EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES

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and

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EPIDEMIOLOGY

= interdisciplinary method

- relationship between diseases, their occurence and influencing factors

WHAT ARE CARDIOVASCULAR DISEASES?

?

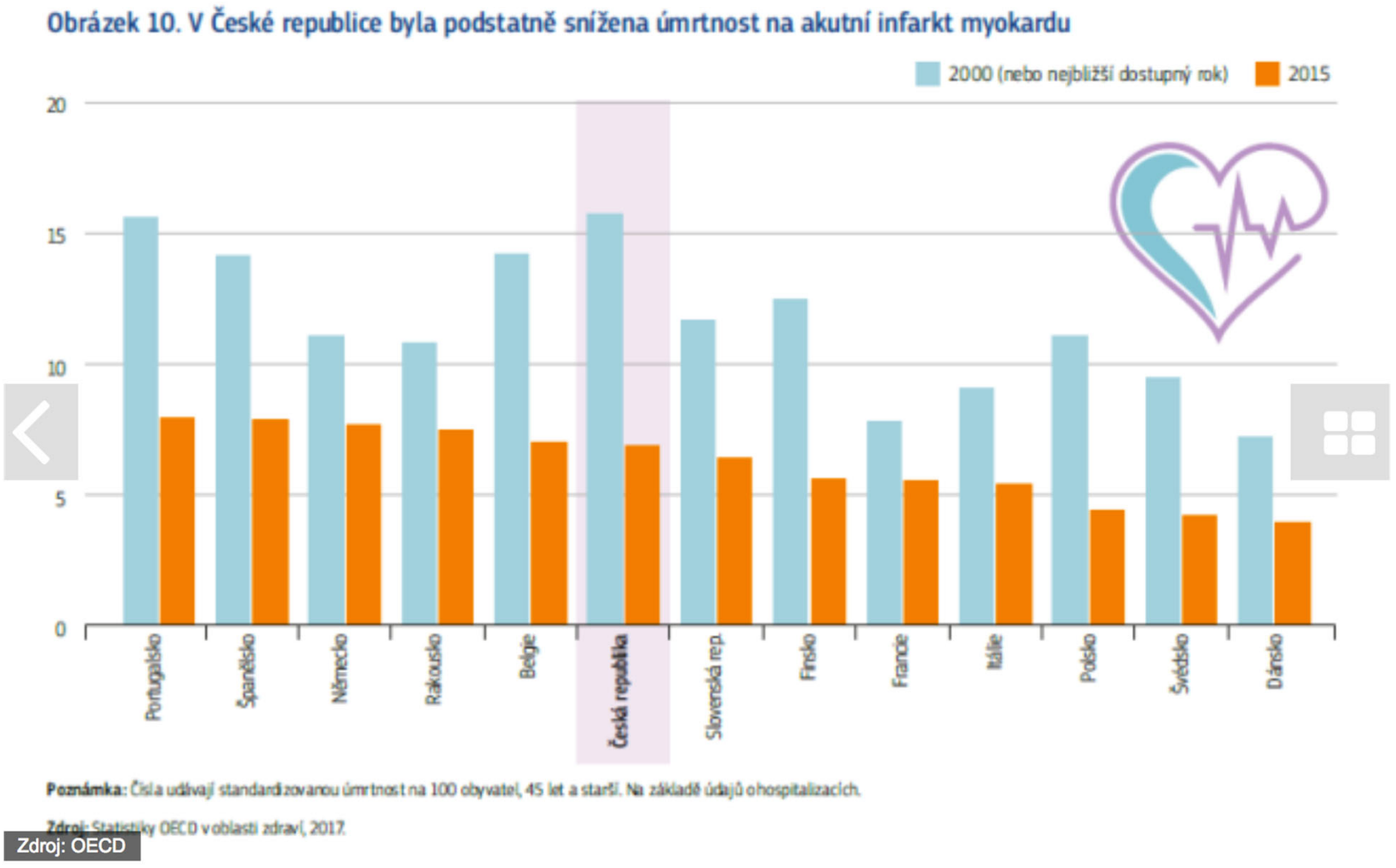
CVD – CARDIOVASCULAR DISEASES

- **Coronary (mainly CHD, myocardial infarction, IHD, ischaemic heart disease…)**
- **Cerebral** (mainly stroke…)
- **Peripheral** (mainly ischaemic disease of lower extremities….)

PREVALENCE AND MORTALITY

- global mortality ≈ 30% of all deaths
- developed countries ≈ 40% of all deaths
- developing countries ≈ 25% all deaths
- most frequent: ischaemic heart disease, followed by stroke

MI MORTALITY IN THE CR 2000/2015

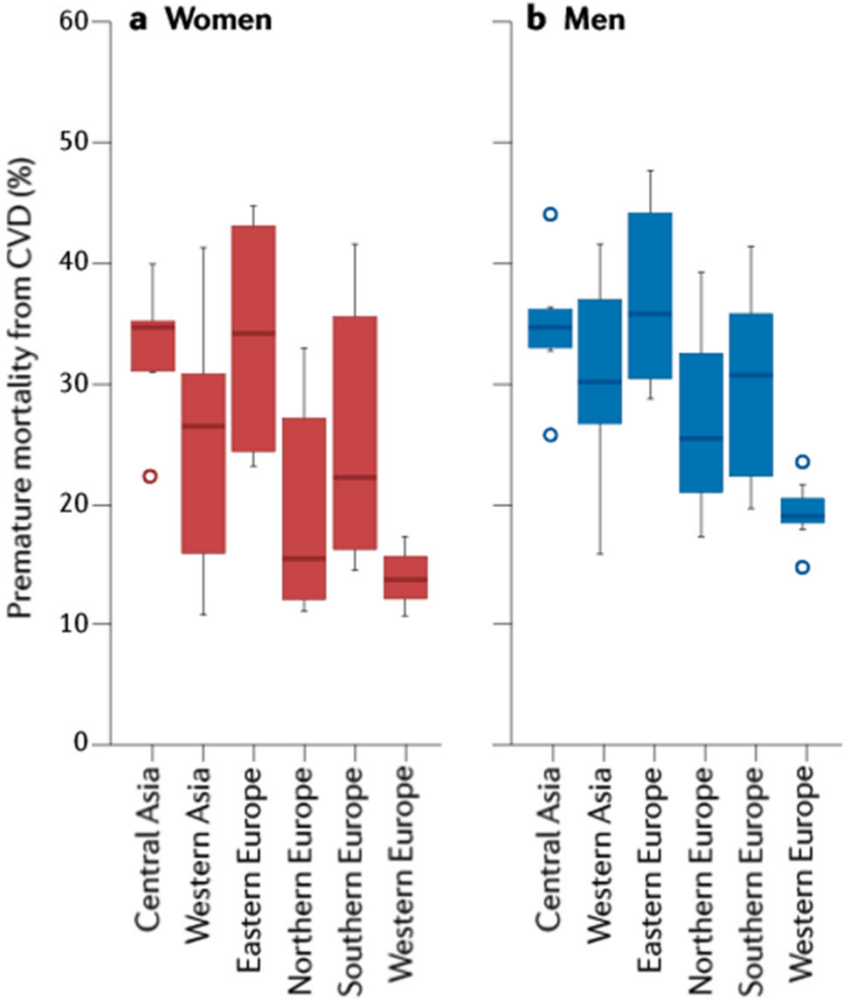


Zdroj: OECD

CV MORTALITY IN EUROPE

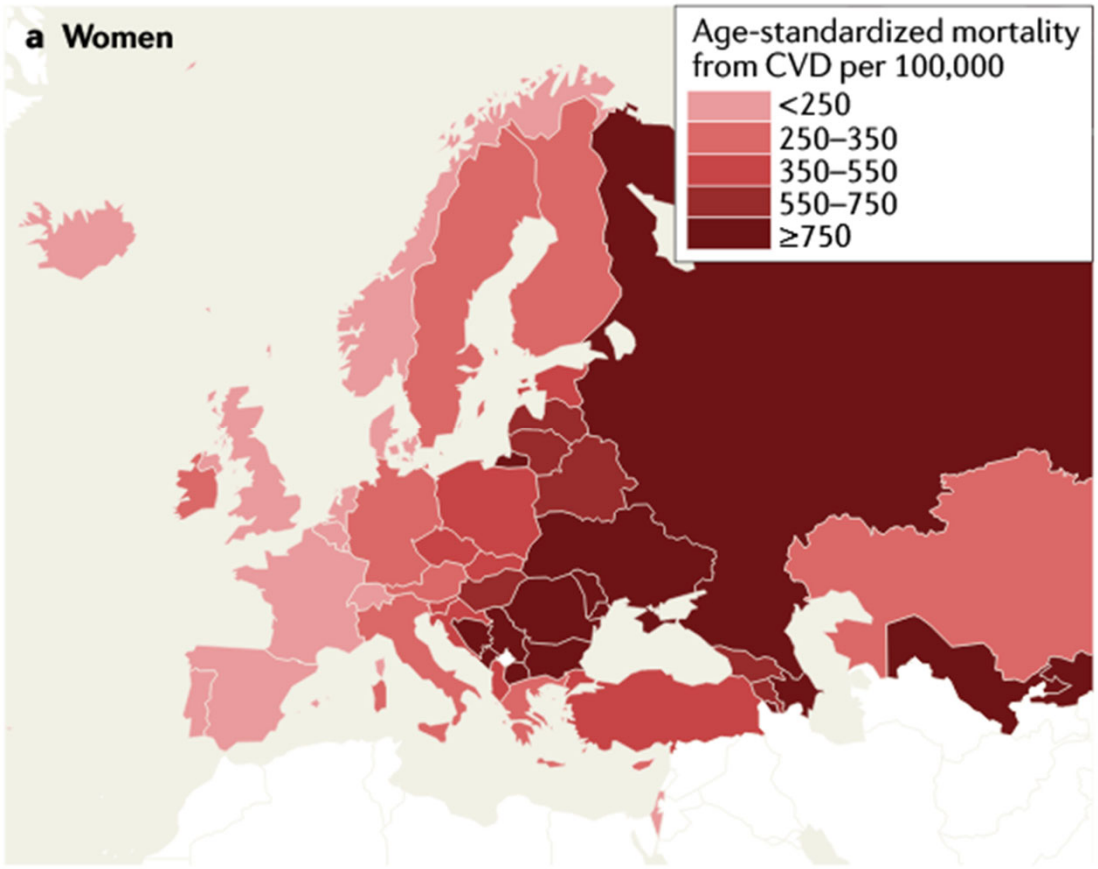
- CVD - the most common cause of death in the EU
- more than 60 million potential years of life are lost to CVD in Europe annually
- more ♀ than ♂ die from CVD in EU
- age-standardized rates of both morbidity and death from CVD are higher in ♂ than in ♀
- large disparities in data coverage and in country-level morbidity, treatment outcomes and mortality from CVD exist across Europe

Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, Gale CP, Achenbach S, Weidinger F, Vardas P. Epidemiology of cardiovascular disease in Europe. Nat Rev Cardiol. 2022 Feb;19(2):133-143.



Percentage of premature deaths from CVD in Europe. Percentage of deaths from cardiovascular disease (CVD) in women (part a) and men (part b) aged <70 years by European region (using the United Nations subregional classification) in the latest year available (which differs between countries; see Supplementary Data 1). Plots display a box representing the median value and first and third quartile values, with whiskers positioned at the furthest data points within 1.5 times the interquartile range. Any countries outside this range are defined as outliers, plotted as individual circles. Data not available for Andorra, Monaco and San Marino. Mortality and population data obtained from the WHO Mortality Database.

Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, Gale CP, Achenbach S, Weidinger F, Vardas P. Epidemiology of cardiovascular disease in Europe. Nat Rev Cardiol. 2022 Feb;19(2):133-143.



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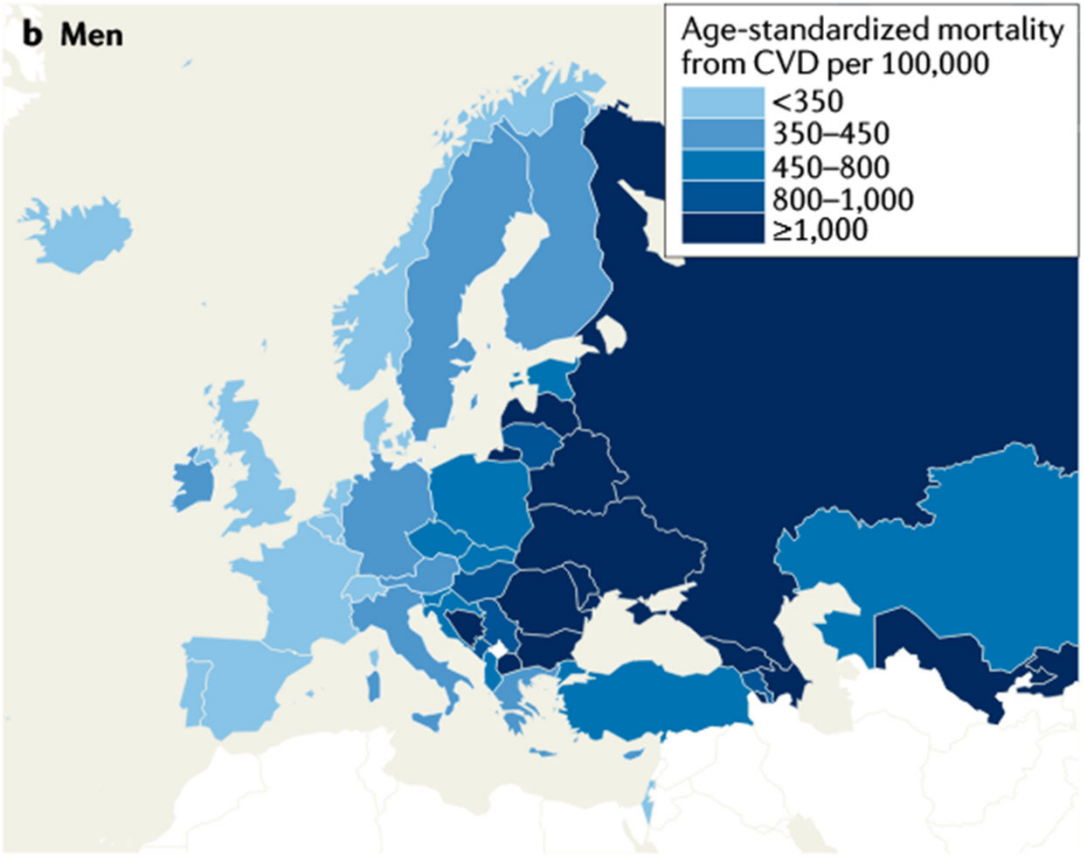

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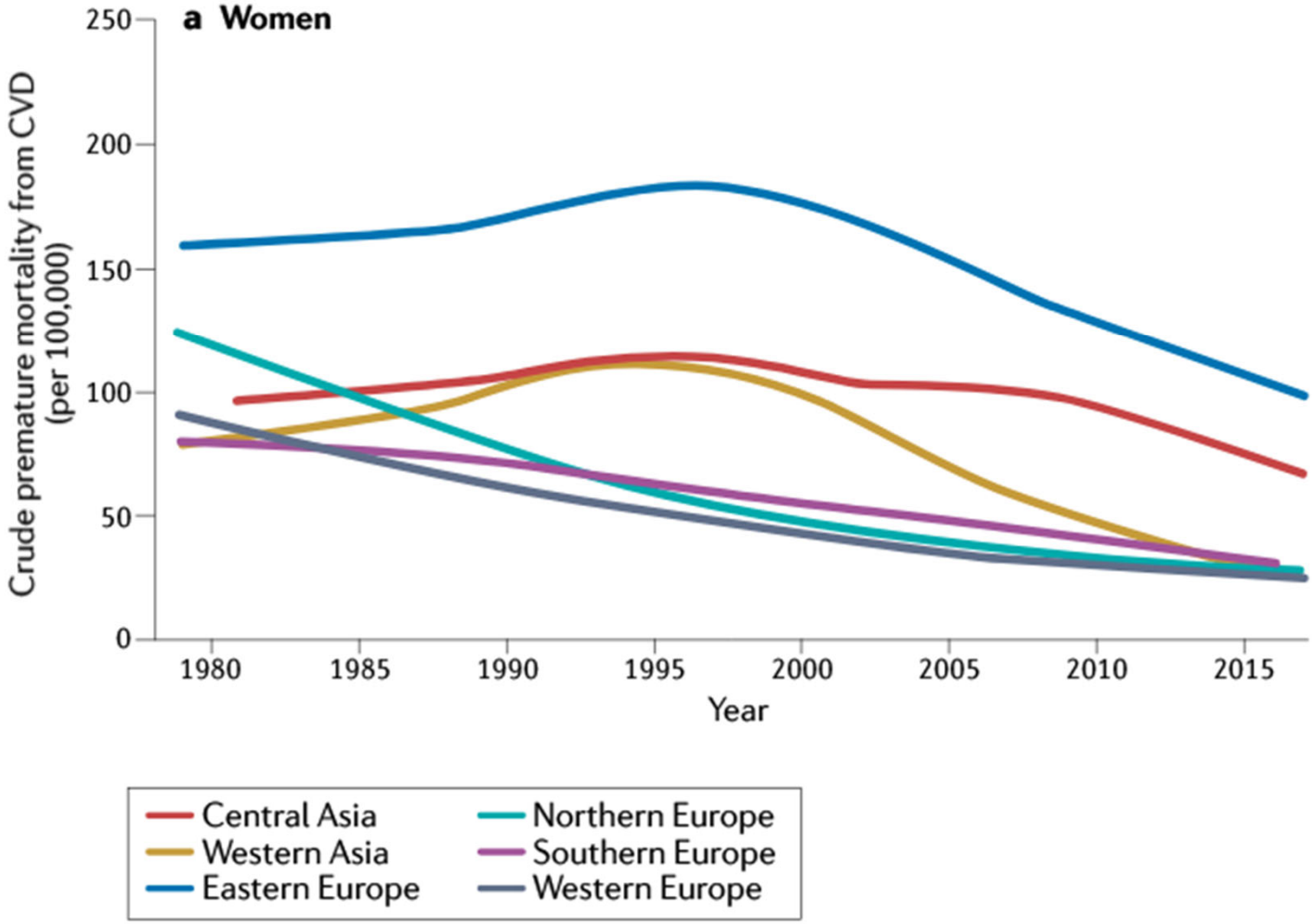

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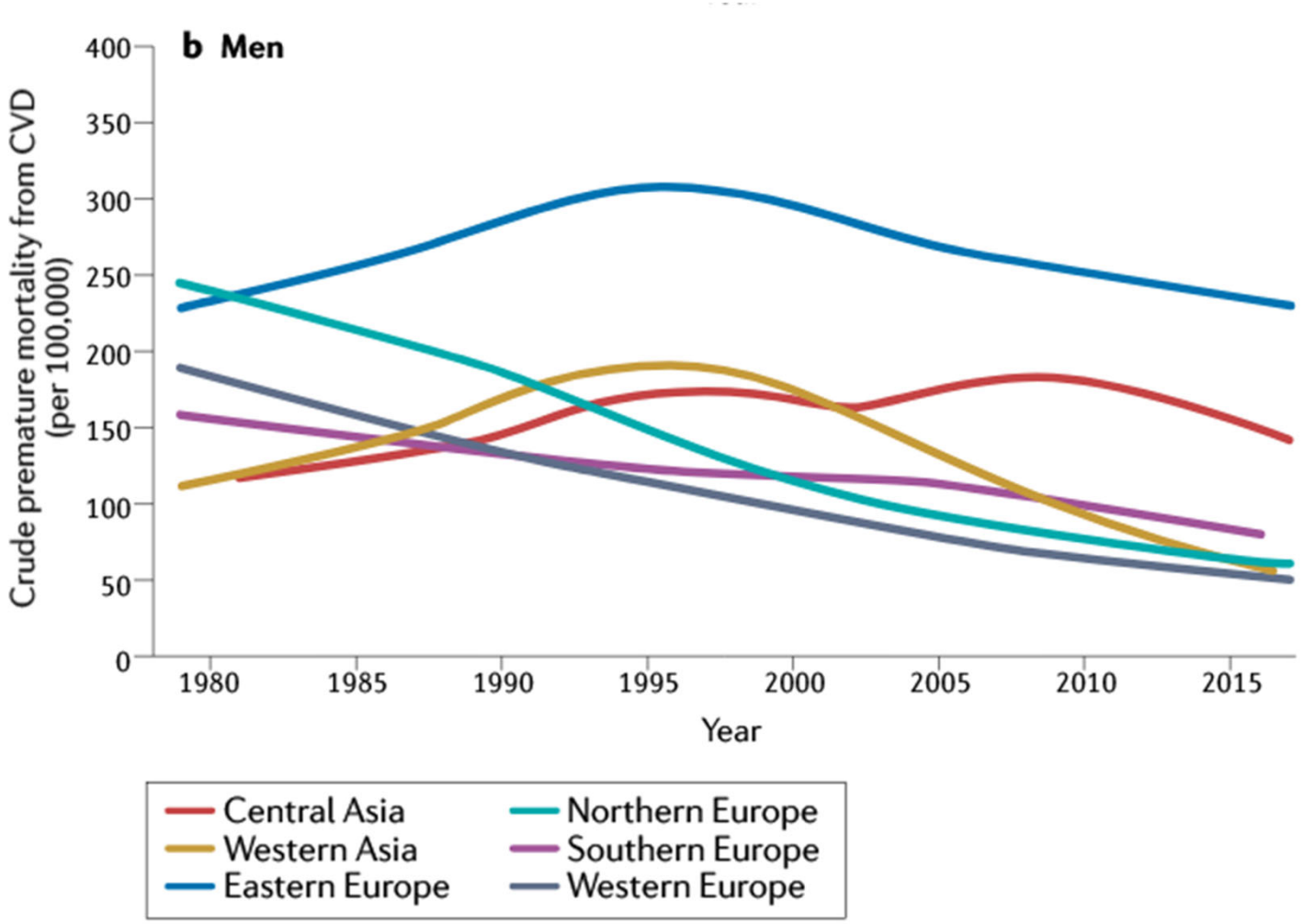

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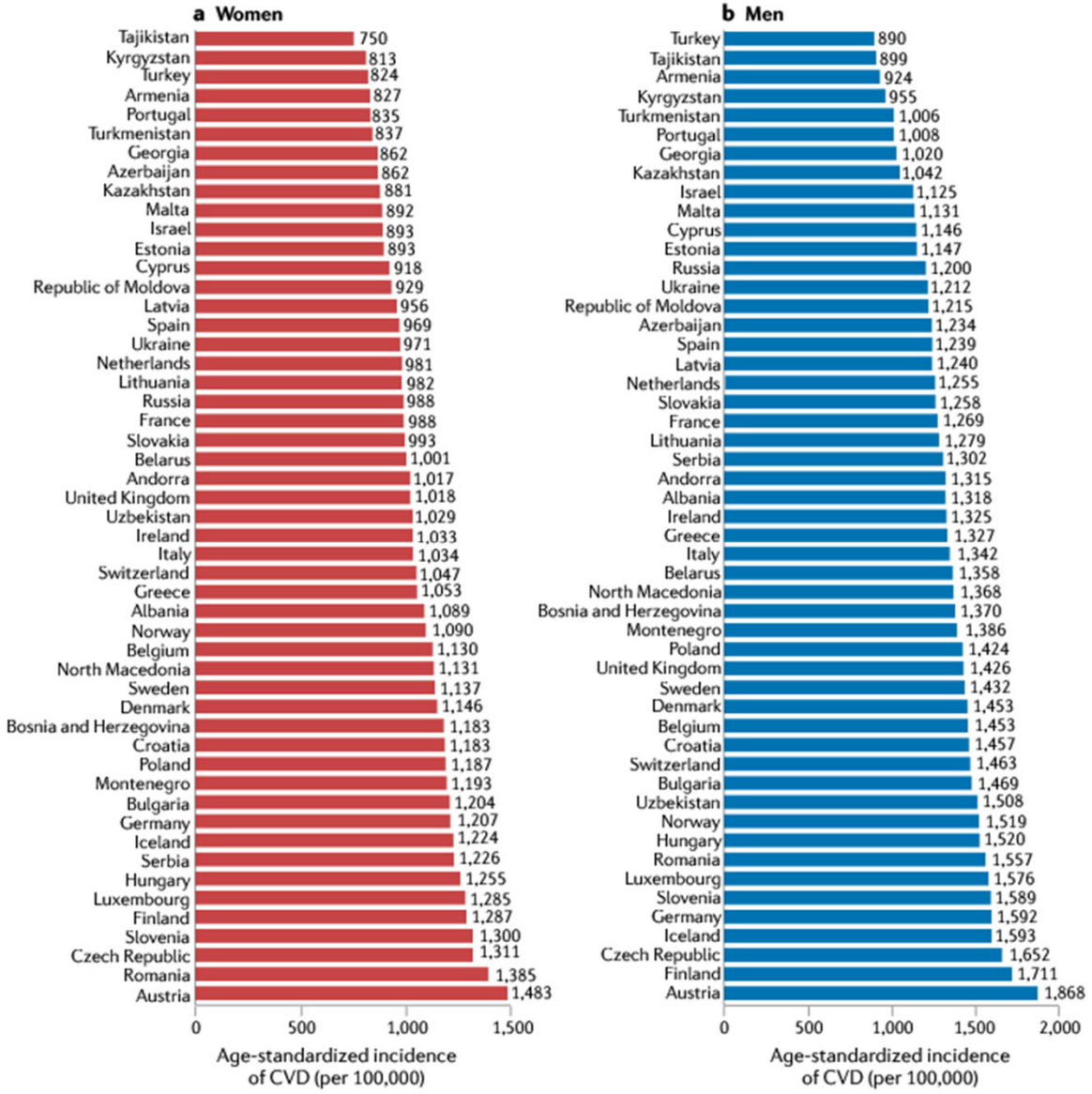
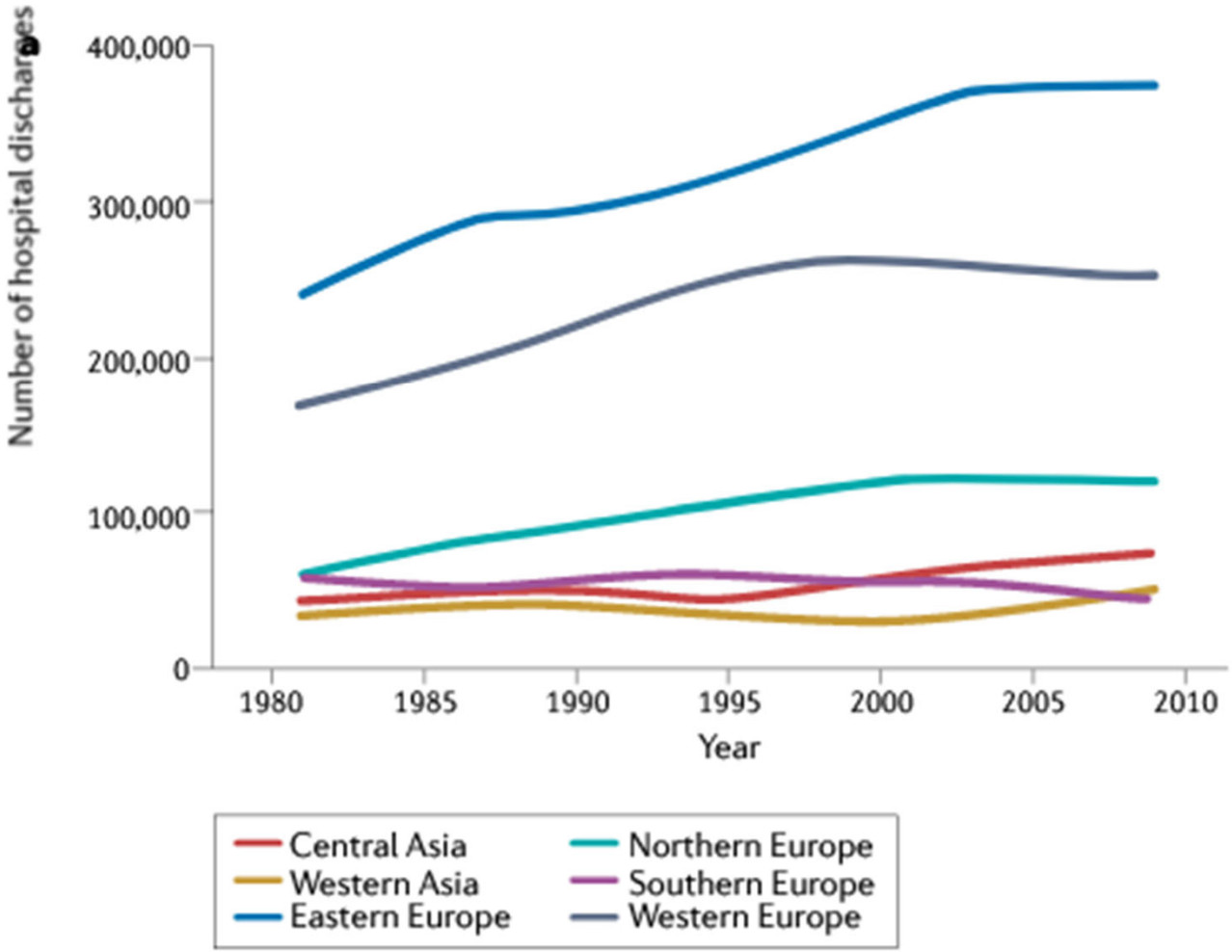


Fig. 5 | **Age-standardized incidence of CVD in Europe.** Age-standardized incidence of cardiovascular disease (CVD) per 100,000 of the population in European countries in 2017 in women (part **a**) and men (part **b**). Data not available for Monaco or San Marino. Data obtained from the Global Burden of Disease (GBD) study 2017 and age-standardized to the GBD world population standard.

Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, Gale CP, Achenbach S, Weidinger F, Vardas P. Epidemiology of cardiovascular disease in Europe. Nat Rev Cardiol. 2022 Feb;19(2):133-143.



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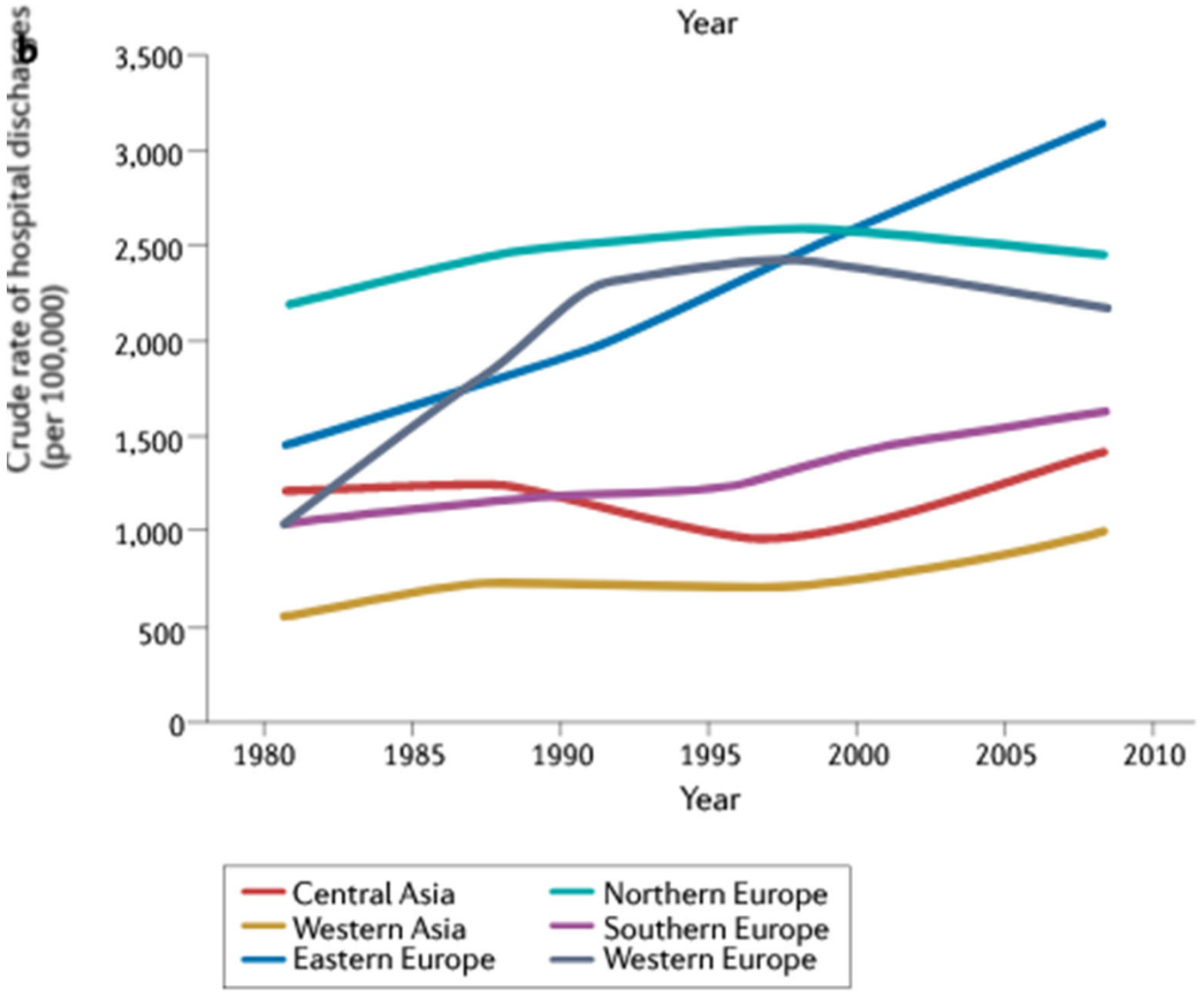

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CVD – BASIC CAUSE OF IN-PATIENT TREATMENT THE CR

Zdroj: UZIS.CZ

CV RISK FACTORS

NON-MODIFIABLE

- …
- …
- …
- …

MODIFIABLE

- …
- …
- …
- …

CV RISK FACTORS

NON-MODIFIABLE

- age
- gender
- race
- Existing IHD
- Genetic factors
- Positive FH

MODIFIABLE

- ?

CV RISK FACTORS

NON-MODIFIALBE

- age
- gender
- race
- Existing IHD
- Genetic factors
- Positive FH

MODIFIABLE

- ↑ cholesterol
- smoking
- high blood pressure
- diabetes
- metabolic syndrome
- ↑ homocystein (?)
- obesity
- ↓ physical activity
- thrombogenic factors
- type A behaviour
- ↓ education level
- ↓ socioeconomic status
- chronic inflammation
- depression
- ……

CV RISK FACTORS

- biological
- environmental
- behavioral
- psychological
- physiological

Komasi S., Saeidi M. Presentation of new classification of perceived risk factors and etiologies of cardiovascular diseases. *ARYA Atheroscler* 2016; 12 (6): 295−296.

BIOLOGICAL CV RISK FACTORS

- genetic
- family history
- age
- gender
- ethnicity (people of South Asian, African or Caribbean descent have a greater risk of developing CVD)

Komasi S., Saeidi M. Presentation of new classification of perceived risk factors and etiologies of cardiovascular diseases. *ARYA Atheroscler* 2016; 12 (6): 295−296

Women-specific risk factors for Cardiovascular Disease.

- Polycystic ovaries (PCOS)
- Premature ovarian failure (POF)
- Menopause
- Surgical menopause
- Complications of pregnancy
  - Gestational diabetes mellitus
  - Preeclampsia
  - Preterm birth
  - Small for gestational age pregnancies (SGA)
  - Miscarriage

Maffei S, Guiducci L, Cugusi L, Cadeddu C, Deidda M, Gallina S, Sciomer S, Gastaldelli A, Kaski JC; Working Group on "Gender difference in cardiovascular disease" of the Italian Society of Cardiology. Women-specific predictors of cardiovascular disease risk - new paradigms. Int J Cardiol. 2019 Jul 1;286:190-197.

ENVIRONMENTAL CV RISK FACTORS

- polluted air
- toxic substances
- dust particles
- polluted water
- passive smoking

Komasi S., Saeidi M. Presentation of new classification of perceived risk factors and etiologies of cardiovascular diseases. *ARYA Atheroscler* 2016; 12 (6): 295–296

(PATO)PHYSIOLOGICAL CV RISK FACTORS

- high blood pressure
- diabetes
- ↑ cholesterol
- obesity

Komasi S., Saeidi M. Presentation of new classification of perceived risk factors and etiologies of cardiovascular diseases. *ARYA Atheroscler* 2016; 12 (6): 295−296

BEHAVIORAL CV RISK FACTORS

- bad nutrition
- smoking
- drug abuse
- heavy physical work
- physical inactivity

Komasi S., Saeidi M. Presentation of new classification of perceived risk factors and etiologies of cardiovascular diseases. *ARYA Atheroscler* 2016; 12 (6): 295–296

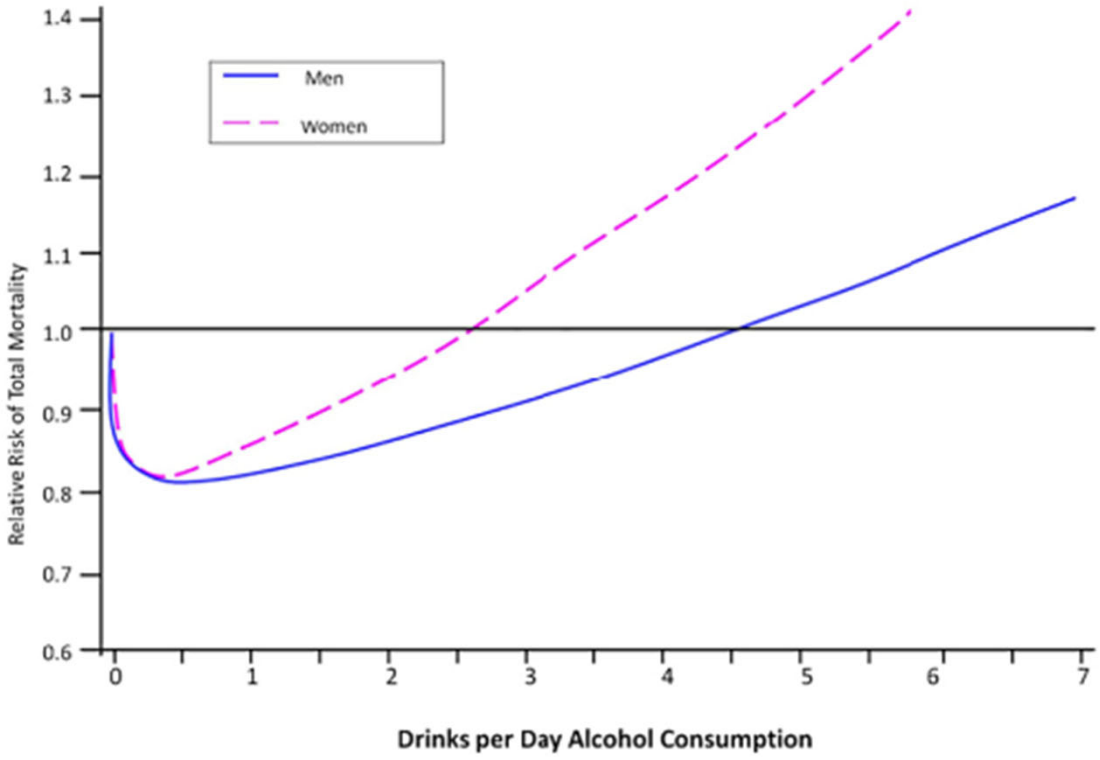
PSYCHOLOGICAL CV RISK FACTORS

- stress
- sadness
- depression
- anger
- hostility
- bad partners' behavior

ALCOHOL

- dose important
- pancreatic irritation/necrosis
- IARC: **cancerogen A (proven human cancerogen)**

ALCOHOL INTAKE AND TOTAL MORTALITY



O'Keefe EL, DiNicolantonio JJ, O'Keefe JH, Lavie CJ. Alcohol and CV Health: Jekyll and Hyde J-Curves. Prog Cardiovasc Dis. 2018 May-Jun;61(1):68-75.

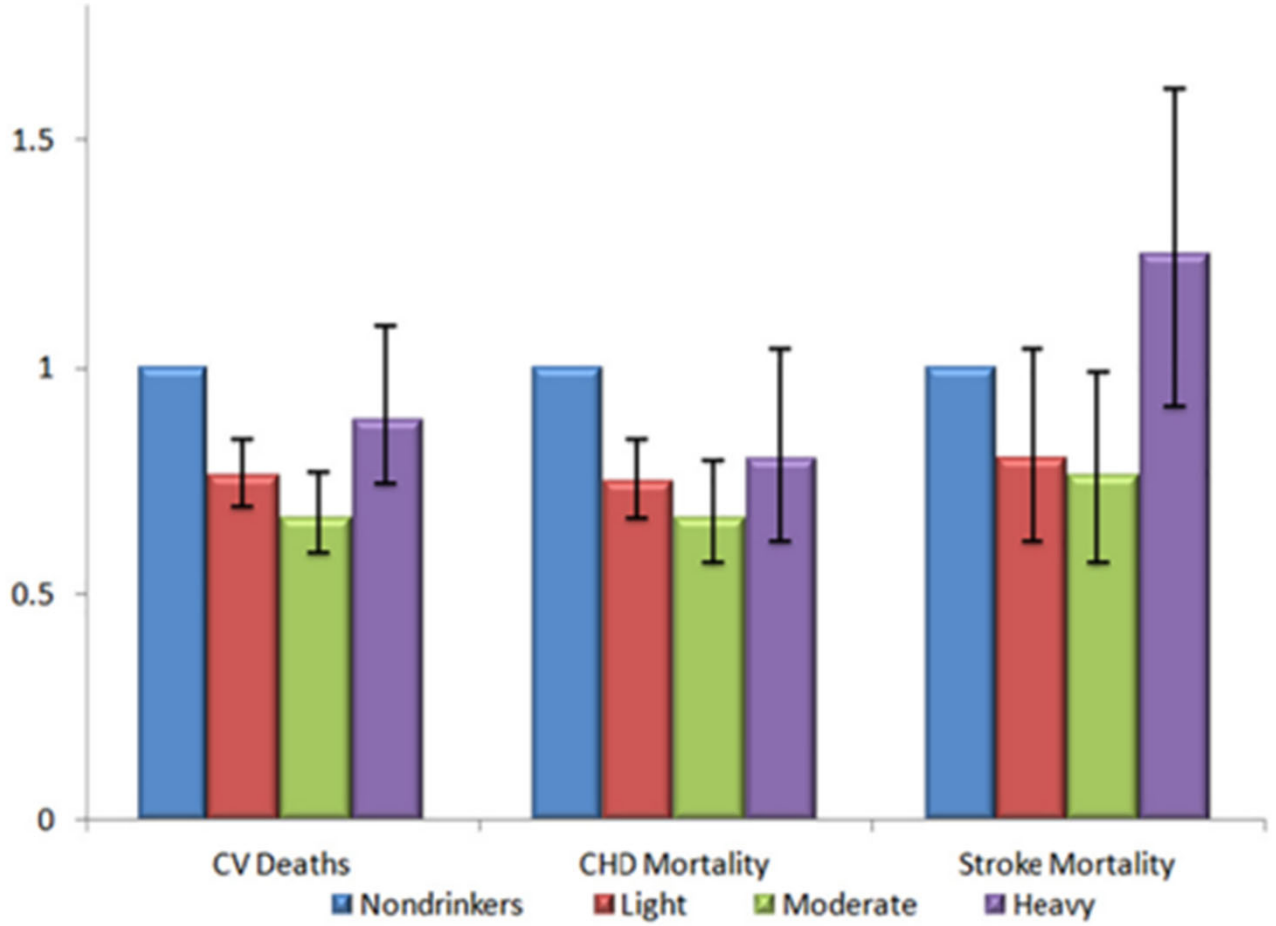


Fig 2. Adjusted risks for cardiovascular (CV) disease as a function of alcohol intake. *Abbreviations*: CHD = coronary heart disease; HR = hazard ratio. Error bars indicate 95% CIs. Data from *Journal of the American College of Cardiology*.[12]

O'Keefe EL, DiNicolantonio JJ, O'Keefe JH, Lavie CJ. Alcohol and CV Health: Jekyll and Hyde J-Curves. Prog Cardiovasc Dis. 2018 May-Jun;61(1):68-75.

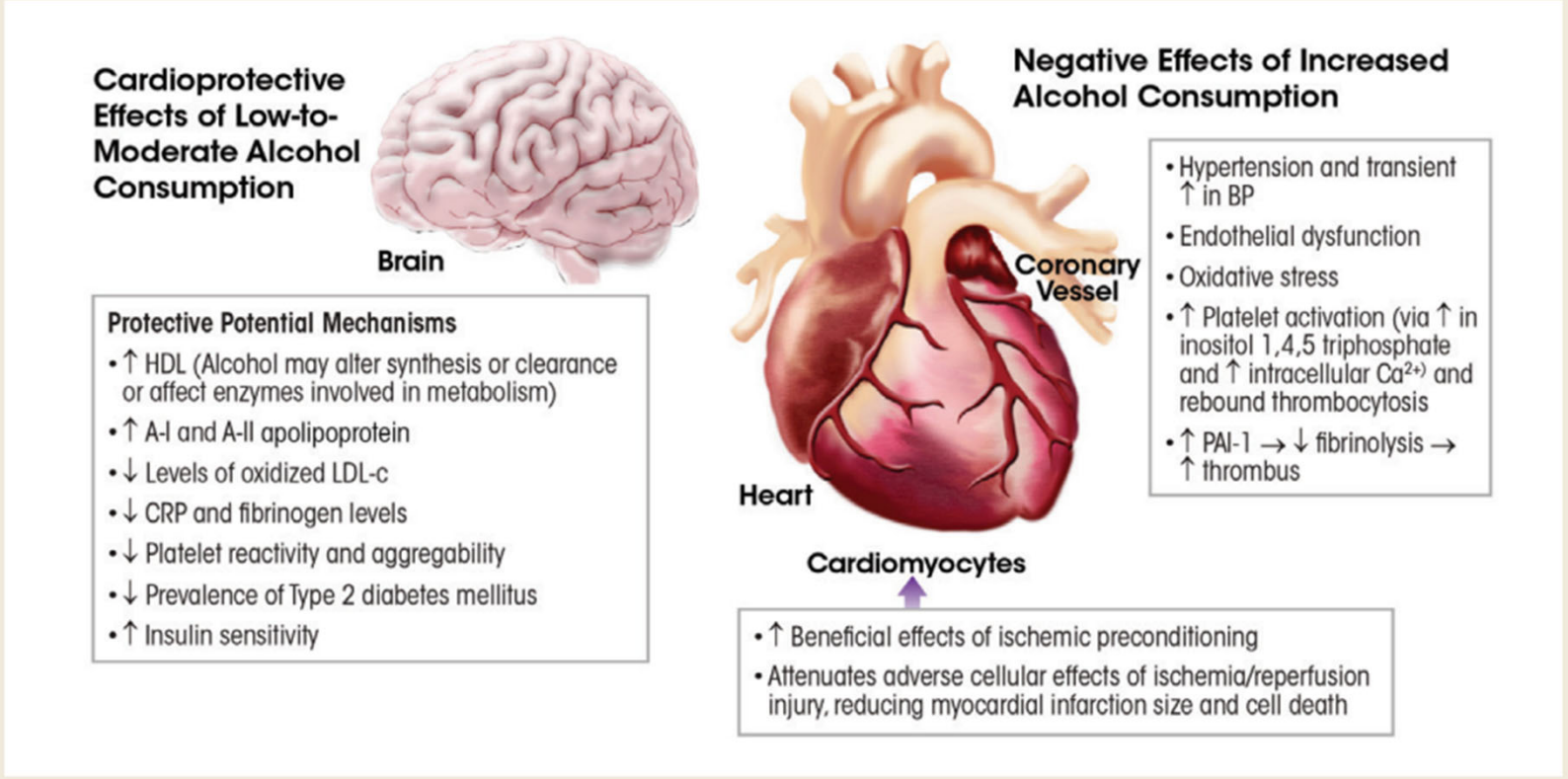


Figure 3 Mechanisms related to the positive and adverse effects of alcohol on cardiovascular conditions, such as coronary heart disease and stroke as well as cardiomyopathy. Different mechanisms may be in effect depending on the dose, duration, and pattern of alcohol consumption.

NOTE: BP = blood pressure, Ca^{2+} = calcium, CRP = C-reactive protein, DM = diabetes mellitus, HDL = high-density lipoprotein, LDL = low-density lipoprotein, PAI-1 = plasminogen activator inhibitor-1.
SOURCE: Adapted from Krenz and Korthuis 2012.

Piano MR. Alcohol's Effects on the Cardiovascular System. Alcohol Res. 2017;38(2):219-241.

ALCOHOL AND CVD

- ethanol at higher doses – proven cardiotoxin
- ↑ risk of arrhythmias (esp. AF) in binge drinkers
- heavy drinking: alcoholic cardiomyopathy
- regular alcohol consumption ↑elevates BP in a dose-dependent fashion
- chronic heavy alcohol intake and chronic alcoholism are potent independent risk factors for stroke

O'Keefe EL, DiNicolantonio JJ, O'Keefe JH, Lavie CJ. Alcohol and CV Health: Jekyll and Hyde J-Curves. Prog Cardiovasc Dis. 2018 May-Jun;61(1):68-75.

WHAT IS A SAFE DOSE?

MAXIMUM OF 100G/WEEK

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, European Heart Journal (2021) 42, 3227-3337

PHYSICAL ACTIVITY

= obesity prevention

- aerobic sports
- decrease of TAG, increase of HDL
- best daily, at least 3x/week one hour

- **Better fit and fat than unfit and unfat**!!!

But…

- chronic excessive endurance exercise might adversely impact CV health:
- ultra-endurance races can inflict acute myocardial damage (↑ TnI and BNP)
- sudden cardiac arrest – more often in marathons and thriathlons vs. in shorter racers
- veteran endurance athletes - often abnormal cardiac remodeling with ↑ risk for myocardial fibrosis and coronary calcification

O'Keefe EL, Torres-Acosta N, O'Keefe JH, Lavie CJ. Training for Longevity: The Reverse J-Curve for Exercise. Mo Med. 2020 Jul-Aug;117(4):355-361.

- chronic excessive exercise – associated with ↑ risks of atrial fibrillation (AF), and along with some attenuation of longevity benefits
- OPTIMAL DOSE OF EXERCISE: uknown (probably differs among individuals)
- current studies: 2.5 to 5 hours/week of moderate or vigorous physical activity will confer maximal benefits
- >10 hours/week may reduce these health benefits

O'Keefe EL, Torres-Acosta N, O'Keefe JH, Lavie CJ. Training for Longevity: The Reverse J-Curve for Exercise. Mo Med. 2020 Jul-Aug;117(4):355-361.

DYSLIPIDAEMIA

Table 1. Impact of specific dietary changes in the management of dyslipidemia with focus on lowering low-density lipoprotein cholesterol (LDL-C) concentration.

Dietary Component	Specific Recommendation	Magnitude of Effect [1]	Strength (Level) of Evidence [2]
Dietary fat			
Reduce intake of saturated fatty acids (SAFA)	<10% of total energy intake (TE)<7% TE in the presence of hypercholesterolemia	++	***
Exchange SAFA with unsaturated fatty acids	Lower SAFA and increase intake of mono- (MUFA) and polyunsaturated fatty acids (PUFA)	++	***
Avoid intake of dietary trans fat	Reduce to <1%TE	++	***
Reduce intake of dietary cholesterol	<300 mg/day	+	**
Dietary fiber (DF)			
Increase total DF intake	25–40 g/day	++	***
Increase intake of soluble fibers, e.g., beta-glucan	≥7–13 g/day as part of total DF intake	++	***
Phytosterols	≥2 g/day	++	***

Modified based on the 2019 ESC/EAS guidelines for the management of dyslipidaemias [2]. [1,2] Magnitude of effect and strength of evidence refer to the impact of each dietary change on lowering TC and LDL-C concentrations. [1] Magnitude of effect: ++ = 5–10% reduction; + = <5% reduction. [2] Level of evidence: *** Data derived from multiple randomized clinical trials (RCTs) or meta-analyses; ** Data derived from a single RCT trial or from large non-randomized studies.

Trautwein EA, McKay S. The Role of Specific Components of a Plant-Based Diet in Management of Dyslipidemia and the Impact on Cardiovascular Risk. Nutrients. 2020 Sep 1;12(9):2671.


TERRA
exotic vegetable chips
ORIGINAL
13:37
BEST BEFORE
01SEP11 MH2104
NO TRANS FAT
PARVE
NET WT
1 oz (28g)

HYPERTENSION

- BP ≥ 135/80 mmHg repeatedly measured **!!!**
- Prevalence in the CR around 35 % (higher in higher age)
- Primary (esencial) hypertension 90%, secondary hypertension 10%
- The most important action:

OBESITY

- After smoking, the most frequent preventable cause of death
- Over 30 % women, over 20 % men in ČR
- Prevalence increases
- Type apple = abdominal fat cummulation
- Type pear = gynoid obesity
- **Waist circumference =** marker of the risk

OBESITY

- **Complex** attitude –behavioral intervention, physical aktivity, food intake… (event. bariatric surgery)
- BUT: clinical trials of nonsurgical obesity treatments have not shown benefits in CVD, although recent diabetes trials have demonstrated major CV benefits.
- however, bariatric (metabolic) surgery – associated with substantial and reproducible CVD benefits

Albaugh VL, Kindel TL, Nissen SE, Aminian A. Cardiovascular Risk Reduction Following Metabolic and Bariatric Surgery. Surg Clin North Am. 2021 Apr;101(2):269-294.

OBESITY PARADOX

= the better prognosis in overweight/obese individuals affected by CVD compared with leaner subjects

- a protective role of obesity proven for overall and CV mortality in patients affected by coronary heart disease (CHD), HF, atrial fibrillation (AF), end-stage renal disease, chronic obstructive pulmonary disease and type 2 diabetes mellitus

Vecchié A, Dallegri F, Carbone F, Bonaventura A, Liberale L, Portincasa P, Frühbeck G, Montecucco F. Obesity phenotypes and their paradoxical association with cardiovascular diseases. Eur J Intern Med. 2018 Feb;48:6-17.

WAIST-TO-HIP RATIO, WHR

- Waist circumference:

Female: > 80 cm high risk

Male: > 94 cm high risk

- WHR (better CV risk indicator than BMI):

Female: > 0,85

Male: > 1,0

% OF BODY FAT

Age	Up to 30 years	30 – 50 years	50 +
Female	14 – 21%	15 - 21%	16 – 25%
Male	9 – 15%	11 – 17%	12 – 19%

METABOLIC SYNDROME

- At least 3 out of following (WHO):

Waist circumference > 88 cm (female), >102 cm (male)

BP > 130/85 mmHg

Glycaemia > 6,0 mmol/l

TAG > 1,7 mmol/l

HDL < 1,25 mmol/l (female), <1,0 mmol/l (male)

METABOLIC SYNDROME AND OBESITY

BMI = weight (*kg*) /height^2 (*m*)

< 18.5 underweight

18.5 – 24.9 normal weight

25.0 – 29.9 overweight

30.0 – 34.99 obesity I. st grade

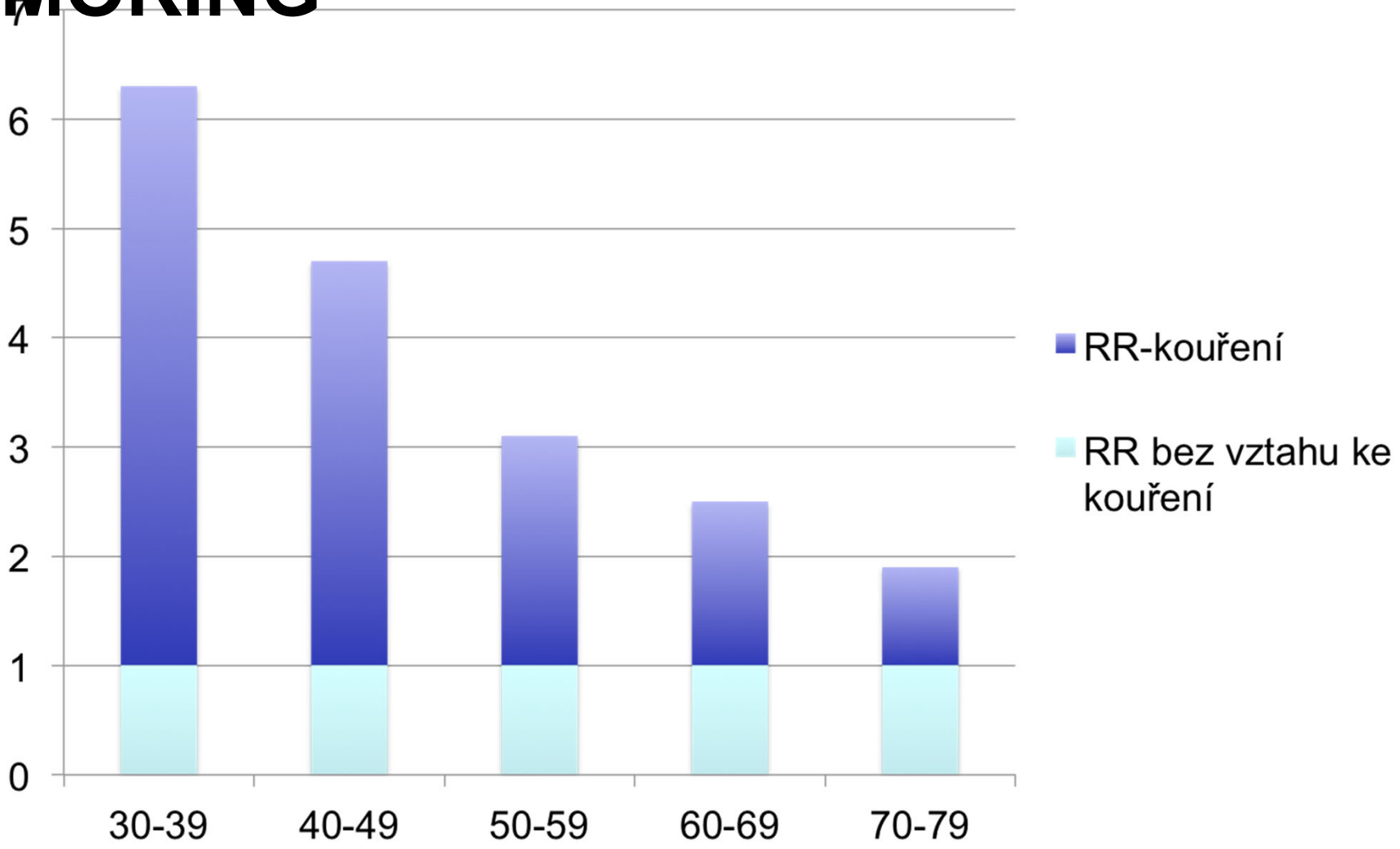
35.0 – 39.9 obesity II. nd grade

> 40.0 obesity III. rd grade

METABOLIC SYNDROME AND OBESITY

- Normal weight - metabolic sy < 3 %
- BMI > 35 almost 100 %

RR IM ACCORDING TO AGE AND SMOKING

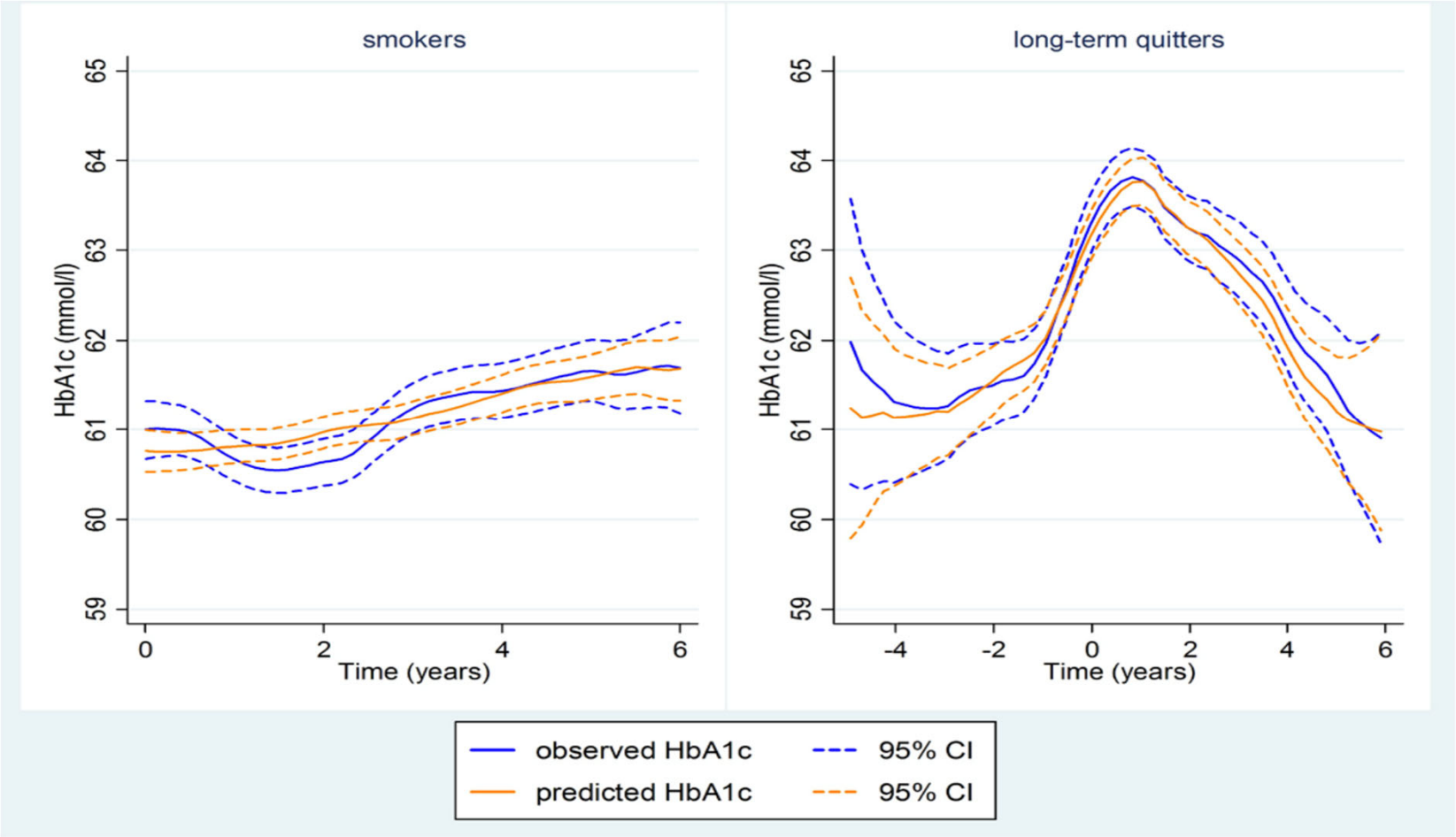


Parish S, Collins R, Peto R, Youngman L, Barton J, Jayne K, Clarke R, Appleby P, Lyon V, Cederholm-Williams S, et al. Cigarette smoking, tar yields, and non-fatal myocardial infarction: 14,000 cases and 32,000 controls in the United Kingdom. The International Studies of Infarct Survival (ISIS) Collaborators. BMJ 1995 Aug 19;311(7003):471-7.

DIABETES MELLITUS

- Diabetes – atherosclerosis manifestation
  Complications: micro/macroangiopatic, metabolic)
- Prevalence in the CR 8 – 10 %
- Metabolic sy connected esp. with type II diabetes (insuline rezistence)

SMOKING CESSATION AND DM COMPENSATION



Lycett D et al.: The association between smoking cessation and glycaemic control in patients with type 2 diabetes: a THIN database cohort Lancet Diabetes Endocrinol. 2015 Jun;3(6):423-430

SUBCLINICAL THYROID DYSFUNCTION

- subclinical thyroid dysfunction (STD) - subclinical hypothyroidism (SHypo)/subclinical hyperthyroidism (SHyper) - abnormal serum thyrotropin (TSH) and normal free thyroid hormones – associated with ↑CV risk and mortality (ie. atherosclerosis, CAD, heart failure, cardiac arrhythmias, predominantly atrial fibrillation…)

Manolis AA, Manolis TA, Melita H, Manolis AS. Subclinical thyroid dysfunction and cardiovascular consequences: An alarming wake-up call? Trends Cardiovasc Med. 2020 Feb;30(2):57-69.

- no consensus (lack of randomized controlled studies), but some evidence exists (observational studies) that treatment of STD reduces CV events
- patients with severe SHypo (TSH > 10 mIU/L) or grade 2 SHyper (TSH < 0.1 mIU/L) should receive treatment, mostly for the increased risk of CV morbidity and mortality

Manolis AA, Manolis TA, Melita H, Manolis AS. Subclinical thyroid dysfunction and cardiovascular consequences: An alarming wake-up call? Trends Cardiovasc Med. 2020 Feb;30(2):57-69.

PSYCHOSOCIAL FACTORS

- Personal characteristics
- **Depression** – prevalence across EU around 15 %
- **Anxiety**

A COMPLEX CIRCLE

- Smoking is the main CV risk factor
- Depressive patients smoke more often
- Smokers suffer more often depression
- Depression increases the CV risk
- CV patiens are more often depressive

STRESS

- Reaction of the organism to some danger
- Originally: activation of the sympato-adrenomedullar system and testosteron – „fight or flight“
- **Long-time, chronic stress:** activation hypophysal-adrenocortical system with production of ACTH, cortocoids and adrogen alteration (lowering testosteron in male and estrogens in female)

STRESS

- chronic stress: lost of metabolism control, reproduction, immunity, depression
- high working load may lead to chronic fatigue syndrome, burn-out syndrome

BURN-OUT SYNDROME

The state of emotional exhaustion and depersonalization that leads to a decrease in work efficiency
Main trigger: chronic stress, permanent pressure, high emotional tension
Z73.0 - Extinction, defined as "state of exhaustion"

CV EPIDEMIC

- About 50 years ago: “manager’s disease”
- Currently: a worker, taxi driver

L. Husten v The Lancet 352:1530, 1998

EBM/EBP – EVIDENCE BASED MEDICINE/PRACTICE

Evidence Based Medicine – EBM

„ the conscientious, explicit, and judicious use of current best **evidence** in making decisions about the care of individual patients.“

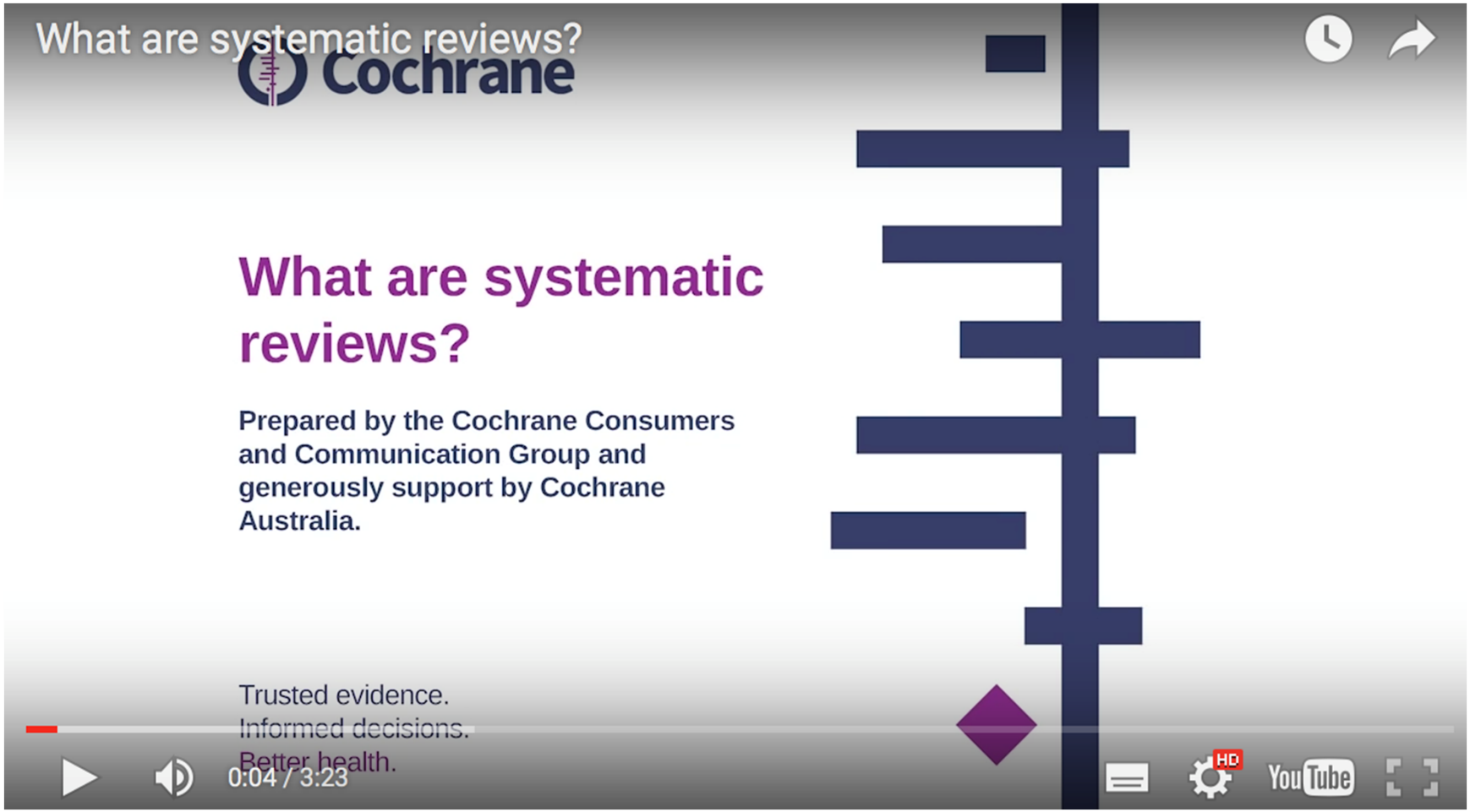
(Sackett et al., 1996)

HIERARCHY OF EVIDENCE

1. Metaanalyses and systematic reviews
2. Randomised controlled trials, RCT)
3. Cohort trials
4. Case-control studies
5. Cross-sectional studies
6. Case reports

COCHRANE REVIEW

WWW.COCHRANE.ORG



THE POWER OF EVIDENCE

(CAN DIFFER!)

A – highest recommendation level based on metaanylyses and best RCT (large studies)

B – middle recommendation based on smaller RCT

C – lower recommendation based on prospective, retrospective or case-control studies

D – very low recommendation level based on „consensus“ or „experts recommendation“

GUIDELINES EXAMPLE…

Recommendation: Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment, except where contraindicated or for specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers, and adolescents). (Strength of Evidence = A)

Fiore M et al.: Treating Tobacco Use and Dependence, 2008, https://www.ncbi.nlm.nih.gov/books/NBK63943/#A28430

…EXAMPLE: GUIDELINES

Table 6.3 Summary of strength of evidence for recommendations

Strength-of-evidence classification	Criteria
Strength of Evidence = A	Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings.
Strength of Evidence = B	Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal. For instance, few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the recommendation.
Strength of Evidence = C	Reserved for important clinical situations in which the Panel achieved consensus on the recommendation in the absence of relevant randomized controlled trials.

From: 6, Evidence and Recommendations

Treating Tobacco Use and Dependence: 2008 Update.
Tobacco Use and Dependence Guideline Panel.
Rockville (MD): US Department of Health and Human Services; 2008 May.

Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[35]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the The Canadian Task Force on Preventive Health Care.[35]

https://www.jogc.com/article/S1701-2163(16)34746-6/pdf

OSTEOARTHROSIS TREATMENT BY STEM CELLS…

…is an experimental method, and it is not realistic to expect EBM 1-2 level recommendation in the near future.....

Journal of Public Health
October 2017, Volume 25, Issue 5, pp 453–460 | Cite as

Tobacco smoking and multiple sclerosis: a systematic review of systematic and narrative reviews of observational studies

Authors Authors and affiliations

Insa Backhaus, Alice Mannocci, Giuseppe La Torre

Results

Seventeen reviews met the inclusion criteria and were categorized as either systematic reviews or narrative reviews. Smoking was associated with increased risk of MS for ever- compared with never-smokers and current compared with non-smokers. The summary **odds ratio of MS for ever-smokers versus never-smokers varied between 1.40 (95% CI: 1.29–1.52) and 1.46 (95% CI: 1.33–1.59).**

Categories: Scientific Conferences & Meetings | **Published:** November 08, 2021

E-cigarette users face 15% higher risk of stroke at a younger age than traditional smokers

This abstract will no longer be presented at Scientific Sessions 2021. Unfortunately, the researchers were not able to complete their presentation.

Circulation

ORIGINAL RESEARCH ARTICLE

Combined Associations of Changes in Noncombustible Nicotine or Tobacco Product and Combustible Cigarette Use Habits With Subsequent Short-Term Cardiovascular Disease Risk Among South Korean Men

A Nationwide Cohort Study

Seulggie Choi, MD; Kiheon Lee, MD, PhD; Sang Min Park, MD, PhD, MPH

BACKGROUND: The associations of changes in noncombustible nicotine or tobacco product (NNTP) and combustible cigarette (CC) use habits with subsequent cardiovascular disease (CVD) risk are still unclear.

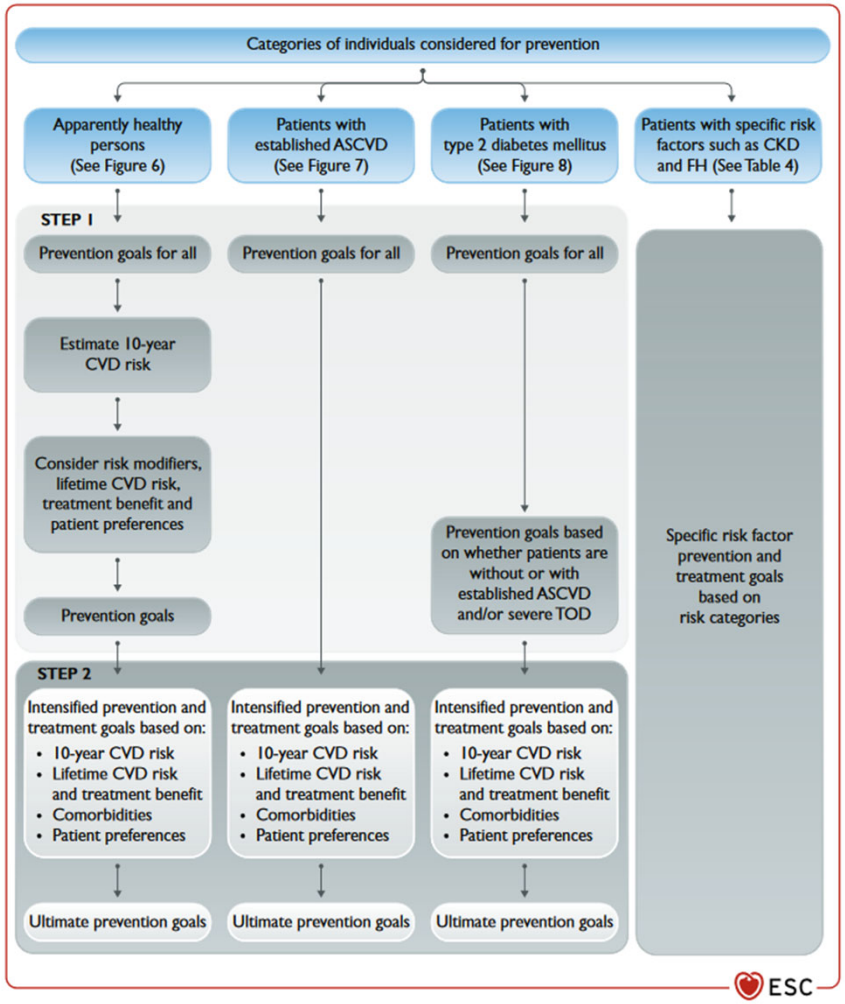
METHODS: The study population consisted of 5 159 538 adult men who underwent health screening examinations during both the first (2014–2015) and second (2018) health screening periods from the Korean National Health Insurance Service database. All participants were divided into continual CC-only smokers, CC and NNTP users, recent (<5 years) CC quitters

CONCLUSIONS: Switching to NNTP use among initial CC smokers was associated with lower CVD risk than continued CC smoking. On CC cessation, NNTP use was associated with higher CVD risk than CC quitting without NNTPs. Compared with CC smokers who quit without NNTP use, CC quitters who use NNTPs may be at higher future CVD risk.

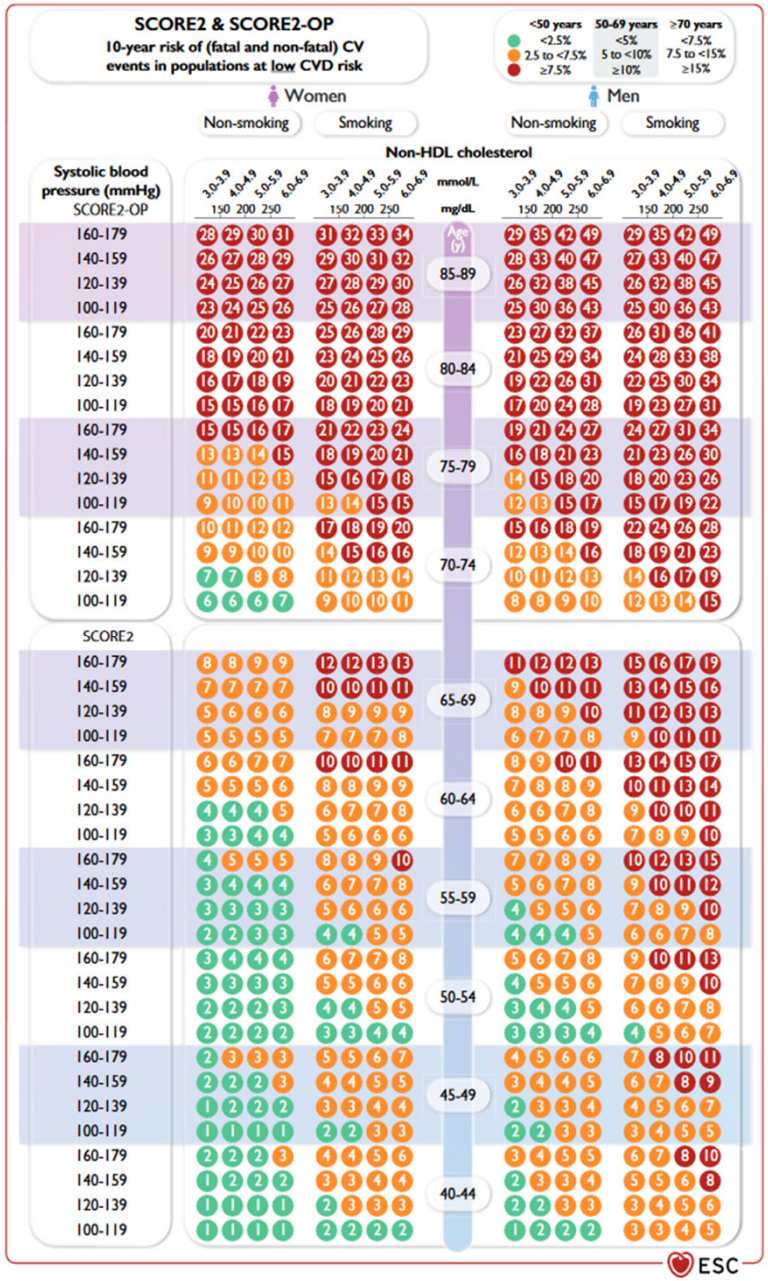
STUDY WITHDRAWN

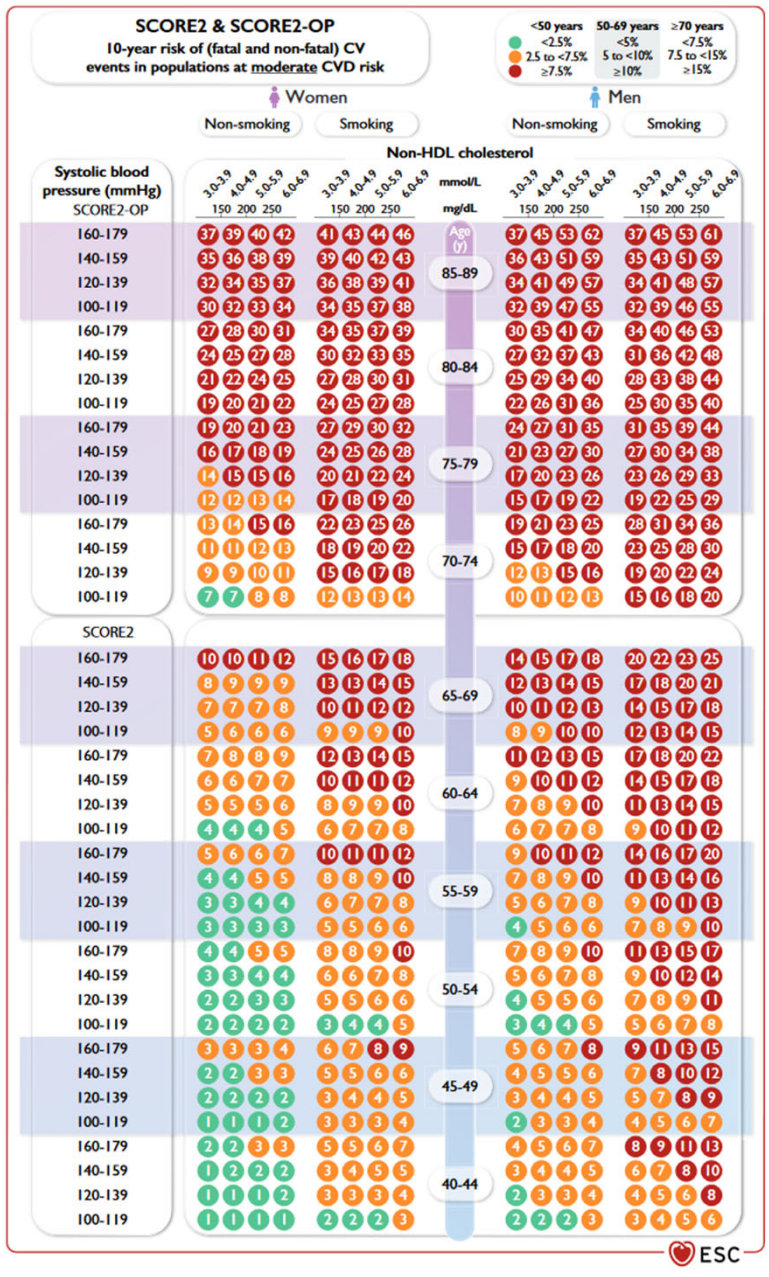
This study does not (or cannot) separate out the effects of prior history of smoking. The author states the limitations, but seems not to fully grasp the limitation of the data she is working with. I recall years ago we observed those wearing a nicotine patch to have a higher rate of Myocardial Infraction (MI). However, the high rate of MI was not due to the patch, but the higher risk status of those attracted to use a nicotine patch (self-section bias).

CV RISK MANAGEMENT



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, European Heart Journal (2021) 42, 3227-3337





2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, European Heart Journal (2021) 42, 3227-3337

THANKS FOR ATTENTION!

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