

LSRO

Evidence and Approach to Establish Guidelines for Dietary Cholesterol



Catherine J. Klein, PhD, RD
December 3, 2008

LSRO

THE SCIENTIFIC EVIDENCE AND APPROACH TAKEN
TO ESTABLISH GUIDELINES FOR CHOLESTEROL INTAKE IN
AUSTRALIA, CANADA, THE UNITED KINGDOM, AND THE UNITED STATES



November 2006

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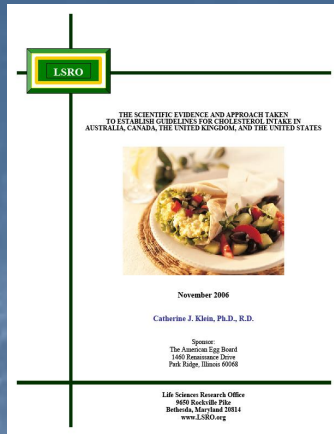
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and

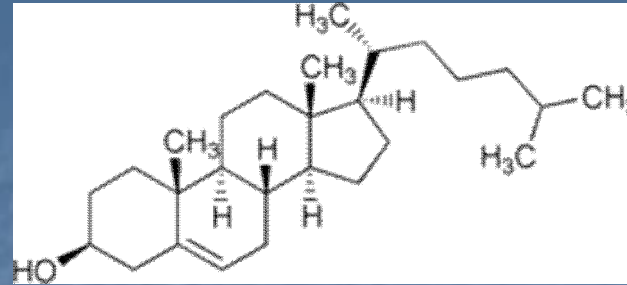
Lewis Kuller, M.D., Dr.P.H.
University of Pittsburgh, PA



LSRO: Scope of Work

- Summarize evidence and methods used to set U.S. guidelines for cholesterol intake
 - based on the relationship of diet and heart disease
- Compare and contrast with approaches by Canada, Australia, and the United Kingdom

Back to Basics



- **Cholesterol**

- **Adults produce 12 to 13 mg/kg**

(Di Buono et al., 2000)

e.g., 154 lb individual = 840 to 910 mg/d

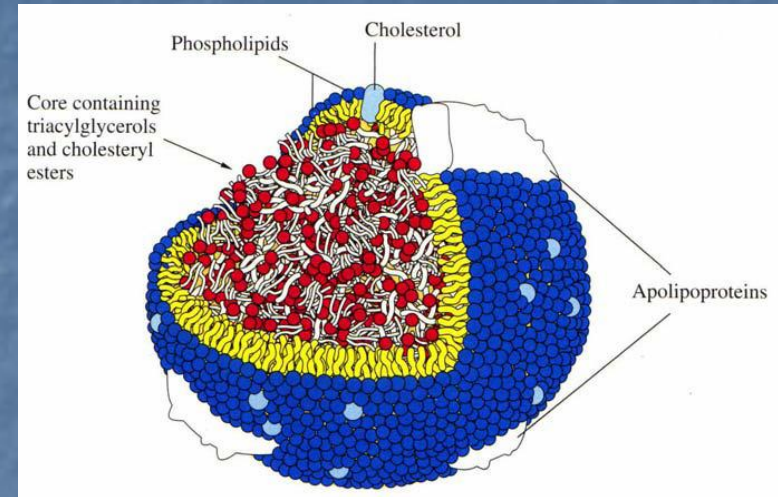
- **Bioavailability**

- **Absorption 40% to 60%**
- **Absorption ↓ by viscous fiber (soluble fiber)**
- **Absorption ↓ plant sterol (phytosterols)**

Back to Basics

- **Blood cholesterol**
 - Serum 2% - 3% > plasma
 - TOTAL-C
 - Lipoprotein fractions
 - LDL-C = therapy target**

Structure of a lipoprotein



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- **Measures improved**
 - Standard reference material, 1989
 - Gas chromatography replaced colorimetry
- Example: 50 gram egg**
274 mg (1976) → 212 mg (2006)

Cholesterol and Saturated Fat in Food (USDA, 2006)

	Portion	Cholesterol DV = 300 mg/d % DV (mg)	Sat fat DV = 20 g/d % DV (g)
High-cholesterol			
Beef liver, fried	3 oz	108% (324)	7% (1.3)
Egg	1 large	71% (212)	8% (1.6)
Shrimp, breaded, fried	6 – 8 shrimp	67% (200)	27% (5.4)
High-saturated fat			
Taco	1 large	29% (87)	88% (17.5)
Egg and sausage biscuit	1 sandwich	101% (302)	75% (15.0)
Candy, chocolate	1/4 cup	0	38% (7.5)

Dietary cholesterol is only weakly correlated, with intake of saturated fat ($r = 0.31$) (Hegsted, 1986); %DV, percent daily value on food label

Dietary Cholesterol in USA Authoritative Guidelines

- **Food Label % Daily Value
(FDA, 1993)**
- **Dietary Reference Intakes
(IOM, 2005)**
- **Dietary Guidelines for Americans
(HHS, USDA, 2005)**

Format Example

**#2 Approach
And
Decisions**



Recommendation

**#2 Key Evidence
and Considerations**

**#1 Approach
And
Decisions**

**#1 Key Evidence
and Considerations**

**Underlying Assumptions and
Past Experience**



Food Label

Daily Reference Value for Cholesterol

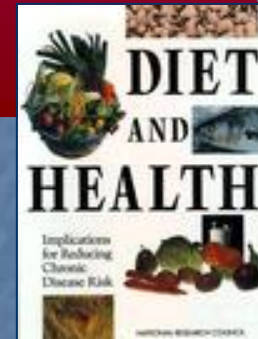
FDA/CFSAN
Change DRV?

FDA/CFSAN
Set DRV 1993
Consistent with
Diet and Health

NLEA (1990)
% Daily Value
Mandatory

DRV
< 300 mg

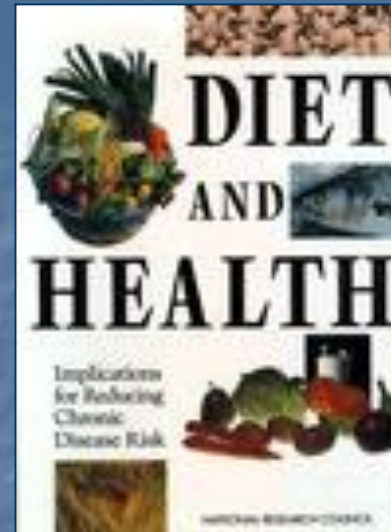
Diet and Health (NRC, 1989)
300 mg upper limit



DIET-C → ↑ TOTAL-C & LDL-C → ↑ CHD

Diet and Health (NRC, 1989)

**Early
Consensus
Groups**
**250 – 300
mg/d**



1988 Canada
1985 NIH
1984 ISCHDR
1983 AHA
1982 WHO
1973 Netherlands
1972 AHF

Diet and Health (NRC, 1989)

DIET-C and Blood-C

Early Consensus

250-300 mg/d

Feeding Studies (1952- 1987)

DIET-C 15 - 600 mg

↑ TOTAL-C

Diet and Health (NRC, 1989)

DIET-C and Blood-C

D&H estimated

↑ 100 mg DIET-C / 1000 kcal
↑ LDL-C by 8 to 10 mg/dL

Early Consensus

250-300 mg/d

Katan et al
(1986, 1988)

88% Δ TOTAL-C
= Δ LDL-C

Hegsted (1965, 1986)

+ 100 mg/d DIET-C
↑ TOTAL-C ~ 4 mg/dL

Feeding Studies (1952- 1987)

DIET-C + 15 - 600 mg
↑ TOTAL-C

Diet and Health (NRC, 1989)

D&H estimated
1/3rd population
Responds to DIET-C
(McNamara, 1987)

D&H estimated
↑ 100 mg DIET-C / 1000 kcal
↑ LDL-C by 8 to 10 mg/dL

Early Consensus
250-300 mg/d

DIET-C and Blood-C

McNamara
(1987)

Katan et al
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88% Δ TOTAL-C
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Hegsted (1965, 1986)
+ 100 mg/d DIET-C
↑ TOTAL-C ~ 4 mg/dL

Feeding Studies (1952- 1987)
DIET-C + 15 - 600 mg
↑ TOTAL-C

Diet and Health (NRC, 1989)

D&H estimated
TOTAL-C ↓ 1%
↓ 2% CHD

D&H estimated
1/3rd population
Responds to DIET-C

D&H estimated
↑ 100 mg DIET-C / 1000 kcal
↑ LDL-C by 8 to 10 mg/dL

Early Consensus
250-300 mg/d

Blood-C and CHD

Peto
(1987, unpublished)
TOTAL-C ↓ 10%
↓ 16% CHD

DIET-C and Blood-C

McNamara
(1987)

Katan et al
(1986, 1988)

Hegsted (1965, 1986)

Feeding Studies (1952- 1987)

Diet and Health (NRC, 1989)

NRC Recommended →

TOTAL-C ↓ 1%
↓ **CHD rates ~2%**

DIET-C ↓ 140 mg/d
↓ **LDL-C 5 to 7 mg/dL**

NCEP (1988)
LDL-C = Key Target

Early Consensus
250-300 mg/d

< 300 mg

CSFII (1985)
Men: 439 mg/d
Women: 280 mg/d

Peto (1987)
TOTAL-C ↓ 10%
↓ 16% CHD



DRI Cholesterol (2005)

DIET-C and Blood-C

6 Meta-analyses
(1986-2005)

Δ DIET-C = Δ TOTAL-C

50 Human Trials
(1960-1998)

Δ DIET-C = Δ in TOTAL-C

15 Epi reports

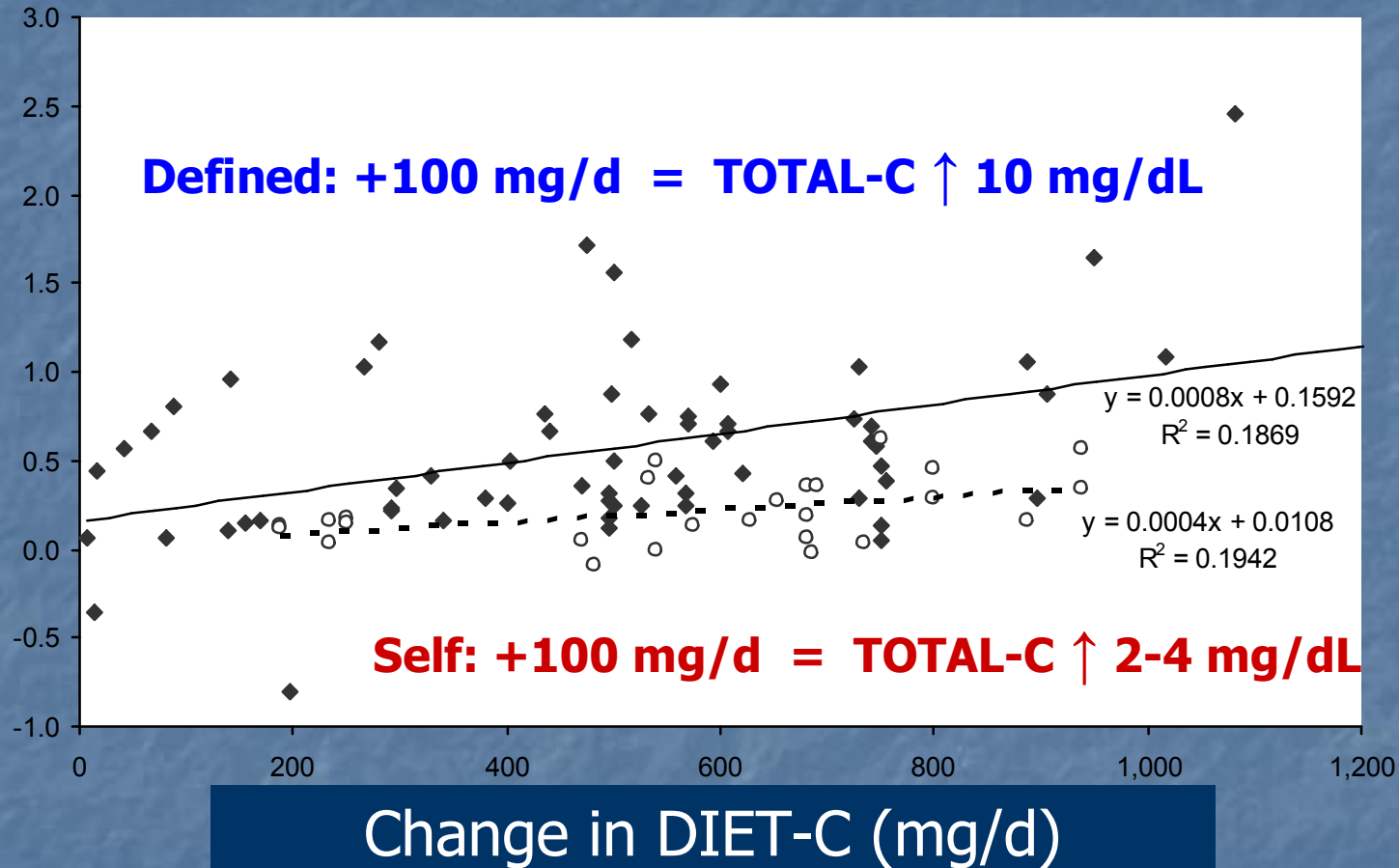
“Did not provide a meaningful basis for
establishing adverse health effects
of dietary cholesterol”

Animal Models

Cannot extrapolate data to humans

Linear relationship Δ in DIET-C and Δ in TOTAL-C (IOM, 2005)*†

Change TOTAL-C (mmol/L)



* Defined: \blacklozenge Self-Selected: \diamond Linear(Defined): — Linear(Self-Selected): ---

† Corrected equation of the line for defined diets

DRI Cholesterol (2005)

IOM recommended →

IOM suggested

~80% Δ in TOTAL-C
= Δ LDL-C

Clarke et al (1997)

Hegsted et al (1993)

IOM

↑ Blood lipoproteins
“would be predicted to result
in ↑ risk for CHD”

**DIET-C
as low as
possible**

**6 Meta-analyses
(1986-2005)**

Δ DIET-C = Δ TOTAL-C

**50 Human Trials
(1960-1998)**

Δ DIET-C = Δ in TOTAL-C



Dietary Guidelines for Americans 2005

DG-Advisors

**#1. Scientific report to
revise 2000 DG**

Food Label

300 mg/d

Food-modeling

(USDA, 2005)

~160 to 212 mg/d

IOM (2005)

DIET-C "as low as possible"



Dietary Guidelines for Americans 2005

Secretaries DHHS/USDA
#2. Set recommendations

DG-Advisors
**#1. Scientific report to
revise 2000 DG**

Food Label
300 mg/d

Public comment
Citizens, industry

Food availability
Consumption patterns

Food-modeling
(USDA, 2005)
~160 to 212 mg/d

IOM (2005)
DIET-C "as low as possible"



Dietary Guidelines for Americans 2005

Secretaries DHHS/USDA
#3. Set guidelines

Secretaries DHHS/USDA
#2. Set recommendations

DG-Advisors
**#1. Scientific report to
revise 2000 DG**

Food Label
300 mg/d

< 300 mg

Experts
Test key messages

Public comment
Citizens, industry

Food availability
Consumption patterns

Food-modeling
(USDA, 2005)
160 to 212 mg/d

IOM (2005)
DIET-C "as low as possible"

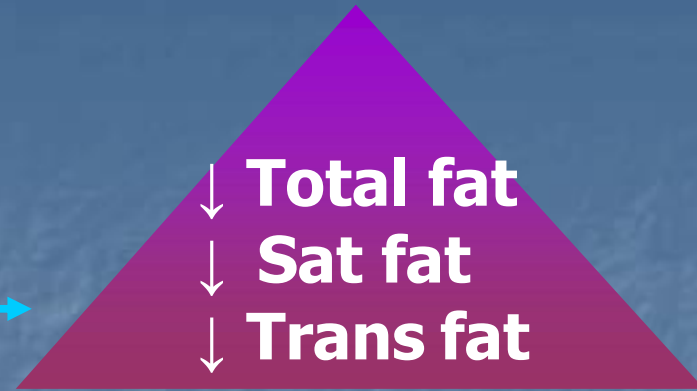
Summary of U.S. Recommendations

- **Dietary Guidelines (HHS, USDA, 2005)**
300 mg
- **DRI (IOM, 2005)**
“as low as possible”
- **Food Label (FDA, 1993)**
300 mg



World Health Organization

WHO (2004) recommended



Diet Fat and CHD

Hooper et al (2001)

RCT

↓ diet fat ↓ CVD

DIET-C and MI/death

Hu et al (2000)

FFQ men (n=44,875)

Western diet 335 mg

Prudent diet 288 mg

WHO (2003)
Recommended
Average per capita
< 300 mg/d

No rationale for specific cut-off

Concluded

High DIET-C leads
to increased CHD

Kris-Etherton et al (2001)

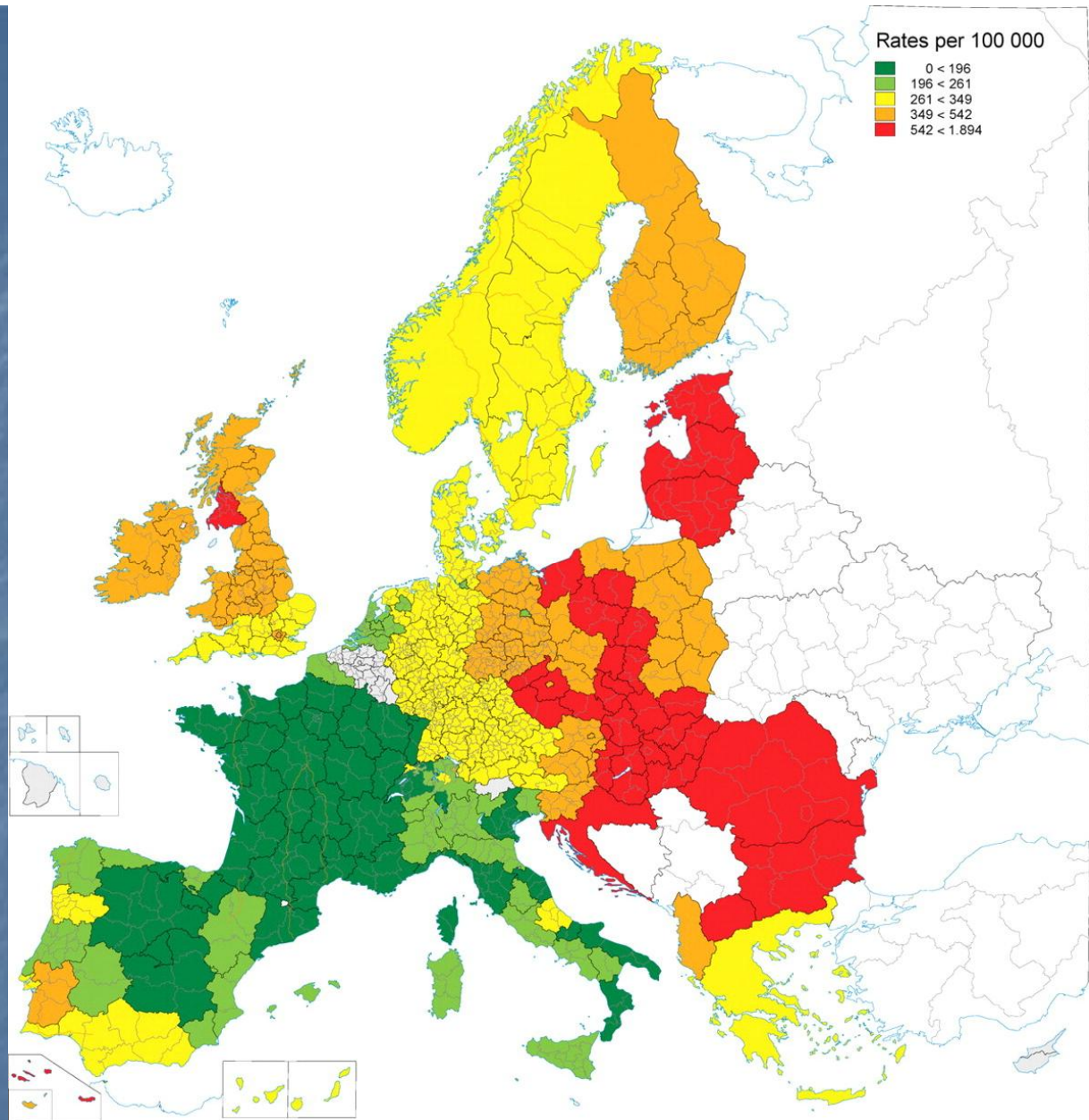
Early consensus < 300 mg/d

Europe

CVD of men (2000)

Ischemic Heart
Disease

Cerebrovascular
Disease



Muller-Nordhorn, J. et al. Eur Heart J 2008 29:1316-1326;
doi:10.1093/eurheartj/ehm604

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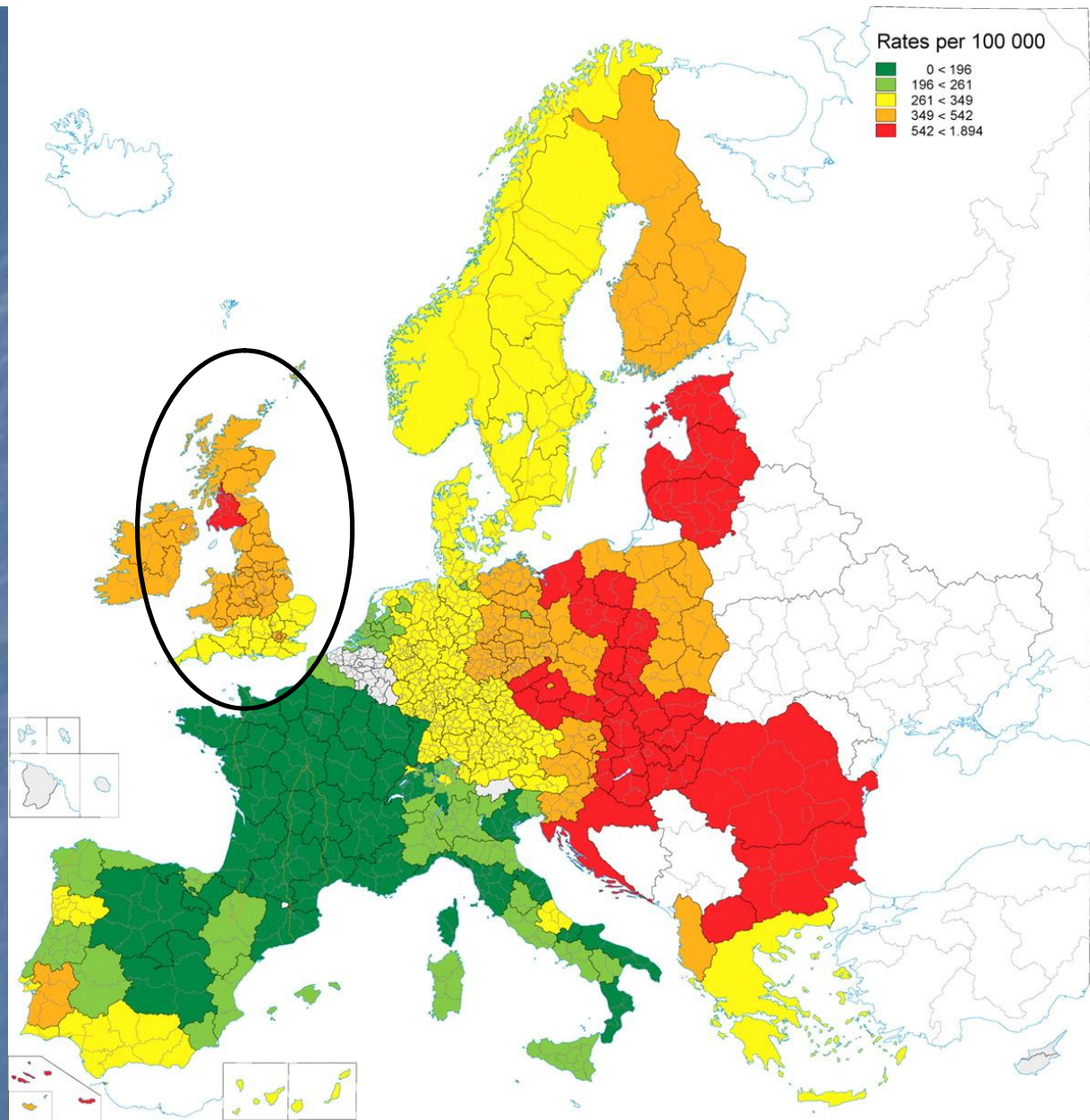
European
Heart Journal

Europe

CVD of men (2000)

Ischemic Heart
Disease

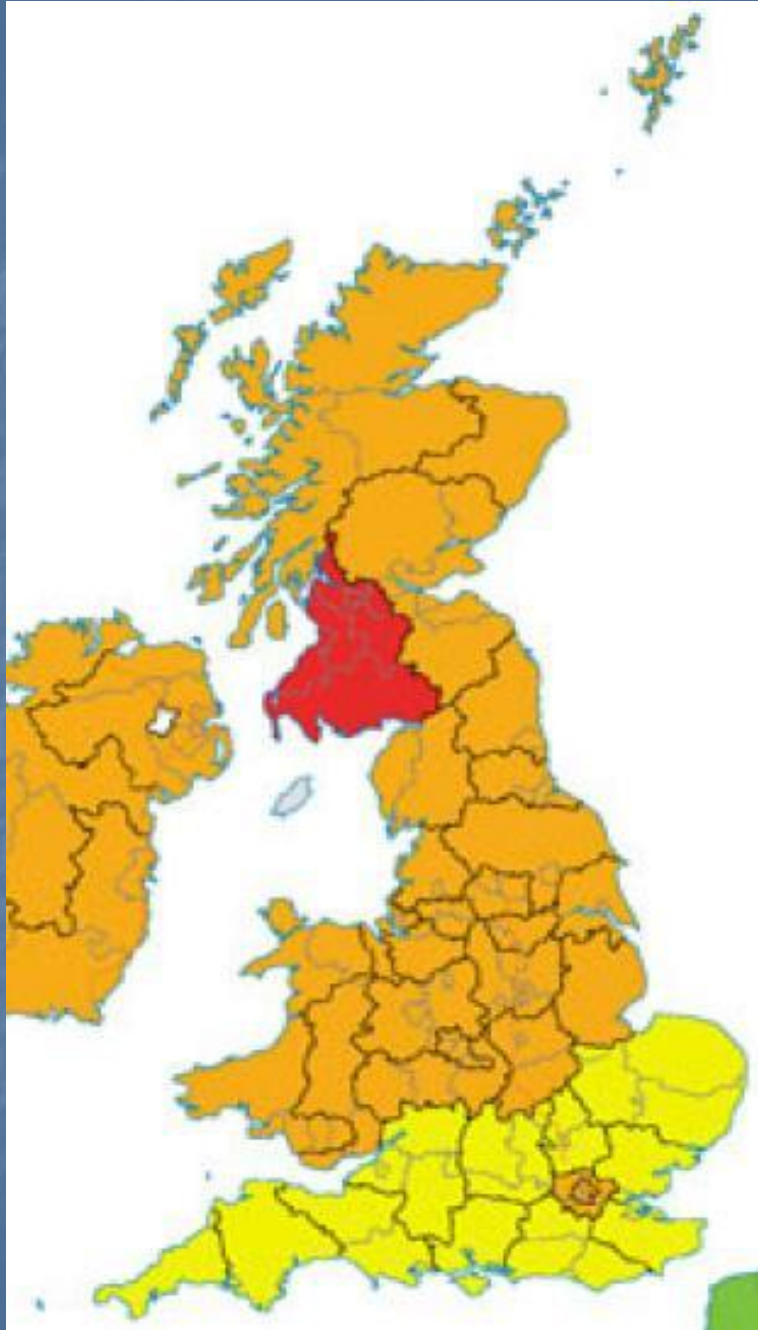
Cerebrovascular
Disease



Muller-Nordhorn, J. et al. Eur Heart J 2008 29:1316-1326;
doi:10.1093/eurheartj/ehm604

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European
Heart Journal



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Europe

↓ Total fat
↓ Sat fat
↓ Trans fat

European Heart Network (2002)

1. DIET-C ↑ LDL-C vs. Sat fat ↑ ↑ ↑ LDL-C
2. ↓ Sat fat ... will probably ↓ DIET-C
3. DIET-C in EU < 300 mg

Eurodiet Project (1998-2000)

↓ Total, saturated, trans fat

Weggemans et al. (2001)

meta-analysis

+ 100 mg DIET-C

↑ TOTAL-C to HDL-C ratio

Early Consensus

300 mg/d

United Kingdom



FOOD STANDARDS AGENCY

Eat well, be well

Helping you make healthier choices

**Food Standards Agency
UK Dept of Health
(2005, 2006)**

↓ **Total and saturated fat**

Scottish Office (2003, 2005)

↓ **Total and saturated fat**

UK SACN (1994 - 2001)

Population goal

Avg DIET-C should not rise

Early Consensus

300 mg/d

↓ **Total fat**
↓ **Sat Fat**

**DIET-C Great Britain
(2000-2001)**

304 mg/d men

213 mg/d women

DIET-C UK (1990's)

~ 245 mg/d



Australia and New Zealand

NHMRC (2006)

Limit fat to 35% of total kcal
Limit Sat and Trans fat to 10% of kcal



Nutrient Reference Values

Review IOM DRI (2005)

Adopt, Adopt with changes or Reject



Truswell (2003)

Reduce Sat fat
Eat, at most, one egg/day

Limit
Total fat,
Sat fat
and Trans fat

Other guidelines
Other data
WHO, other countries

IOM DRI (2005)
"any incremental
increase in cholesterol
intake increases CHD risk"

Hu et al. (1999)
1 egg/day does not ↑ CHD or stroke



**Eating Well with
Canada's Food Guide
(Feb, 2007)**

**Limit
high fat food**

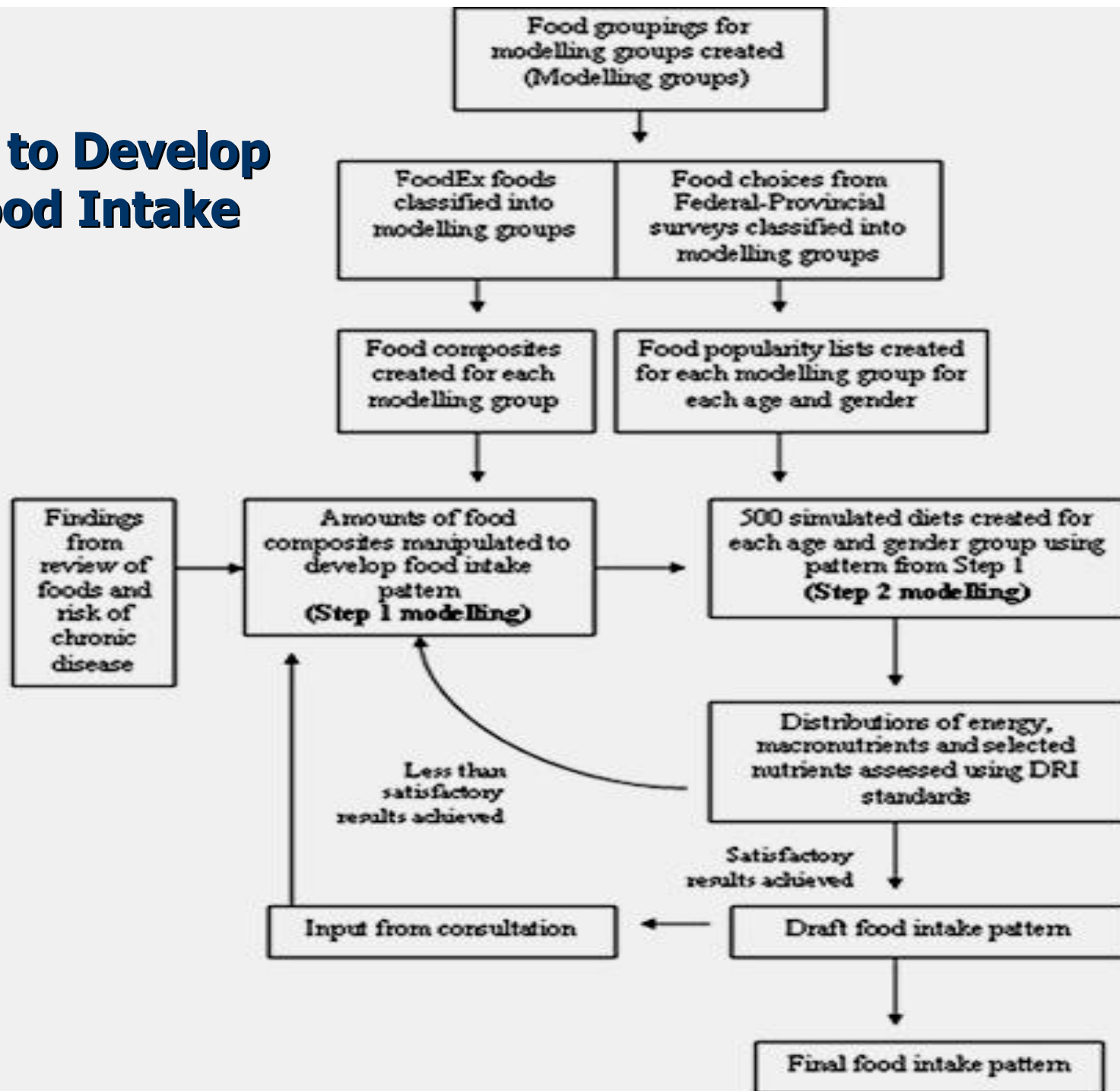
**Food Intake Pattern (2007)
Evaluate relative to DRI**

**Dietary Guidelines
Science Advisory Report
(USDA, 2005)
< 300 mg**

**IOM DRI (2005)
any increase in DIET-C increases CHD risk**

**WHO (2003)
Recommended Average per capita < 300 mg/d**

Canada Process to Develop 2007 Food Intake Pattern





Food Label (Dec, 2007)
Mandatory DIET-C mg
Optional % Daily Value

Food Guide (Feb, 2007)
Limit high fat food

**Limit
high fat food**

Reference Standard
300 mg/d
Amounts harmonized with USA

Summary

