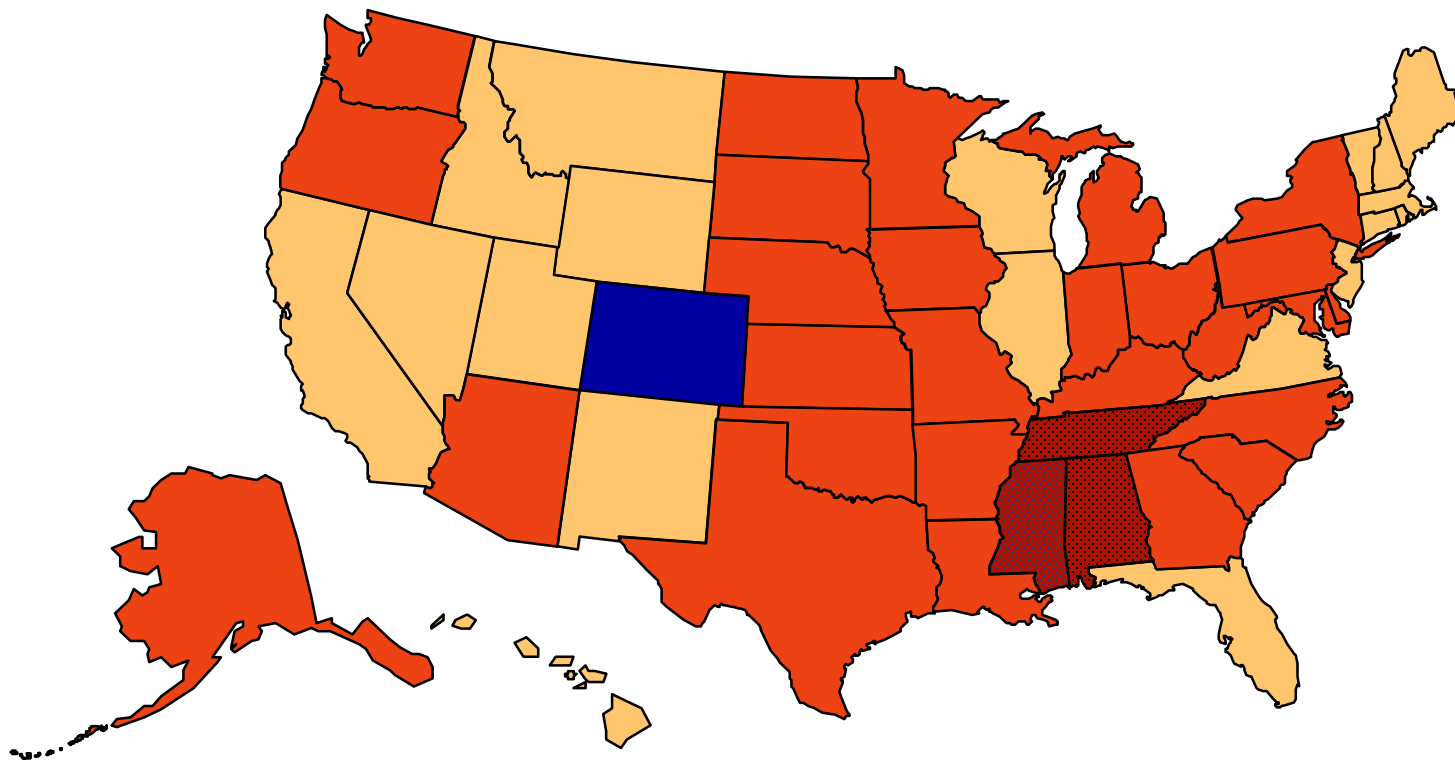
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Obesity Trends* Among U.S. Adults

BRFSS, 2007

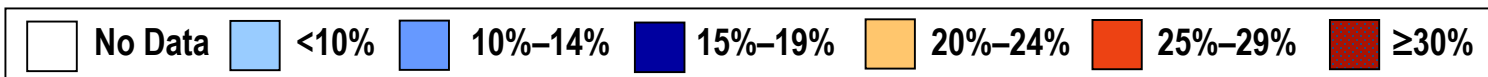
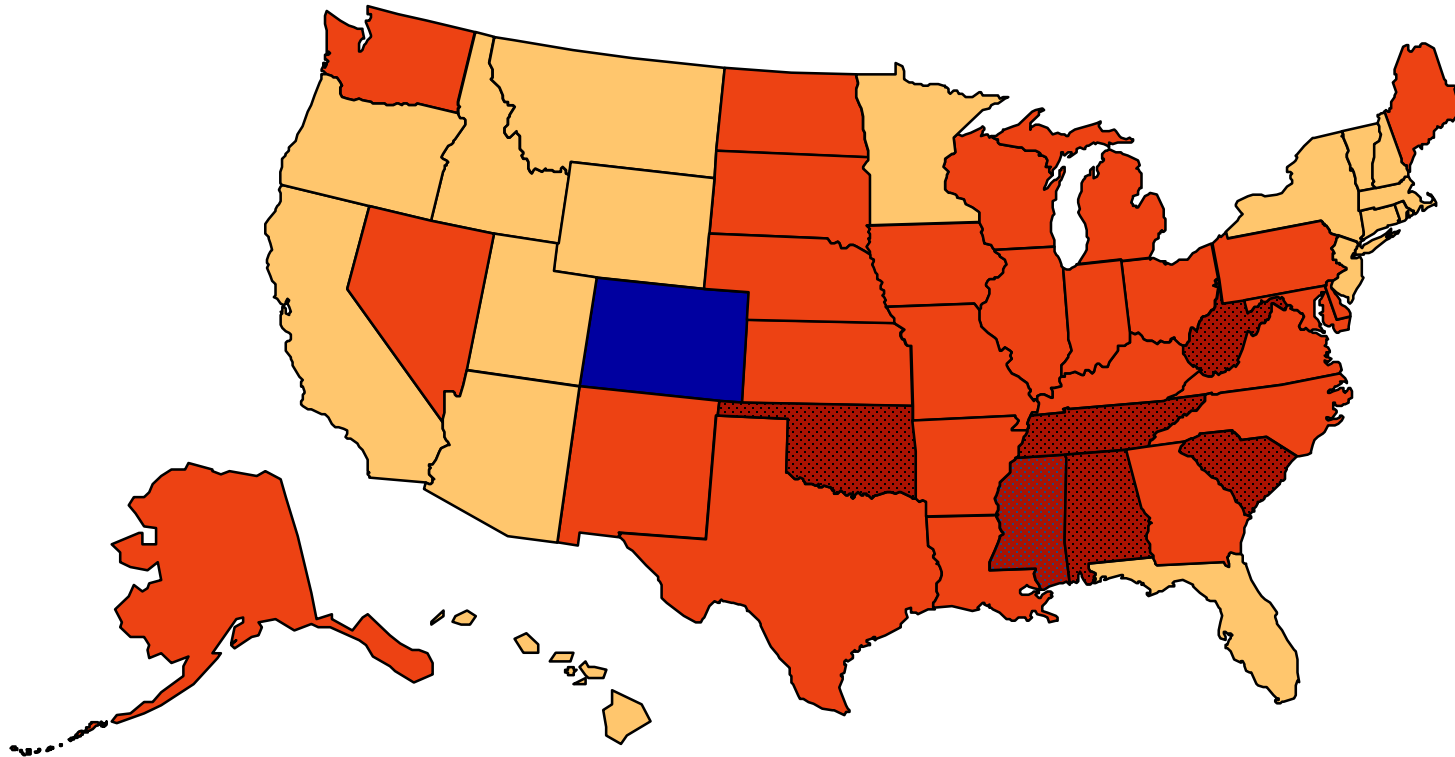
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Obesity Trends* Among U.S. Adults

BRFSS, 2008

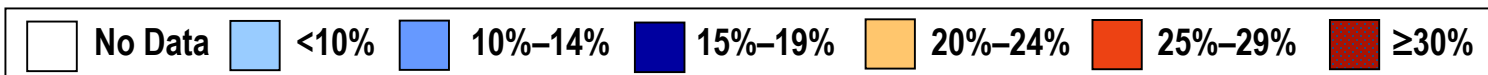
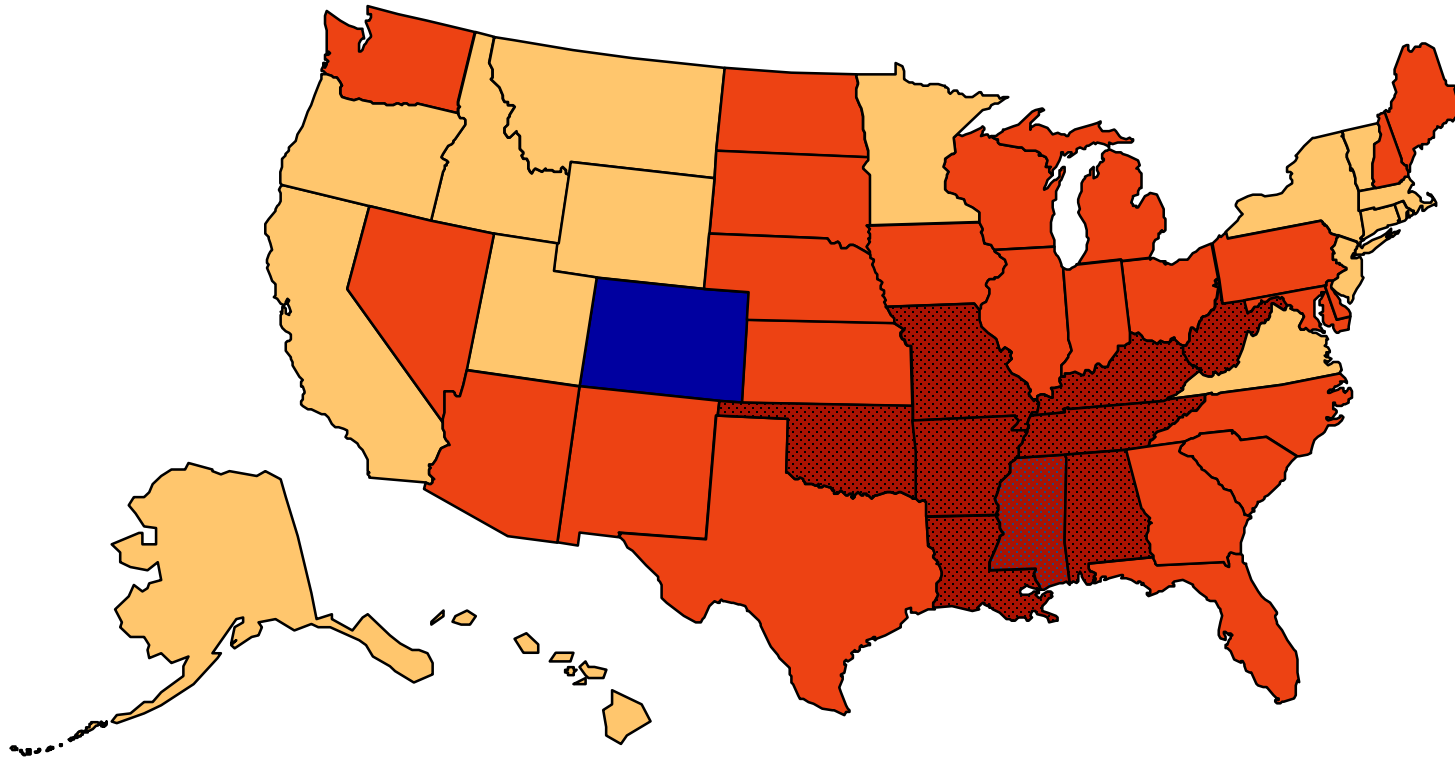
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Obesity Trends* Among U.S. Adults

BRFSS, 2009

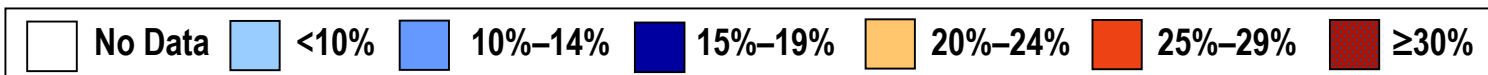
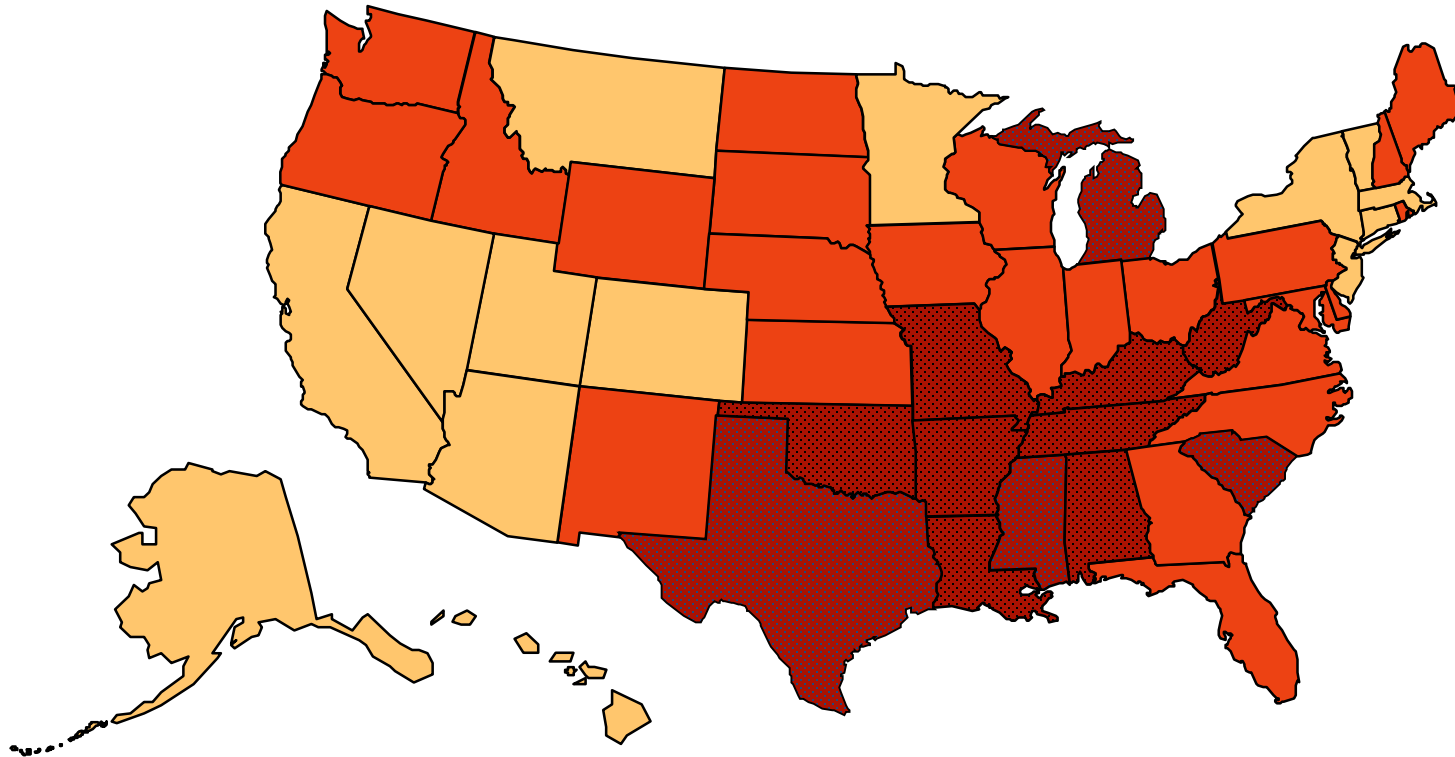
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Obesity Trends* Among U.S. Adults

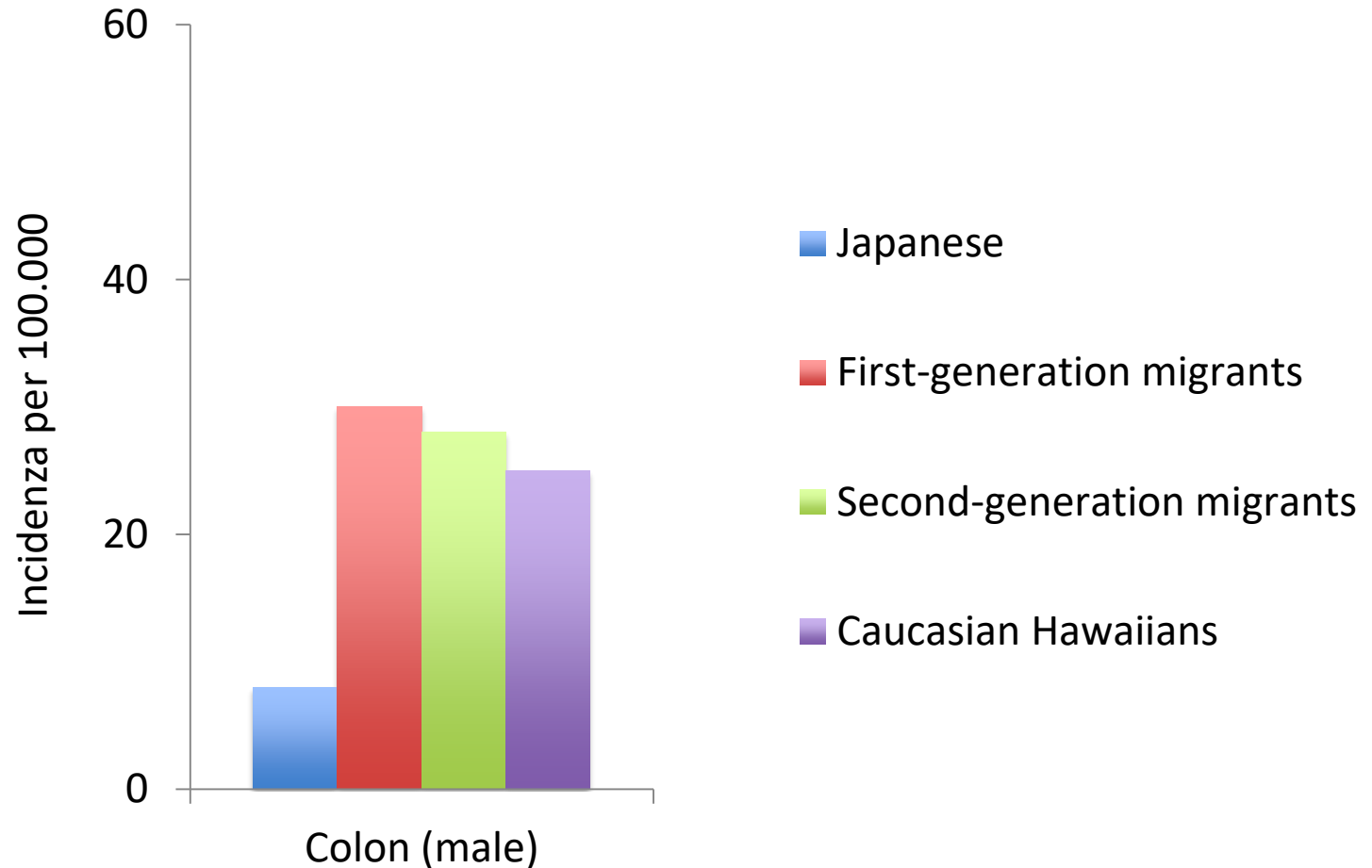
BRFSS, 2010

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



Fattori Ambientali e CRC

The multiethnic cohort study



BMI e Cancro del Colon

Adulti

	Uomini			Donne		
	Relative risk (95% CI)	Heterogeneity		Relative risk (95% CI)	Heterogeneity	
		P	I ²		P	I ²
Nord America	1.35 (1.21-1.50)	0.094	40.8	1.13 (1.06-1.19)	0.238	23
Europa e Australia	1.21 (1.18-1.24)	0.727	0	1.04 (1.00-1.07)	0.382	5.9
Asia e Pacifico	1.32 (1.20-1.46)	0.242	25.7	1.13 (0.88-1.44)	0.259	26.1
Totale	1.24 (1.20-1.28)	0.189	20.7	1.09 (1.04-1.14)	0.042	39.1

5 kg/m² BMI increase

BMI in adolescenza e rischio di Cancro Colorettae da adulti

Cancro	Adjusted HR (95% CI)	<i>P</i>
Colon*	1.53 (1.17-2.00)	0.002
Retto*	1.09 (0.68-1.73)	0.723
Colon, non mucinoso*	1.68 (1.26, 2.23)	0.001

* BMI \geq 85th vs <85th

Il fumo è associato ad un' aumentata formazione di polipi e cancro colorettaali

Strata

RR^a (95% CI)

Smoking status

Current

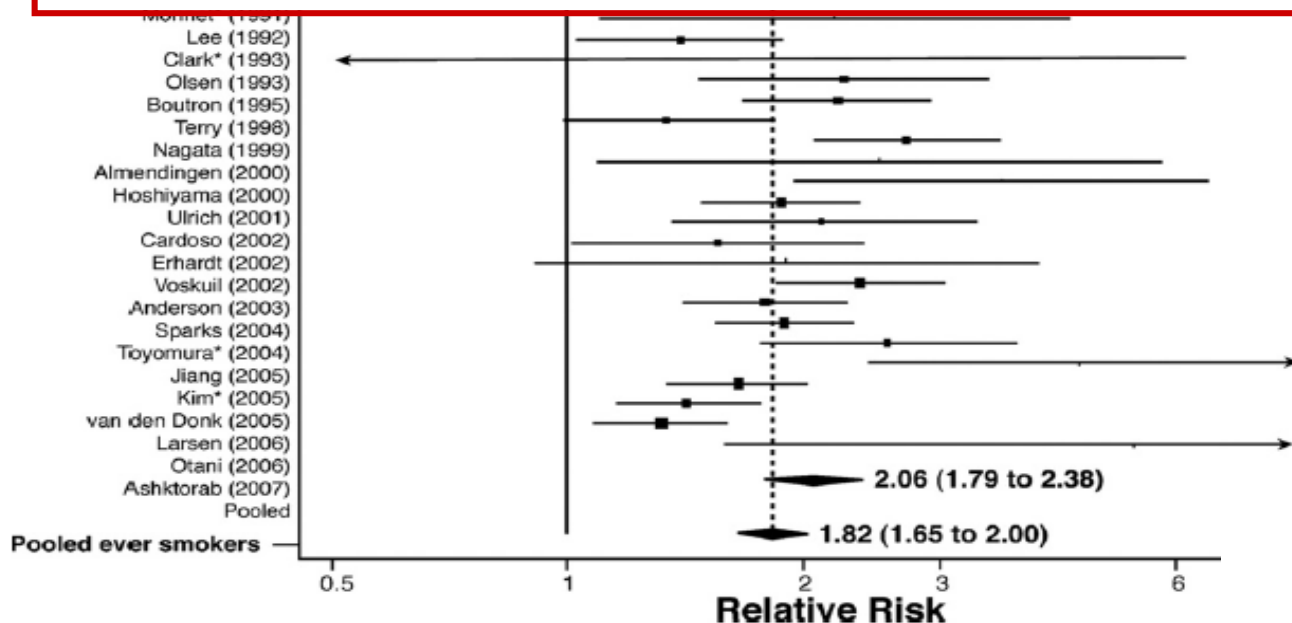
2.14 (1.86–2.46)

Former

1.47 (1.29–1.67)

Ever

1.82 (1.65–2.00)



Botteri et al. JAMA 2008

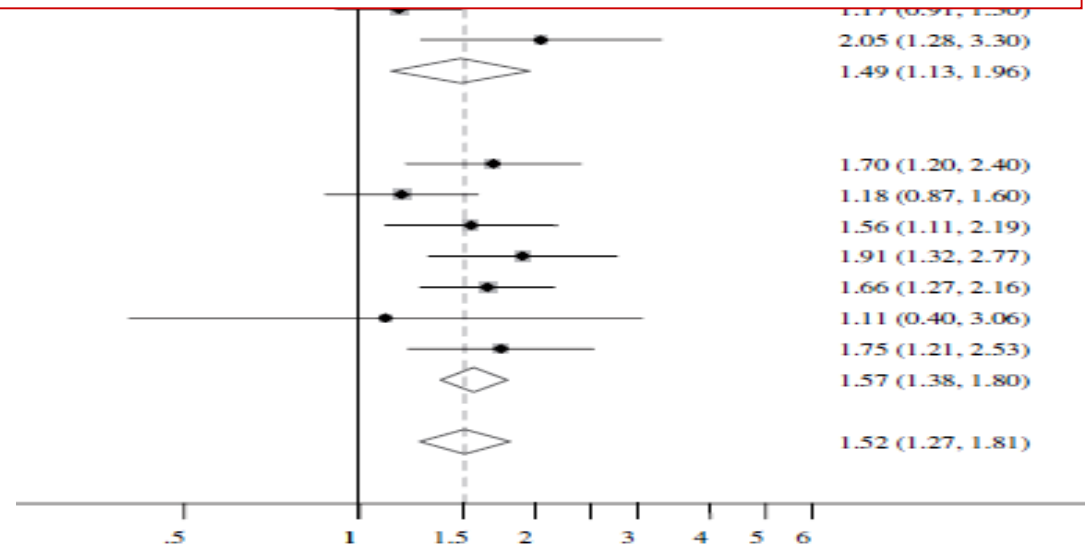
Botteri et al. Gastroenterology 2008

Bevande alcoliche e rischio di CRC

RR 1.21 [1.13-1.28] per consumo moderato

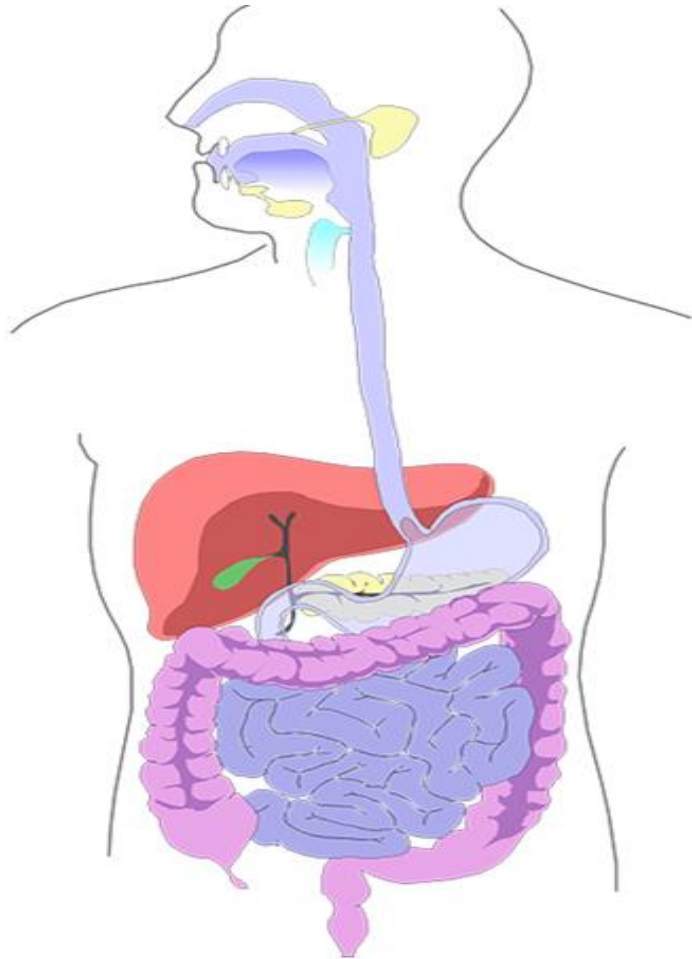
RR 1.52 [1.27-1.81] per alto consumo (≥ 4 alcolici/giorno)

Associazione tra il rischio di CRC e consumo di >1 bevanda alcolica (12,5 g) al giorno



Fedirko et al., Annals of Oncology 2011

Dieta e rischio di cancro colorettales



- 1) Nutrienti
- 2) Tipo di dieta

Carne e rischio di CCR

World Cancer Research Fund (WCRF) 2011 classifica come 'convincenti' le evidenze che associano la carne al CCR

Meta-analisi dose risposta per incrementi di 100g/die	RR	95% CI
Colorectal cancer	1,14	1,04-1,24
Proximal colon cancer	1,11	0,88-1,40
Rectal Cancer	1,31	1,13-1,52

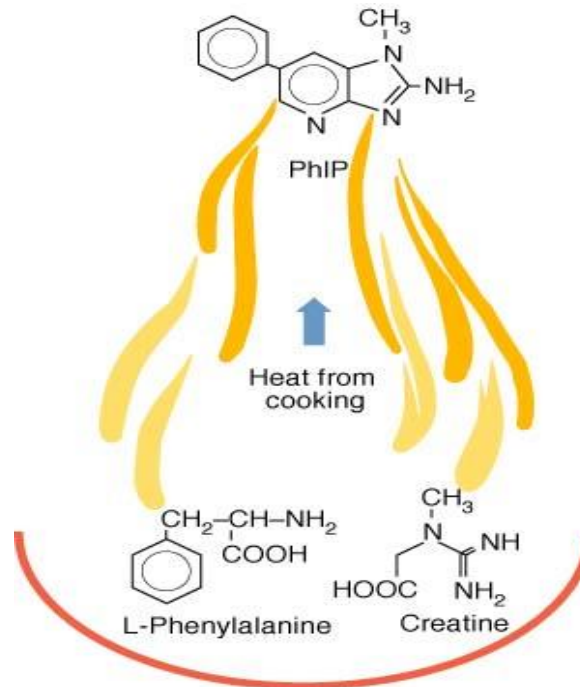
➤ *L'associazione appare più evidente per i tumori del colon distale e del rettosigma*

Chan DS et al., PLoS One 2011

World Cancer Research Fund / American Institute for Cancer Research 2011

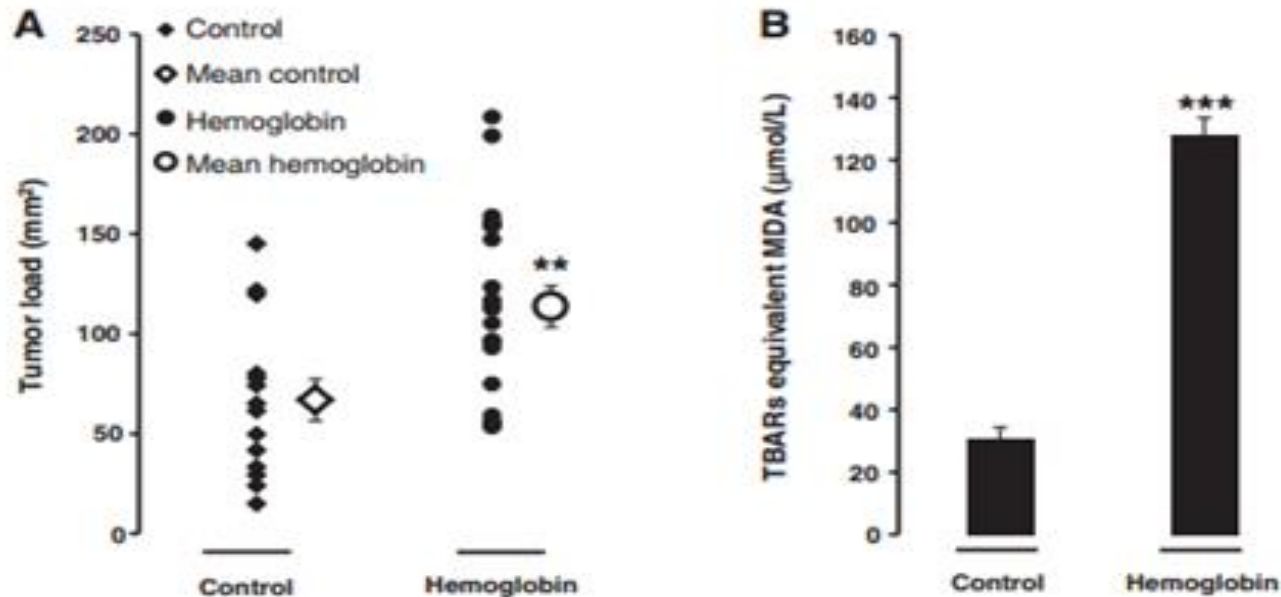
Potenziali meccanismi che collegano il consumo di carne ai tumori digestivi

Carne cotta ad alte temperature è una fonte di mutageni, comprese **amine eterocicliche** e **idrocarburi policiclici aromatici**



Potenziali meccanismi che collegano il consumo di carne ai tumori digestivi

L'eme ferro nella carne rossa può indurre uno stress ossidativo attraverso la perossidazione lipidica, la proliferazione dei colonociti e la formazione endogena di sostanze cancerogene nel tratto GI (N-nitroso)



Cross et al, Cancer res 2003
Bastide et al., Cancer res 2015

Consumo di fibre e rischio di CCR

Meccanismi anti-cancro:

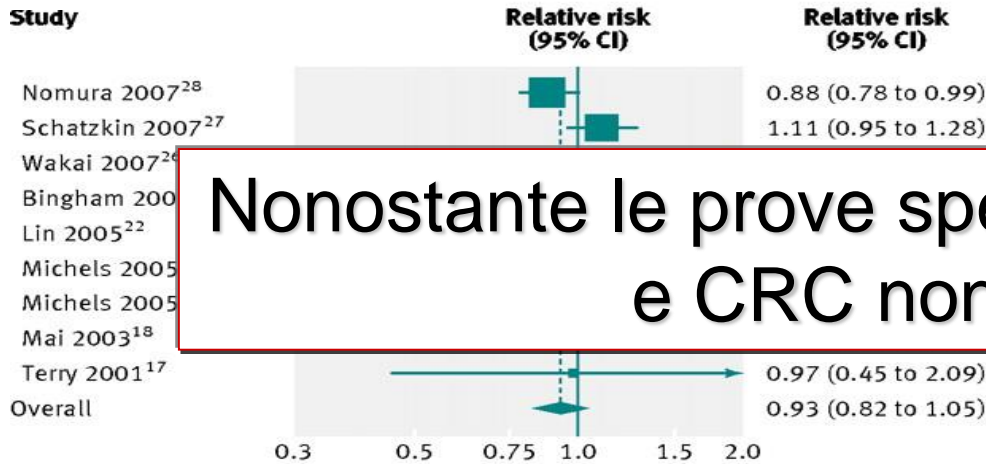
- Aumentato peso delle feci
- Ridotto tempo di transito
- Diluizione del contenuto cancerogeno
- Ridotta adiposità
- Proprietà anticancro degli acidi grassi a catene corta prodotti dalla fermentazione batterica



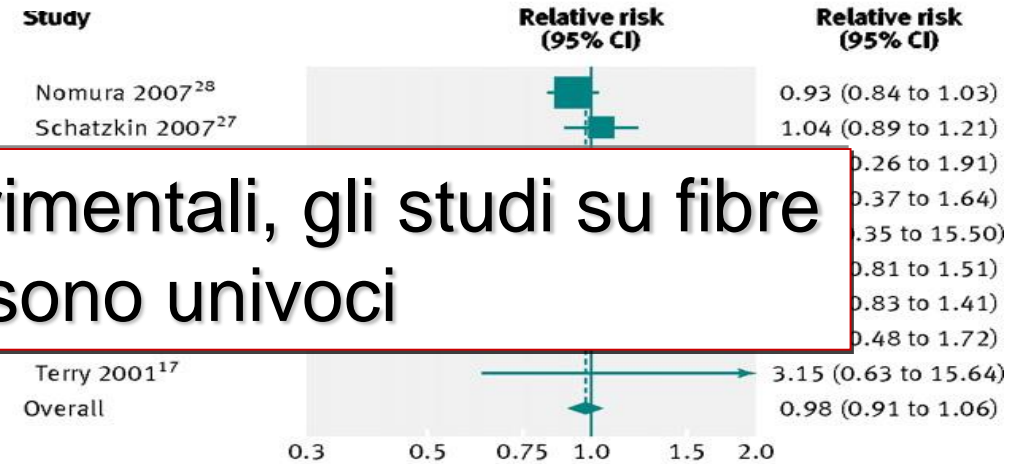
Song M. et al. Gastroenterology 2015

Rischio di CCR in base al tipo di fibre

FRUIT FIBRE

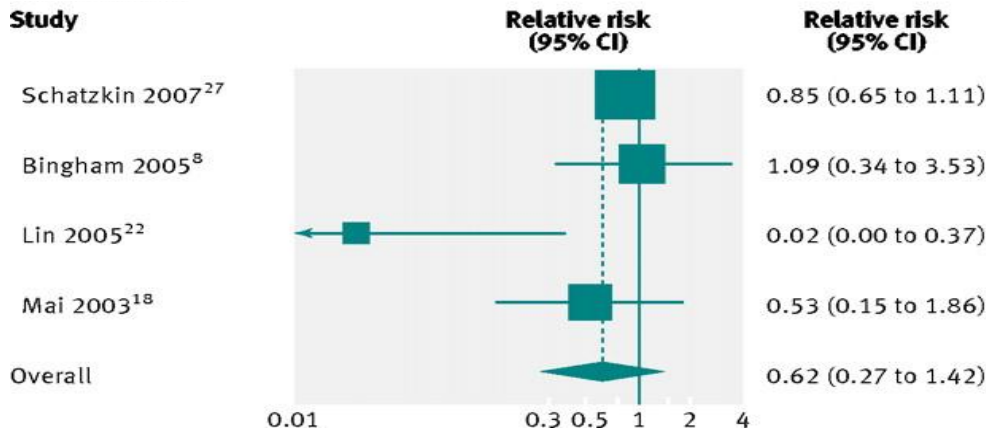


VEGETABLE FIBRE

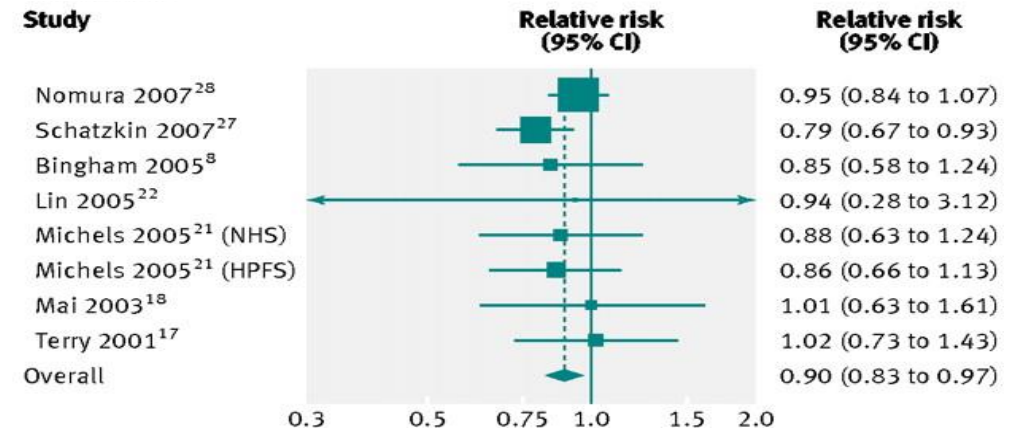


Nonostante le prove sperimentali, gli studi su fibre e CRC non sono univoci

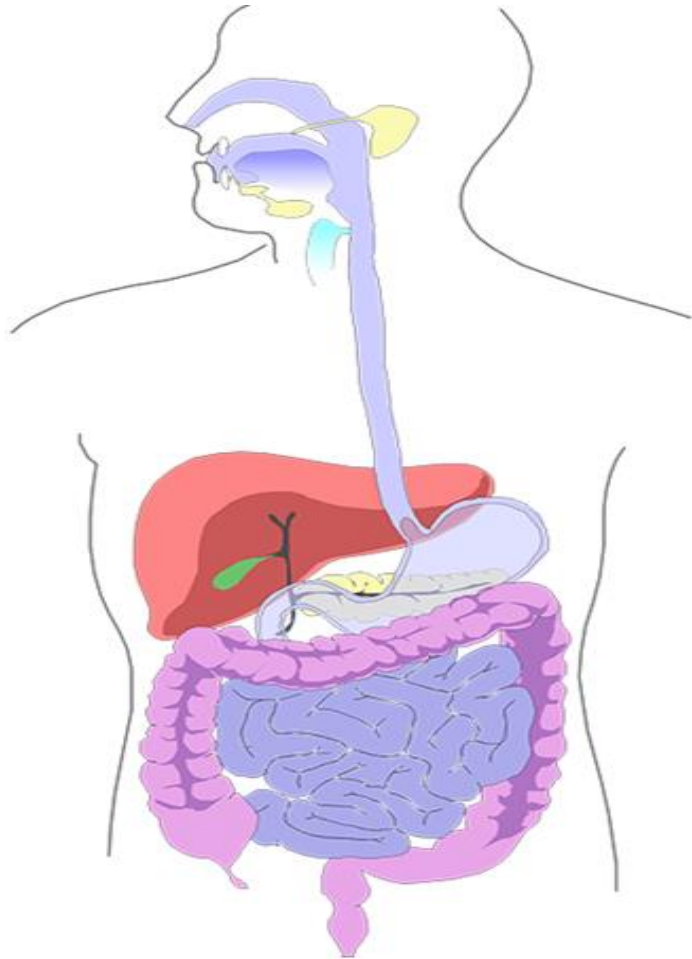
LEGUME FIBRE



CEREAL FIBRE



Dieta e rischio di cancro colonrettale



- 1) Nutrienti
- 2) Tipo di dieta

Tipi di dieta

“Complessa integrazione di alimenti e nutrienti consumato da una determinata popolazione”



Western/unhealthy: caratterizzato dal consumo di diversi tipi di carne, latticini ad alto contenuto di grassi, alimenti ricchi di amido e zuccheri, cereali raffinati

VS.



Prudent/healthy: basato principalmente su un elevato consumo di frutta e verdura, pesce, pollame e prodotti integrali

*Hu et al. Curr Opin Lipidol 2002
Reedy et al. Am J Epidemiol 2010*

Regime dietetico “Western/unhealthy” e rischio di CCR

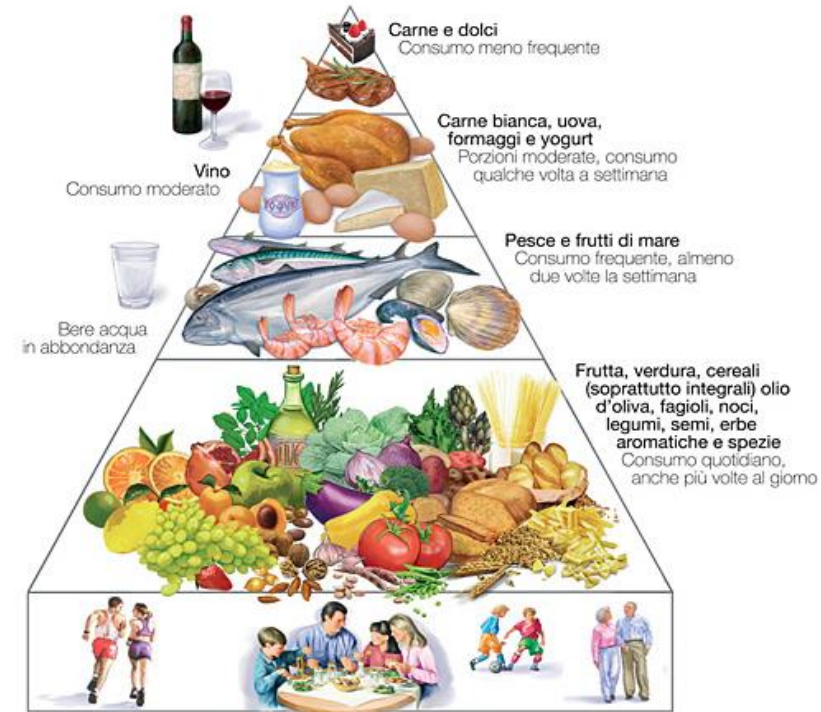
	Western Dietary Pattern by Quintile ^b					P for Trend
	1 (n = 201)	2 (n = 202)	3 (n = 202)	4 (n = 202)	5 (n = 202)	
Cancer recurrence or death from any cause (disease-free survival) No. of events/person-time at risk ^c	71/795	57/808	73/772	68/768	83/759	
Overall mortality No. of events/person-time at risk ^c	57/916	35/920	51/867	53/842	55/860	
Energy-adjusted only	1[Reference]	0.74 (0.48-1.15)	1.39 (0.93-2.09)	1.81 (1.17-2.80)	2.61 (1.59-4.30)	<.001
Multivariate adjusted ^d	1[Reference]	0.74 (0.48-1.17)	1.38 (0.90-2.11)	1.66 (1.04-2.65)	2.32 (1.36-3.96)	<.001

Associato con un più alto rischio di recidiva e di mortalità tra i pazienti con tumore del colon in stadio III trattati con chirurgia e chemioterapia adiuvante

Dieta mediterranea e tumori digestivi

Studio prospettico multicentrico Europeo (n=485'000 persone)

	OR	95% CI
Mediterranean diet	0.67	0.47-0.94



Dieta Mediterranea: alto consumo di frutta, verdura, olio di oliva, pesce e frutti di mare, legumi, frutta secca, e basso consumo di carne rossa e processata, latticini e consumo moderato di alcool (vino rosso)

Buckland et al. 2010

Fattori di rischio per CCR

Età
Familiarità
Sindromi genetiche
MICI



Fattori che influenzano la
prevenzione secondaria

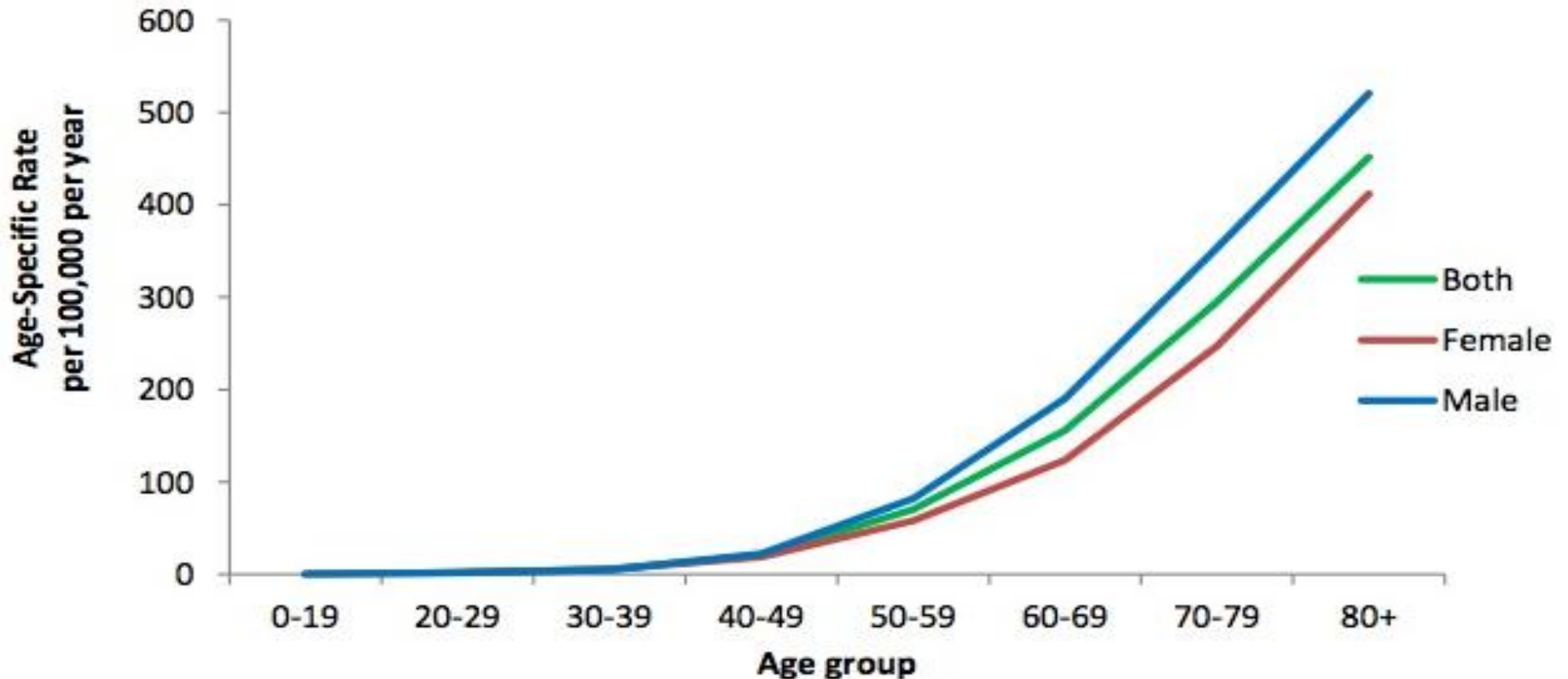
Fattori che influenzano la
prevenzione primaria



Fumo
Alcool
Dieta
Obesità

Fattori di rischio che influenzano la **prevenzione secondaria**

Generico



Tutti gli individui di età superiore ai 50 anni

Fattori di rischio che influenzano la **prevenzione secondaria**

Aumentato

- Familiarità
- Sindromi ereditarie
 - Poliposi adenomatosa familiare
 - Sdr di Lynch
- Malattie infiammatorie croniche intestinali (IBD)

Rischio di sviluppare Cancro Coloretale

Rischio generico

- Rischio cumulativo popolazione generale.....**6%**

Rischio familiare

- Un familiare di I° grado con CCRrischio aumentato di **2-3 volte**
- Due familiari di I° grado con CCR.....rischio aumentato di **3-4 volte**
- Un familiare di I° grado con CCR
diagnosticato ad età < 50 anni.....rischio aumentato di **3-4 volte**
- Un familiare di 2° o 3° grado con CCR.....rischio aumentato di **~1.5 volte**
- Due familiari di secondo grado con CCR.....rischio aumentato di **~2-3 volte**
- Un familiare di I° grado con un
polipo adenomatoso.....rischio aumentato di **~2 volte**

FORME EREDITARIE DI CANCRO COLORETTALE

POLIPOSI ADENOMATOSA FAMILIARE (FAP)

- Circa 1% dei casi di cancro coloretale
- Mutazione germinale gene APC
- Da centinaia a migliaia di polipi adenomatosi in tutto il colon
- Adenomi del tratto GI superiore
- Sviluppo di CCR a 39 anni
- Adenomi a partire dai 16 anni (media)
- **Colectomia totale**
- **Studio dei familiari di primo grado dai 10 anni con endoscopia**

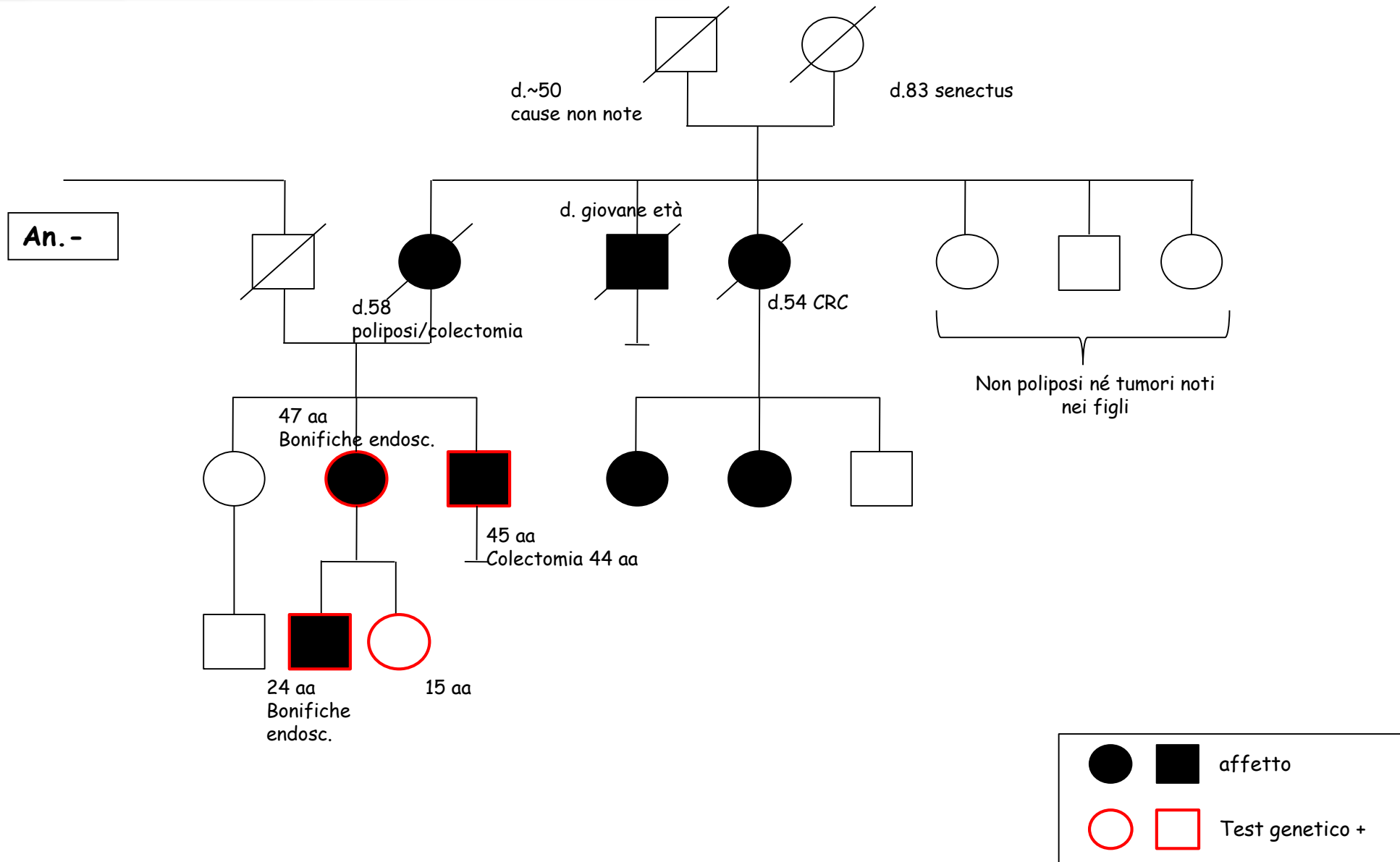


Sindrome di Lynch

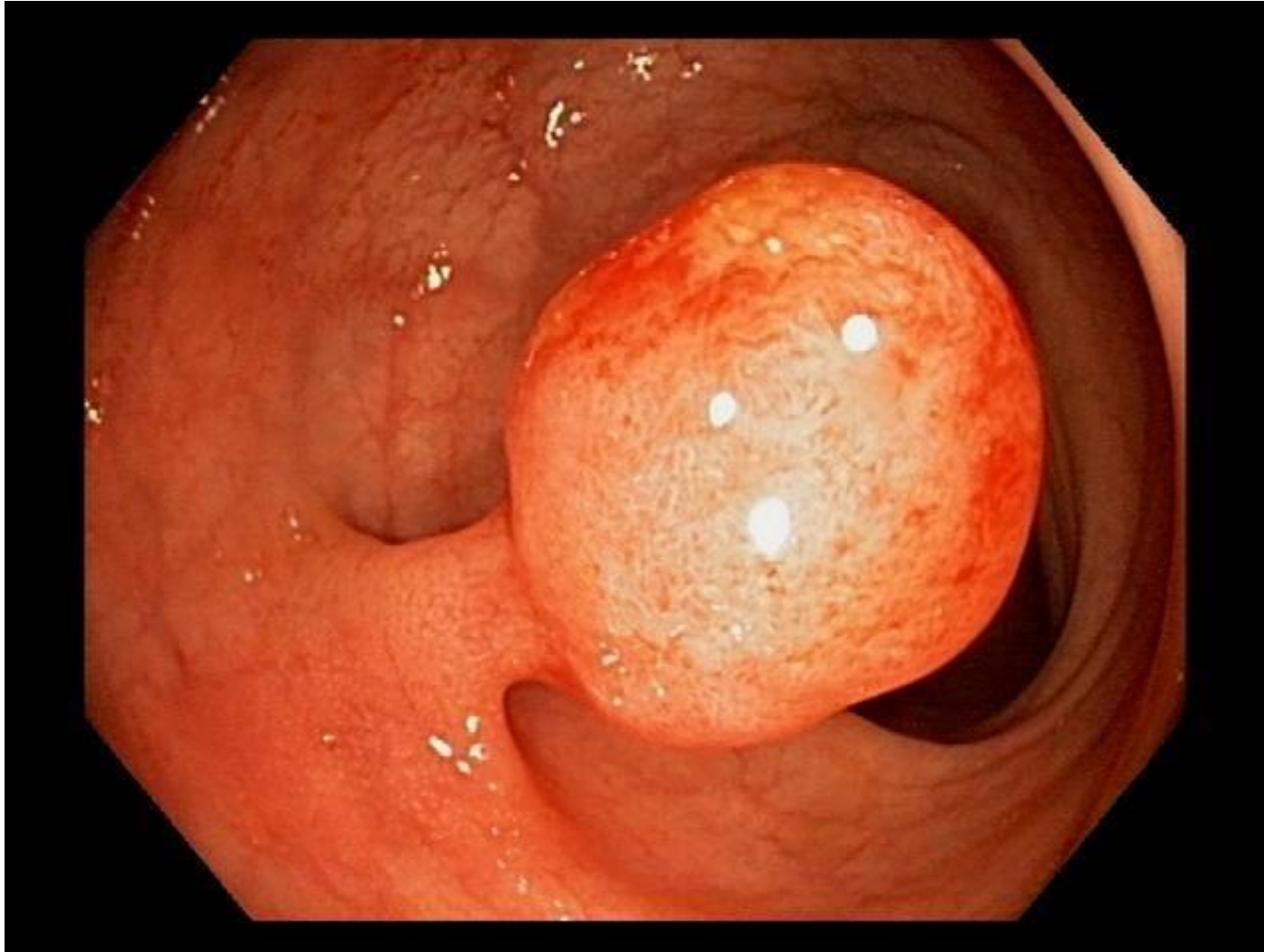
- Autosomico dominante
- 3% di tutti i casi di CRC
- Età < 40 anni
- Mutazione dei geni che riparano il DNA (MMR)
- Adenomi a rapida progressione verso il CRC
- Associata a neoplasie extra-coliche (endometrio, pelvi, ovaio, uretere)



Pedigree Sindrome Ereditaria (FAP)

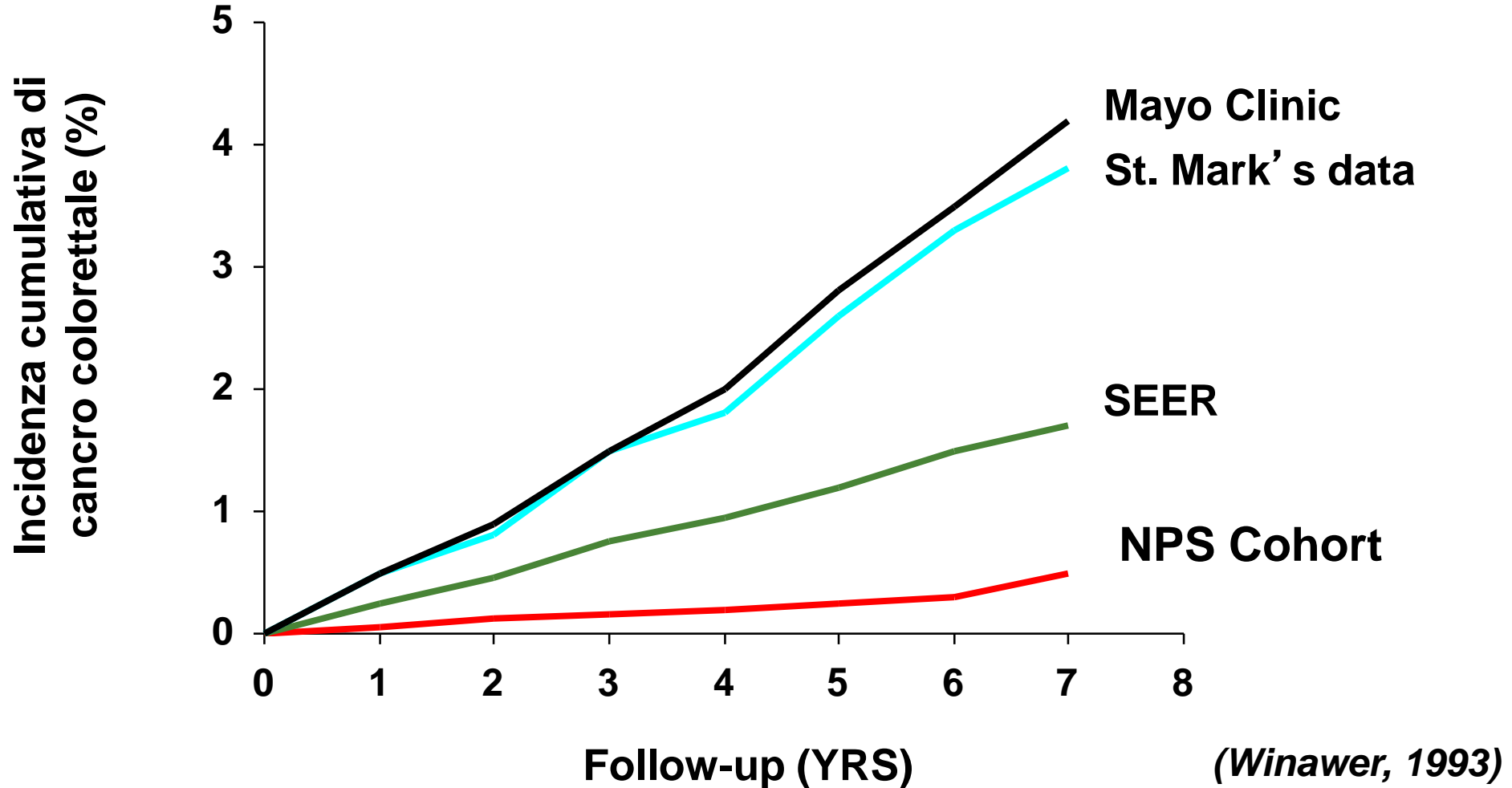


Polipo adenomatoso



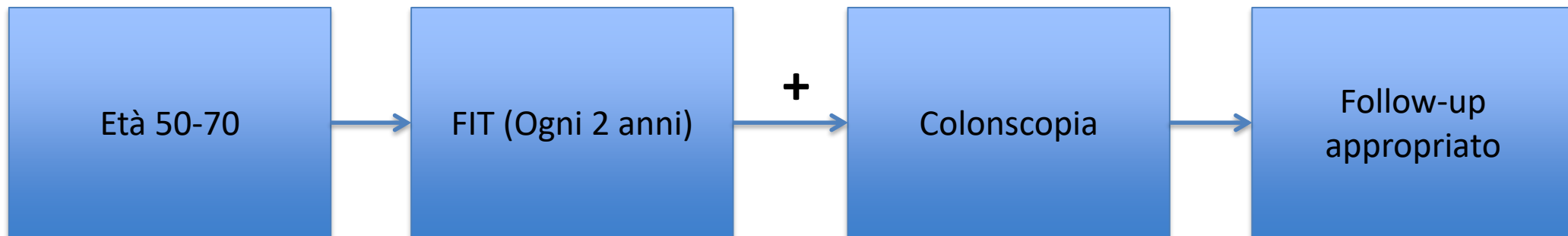
Prevenzione Secondaria

La polipectomia

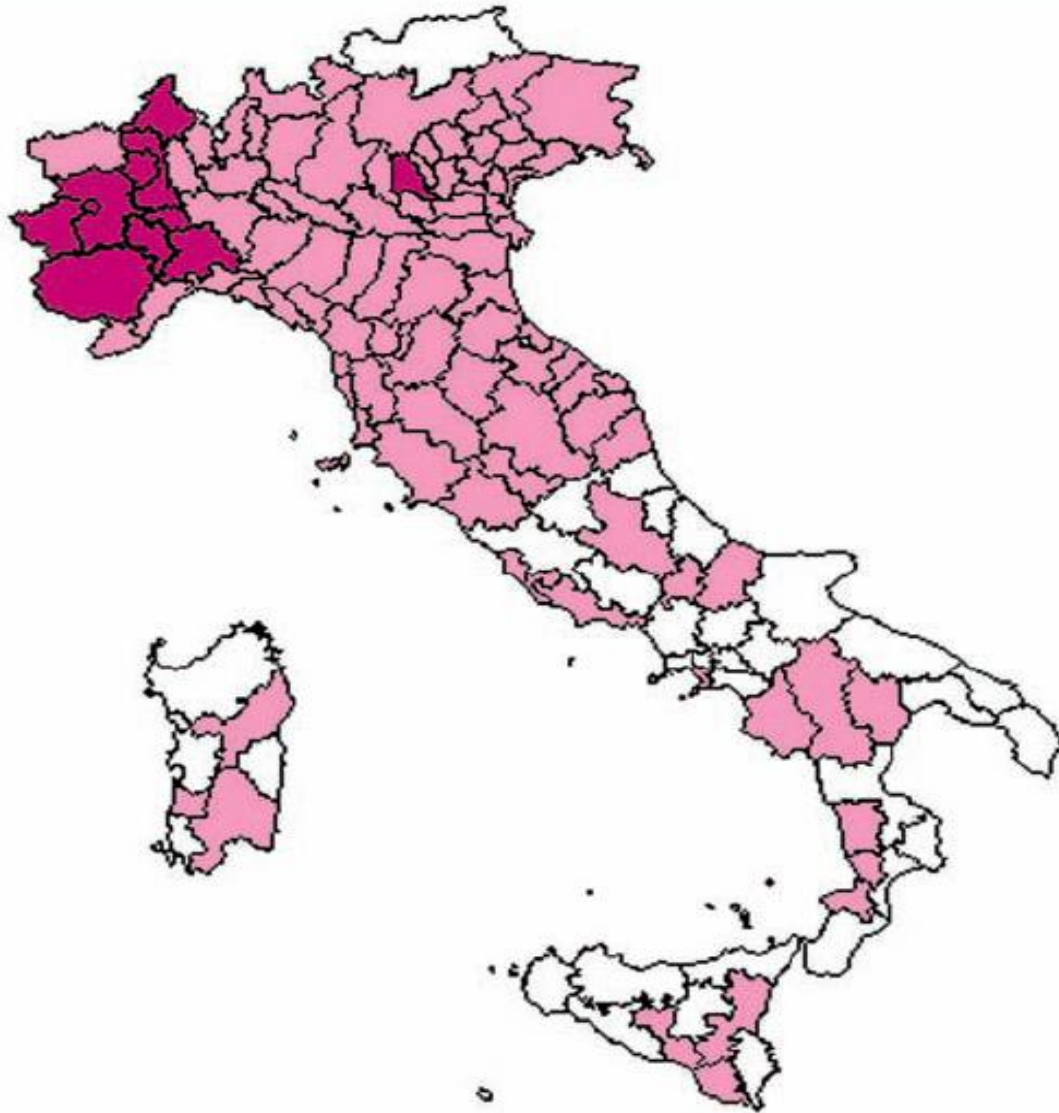


Screening del cancro colorettaie

Emilia-Romagna

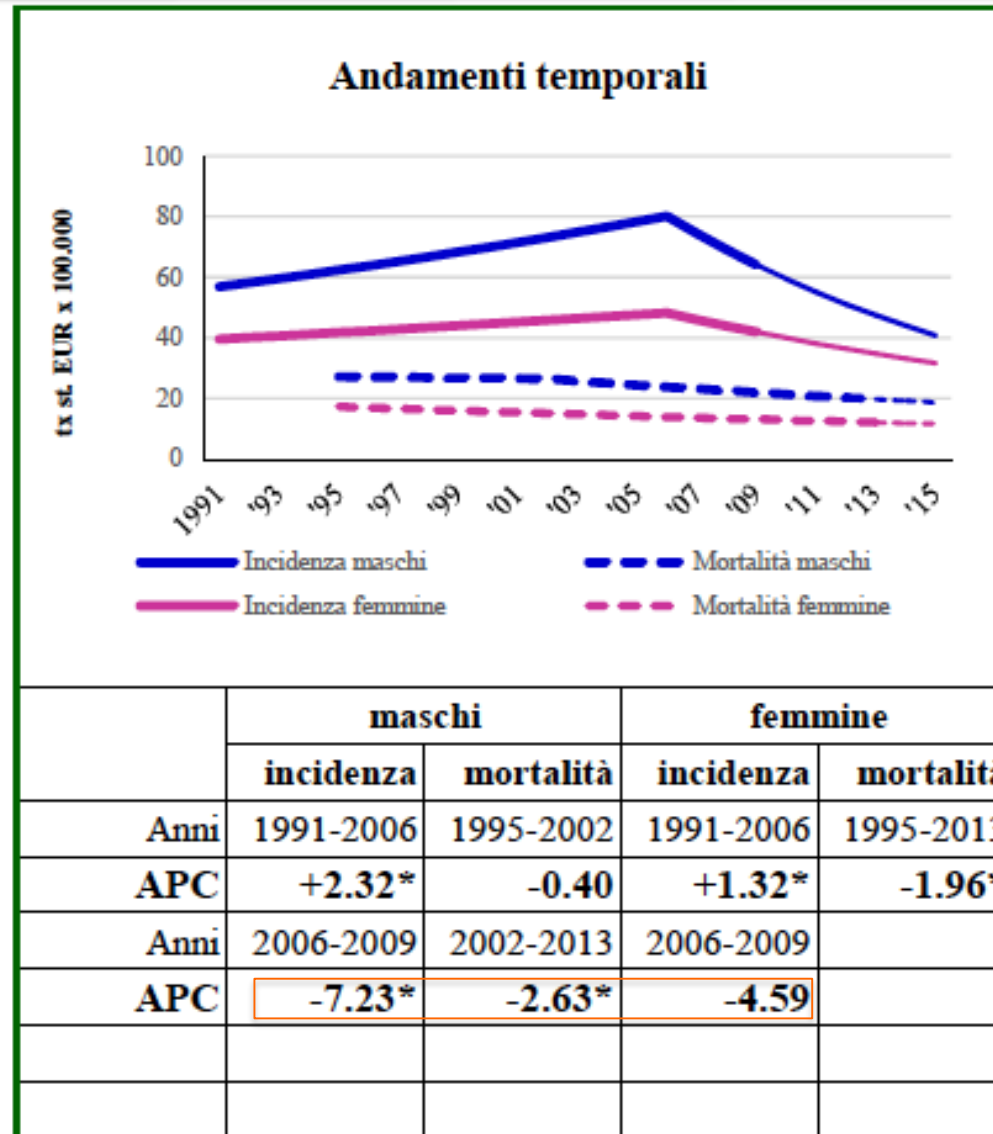


Screening del CRC in Italia



FIT 50-69/74 years
FS 58/60 + FIT 59-69 years

CRC in Emilia Romagna



APC: variazione percentuale annua * p<0,05

Conclusioni

- Il cancro coloretale è una malattia che può essere prevenuta
- Cancro Sporadico
 - Prevenzione secondaria
 - SOF
 - Tutte le strade portano alla colonscopia
- Sindromi ereditarie
 - La diagnosi genetica è codificata → fondamentale per sorveglianza e screening nelle famiglie
 - Gestione ottimale delle sindromi ereditarie riduce i costi ed esami inutili a familiari
- Prevenzione primaria difficile, ma deve essere l'obiettivo futuro

