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The World Health Organization (WHO)

Specializovaná agentura Spojených národů vytvořená v r. 1948. Je primárně zodpovědná za věci týkající se zdraví v mezinárodním měřítku.
Regionální úřad WHO v Evropě je jedním ze 6 regionálních úřadů na světě, z nichž každý má svůj vlastní program zaměřený na specifické zdravotní podmínky v zemích, kde fungují.

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FOOD AND HEALTH IN EUROPE: A NEW BASIS FOR ACTION

Edited by: Aileen Robertson, Cristina Tirado, Tim Lobstein, Marco Jermini, Cecile Knai, Jørgen H. Jensen, Anna Ferro-Luzzi and W.P.T. James

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This publication, aimed at health professionals, discusses in depth the components of food and nutrition policies and the evidence supporting them. It describes food- and nutrition-related ill health and its costs, shows the need for action and describes the steps for decision-makers to take. This book highlights the urgent need for integrated, multisectoral food and nutrition policies to encourage the sustainable production of food, its safety and the provision of food of high nutritional quality for all. A summary of the book's content, aimed at policy-makers, was published in English and Russian in 2002.

Poor nutrition, foodborne disease and lack of secure access to good food make an important contribution to the burden of disease and mortality in the WHO European Region. Better diets, food safety and food security will not only reduce or prevent suffering to individuals and societies but also help cut costs to health care systems and bring social and economic benefits to countries.

Food and nutrition strategies

A comprehensive food and nutrition policy comprises three strategies: on nutrition, food safety and a sustainable food supply (food security), based on the principles of HEALTH21 and Agenda 21 (for definitions of selected terms see Annex 2). This framework (see Fig. 2) provides a starting point from which to address the question of how to promote public health through food.

Fig. 2. A comprehensive policy contains nutrition, food safety and sustainable food supply strategies

Food can be contaminated during the various stages of primary agricultural production, storage, transport, processing, packaging and final preparation. Each link in the chain must be as strong as every other if the health of consumers is to be protected (see Fig. 1). In addition, the increase in global food trade creates the potential for very large amounts of food, from one single source, to be distributed over far greater distances than ever before. While this does allow cheaper and more varied foods to be produced, it also creates an increased risk of larger and more widespread outbreaks of foodborne illnesses.

Fig. 1. Principal stages of the food supply chain

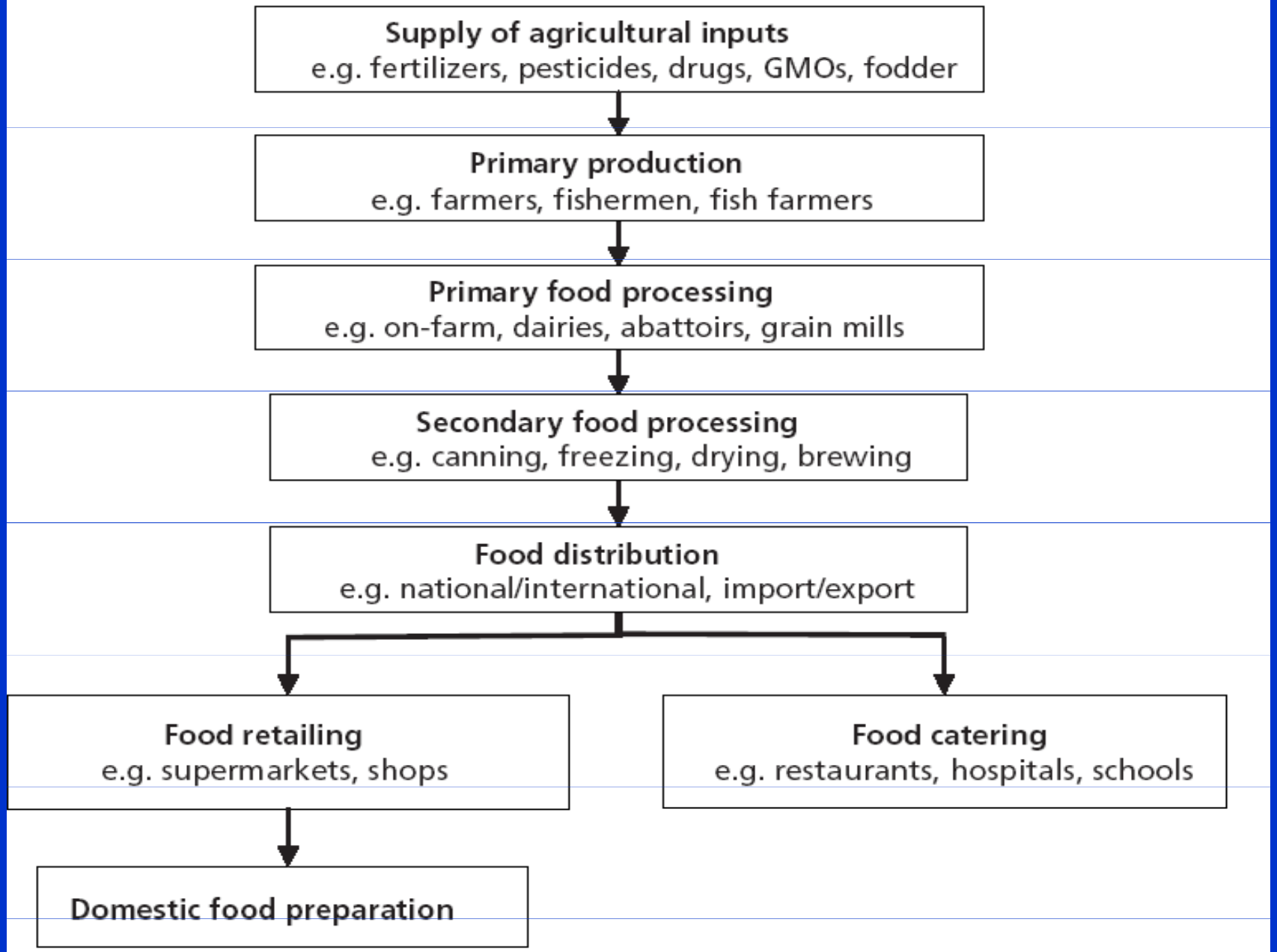
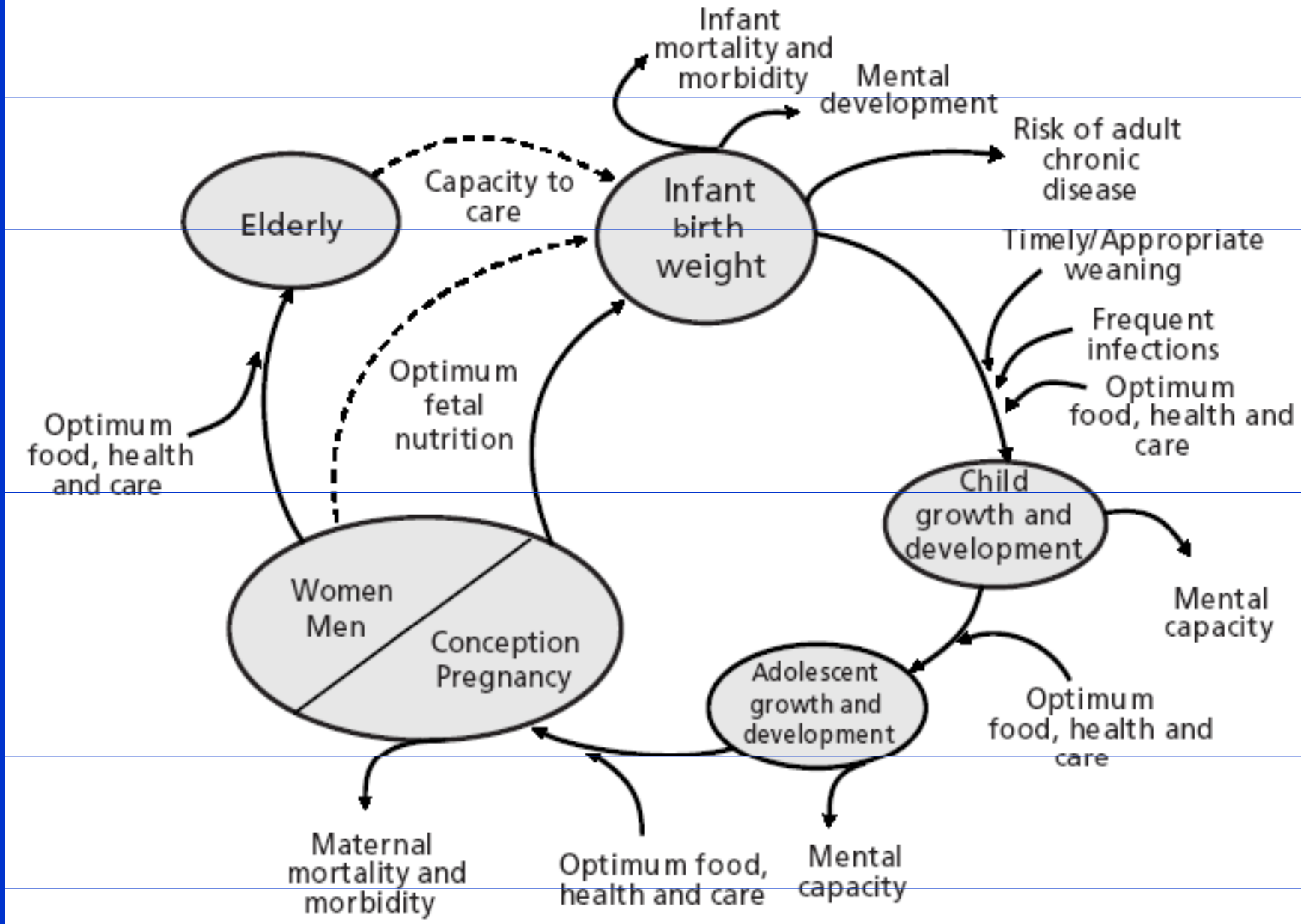


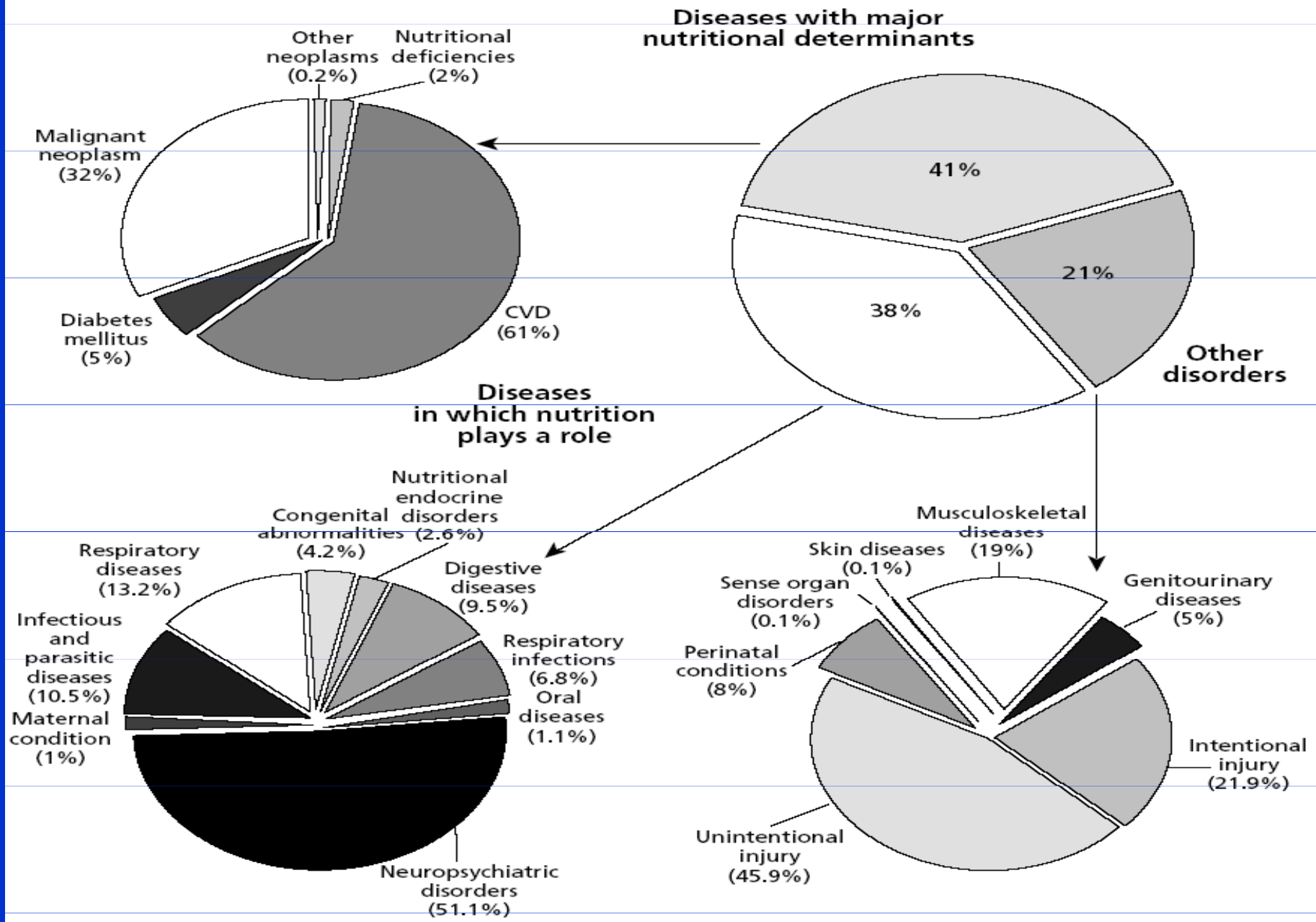
Fig. 3. Life cycle: the proposed causal links



Diet-related diseases: the principal health burden in Europe

The burden of disease has been assessed in terms of disability-adjusted life-years (DALYs). These incorporate an assessment of the years of life lost to different diseases before the age of 82.5 years for females and 80 for males *(1)* and the years spent in a disabled state *(2)*. Non-fatal health states are assigned values (disability weights) for estimating years lost to disability based on surveys. Years lost (severity adjusted) to disability are then added to years lost to premature mortality to yield an integrated unit of health: the DALY; one DALY represents the loss of one year of healthy life.

Fig. 1.1. Lost years of healthy life in the European Region, 2000



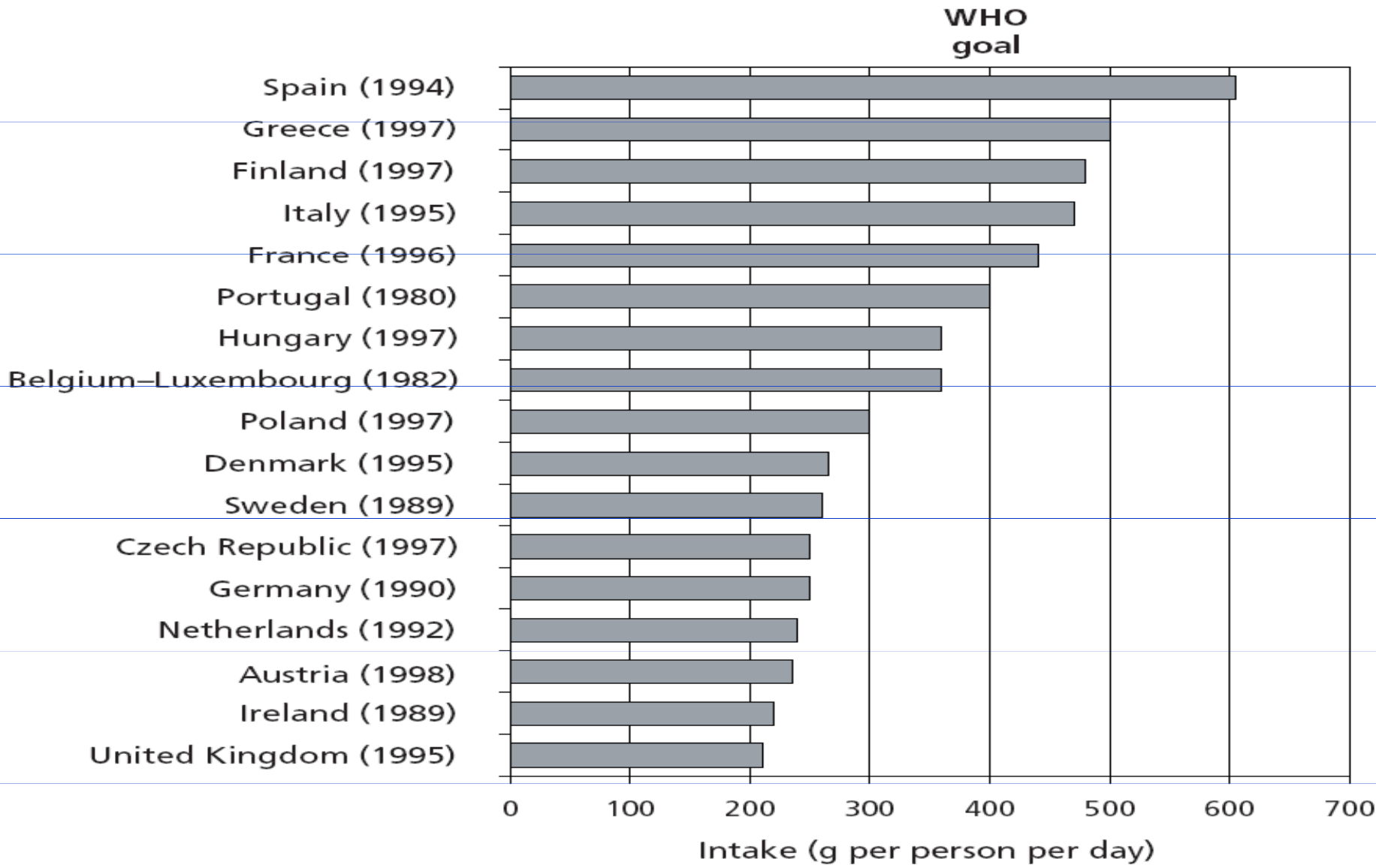
Source: adapted from *The world health report 2000. Health systems: improving performance (3).*

Table 1.1. Contribution of selected factors to the overall burden of disease in the EU

Causal factor	Contribution (%)
Tobacco smoking	9.0
Alcohol consumption	8.4
Overweight	3.7
Occupational risks	3.6
Low fruit and vegetable consumption	3.5
Relative poverty	3.1
Unemployment	2.9
Illicit drugs	2.4
Physical inactivity	1.4
Diet high in saturated fat	1.1
Outdoor air pollution	0.2

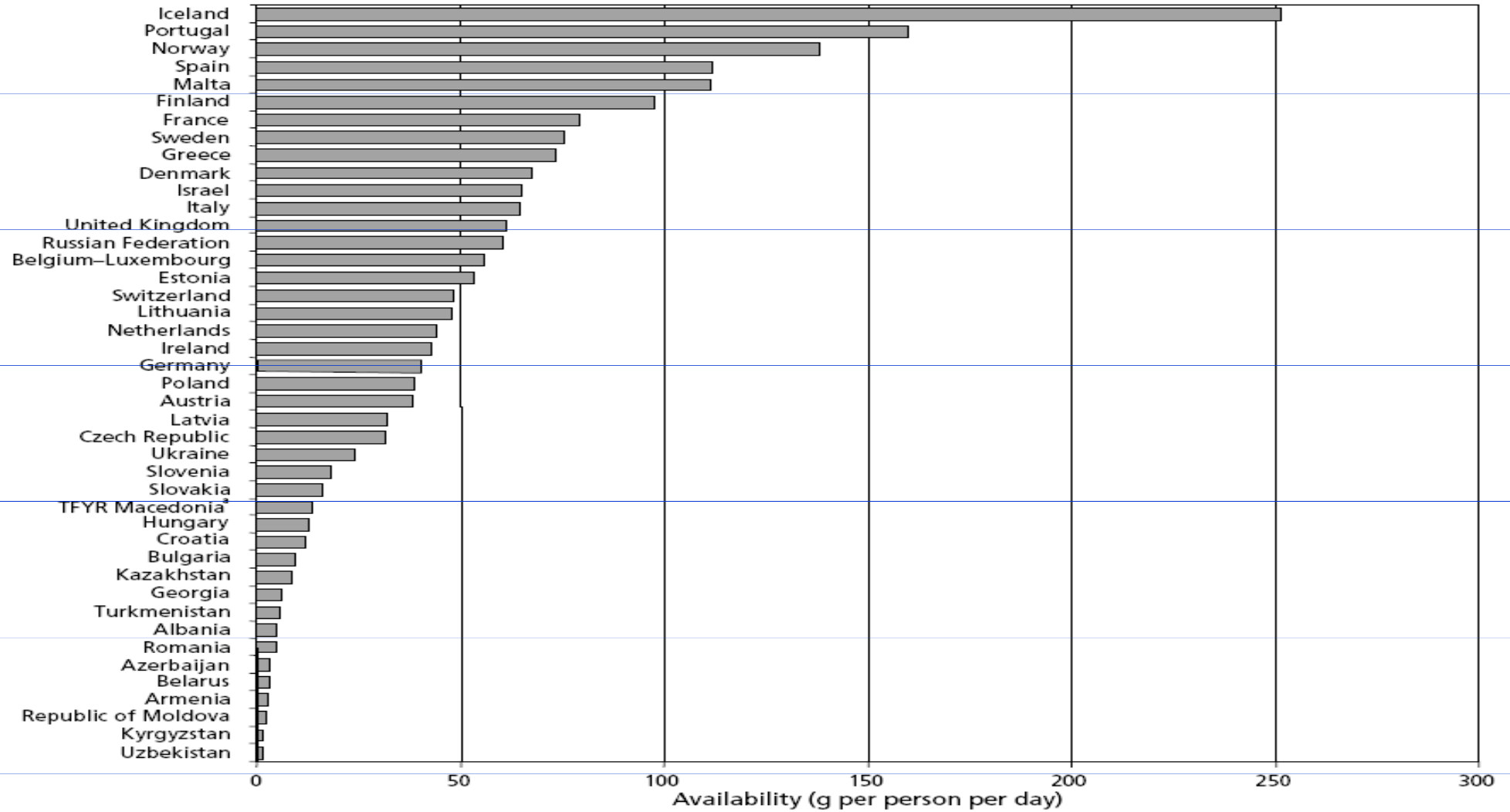
Source: Determinants of the burden of disease in the European Union (6).

Fig. 1.3. Vegetable and fruit intake (mean g/day) in selected European countries



Source: Comparative analysis of food and nutrition policies in the WHO European Region 1994–1999. Full report (20).

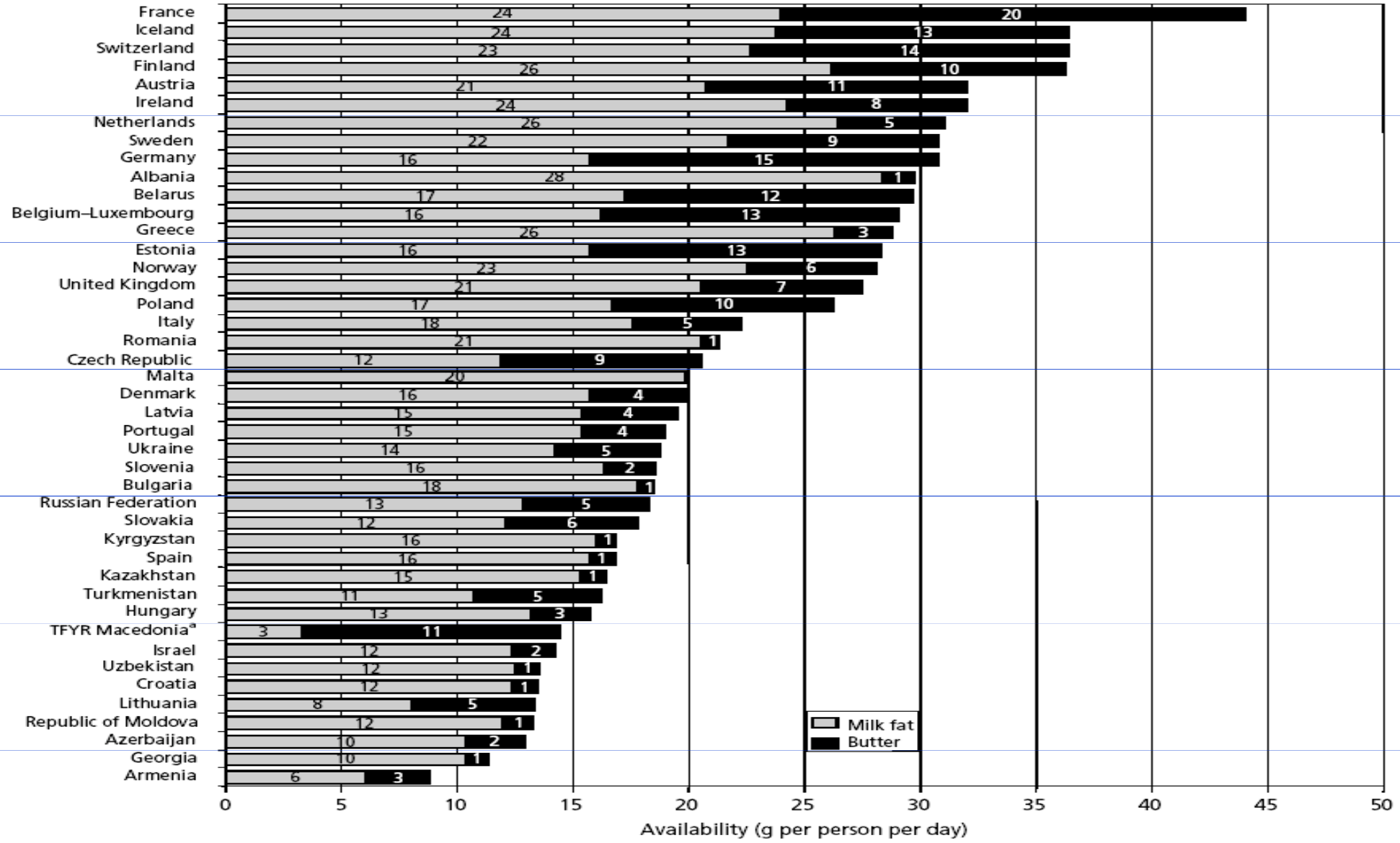
Fig. 1.5. Availability of fish, selected countries in the WHO European Region, 1998



[a] The former Yugoslav Republic of Macedonia.

Source: Food and Agriculture Organization of the United Nations (http://apps.fao.org/lim500/wrap.pl?FoodBalanceSheet&Domain=FoodBalanceSheet&Language=english, accessed 25 September 2003).

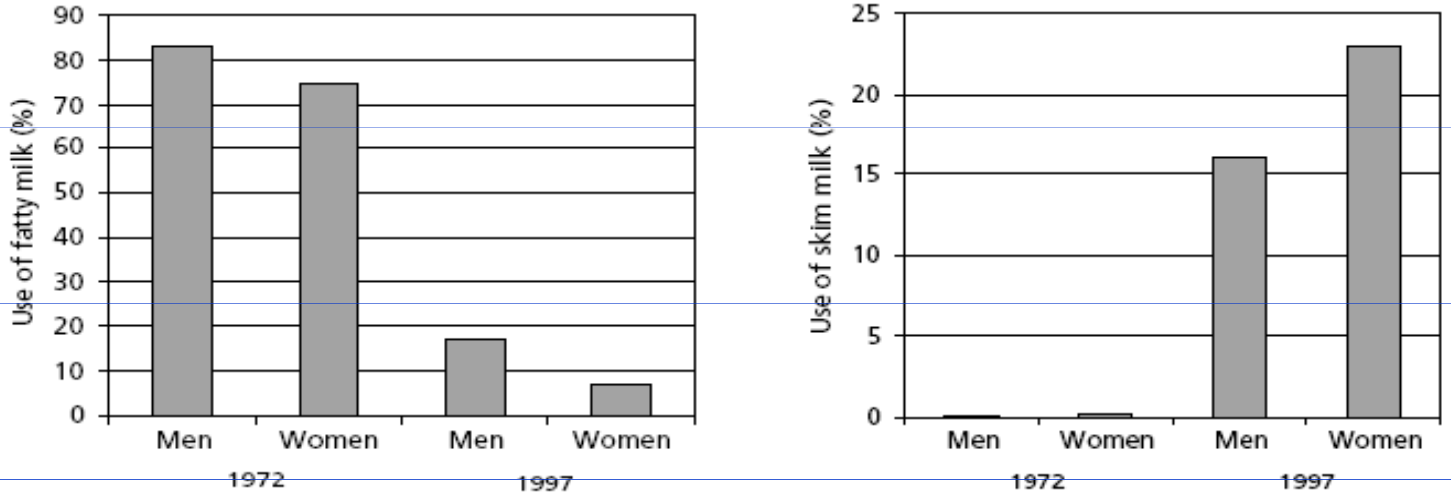
Fig. 1.4. Availability of milk fat, selected countries in the WHO European Region, 1998



[a] The former Yugoslav Republic of Macedonia.

Source: Food and Agriculture Organization of the United Nations (http://apps.fao.org/lim500/wrap.pl?FoodBalanceSheet&Domain=FoodBalanceSheet&Language=english, accessed 25 September 2003).

Fig. 1.6. Percentage of men and women aged 35–59 years in North Karelia, Finland drinking fat-containing milk and skim milk, 1972 and 1997



Source: Puska *(25)*.

Fig. 1.7. Percentage of men and women aged 35–59 years in North Karelia, Finland using butter and vegetable oil, 1972 and 1997

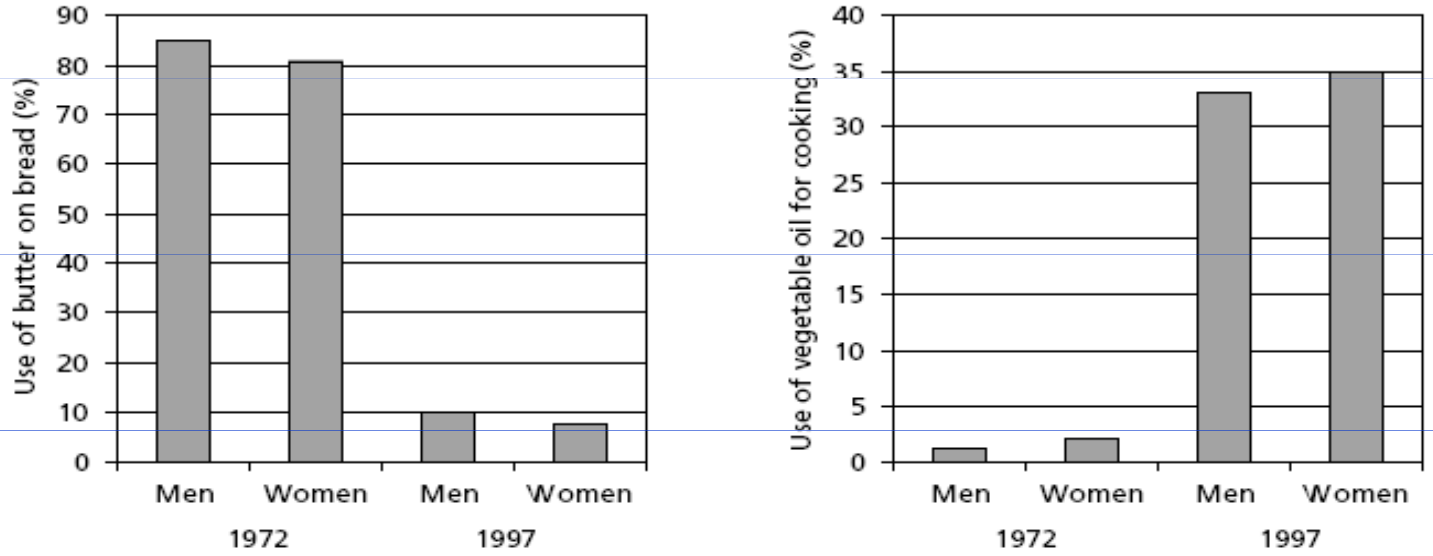
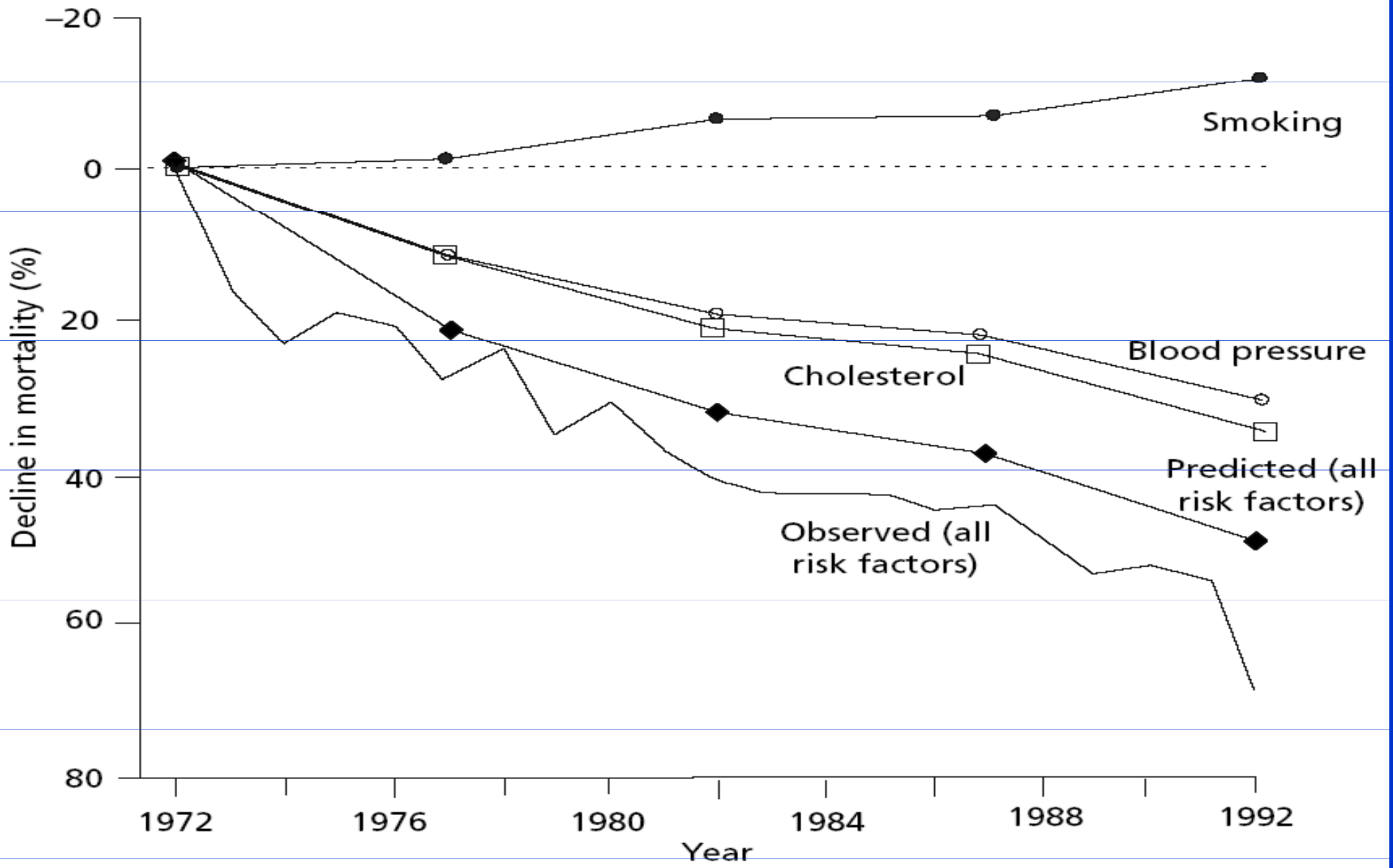


Fig. 1.8. Predicted and observed mortality from CHD in females aged 35–64, north-eastern Finland



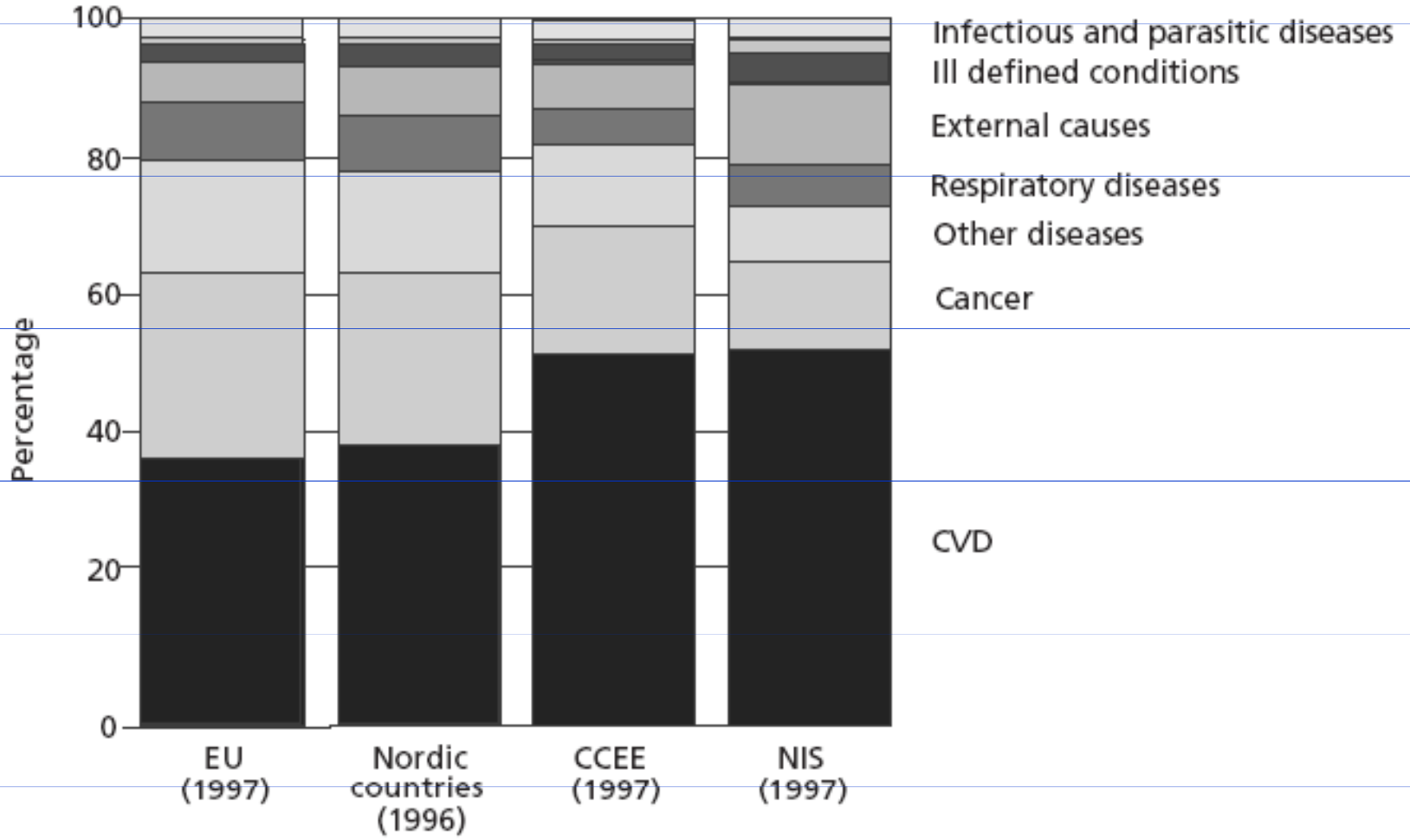
Source: Vartiainen et al. *(26).*

Table 1.2. Costs of diet-dependent conditions in Germany, 1990s

Conditions	Estimated costs (DM billion)		
	Total	Direct	Indirect
CVD	32.9	15.4	17.6
Dental caries	20.2	20.2	<0.1
Cancer	9.6	1.6	8.1
Diabetes	3.8	2.3	1.5
Alcoholism	3.5	0.7	2.8
Diseases of the liver	3.1	0.4	2.6
Other conditions	2.6	1.4	0.5
Diseases of the pancreas	2.6	1.9	0.6
Lipid metabolism	1.4	1.2	0.9
Food poisoning	1.4	0.3	1.1
Goitre	1.3	1.1	0.2
Diseases of the gallbladder	1.1	0.8	0.3
All diet-related conditions	83.5	47.3	36.2

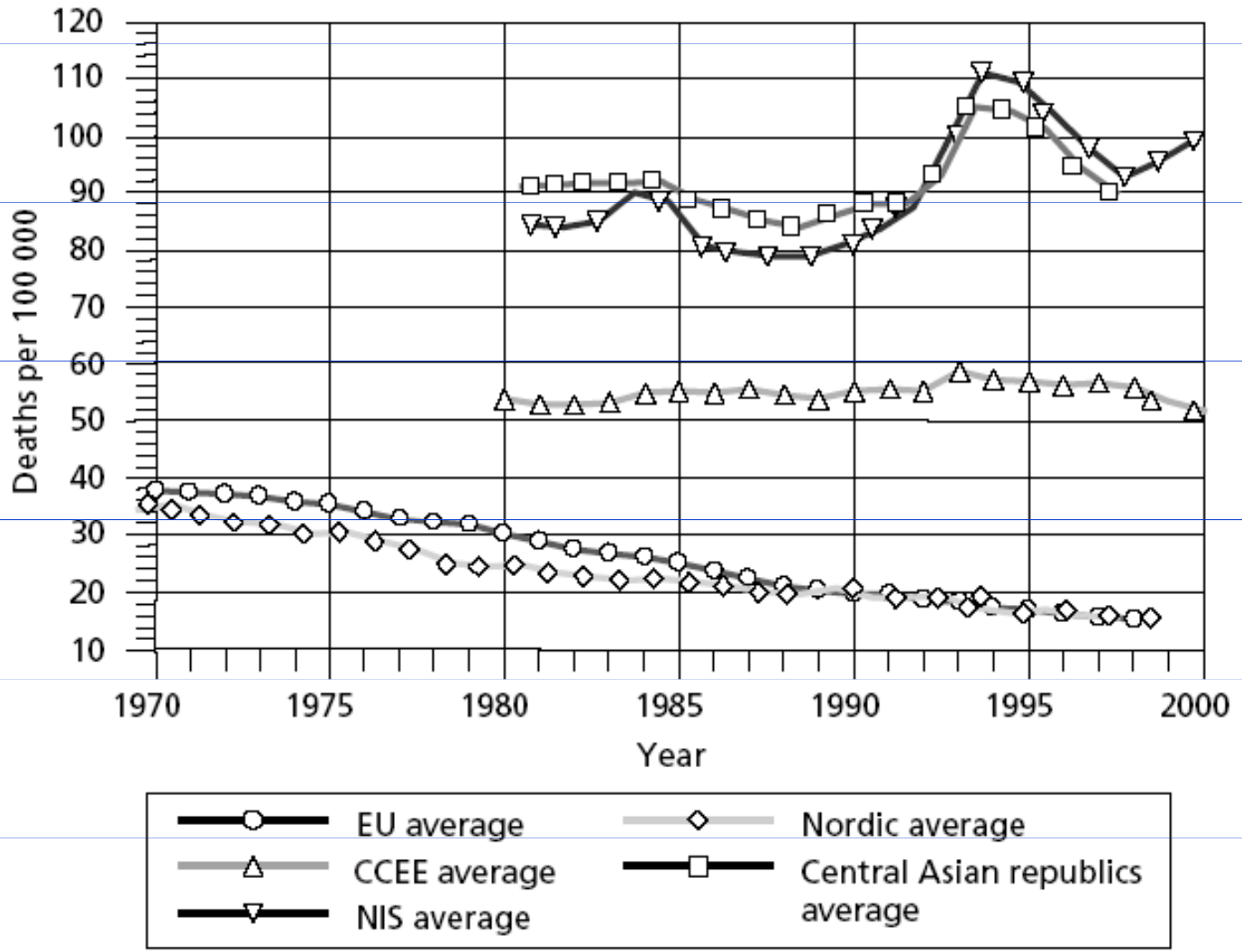
Source: adapted from Kohlmeier et al. *(30)*.

Fig. 1.9. Main causes of death in groups of countries in the European Region



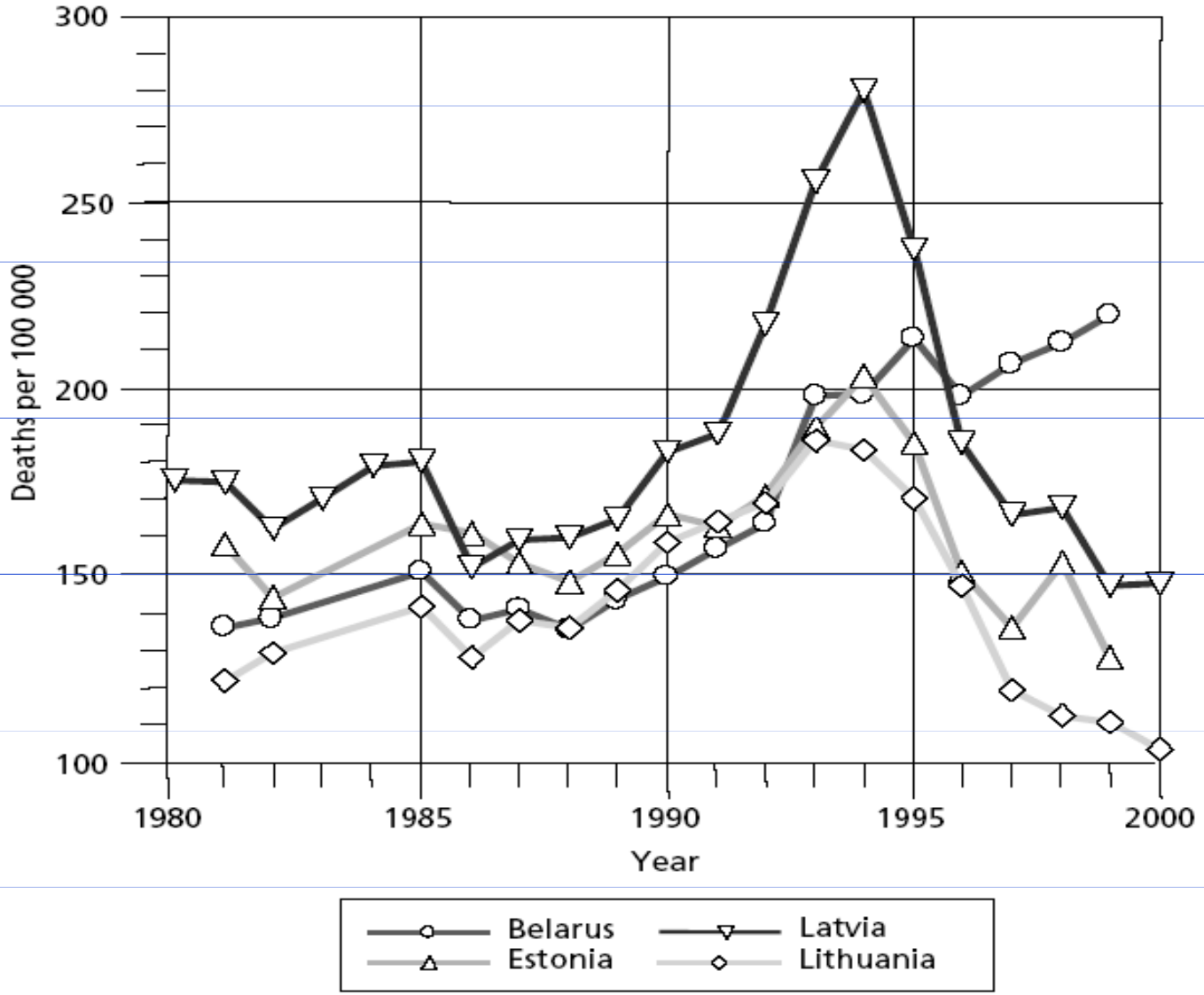
Source: European health for all database, WHO Regional Office for Europe, 2001.

Fig. 1.10. Average age-standardized mortality from cerebrovascular disease in men and women aged 25–64 years, European Region



Source: Mortality indicators by cause, age and sex (database), WHO Regional Office for Europe, 2002.

Fig. 1.11. Age-standardized premature mortality from ischaemic heart disease in men and women aged 0–64 years, Belarus and the Baltic countries



Source: Mortality indicators by cause, age and sex (database), WHO Regional Office for Europe, 2002.

Fig. 1.31. Projected numbers of yearly incident hip fractures in EU countries, 1995–2050

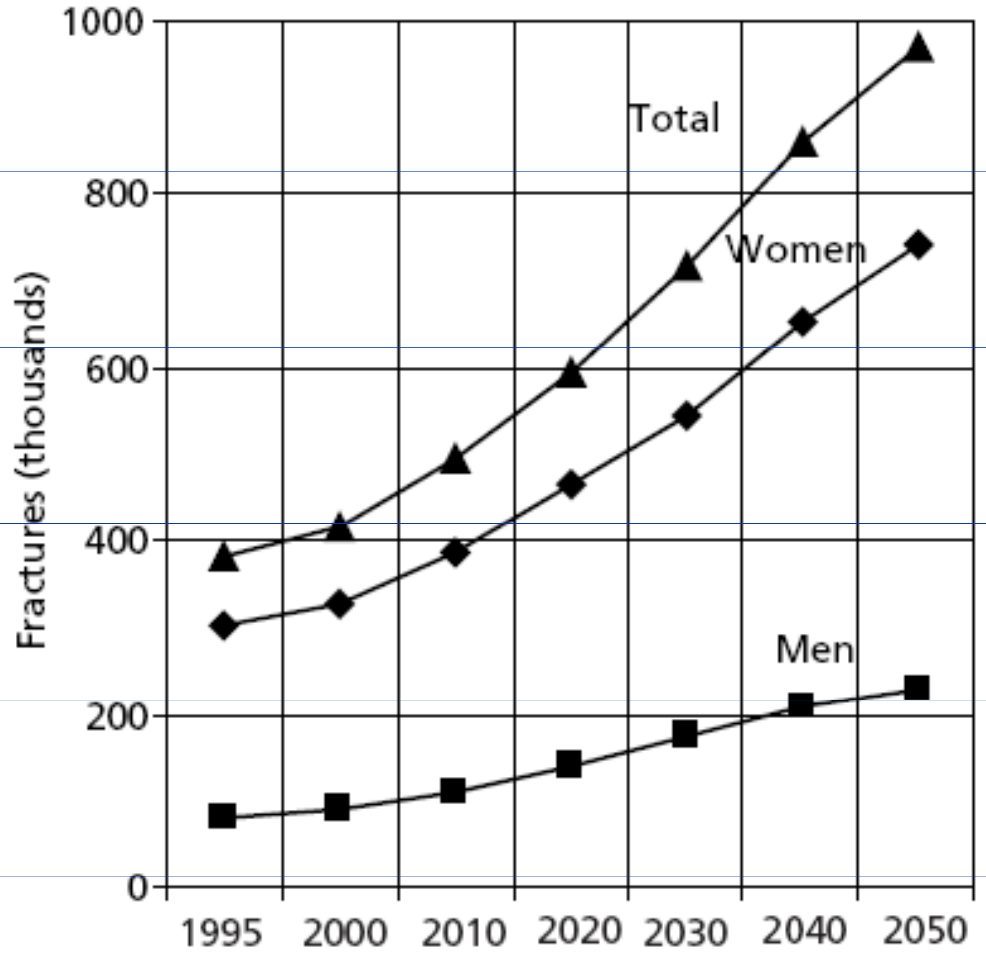
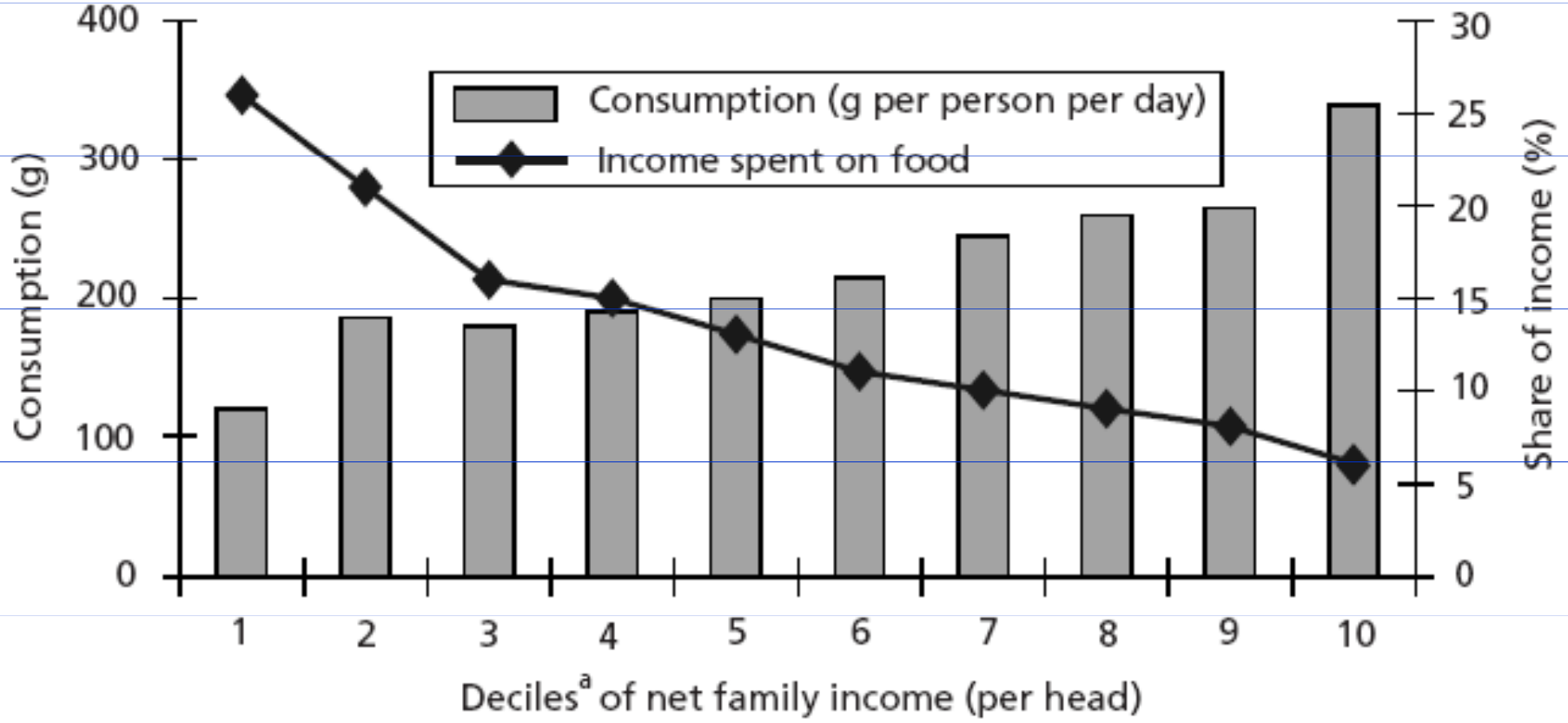


Fig. 1.33. Relationship of income to consumption of fresh fruits and vegetables and the share of income spent on food in the United Kingdom

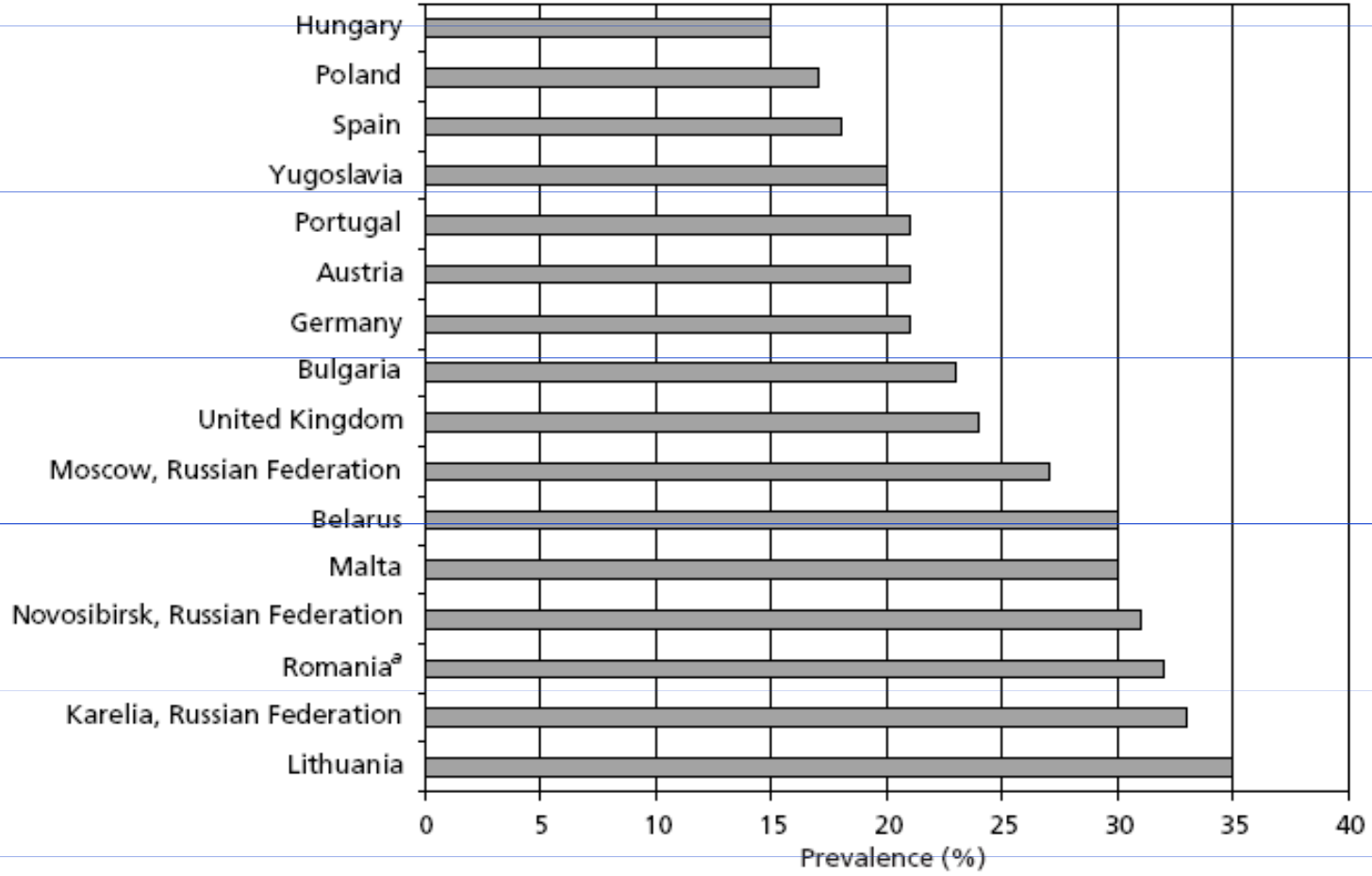


[a] 1 = lowest incomes; 10 = highest incomes.

Table 1.7. Social class and ill health: prevalence of diseases and risk factors in adults in the United Kingdom, 1994

Diseases and risk factors	Social class					
	Highest		Intermediate non-manual		Lowest	
	Men	Women	Men	Women	Men	Women
Ischaemic heart disease (%)	5.1	1.8	6.0	5.2	6.4	7.2
Stroke (%)	1.3	0.5	1.7	2.3	2.1	2.5
Mean blood pressure (mm/Hg)	136/76	130/72	138/76	136/73	139/77	141/75
Cholesterol > 6.5 mmol/l (%)	26	26	27	35	26	36
Haemoglobin < 13 g/dl (%)	3	9	5	12	5	13
Obesity (BMI > 30) (%)	9.9	11.8	13.7	15.0	14.0	22.6
Physically inactive (%)	14	15	15	17	21	22

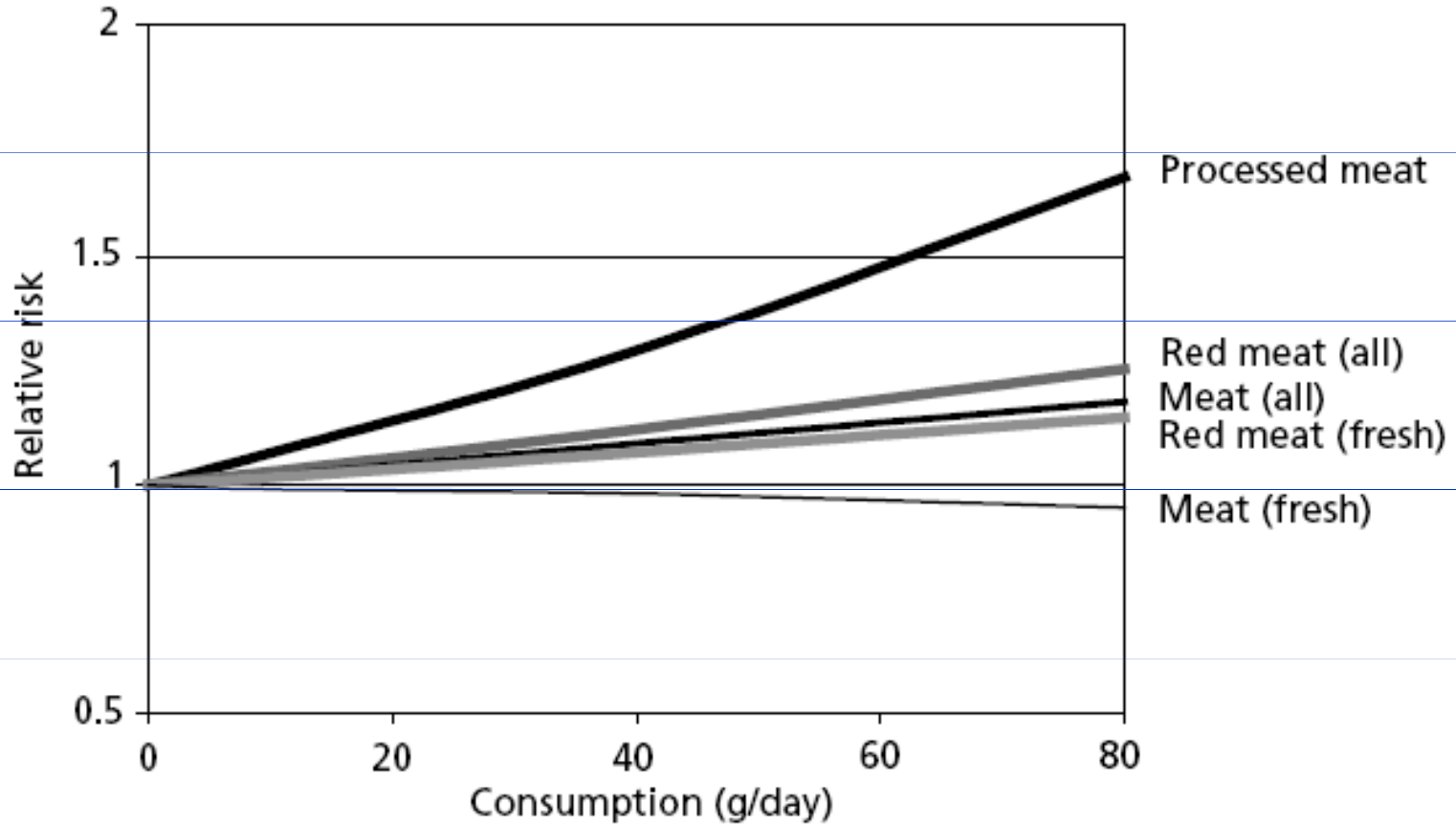
Fig. 1.13. Age-adjusted prevalence of high blood pressure (160/95 mmHg) in men aged 35–64, selected countries and regions in the European Region



[a] In Romania, the data are for men aged 41–65 years with blood pressure over 140/90 mmHg *(61)*.

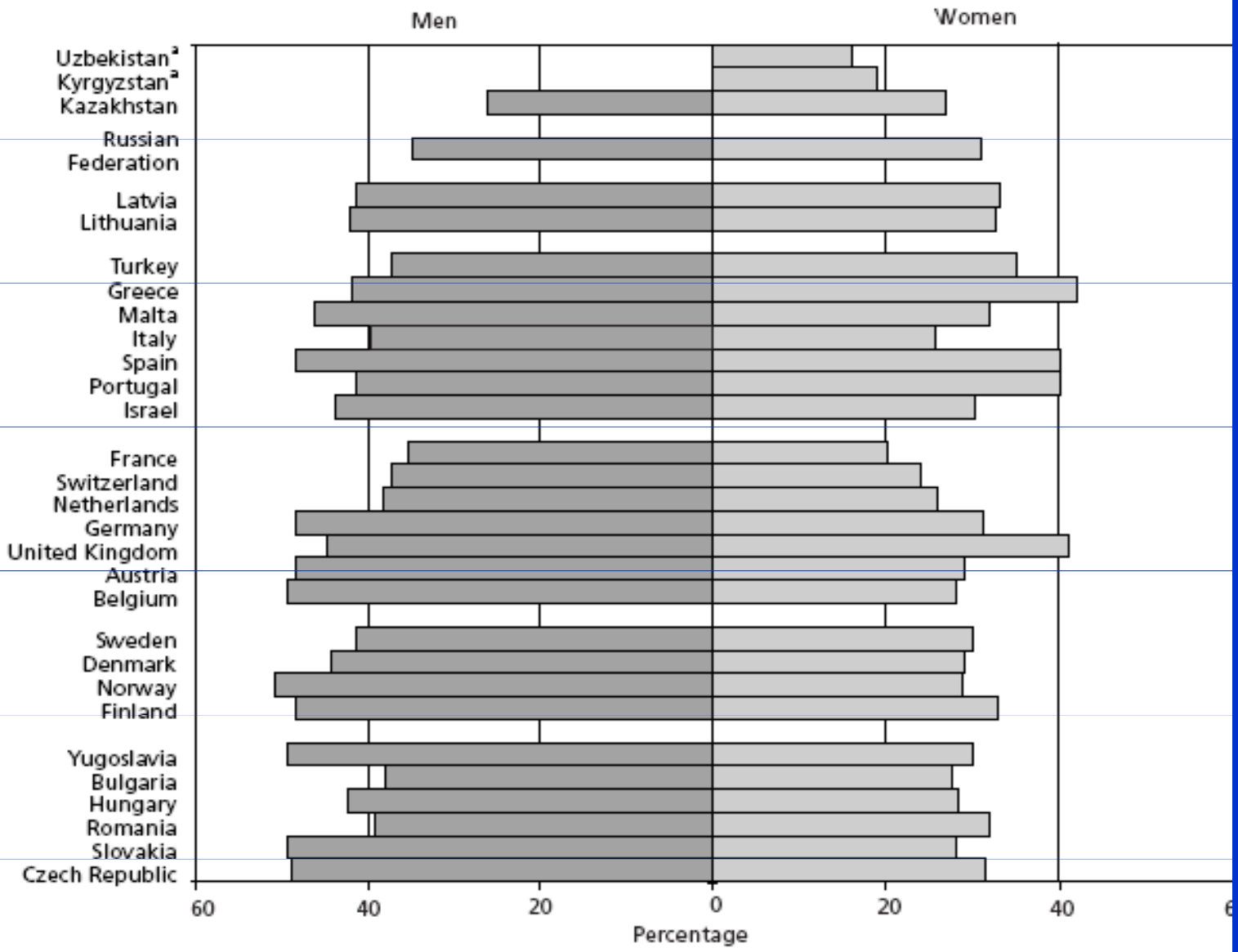
Source: data from a risk factor population survey conducted in demonstration centres of the WHO countrywide integrated noncommunicable disease intervention (CINDI) programme, 1999.

Fig. 1.14. Dose–response relationship between the consumption of red and processed meat and the risk of colorectal cancer



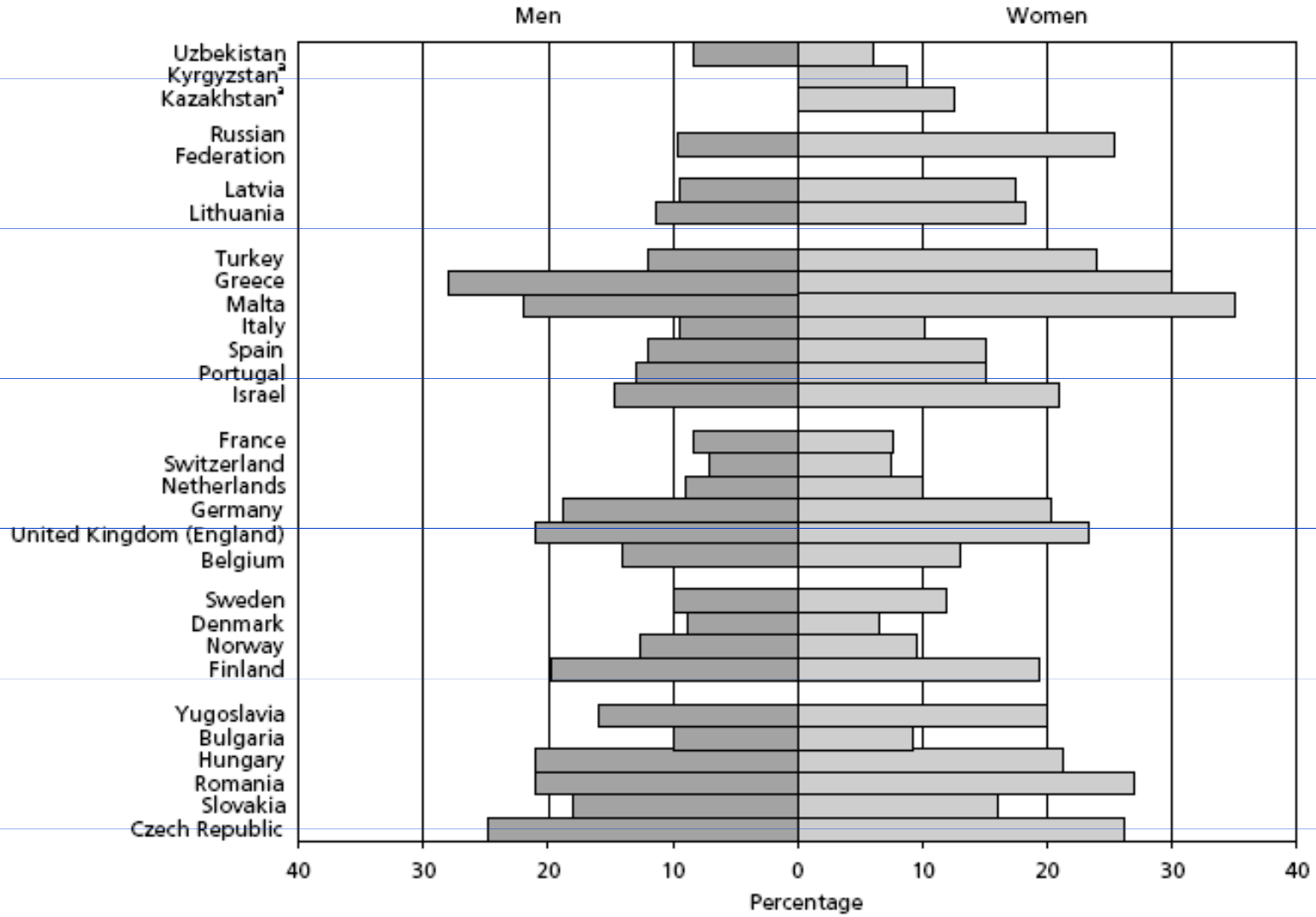
Source: Norat et al. *(72)*. Reprinted by permission of Wiley-Liss, Inc, a subsidiary of John Wiley & Sons, Inc.

Fig. 1.15. Overweight adults (BMI 25–29.9), European Region (%



[a] No data are available on overweight in men.

Fig. 1.16. Obese adults (BMI ≥30), European Region (%)



[a] No data are available on obesity in men.

Fig. 1.17. Proportion of 15-year-olds who report exercising vigorously twice a week or more, European Region

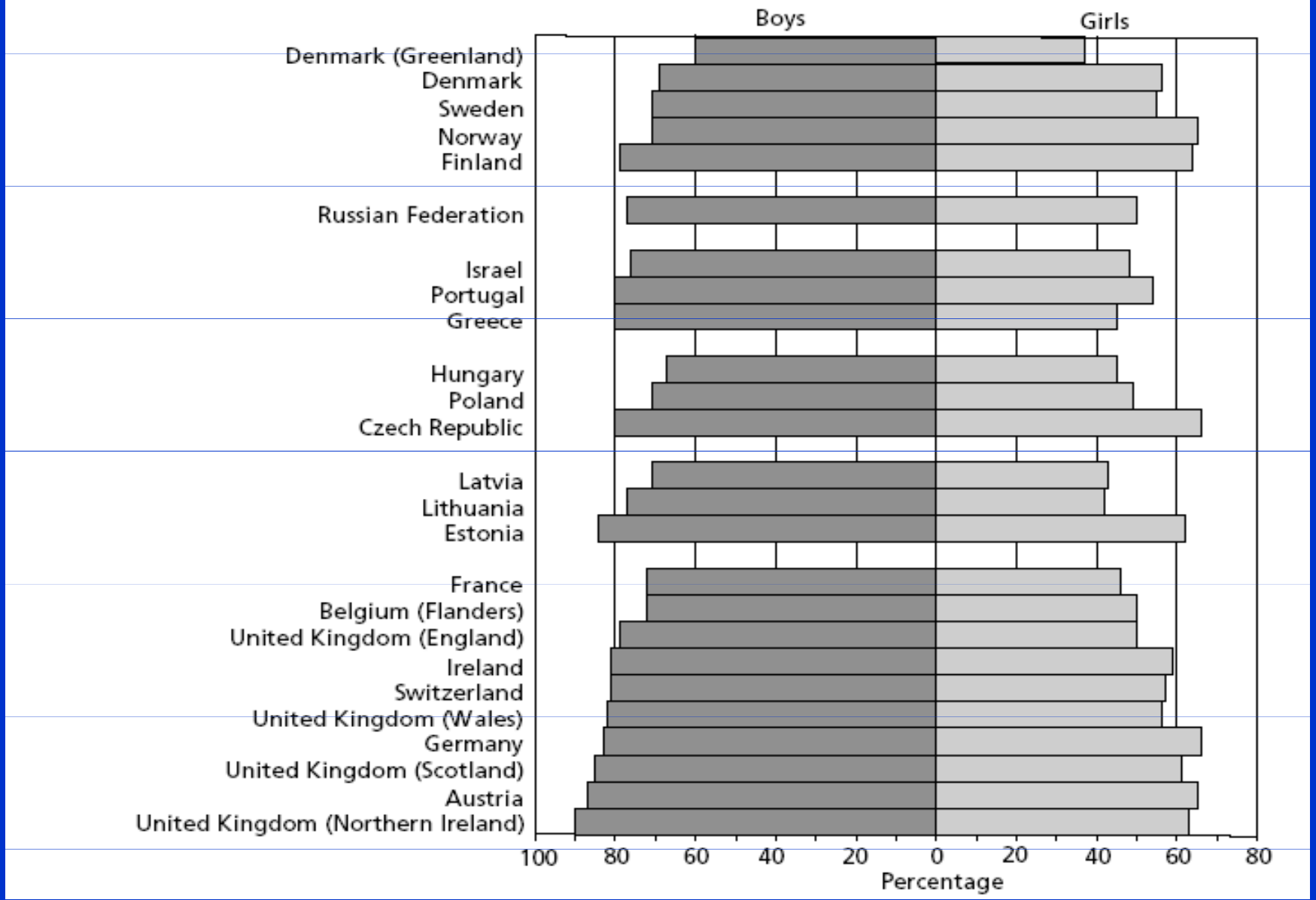
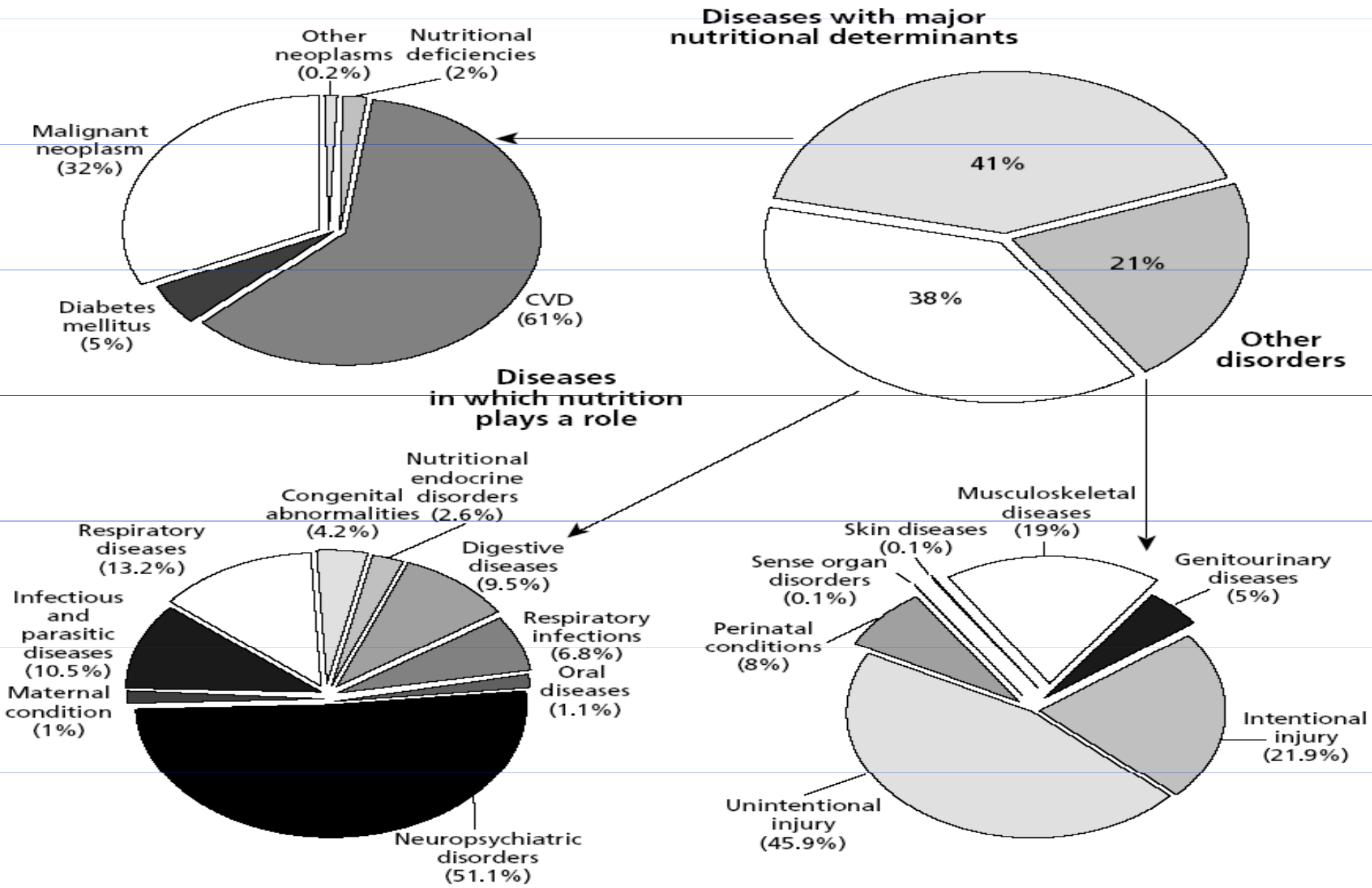
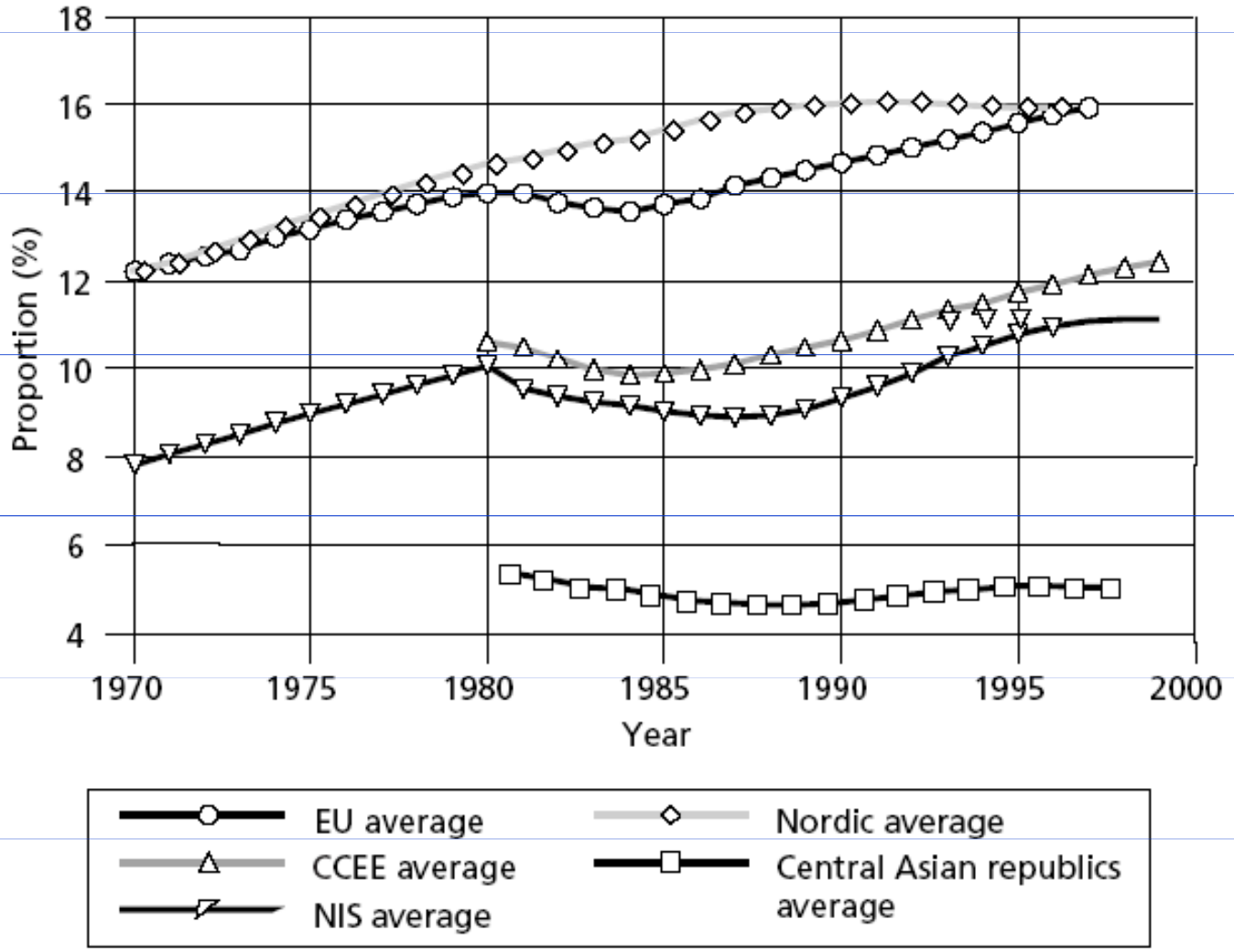


Fig. 1.1. Lost years of healthy life in the European Region, 2000



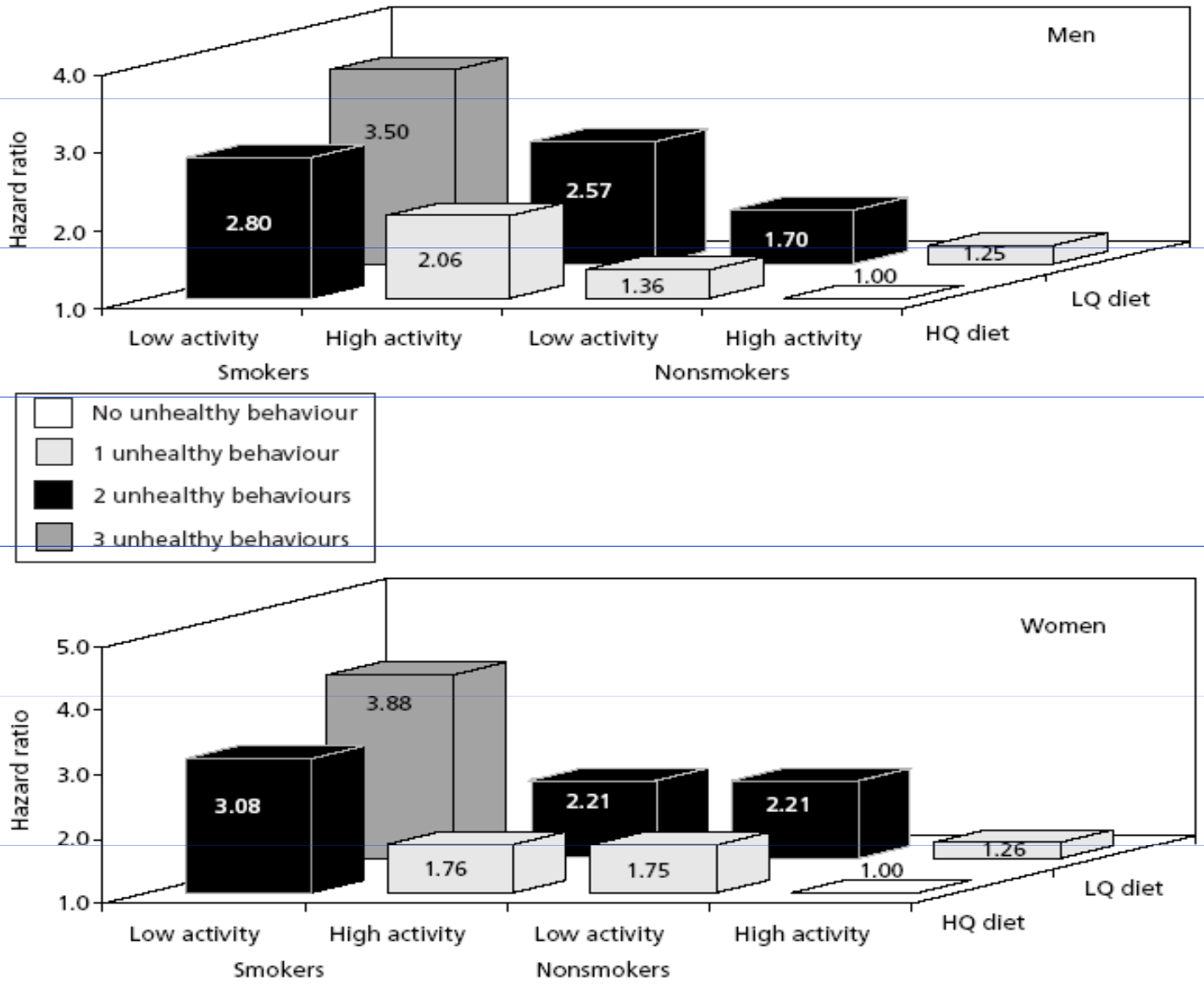
Source: adapted from *The world health report 2000. Health systems: improving performance (3).*

Fig. 1.28. Trends in the proportion of the population 65 years or older in the WHO European Region, 1970–1998



Source: European health for all database, WHO Regional Office for Europe.

Fig. 1.29. Adjusted hazard ratios of the individual and combined effects of diet, nonsmoking and physical activity on mortality in a sample of European men and women born between 1913 and 1918



Note: The ratios were adjusted for age at baseline, region and the number of chronic diseases. HQ diet = high-quality diet; LQ diet = low-quality diet.
Source: Haveman-Nies et al. *(197).*

Fig. 1.23. Percentage of infants being partially breastfed at 3 and 6 months, European Region, 1990s

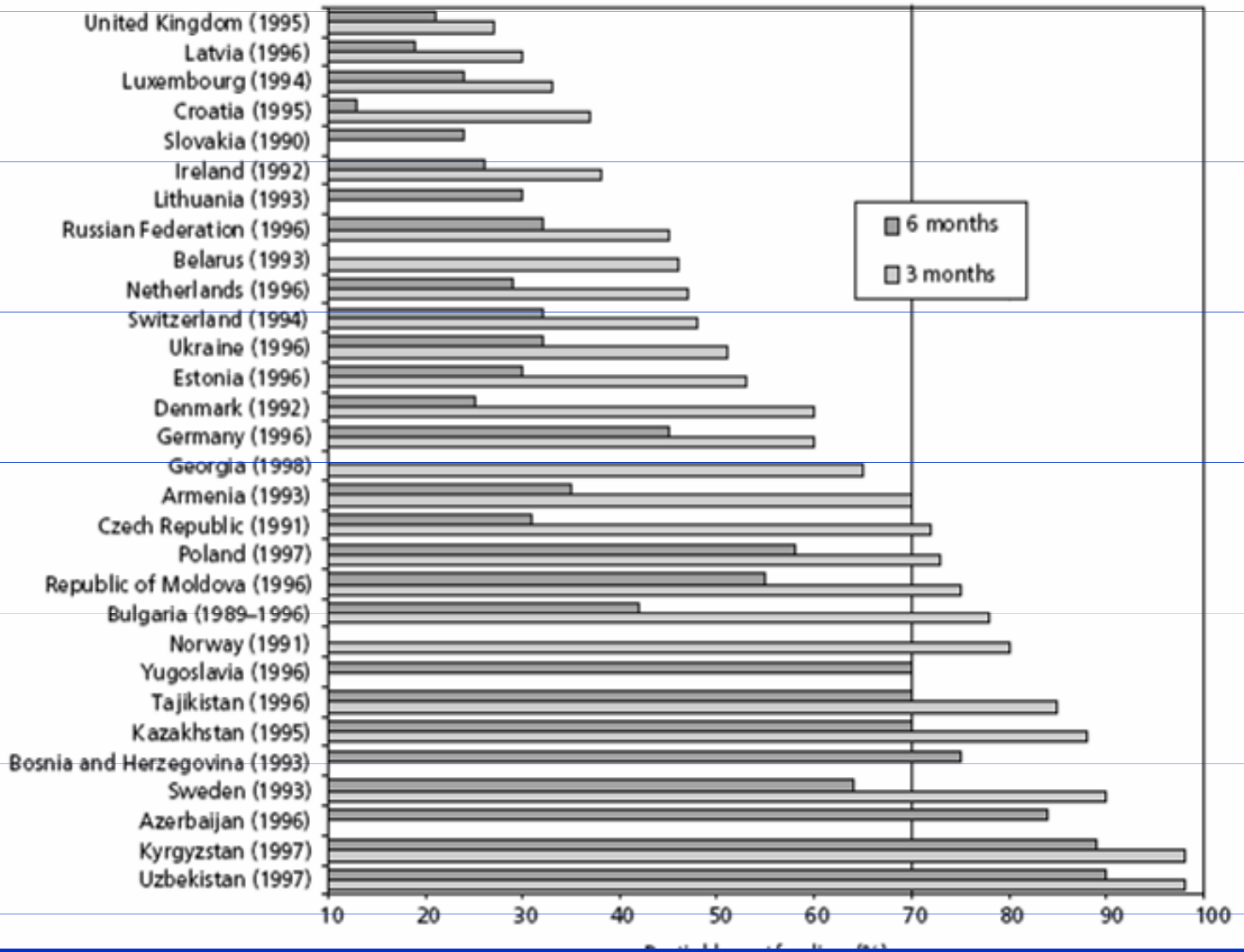
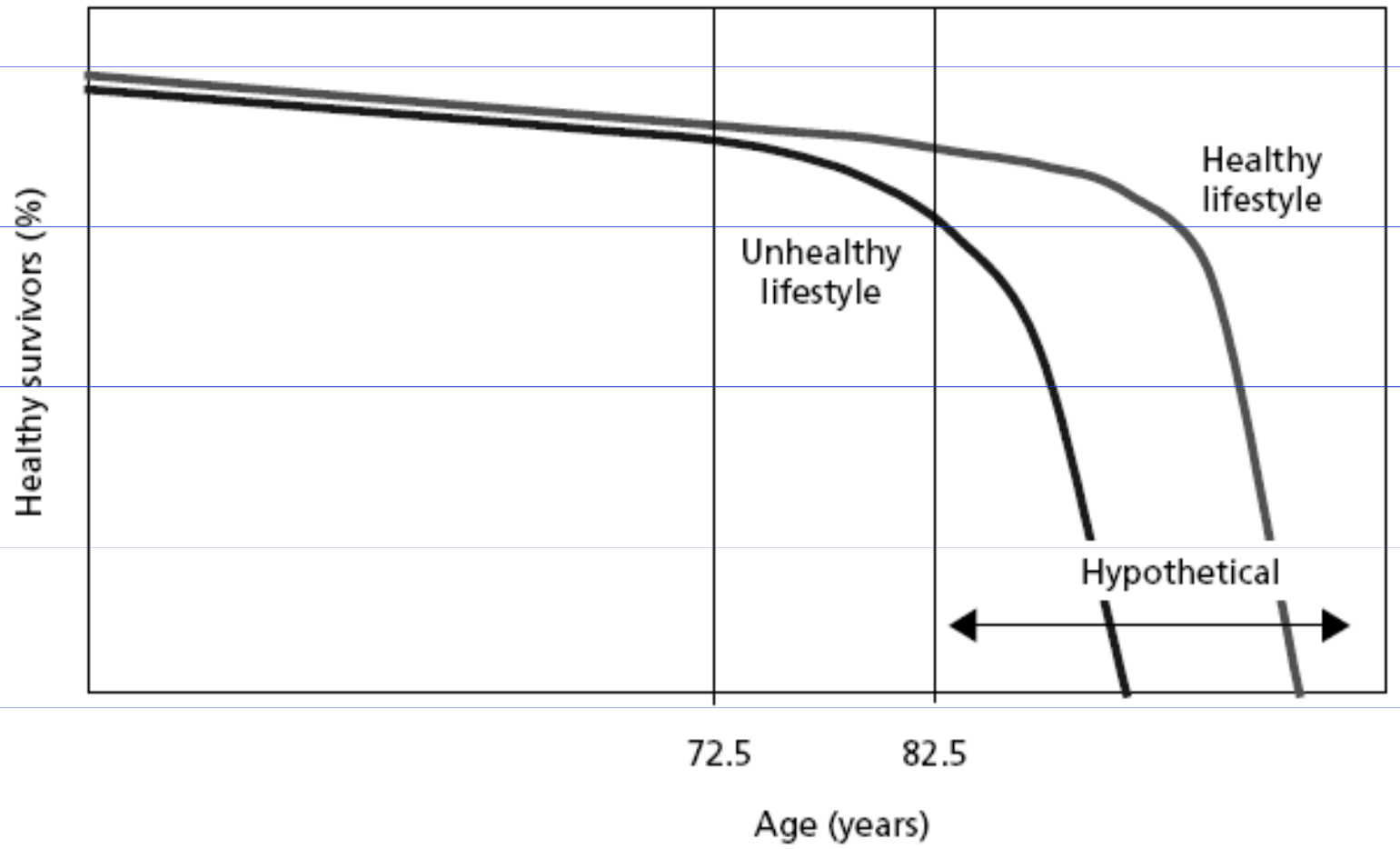


Table 1.6. Breastfeeding rates in high and low socioeconomic groups in the United Kingdom, 1999

Time	Breastfeeding rates (%)	
	Social class I	Social class V
At 1 week	84	40
At 6 weeks	73	23
At 4 months	56	13

Fig. 1.30. Effect of healthy lifestyles on healthy ageing in a sample of Europeans born between 1913 and 1918, including hypothesized effects after 2000



DIET & HEALTH GUIDELINES FOR CANCER PREVENTION
Short guidelines from the American Inst. for Cancer Research

1. Choose a diet rich in a variety of plant-based foods.
2. Eat plenty of vegetables and fruits.
3. Maintain a healthy weight and be physically active.
4. Drink alcohol only in moderation, if at all.
5. Select foods low in fat and salt.
6. Prepare and store foods safely.

And, more important, do not smoke at all!

For each one, you or me, for individuals: What shall I eat? How can I reduce my cancer risk? Which diet shall I choose to lower the chance of getting a cancer?

ADVICE to INDIVIDUALS

FOODS, EATING and related factors

From theAmerican Inst. for Cancer Research and the World Cancer Research Fund

1. Food supply and eating

• Choose predominantly plant-based diets rich in a variety of vegetables and fruits, pulses (legumes) and minimally processed starchy staple foods

2. Maintaining body weight

• Avoid being underweight or overweight and limit weight gain during adulthood to less than 5 kg (11 pounds)

3. Maintaining physical activity

• If occupational activity is low or moderate, take an hour's brisk walk or similar exercise daily, and also exercise vigorously for a total of at least one hour in a week

FOODS AND DRINKS

4. Vegetables and fruits
• Eat 400 - 800 grams (15 - 30 ounces) or five or more portions (servings) a day of a variety of vegetables and fruits, all year round
5. Other plant foods
• Eat 600 - 800 grams (20 - 30 ounces) or more than seven portions (servings) a day of a variety of cereals (grains), pulses (legumes), roots, tubers and plantains.c, f Prefer minimally processed foods. Limit consumption of refined sugar
6. Alcoholic drinks
• Alcohol consumption is not recommended. If consumed at all, limit alcoholic drinks to less than two drinks a day for men and one for women
7. Meat
• If eaten at all, limit intake of red meat to less than 80 grams (3 ounces) daily. It is preferable to choose fish, poultry or meat from non-domesticated animals in place of red meat
8. Total fats and oils
• Limit consumption of fatty foods, particularly those of animal origin. Choose modest amounts of appropriate vegetable oils

FOOD PROCESSING

9. Salt and salting
• Limit consumption of salted foods and use of cooking and table salt. Use herbs and spices to season foods
10. Storage
• Do not eat food which, as a result of prolonged storage at ambient temperatures, is liable to contamination with mycotoxins
11. Preservation
• Use refrigeration and other appropriate methods to preserve perishable food as purchased and at home
12. Additives and residues
• When levels of additives, contaminants and other residues are properly regulated, their presence in food and drink is not known to be harmful. However, unregulated or improper use can be a health hazard, and this applies particularly in economically developing countries
13. Preparation
• Do not eat charred food. For meat and fish eaters, avoid burning of meat juices. Consume the following only occasionally: meat and fish grilled (broiled) in direct flame; cured and smoked meats

DIETARY SUPPLEMENTS

14. Dietary supplements

• For those who follow the recommendations presented here, dietary supplements are probably unnecessary, and possibly unhelpful, for reducing cancer risk m TOBACCO

• Do not smoke or chew tobacco

At the country level, for a population: What should be done? Which foods, what diet could reduce cancer toll? What to do against cancer? How could we reduce cancer incidence and mortality?

PUBLIC HEALTH GOALS

FOOD SUPPLY, EATING and related factors
From theAmerican Inst. for Cancer Research
and the World Cancer Research Fund

1. Food supply and eating
• Populations to consume nutritionally adequate and varied diets, based primarily on foods of plant origin
2. Maintaining body weight
• Population average body mass indices throughout adult life to be within the range BMI 21 - 23, in order that individual BMI be maintained between 18.5 and 25
3. Maintaining physical activity
• Populations to maintain, throughout life, an active lifestyle equivalent to a physical activity level (PAL) of at least 1.75, with opportunities for vigorous physical activity

FOODS AND DRINKS

4. Vegetables and fruits
• Promote year-round consumption of a variety of vegetables and fruits, providing 7% or more total energy
5. Other plant foods
• A variety of starchy or protein-rich foods of plant origin, preferably minimally processed, to provide 45 - 60% total energy. Refined sugar to provide less than 10% total energy
6. Alcoholic drinks
• Consumption of alcohol is not recommended. Excessive consumption of alcohol to be discouraged. For those who drink alcohol, restrict it to less than 5% total energy for men and less than 2.5% total energy for women
7. Meat
• If eaten at all, red meat to provide less than 10% total energy
8. Total fats and oils
• Total fats and oils to provide 15% to no more than 30% total energy

FOOD PROCESSING

9. Salt and salting
• Salt from all sources should amount to less than 6 grams/day (0.25 ounces) for adults
10. Storage
• Store perishable food in ways that minimise fungal contamination
11. Preservation
• Perishable food, if not consumed promptly, to be kept frozen or chilled
12. Additives and residues
• Establish and monitor the enforcement of safety limits for food additives, pesticides and their residues, and other chemical contaminants in the food supply
13. Preparation
• When meat and fish are eaten, encourage relatively low temperature cooking

DIETARY SUPPLEMENTS

14. Dietary supplements

- Community dietary patterns to be consistent with reduction of cancer risk without the use of dietary supplements

TOBACCO

- Discourage production, promotion and use of tobacco in any form

Causes of foodborne disease

Foodborne disease is defined as any disease of an infectious or toxic nature caused, or thought to be caused, by the consumption of food or water. It can result from contamination with an extrinsic chemical or biological hazard and sometimes from the intrinsic toxicity associated with food (Table 2.1).

Table 2.1. Causes of foodborne disease

Causes	Examples
Extrinsic hazards	
Chemical contaminants	Dioxins, polychlorinated biphenyls, heavy metals, cadmium, mercury, lead, pesticide residues, veterinary drug residues
Biological contaminants	Bacteria causing infection (such as *Salmonella*) or intoxication (such as *Clostridium botulinum*), helminths (such as roundworms), protozoa (such as *Giardia lamblia*), viruses (such as hepatitis A and Norwalk-like human caliciviruses), fungi and mycotoxins (such as aflatoxin), algae (such as dinoflagellates leading to paralytic shellfish poisoning), prions
Intrinsic hazards (natural toxins or antinutritional factors)	Oxalic acid (in rhubarb and spinach), alkaloids, solanine (in potatoes), dioscorine (in yams), cyanide (in cassava and lima beans), haemagglutinin (in red kidney beans), protease inhibitors (in legumes), phytic acid (in bran), amatoxin, psilocybin and others (in toxic mushrooms)

Adverse health effects can result from both acute and chronic exposure to foodborne chemicals and may include kidney and liver damage, fetal developmental disruption, endocrine system disruption, immunotoxicity and cancer *(2)*. Chemical hazards in foods can arise from several sources:

- environmental pollutants such as lead, mercury, polychlorinated biphenyls (PCBs), dioxins and radionuclides;
- agricultural and veterinary practices such as pesticides, fertilizers and veterinary drugs; and
- food-processing and packaging techniques (such as the use of chloropropanols and nitrosamines).

Most foodborne disease is thought to be of microbial origin. Microorganisms cause foodborne illness by one of essentially two mechanisms:

- infection: when viable organisms (bacteria, viruses or parasites) are present in food and enter the body, where their growth and metabolism produce the disease response; and

- intoxication: when the presence and (usually) growth of an organism in the food because of incorrect storage are accompanied by the accumulation of a toxin that is ingested with the food and causes illness.

For example, organisms causing intoxication include the bacteria *Bacillus cereus*, *Clostridium botulinum* and *Staphylococcus aureus*, algae and mycotoxins (mould toxins).

Prions, which are thought to be responsible for bovine spongiform encephalopathy (BSE) in cattle and new variant Creutzfeldt-Jacob disease (vCJD) in humans, are very different. They are proteins rather than complete organisms and recruit or convert proteins on the surface of neurons to an abnormal form that accumulates, which causes symptoms in the nervous system.

Fig. 2.1. Reported incidence of campylobacteriosis in selected European countries, 1985–1998

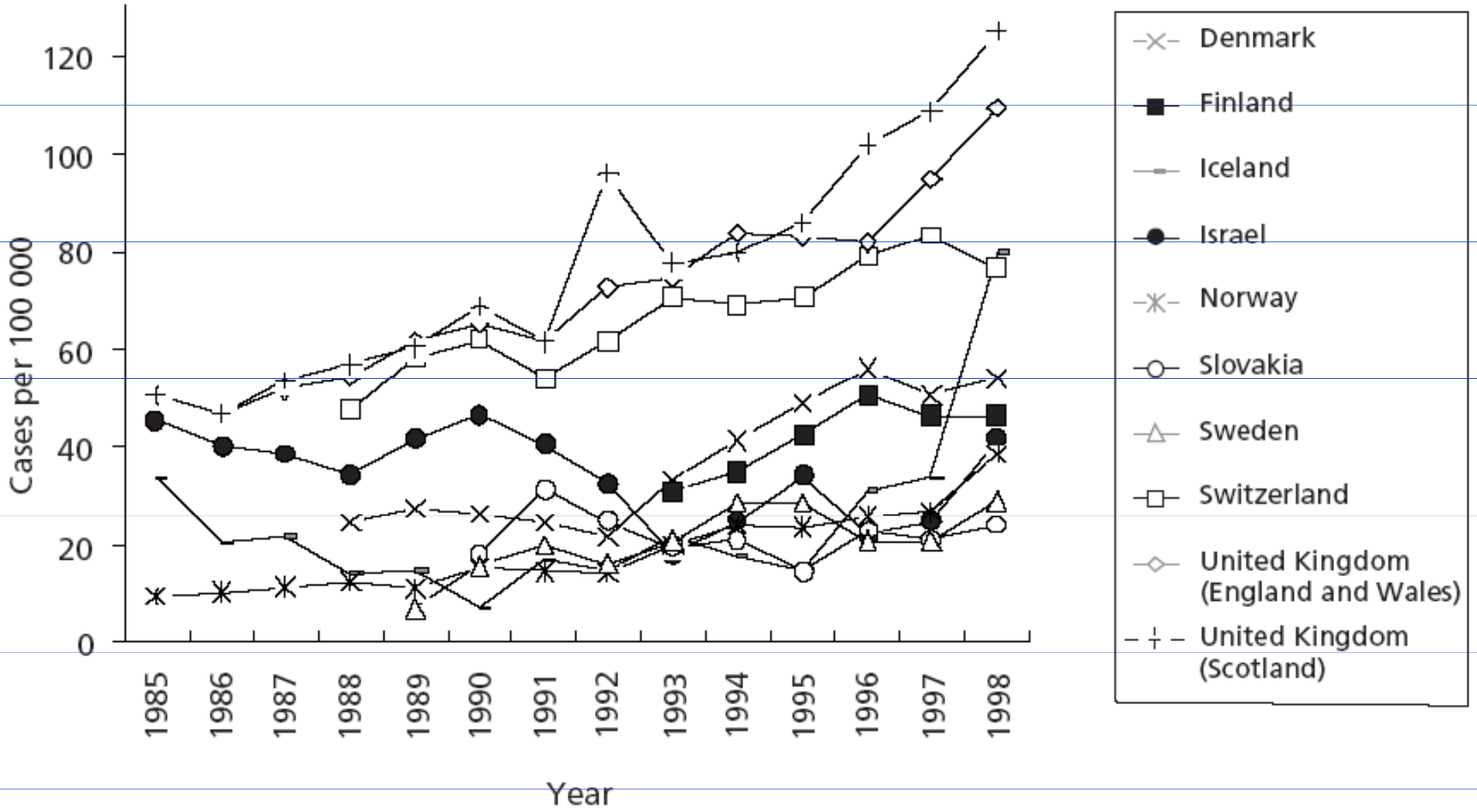


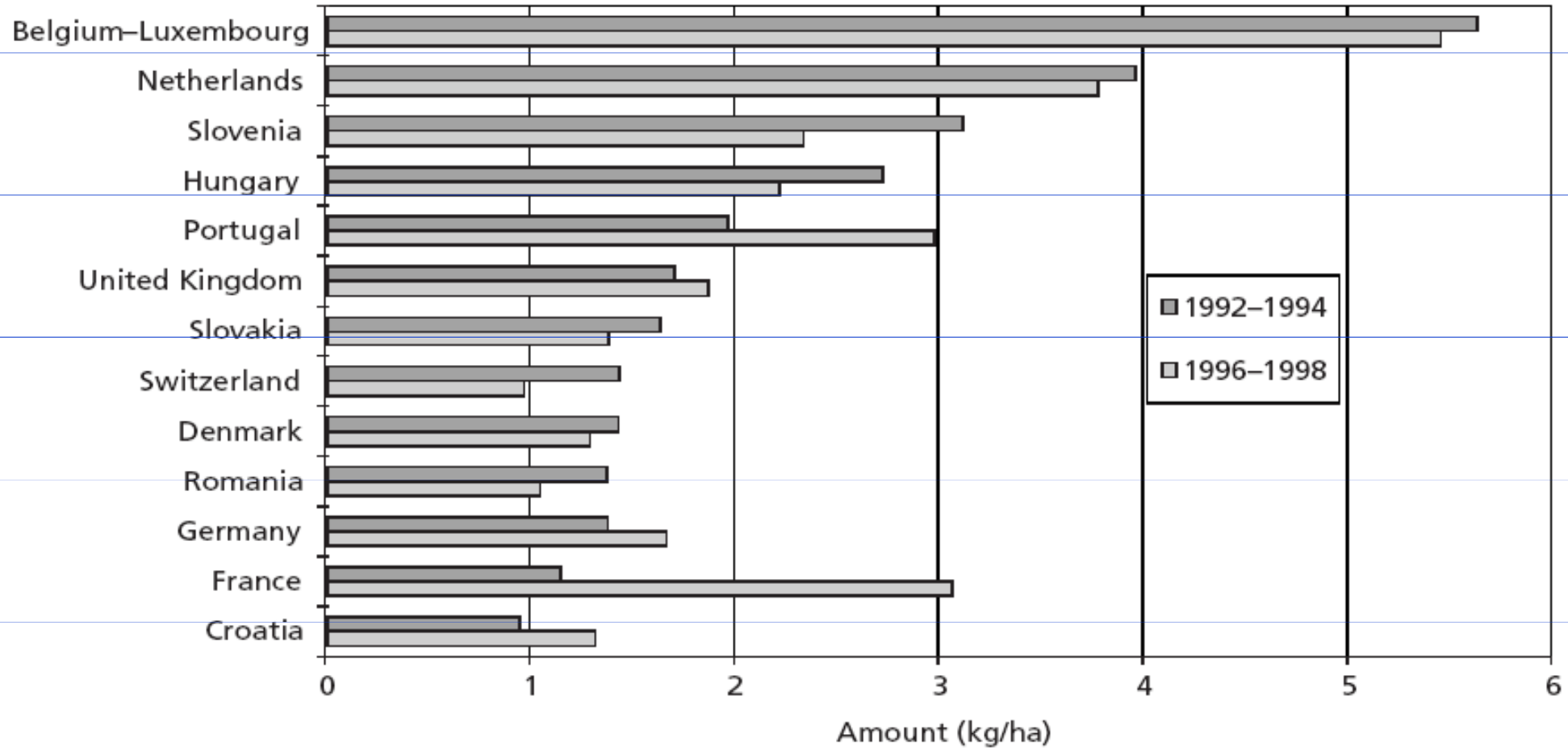
Table 2.2. GEMS/Food Europe comprehensive list of contaminants and foods

Contaminants	Foods
Aldrin, dieldrin, DDT (*p,p′*- and *o,p′*-), TDE (*p, p′*-), DDE (*p,p′*- and *p,o′*-) endosulfan hexachlorobenzene, heptachlor, heptachlor epoxide, chlordane, polychlorinated biphenyls (congeners no. 28, 52, 77, 101, 105, 114, 118, 123, 126, 138, 153, 156, 167, 169, 180 and 189), and dioxins (polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs))	Whole milk, dried milk, butter, eggs, animal fats and oils, fish, cereals,[a] vegetable fats and oils, human milk, total diet, drinking-water
Lead	Milk, canned/fresh meat, kidney, fish, mollusks, crustaceans, cereals,[a] pulses, legumes, canned/fresh fruit, fruit juice, spices, infant food, total diet, drinking-water
Cadmium	Kidney, molluscs, crustaceans, cereals,[a] flour, vegetables, total diet
Mercury	Fish, fish products, mushrooms, total diet
Aflatoxins	Milk, milk products, maize, cereals,[a] groundnuts, other nuts, spices, dried figs, total diet
Ochratoxin A	Wheat, cereals,[a] wine
Dioxynivalenol	Wheat, cereals[a]
Patulin	Apple juice
Fumonisins	Maize, wheat
Diazinon, fenitrothion, malathion, parathion, methyl parathion, methyl pirimiphos, chlorpyrifos	Cereals,[a] vegetables, fruit, total diet
Aldicarb, captan, dimethoate, folpet, phosalone	Cereals,[a] vegetables, fruit, total diet
Dithiocarbamates	Cereals,[a] vegetables, fruit, total diet, drinking-water
Radionuclides (caesium-137, strontium-90, iodine-131, plutonium-239)	Cereals,[a] vegetables, fruit, total diet, drinking-water
Nitrate/nitrite	Drinking-water
Inorganic arsenic	Drinking-water

[a] Includes other staple foods.

Source: Improved coordination and harmonization of national food safety control services: report on a joint WHO/EURO–FSAI meeting, Dublin, Ireland 19–20 June 2001 (12).

Fig. 2.6. Use of pesticides (kg active ingredient per hectare of agricultural land) in selected European countries, 1992–1994 and 1996–1998



Environmentální (chemické) karcinogeny

What is a chemical carcinogen?

- Any discrete chemical compound which has been shown to cause cancer in human or animal studies.
- Hundreds of individual compounds have been shown to induce cancers. Many thousands of additional compounds are “suspect” carcinogens.
- Many are commonly used in laboratory operations, shops and factories.
- NTP; IARC - carcinogen classification based on rodent tests.

How is chemical carcinogenicity determined?

- Epidemiological studies determine the relationship between a cancer suspect chemical and a human population over a long period of time.
- Animal studies directly induce cancer in test animals using a large sample of animals, usually of two or more species with varying dose and time parameters.
- Experiments with animals are based on the premise that chemicals that produce cancer in animals will have similar effects on human cells. Most known human carcinogens produce cancer in experimental animals.

What materials are carcinogens?

- Asbestos
- Certain chemicals
- Coal tars and coke oven emissions
- Natural products (progesterone, safrole)
- Tobacco smoke
- Ionizing radiation
- Ultraviolet radiation

Examples of chemical carcinogens?

- Epoxides:
  - Ethylene oxide
  - Propylene oxide
- Organohalogen comp.:
  - Vinyl chloride
  - Carbon tetrachloride
  - Chloroform
  - Hexachlorobenzene
  - Trichloroethylene
- Hydrazines:
  - Hydrazine (and salts) 1,2-Dimethylhydrazine
- N-Nitroso compounds:
  - N-Nitrosodimethylamine
- Aromatic Amines:
  - Benzidine
  - Aniline
  - o-Anisidine
  - o-Toluidine
- Aromatic hydrocarbons:
  - Benzene
  - Benz[a]anthracene
  - Benzo[a]pyrene

Human carcinogens - environmental:

- Aflatoxins
- Asbestos
- Benzene
- Cadmium
- Coal tar
- Second hand smoke
- Creosote
- DDT
- Polycyclic aromatic hydrocarbons
- Radon
- Solar Radiation

What factors influence the development of cancer?

- Dose--amount and length of exposure. The lower the dose the least likely you are to develop cancer or related diseases.
- Environmental or "lifestyle" factors.
  - Cigarette smoking (co-carcinogen)
  - Alcohol consumption (co-carcinogen)
  - Diet--high fat consumption, natural antioxidants
  - Geographic location--industrial areas, UV light
  - Therapeutic drugs--some are known carcinogens
  - Inherited conditions

PERZISTENTNÍ ORGANICKÉ POLUTANTY (POPs)

VLASTNOSTI

PERZISTENCE
LIPOFILITA
NA HRANICI DETEKOVATELNOSTI V ABIOTICKÝCH SLOŽKÁCH
KUMULACE V BIOTICKÝCH SLOŽKÁCH
CHRONICKÉ DLOUHODOBÉ PŮSOBENÍ

ZDROJE

SPALOVÁNÍ KOMUNÁL. A PRŮMYSL. ODPADU
SPALOVÁNÍ FOSILNÍCH PALIV
METALURGICKÉ PROCESY
PROVOZ SPALOVACÍCH MOTORŮ
BĚLENÍ BUNIČINY
CIGARETOVÝ KOUŘ

VÝSKYT

GLOBÁLNÍ ROZŠÍŘENÍ
ATMOSFÉRA (EMISE)
HYDROSFÉRA (ODP. KANÁLY, PRŮSAKY)
PEDOSFÉRA (APLIKACE)
VOLATILNÍ
SEMIVOLATILNÍ
RŮZNÁ POHYBLIVOST
PŘECHOD DO VĚTŠÍCH ZEMĚPIS. ŠÍŘEK

POLYCYKLICKÉ AROMATICKÉ UHLOVODÍKY (PAHs)

Modelová látka: benzo[a]pyren (BaP)
Metabolismus, mutagenita a karcinogenita závisí na struktuře (počet a uspořádání kondenzovaných jader). Karcinogenní sloučeniny vznikají metabolizací v játrech.
V prostředí reakce s jinými látkami - chlorované deriváty, nitro deriváty (nitro-PAH) - větší toxicita

HALOGENOVANÉ AROMATICKÉ UHLOVODÍKY

polychlorované bifenyly (PCB), dibenzo-p-dioxiny (PCDD), dibenzofurany (PCDF).
Účinky závisí na struktuře, stupni chlorinace a typu substituce.
Modelová látka: 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD)
Toxický ekvivalentový faktor (TEF)
Mechanismus působení: AhR - aryl hydrocarbon receptor

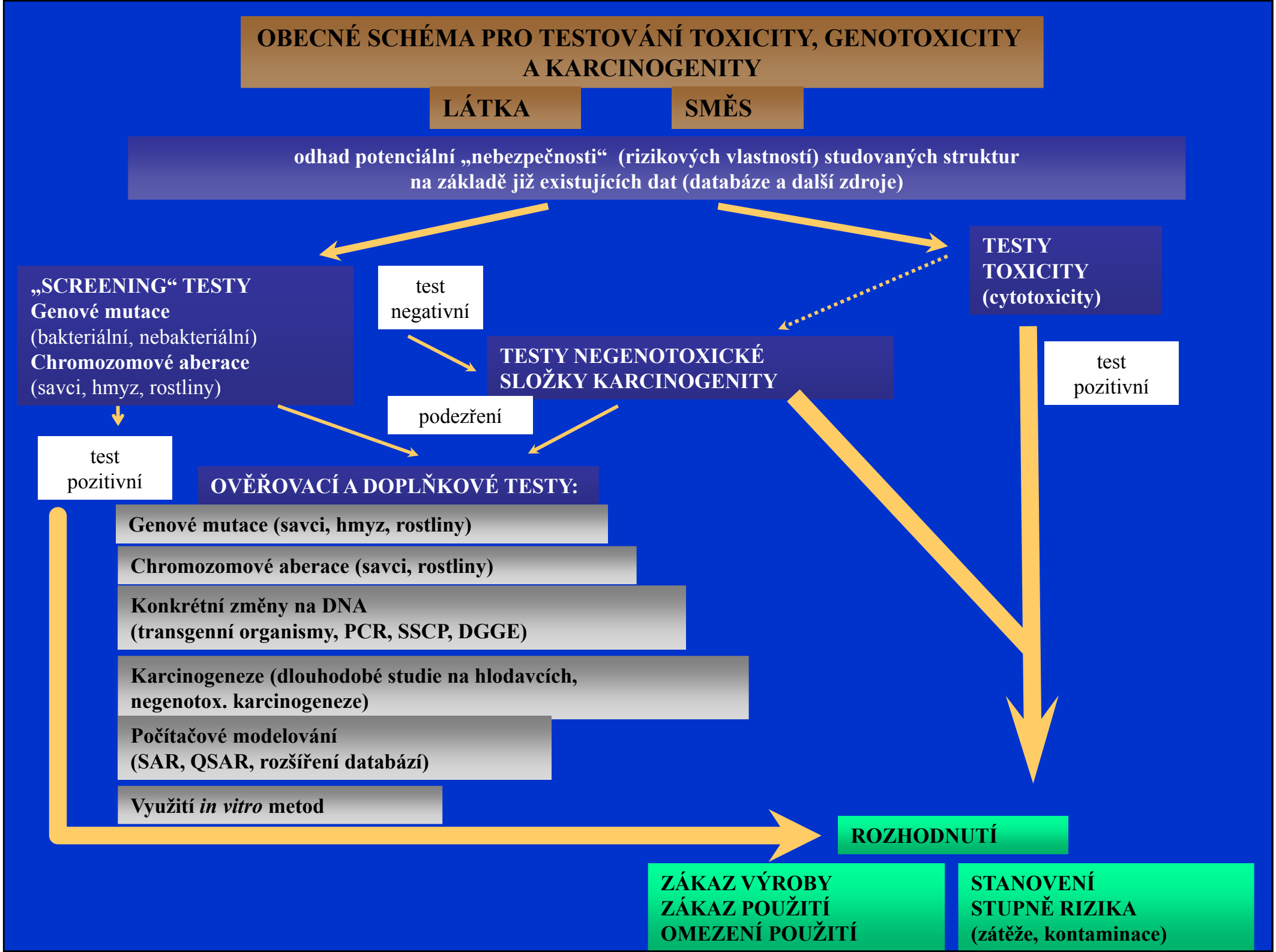
CHLOROVANÉ PESTICIDY
DDT, izomery hexachlorcyklohexanu (lindan)

FTALÁTY
estery kyseliny ftalové - průmysl plastických hmot

INDUKTORY PROLIFERACE PEROXISOMŮ (peroxisome proliferators)
Mechanismus působení: PPAR - perox. proliferator activated receptor
proliferace peroxisomů a aktivace P450 v játrech hlodavců
hepatokarcinogeneze

ESTROGENNÍ AKTIVITY
DDT, chlorované pesticidy, PCB, PBB - závisí na struktuře

XENOBIOTICKÉ LIPIDY
vznik konjugátů lipidů a organických chlorovaných látek -
bioakumulace, perzistence, škodlivé účinky


OBECNÉ SCHÉMA PRO TESTOVÁNÍ TOXICITY, GENOTOXICITY A KARCINOGENITY
LÁTKA
SMĚS
odhad potenciální „nebezpečnosti“ (rizikových vlastností) studovaných struktur na základě již existujících dat (databáze a další zdroje)
„SCREENING“ TESTY
Genové mutace
(bakteriální, nebakteriální)
Chromozomové aberace
(savci, hmyz, rostliny)
test negativní
TESTY NEGENOTOXICKÉ SLOŽKY KARCINOGENITY
TESTY TOXICITY (cytotoxicity)
test pozitivní
podezření
test pozitivní
OVĚŘOVACÍ A DOPLŇKOVÉ TESTY:
Genové mutace (savci, hmyz, rostliny)
Chromozomové aberace (savci, rostliny)
Konkrétní změny na DNA
(transgenní organismy, PCR, SSCP, DGGE)
Karcinogeneze (dlouhodobé studie na hlodavcích, negenotox. karcinogeneze)
Počítačové modelování
(SAR, QSAR, rozšíření databází)
Využití in vitro metod
ROZHODNUTÍ
ZÁKAZ VÝROBY
ZÁKAZ POUŽITÍ
OMEZENÍ POUŽITÍ
STANOVENÍ STUPNĚ RIZIKA
(zátěže, kontaminace)

KLASIFIKACE KARCINOGENŮ PODLE TYPU PŮSOBENÍ

GENOTOXICKY PŮSOBÍCÍ KARCINOGENY

Látky nebo jejich metabolity reagují s DNA (vznik aduktů, mutace)

Přímo mění strukturu nebo počty chromozómů

Mohou být též mitogenní nebo cytotoxické

Většinou druhově a orgánově nespecifické, molekulární cíl je DNA

NEGENOTOXICKY (EPIGENETICKY)PŮSOBÍCÍ KARCINOGENY (epigenetická toxicita)

Jsou druhově a orgánově specifické, mol. cílem jsou všechny buněčné a mimobuněčné složky různých orgánů vyjma DNA

MITOGENY

Mitogenní (adaptivní) stimulace růstu (často přes receptory)

Sekundárně usnadňují bun. proliferací vznik dalších mutací

Mohou způsobit přednostní růst preneoplastických buněk

CYTOTOXICKÉ LÁTKY

Způsobují letalitu buněk

Indukují regenerativní růst

Sekundárně usnadňují bun. proliferací vznik dalších mutací

Mohou způsobit přednostní růst preneoplastických buněk

BIOLOGICKÉ CHARAKTERISTIKY PRO KLASIFIKACI GENOTOXICKÝCH A NEGENOTOXICKÝCH KARCINOGENŮ

Genotoxické karcinogeny

Mutagenní
Reagují přímo s DNA
Tumorigenicita je dávkově závislá
Práh??
Mohou být kompletními karcinogeny
Ireverzibilní
Obvykle nejsou kmenově nebo druhově specifické
Fungují v iniciační a progresívní fázi nádorového procesu

Příklady:
Nitrosoaminy
Polycyklické aromatické uhlovodíky
Mykotoxiny (aflatoxin B)
Aromatické aminy
Nitrosourea

Negenotoxické karcinogeny

Nemutagenní
Nereagují přímo s DNA
Vykazují práh
Reverzibilní
Obvykle jsou kmenově, druhově nebo tkáňově specifické
Fungují v promoční fázi nádorového procesu

Příklady.
Chlorované sloučeniny (chloroform)
Organické chlorované pesticidy (dieldrin, DDT, chlordan)
Peroxisomové proliferátory (klofibrát, nafenopin)
Ostatní organické chlorované látky (dioxiny-TCDD, PCB)
Hormony (estradiol)
Barbituráty (phenobarbital)

Chemikálie jsou označovány jako **karcinogeny**, jestliže v exponované lidské populaci je vyšší frekvence nádorů než v neexponované populaci nebo jestliže se objevují nádory u zvířat, kterým byla chemikálie podávána.
Mutagenita se nerovná karcinogenitě. Genotoxicky působící karcinogeny (nebo jejich metabolity) jsou mutageny (pozitivní v Amesově testu), ale mutageny nejsou vždy karcinogeny.
Negenotoxické karcinogeny - termín označuje jen, že látka nezpůsobuje genetické mutace (negativní v Amesově testu).
Lépe **epigenetická toxicita**, která naznačuje mechanismus, který reverzibilně mění fenotyp buněk přes biochem. dráhy, které zapínají a vypínají geny (mění jejich expresi) prostřednictvím vnitrobuněčných systémů. Tento proces je pod homeostatickou kontrolou okolních buněk zprotředkovanou GJIC.
Vzhledem k tomu, že řada látek může působit genotoxicky i negenotoxicky, je lépe hovořit o genotoxických a negenotoxických (epigenetických) mechanismech působení.
Stále více je zdůrazňováno, že faktory z vnějšího prostředí je třeba studovat ne testovat. Je třeba vytvářet vědecké hypotézy a studovat mechanismy působení chemických látek a jiných faktorů.
Celý problém je dále komplikován tím, že většinou dochází k expozici směsí různých látek a pak je třeba brát ohled na aditivní, synergické či antagonické interakce jak na buněčné tak organismální úrovni.

JE DANÁ LÁTKA KARCINOGEN?

Způsobuje iniciaci, podporuje růst preneoplastických buněk nebo způsobuje stálou přeměnu nebo progresi těchto buněk?

Údaje z experimentů na lab. zvířatech a z epidemiol. studií - expozice akutními nebo chronickými dávkami - vysoké dávky

Extrapolace na nízké chronické expozice je velmi obtížná
- mnohoúrovňová hierarchická struktura mnohobuněčných organismů
- obranné a reparační mechanismy na všech úrovních
- existence adaptivních mechanismů - příčina tzv. hormeze
- expozice směsí látek (aditivita, synergismus, antagonismus)

Odpověď záleží na mnoha faktorech, mj.:
- kdy během vývoje dojde k expozici (embryogeneze, adolescence, dospělost, stáří)
- na typu buněk (kmenové, progenitorové, diferencované, dělící se, klidové)
- na následujících dávkách - adaptace, aditivita, synergismus

BIOLOGICKÉ TESTY – DESIGN, ODHADY RIZIK

Cílem je zabránit potenciálním toxikologickým důsledkům a vysvětlovat (a je-li to možné predikovat) děje následující po interakci chemikálií a léčiv s biologickými systémy.
Studie chronické toxicity a karcinogenity na laboratorních zvířatech – kvalitativní a kvantitativní dose-response data využitelná po extrapolaci k hodnocení potenciálních rizik pro člověka po expozici danou látkou.
Dávka ovlivňuje mechanismus. Proto karcinogenní účinky pozorované po vysokých dávkách, nemusí nastat po nízkých dávkách, zvláště jedná-li se o negenotoxicky působící látky.
Proto jsou velmi důležité průběhy křivek dávka-odpověď.
Stanovení tzv**. maximální tolerované dávky (MTD)**
různé způsoby výpočtů, počet dávkových skupin a rozvrstvení dávek. Pro odhad rizika po reálných expozicích u lidí je důležitý výběr dávek, dávkové odpovědi a exptrapolace z jiných druhů.
MTD je definována jako nejvyšší dávka chemikálie podaná zvířatům, která nezpůsobuje rozsáhlou toxicitu nebo snížení přežití (vyjma po indukci nádoru) – minimální toxická dávka.
Pro správné posouzení mechanismu účinku je důležité sledovat všechny úrovně – organismus, specif. tkáně, buňky – kombinace metod *in vivo* a *in vitro*

TESTY KARCINOGENITY

IN VIVO - vznik nádorů u laboratorních zvířat – neodlišují jednotlivá stadia karcinogeneze.

Studia na modelových orgánech –zvýšená proliferace, apoptóza

Iniciačně/promoční modely vícestupňové karcinogeneze – na kůži hlodavců.

IN VITRO – buněčné línie

Testy buněčné transformace – iniciace + promoce

tvorba morfologicky odlišných fokusů transformovaných buněk na speciálních líniích, např. permanentní myší línie BALB/3T3 nebo

morfologicky transformované kolonie primárních buněk SHE (embrya syrského křečka) - směs fibroblastů a epiteliálních buněk

Morfologická transformace (MT) je rozpoznatelný krok vícestupňového procesu konverze z nenádorového do neoplastického stadia. MT fenotyp je charakterizován ztrátou kontaktní inhibice, růstem v trojrozměrných útvarech v koloniívh s tzv. “criss cross” orientací. Buňky v MT koloniích jsou více basofilní a vykazují zvýšený poměr jádro/cytoplasma.

Epigenetická toxicita

Testy GJIC – na speciálních líniích se sledují změny GJIC (metabolická kooperace, přenos fluoresc. barviv), příp. změny v expresi konexinů
Změny v metylaci DNA
Exprese enzymu poly(ADP-riboso)polymerázy (PARP) a syntéza polymeru poly(ADP-ribosy) (pADPr) - úloha v metabolismu a reparaci DNA, kontrola bun. cyklu, diferenciace, embryogeneze
Buněčné markery - změny cytokinetiky, biochemické markery - změny aktivity specif. enzymů (P450 atd.)
????-hledání nových metod a přístupů

Tab. 1.2.1 Příklady prokázaných profesních humánních karcinogenů, u nichž je v ČR možno teoreticky zvažovat zhoubný nádor jako nemoc z povolání

Agens	Terčový orgán	Kodifikace dle seznamu nzp
4-aminobifenyl	močový měchýř	I/40
arsen a jeho sloučeniny	plíce, kůže	I/3
azbest (minerální křemičitan hořečnatý)	plíce, pleura, peritoneum,	
(larynx, GIT)		III/2
benzen	hematopoetický systém	I/35
benzidin	močový měchýř	I/40
berylium a jeho sloučeniny	plíce	I/5
bis(chlormetyl)eter	plíce	I/55
etylenoxid	plíce	I/54
hořčičný plyn (yperit,2,2´-dichlordietylsulfid)	plíce, larynx, farynx	I/27
chrom – sloučeniny šestimocného Cr	plíce, paranazální dutiny	I/7
kadmium a jeho sloučeniny	plíce, (prostata, ledviny)	I/6
2-naftylamin	močový měchýř (játra)	I/40
nikl-sloučeniny	paranazální dutiny, plíce	I/9
radon a produkty jeho přeměny	plíce	III/6
talek s obsahem azbestových vláken	plíce	III/2
vinylchlorid	játra, (cévy plic, mozku)	I/27
silné anorganické kyseliny s obsahem H_2SO_4	plíce	I/53
výroba auraminu*	močový měchýř	I/40 (?)
výroba isopropylalkoholu*	paranazální dutiny, (larynx)	I/29 (?)
práce spojená s expozicí polycyklickým aromatickým uhlovodíkům přítomným v uhelných sazích, dehtu, smole, parách a prachu	dýchací cesty a plíce, kůže, moč. měchýř, skrotum	III/7, I/42, IV/1
prach dřeva	paranazální dutiny	III/8
sluneční (UV) záření	kůže	IV/1

()... terčový orgán není bezpečně prokázán; nzp... nemoc z povolání; GIT gastrointestinální trakt; *… samotné chemické látky mezi karcinogeny 1 skupiny IARC nepatří

Z. Adam, J. Vorlíček, J. Koptíková:
Obecná onkologie a podpůrná léčba

Tab. 1.2.2 Kumulativní počet zhoubných novotvarů ohlášených jako nemoci z povolání v České republice v letech 1991 až 2001

Typ – lokalizace	Počet	%
bronchogenní karcinom	649	91,7
mezoteliom pleury	31	4,4
zhoubný novotvar vývodných cest močových (moč. měchýř)	16	2,3
zhoubný novotvar kůže	4	0,6
zhoubný novotvar kořene jazyka	2	0,3
zhoubný novotvar laryngu	1	0,1
akutní myeloidní leukemie	1	0,1
zhoubný novotvar ledviny	1	0,1
zhoubný novotvar nitrohrudních orgánů	1	0,1
zhoubný novotvar mozku	1	0,1
jiné	1	0,1
Celkem	708	100,0

Z. Adam, J. Vorlíček, J. Koptíková:
Obecná onkologie a podpůrná léčba

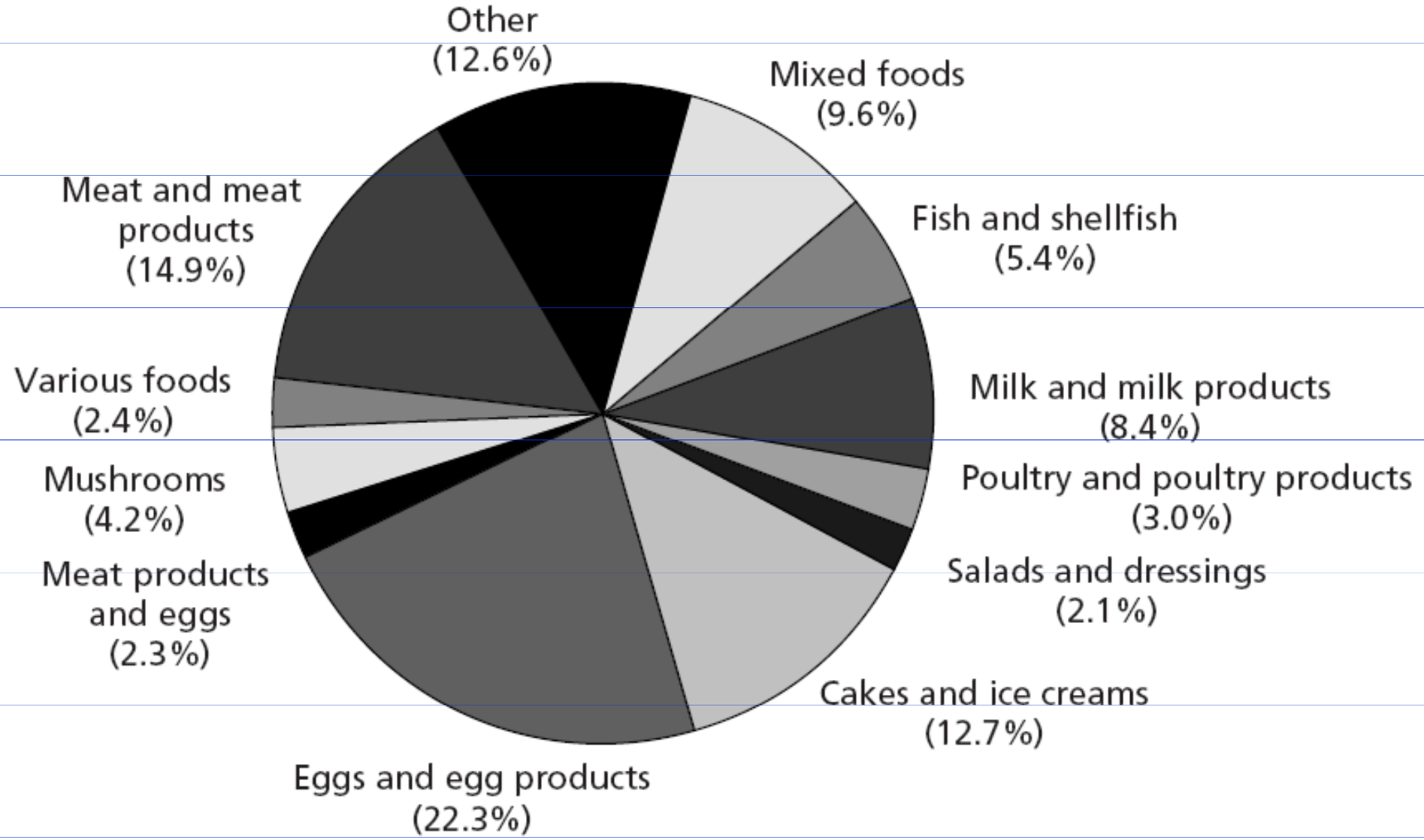
Tab. 1.2.3 Přehled profesních etiologických nox (kumulativní počet) u zhoubných novotvarů ohlášených jako nemoci z povolání v České republice v letech 1991 až 2001

Profesionální noxa	Počet	%
ionizující záření	616	87,0
azbest	48	6,8
koksárenské plyny (zvl. PAU)	14	2,0
PAU	7	1,0
aromatické aminosloučeniny (nebo nitrosloučeniny)	6	0,9
chrom nebo jeho sloučeniny	2	0,3
nikl nebo jeho sloučeniny	1	0,1
benzen	1	0,1
antimon nebo jeho sloučeniny	1	0,1
halogenované uhlovodíky	1	0,1
anorganické kyseliny	1	0,1
bez bližší specifikace	10	1,4
celkem	708	100,0

PAU … polycyklické aromatické uhlovodíky

Z. Adam, J. Vorlíček, J. Koptíková:
Obecná onkologie a podpůrná léčba

Fig. 2.2. Food involved in foodborne disease outbreaks in the WHO European Region, 1993–1998



Source: Tirado & Schmidt *(7)*.

Table 2.7. Sources of outbreaks of infectious intestinal diseases traceable to specific primary food types in six European countries

Food types	Percentage in:					
	Croatia	Norway	Portugal	Spain	United Kingdom	Yugo-slavia
Meat and meat products	40	20	35	6	38	13
Fish and shellfish		11	6	8	14	–
Eggs and egg products	14		6	37	10	38
Milk and dairy products	3	7	3	3	3	4
Ready meals and sauces	4	4	9	–	3	–
Rice dishes	–	–	–	–	4	–
Salads, fruits and vegetables	3	5	–	–	6	4
Cakes and pastries	–	–	26	6	–	–
Desserts and confectionery	34	–	–	–	14	29
Miscellaneous or uncertain	3	30	16	39	7	13
Water	–	23	–	–	1	–
Total	100	100	100	100	100	100

Source: Tirado & Schmidt *(7)*.

Table 2.9. BSE in selected European countries: total cases, incidence in national herds and positive test results in healthy adult cattle entering the food chain

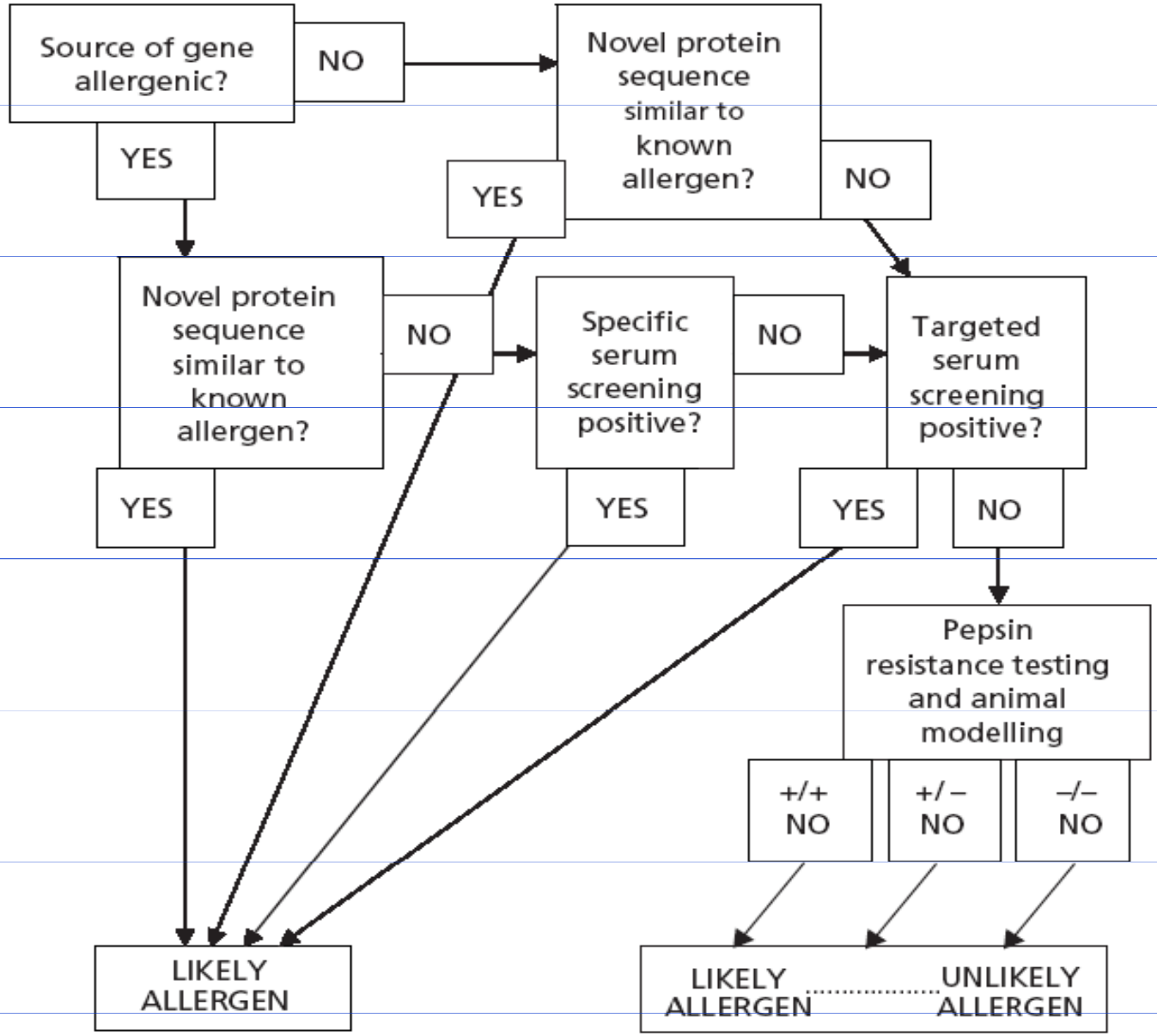
Country	Cases, 1986 to 5 November 2002[a]	Incidence per million adult cattle, 2001[a,b]	Positive cases per 100 000 tests on healthy cattle, January–August 2002[c]
Austria	1	1.0	0
Belgium	90	28.2	3.4
Czech Republic	4	2.9	–[d]
Denmark	9	6.8	0.7
Finland	1	2.4	0
France	692	19.7	2.6
Germany	221	20.0	1.6
Greece	1	3.3	0
Ireland	1 091	61.8	7.3
Italy	54	14.1	3.0
Liechtenstein	2	–	–
Luxembourg	2	0	0
Netherlands	43	10.3	1.6
Poland	4	–	–
Portugal	688	137.9	66.8
Slovakia	10	18.3	–
Slovenia	3	4.3	–
Spain	190	24.2	8.0
Switzerland	420	49.1	–
United Kingdom	182 581	102.4	1.2

Table 2.7. Sources of outbreaks of infectious intestinal diseases traceable to specific primary food types in six European countries

Food types	Percentage in:					
	Croatia	Norway	Portugal	Spain	United Kingdom	Yugo-slavia
Meat and meat products	40	20	35	6	38	13
Fish and shellfish		11	6	8	14	–
Eggs and egg products	14		6	37	10	38
Milk and dairy products	3	7	3	3	3	4
Ready meals and sauces	4	4	9	–	3	–
Rice dishes	–	–	–	–	4	–
Salads, fruits and vegetables	3	5	–	–	6	4
Cakes and pastries	–	–	26	6	–	–
Desserts and confectionery	34	–	–	–	14	29
Miscellaneous or uncertain	3	30	16	39	7	13
Water	–	23	–	–	1	–
Total	100	100	100	100	100	100

Source: Tirado & Schmidt *(7).*

Fig. 2.8. Decision tree for assessing the allergenic potential of foods derived from biotechnology



Source: Evaluation of allergenicity of genetically modified foods (131).

The factors that can influence the emergence of or increase in foodborne disease include *(8)*:

1. changes in the pathogenic organism, increased resistance and new virulence properties;

2. new analytical techniques to detect previously unsuspected hazards;
3. new production systems, including more mass production and longer food chains;
4. new environmental pollutants and changing ecology and climate;
5. new food products, processing techniques, ingredients, additives and packaging;
6. changing social conditions and increasing poverty or pollution;
7. changes in the health status of the population or a subpopulation;
8. changing diets and increasing demand for minimally processed foods;
9. changing food purchasing, more street consumption and eating outside the home;
10. travel and migration and the movement of pathogen hosts; and
11. increased trade in food, animal feed and livestock and exposure to contaminants.

Fig. 2.4. Relationships between undernutrition and infection

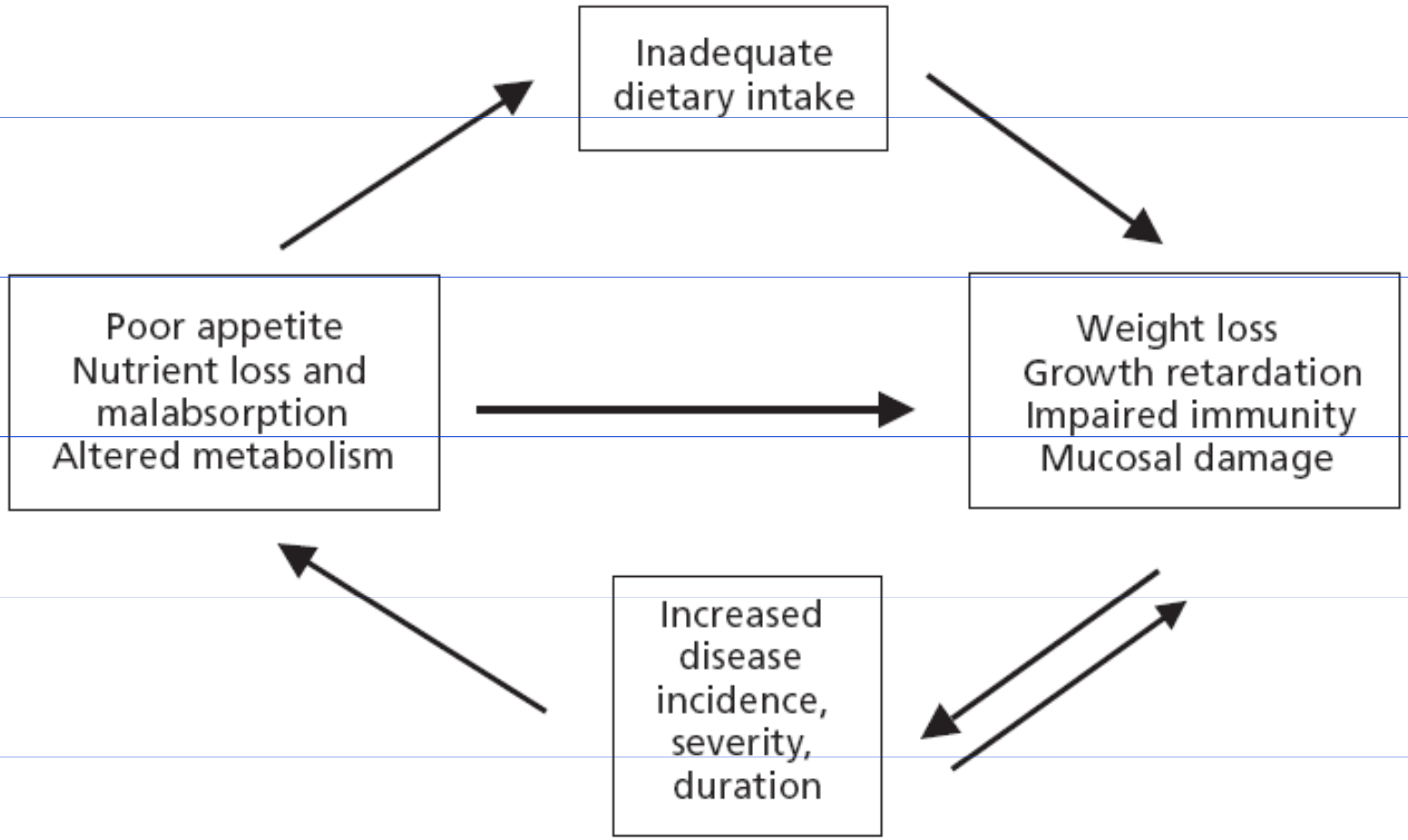
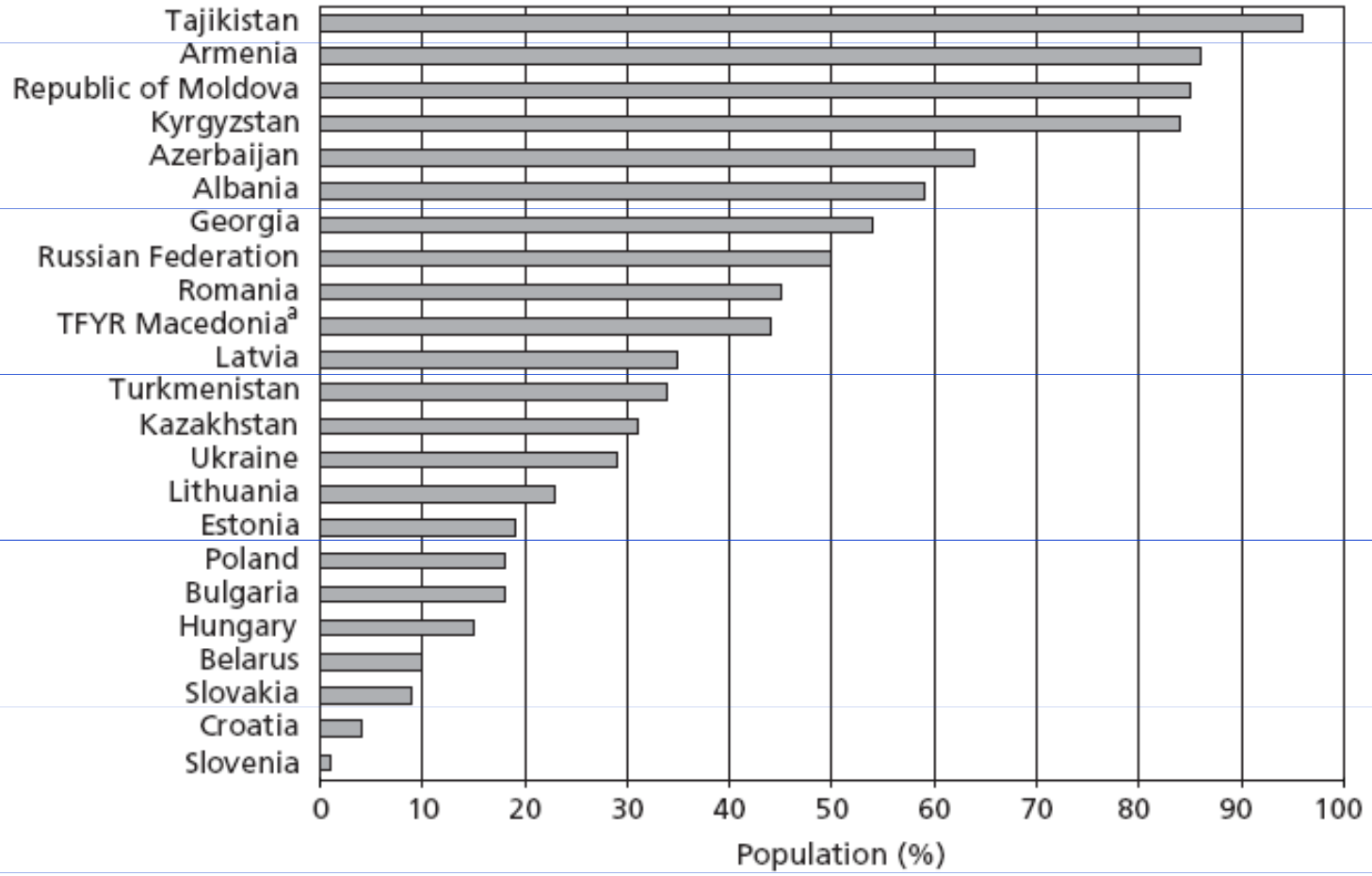


Table 3.1. Changing understanding of food and nutrition security

Term	20th-century model	21st-century model
Food security	Abundance of food through:	Sustainable production methods:
	• increased yields • increased global trading • processing and storage techniques	• reduced input • ecologically sensitive production Reduced risk of foodborne hazards
Nutrition security	Public health dietary targets	Production to meet dietary needs
	Health education messages	More equal access to food
		Control of misleading messages

Fig. 3.1. Proportion of the population in selected CCEE and NIS with personal income below US $4.30 per day, latest available years

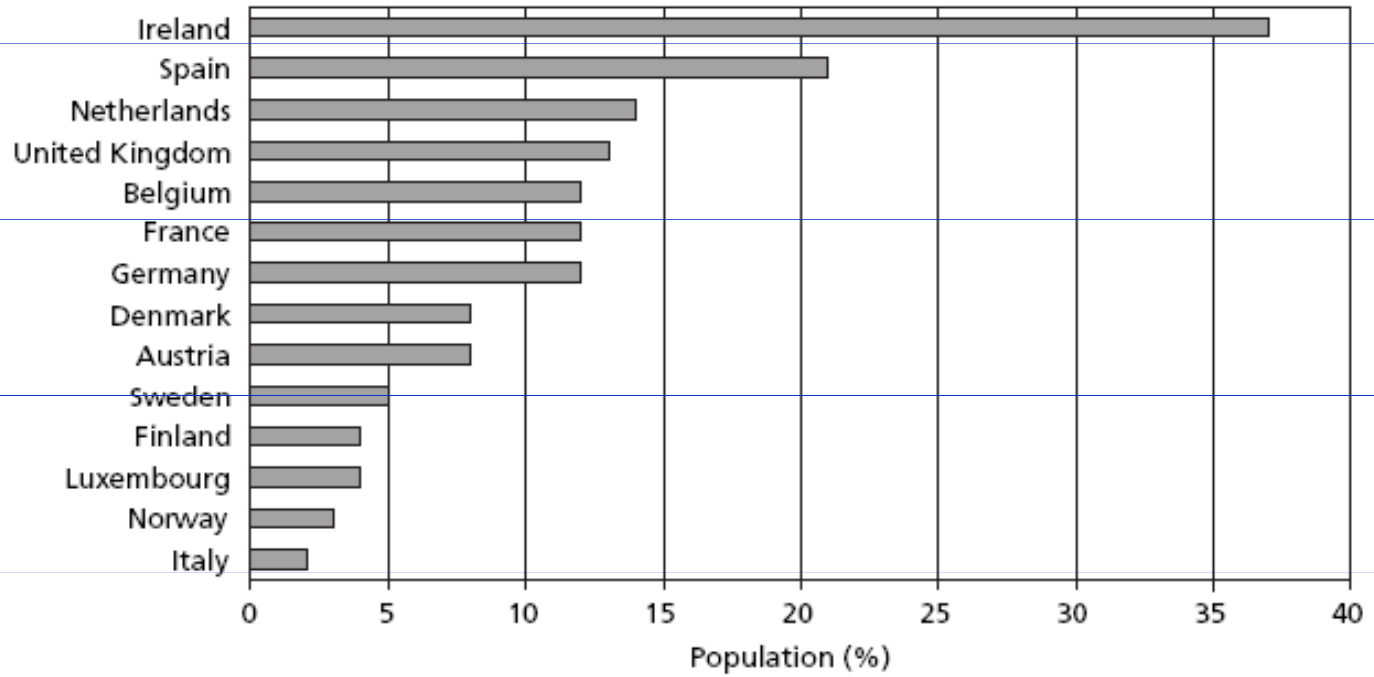


[a] The former Yugoslav Republic of Macedonia.

Note: The Czech Republic and Slovenia have values below 1%.

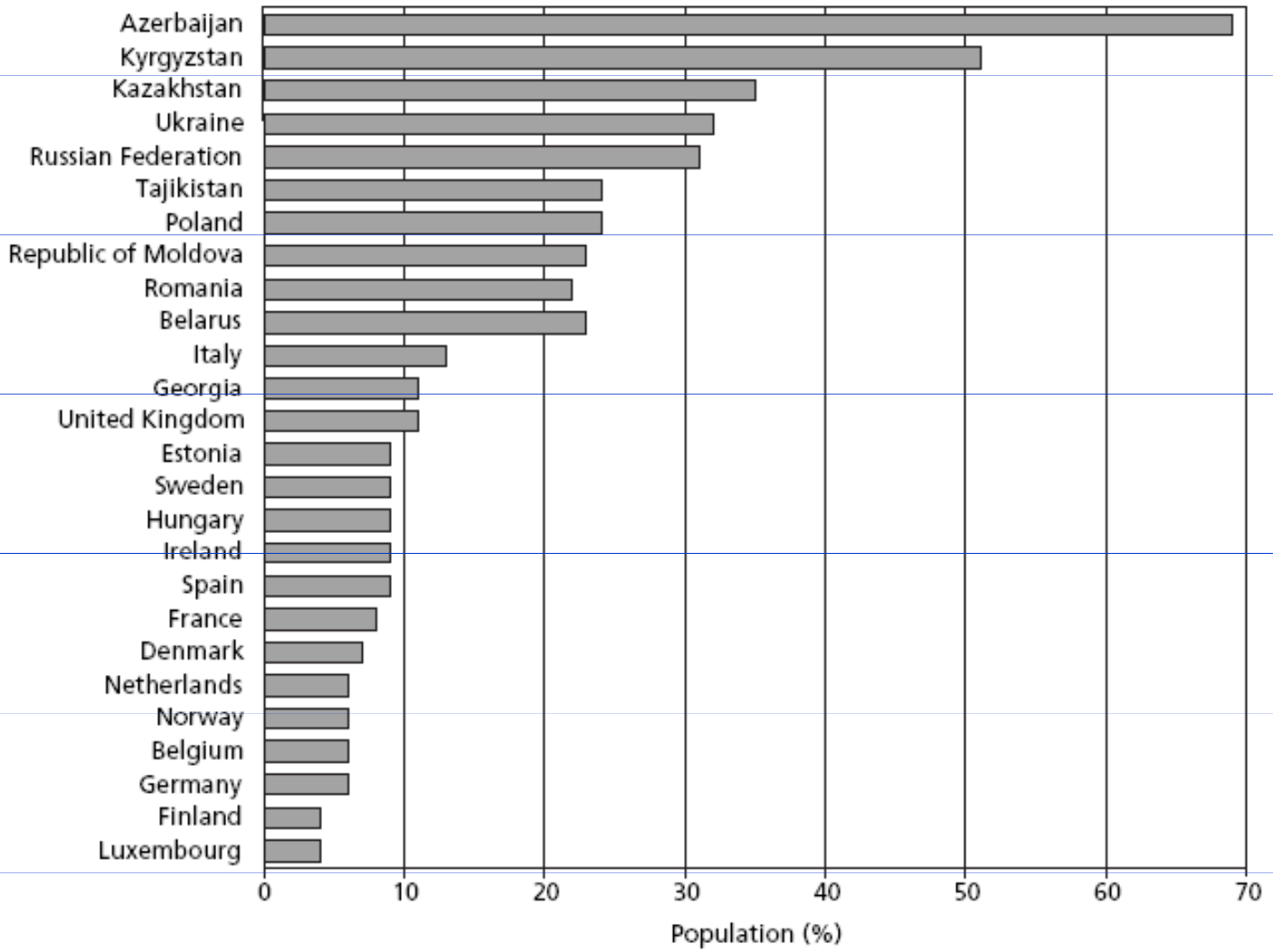
Sources: Human development report 2000 (9), Human development report 2001 (10), World development report 2000–2001 (11) and Falkingham *(12).*

Fig. 3.2. Proportion of the population in selected western European countries with personal income below US $14.40 per day, latest available years



Sources: Human development report 2000 (9), Human development report 2001 (10), World development report 2000–2001 (11) and Falkingham *(12).*

Fig. 3.3. Proportion of the population in selected European countries below the national poverty line, latest available years



Sources: Human development report 2000 (9), Human development report 2001 (10), World development report 2000–2001 (11) and Falkingham *(12).*

Fig. 3.5. Influences on food choices

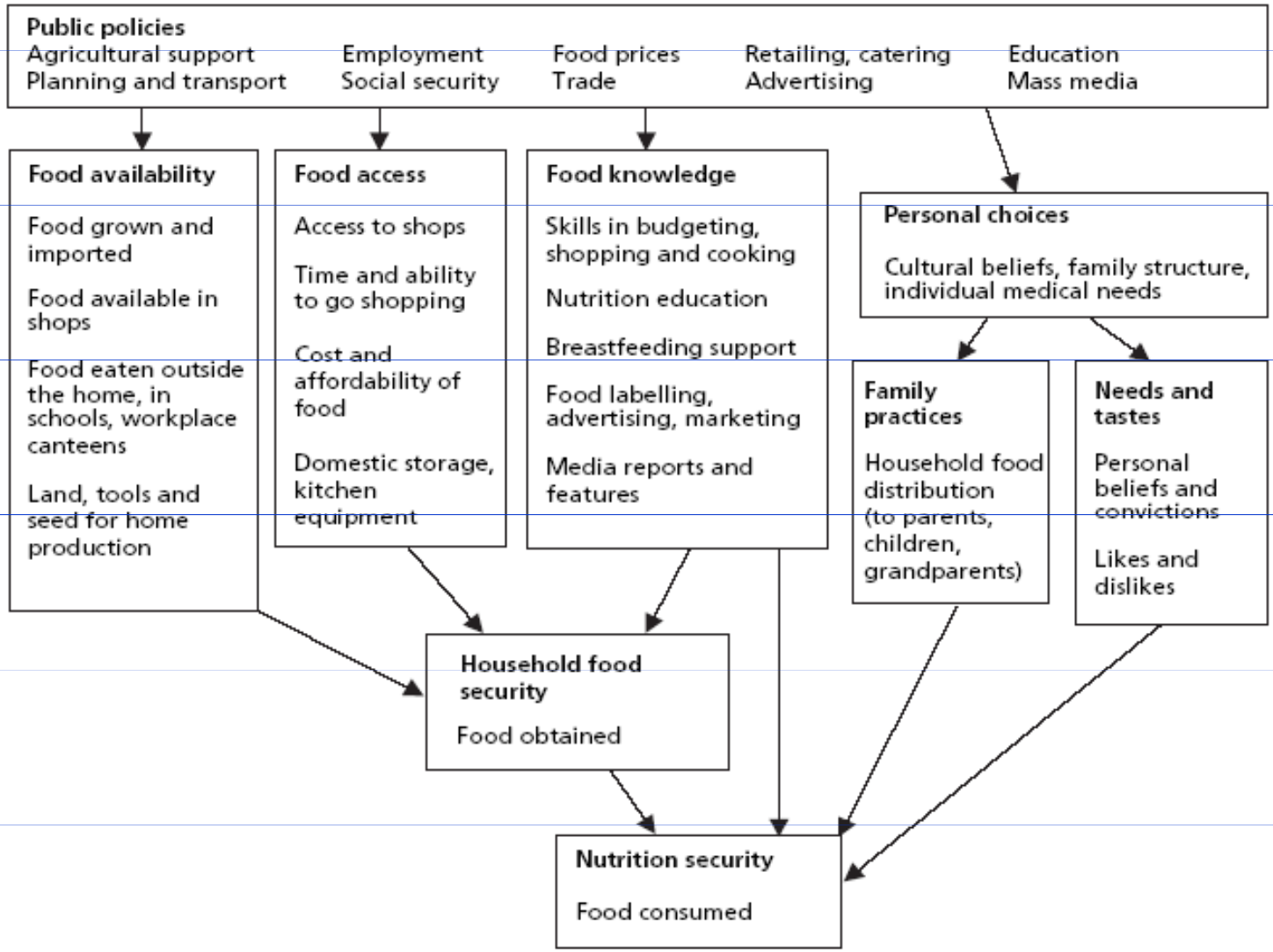


Fig. 3.6. Shares of food sales controlled by the five largest companies in selected European countries

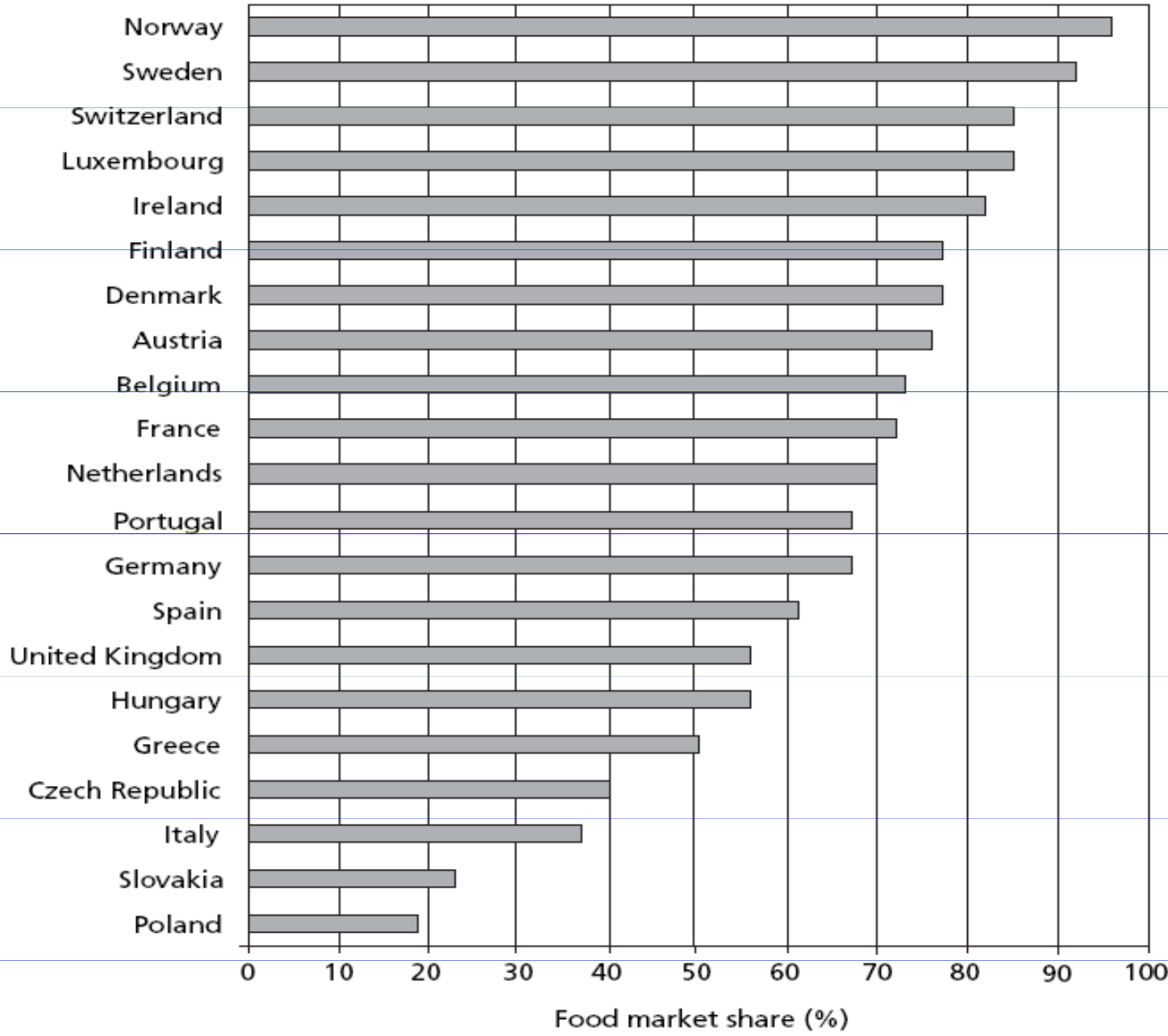


Table 3.10. Comparison of dietary recommendations with food supplies to the populations of Ireland and Italy, 1965 and 1999

Component	Population goals *(78)*	Theoretical food supplies required (per person per day) *(78)*	Actual food supplies (per person per day) *(79)*			
			Ireland		Italy	
			1965	1999	1965	1999
Total fat	< 30% of total energy	< 80 g fat	119 g	136 g	90 g	152 g
Saturated fat	< 10% of total energy	< 60 g fat from animal products	100 g	89 g	38 g	70 g
Sugar	< 10% of total energy	< 65 g raw sugar equivalent	146 g	116 g	73 g	81 g
Fruits and vegetables	> 400 g/day	> 600 g fruit and vegetables (> 400 g edible)	245 g	390 g	720 g	858 g

Table 3.11. Examples of reduced biodiversity in food production in Europe

Country	Crop/Crop-growing land	Varieties used
France	71% of apple production	1 (Golden Delicious)
	30% of bread wheat	2
	70% of bread wheat	10
Netherlands	80% of potato-growing land	1
	90% of wheat production	3
	75% of barley production	1
United Kingdom	68% of early potatoes	3
	71% of wheat area	4

ource: adapted from Pretty *(84)*.

Fig. 3.11. Polyunsaturated fatty acids as a proportion of total fatty acids from various sources

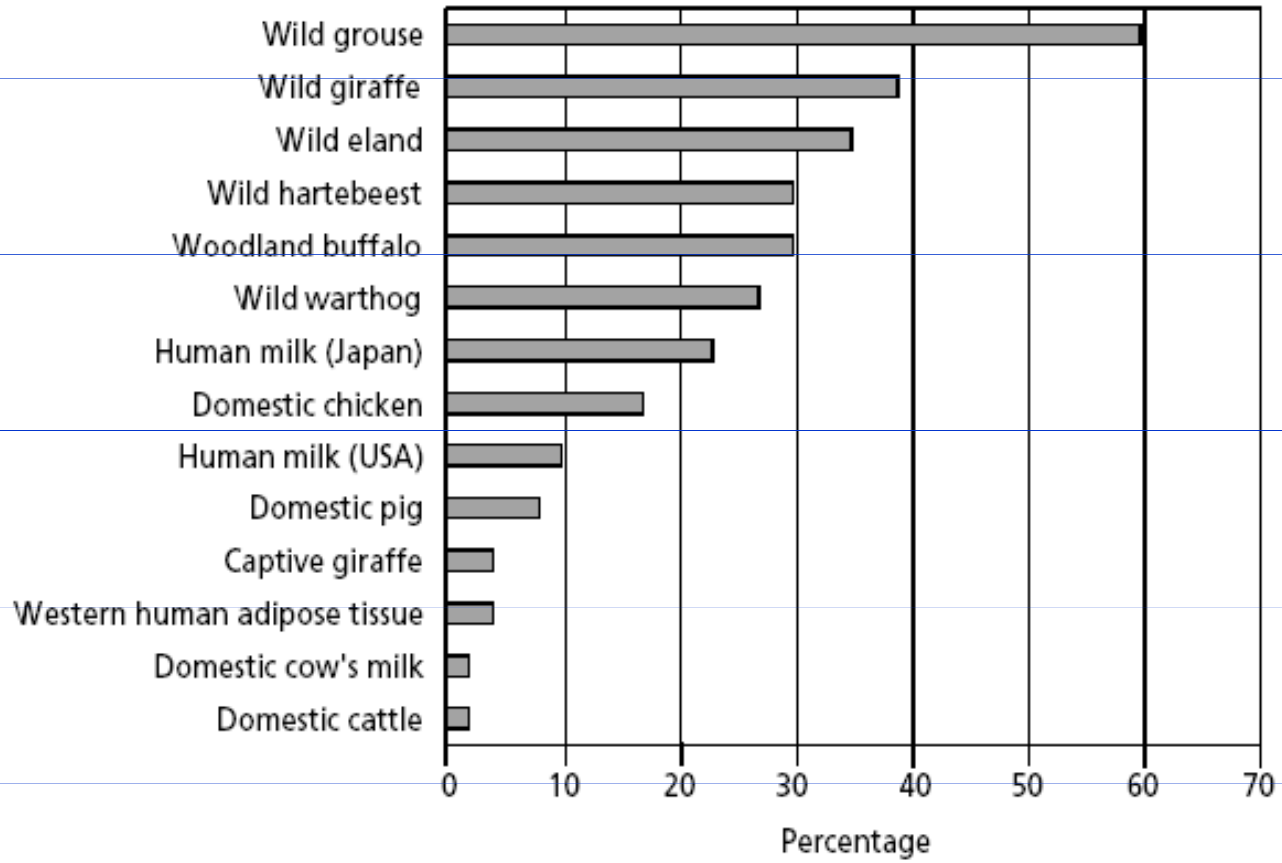


Table 3.12. Fatty acids in the flesh of farmed trout according to their feed

Type	Fatty acids (g per 100 g fatty acids) in trout fed:	
	marine oils	marine and vegetable oils
Polyunsaturated		
Omega-3	31	16
Omega-6	9	19
Monounsaturated	42	38
Saturated	19	28

Fig. 3.12. Loss of vitamins and increase in fat as potatoes are processed

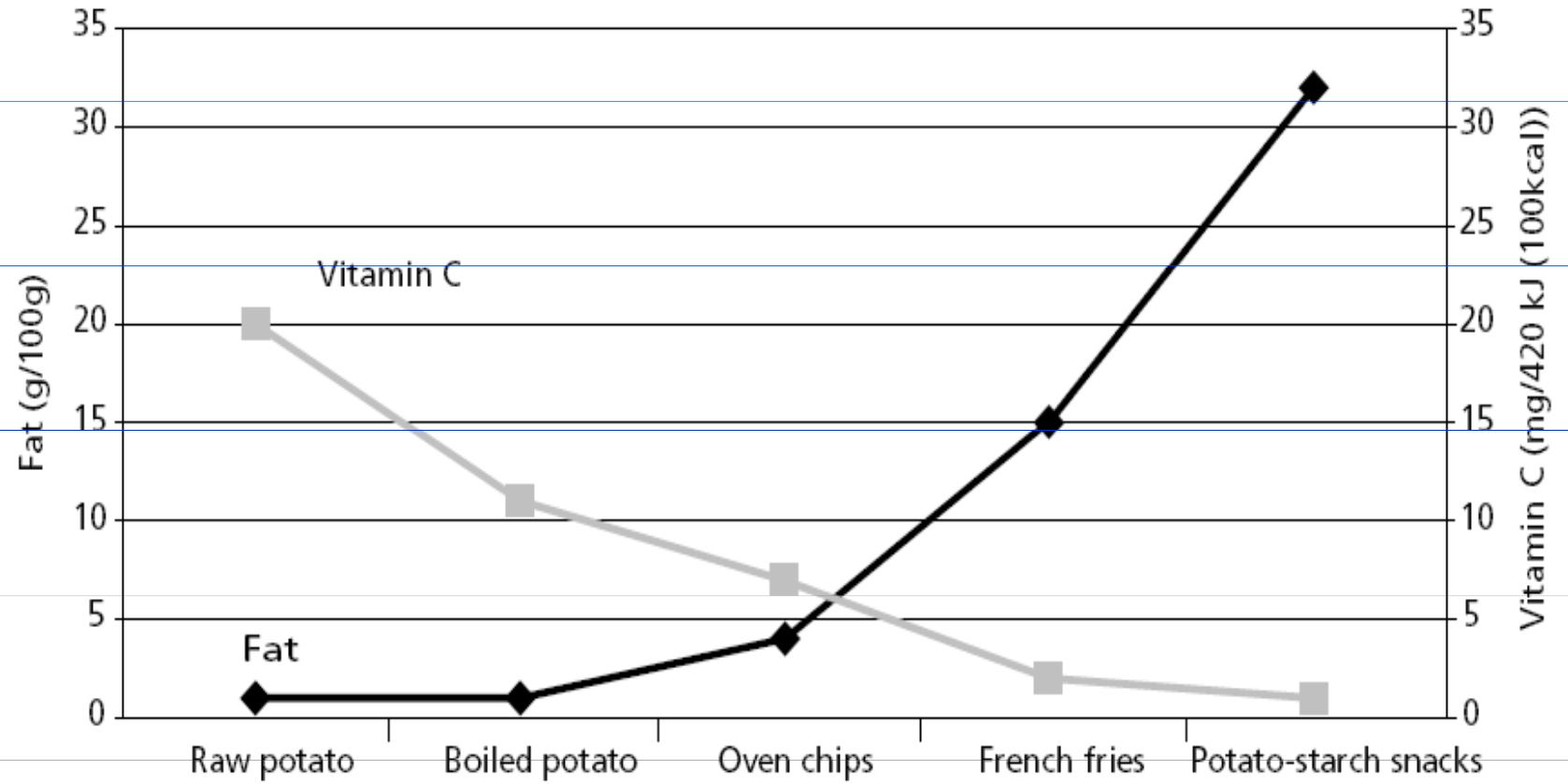


Table 3.15. Five assets for sustainable agriculture and sustainable livelihoods

Assets	Components
Natural capital	Nature's goods and services: food (both farmed and from the wild), wood and fibre; water regulation and supply; waste assimilation, decomposition and treatment; nutrient cycling and fixation; soil formation; biological control of pests; climate regulation; wildlife habitats; storm protection and flood control; carbon sequestration; pollination; and recreation and leisure
Social capital	Cohesiveness of people in their societies: relations of trust, reciprocity and exchanges between individuals that facilitate cooperation; the bundles of common rules, norms and sanctions mutually agreed or handed down within societies; the connectedness of networks and groups that may be formal or informal, horizontal or vertical, and between individuals or organizations; and access to social institutions beyond the immediate household or community
Human capital	Status of individuals: the stock of health, nutrition, education, skills and knowledge of individuals; access to services that provide these, such as schools, health care and adult training; the ways individuals and their knowledge interact with productive technology; and individuals' leadership ability
Physical capital	Nonrenewable resources and infrastructure: technology; housing and other buildings; roads and bridges; energy supplies; communication; markets; and air, road, water and rail transport
Financial capital	Stocks of money: savings; access to affordable credit; pensions; remittances; welfare payments; and grants and subsidies