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Centro Cardiologico Monzino

Milan – June 25 2012

Euroheart II - European Workshop

"DIET, PHYSICAL ACTIVITY AND CARDIOVASCULAR DISEASE PREVENTION IN EUROPE"

An overview and focus on the needs

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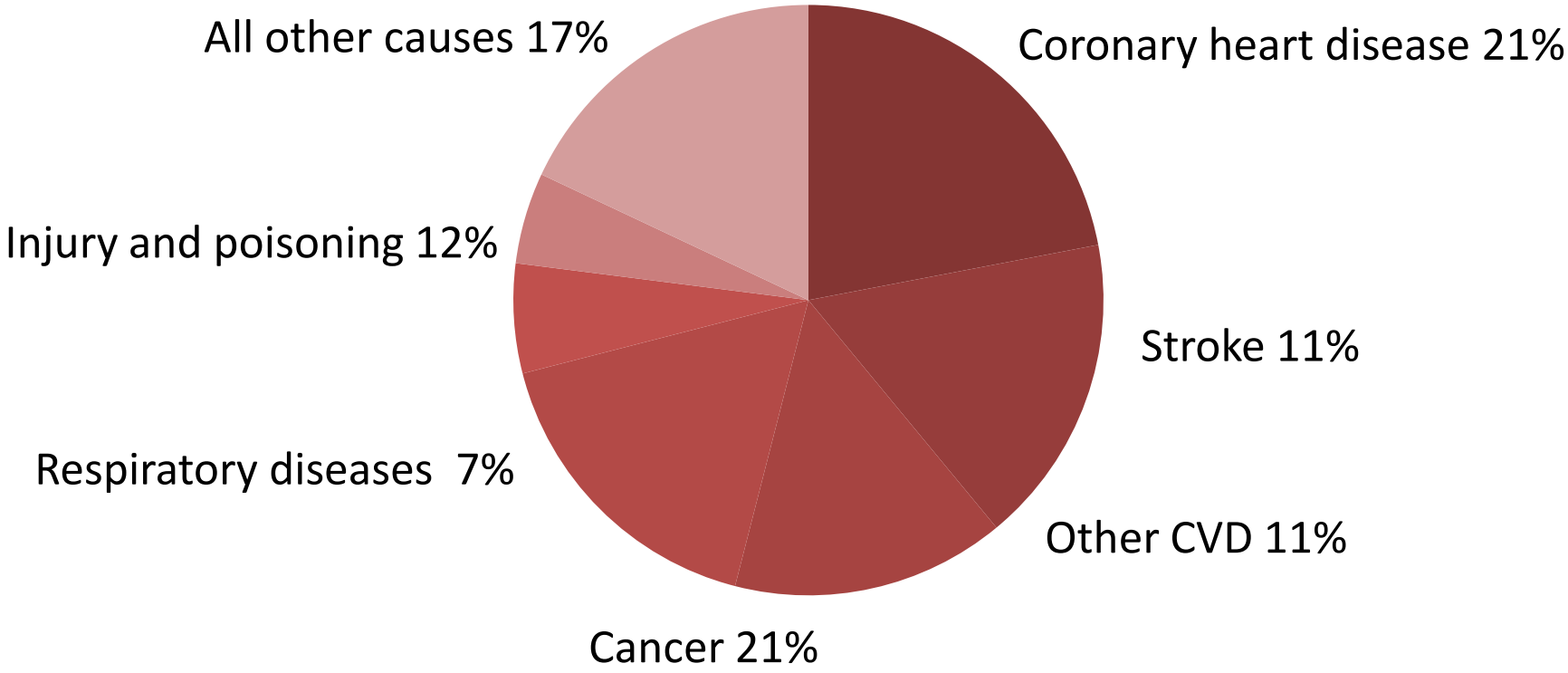
Deaths by cause, men, between 1997 and 2006, in Europe



From "Diet hysical activity and cardiovacular diseases prevention in Europe, "Summary Report EHN November 2011

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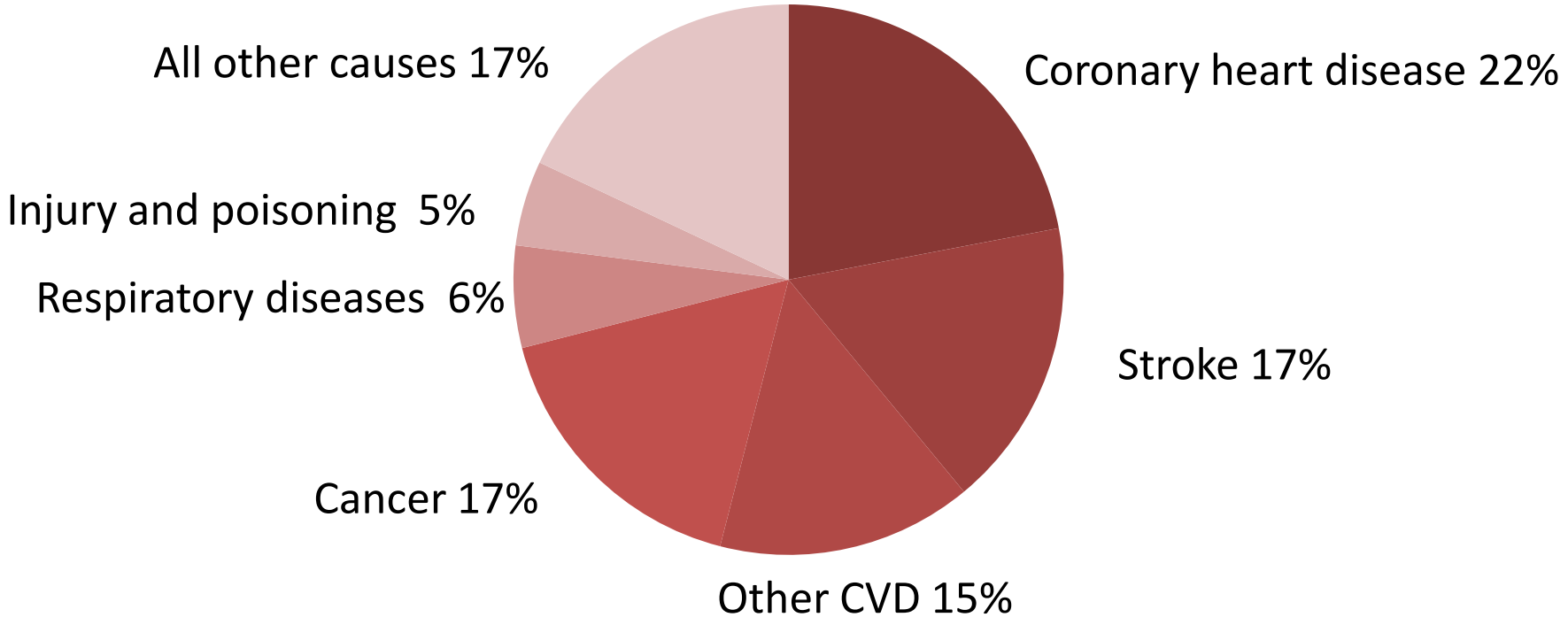
Deaths by cause, women, between 1997 and 2006, in Europe



From "Diet hysical activity and cardiovacular diseases prevention in Europe, "Summary Report EHN November 2011

- Cardiovascular disease remains a serious medical problem that can be associated with death and disability on one hand and considerable resource use on the other.
- Clinical efficacy remains the primary driver for the use of any service. Once efficacy is established and despite its many limitations, cost-effectiveness analysis has an important role in assessing value.

- Assessing the value of prevention in apparently healthy patients is generally more difficult than evaluating therapy for established disease because the time horizon to the clinical manifestation of disease is generally long—many decades in the young.
- Thus, it is difficult, perhaps impossible, to assess long term effectiveness in terms of survival or quality-adjusted life-years (QALYs)
- There are technical and practical limitations to studies of the cost-effectiveness of prevention.

Given the difficulties of conducting long-term clinical trials, many cost-effectiveness analyses about prevention are based on mathematical models or simulations.

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Questions to be answered

1. how many people alive today are candidates for at least one prevention activity
2. how much of the morbidity, mortality, and cost of these diseases is potentially preventable
3. what could realistically be accomplished
4. Which are the most important in terms of their potential effects on health outcomes, costs, and cost-effectiveness
5. what are the main factors that determine the cost-effectiveness of a prevention activity

- **Ideally, the answers to the above questions would be obtained by examining the results of clinical trials.**

- **Lacking clinical trials, the only alternative is to use a mathematical model.**

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Kahn R. et al., **The Impact of Prevention on Reducing the Burden of Cardiovascular Disease.** ***Circulation. 2008;118:576-585.)***

- **The Archimedes model is a person-by-person, object-by- object, large-scale simulation model of physiology, disease, and health care systems written at a high level of detail using object-oriented programming and run on a distributed computing network.**

- **The model uses person-specific data from real populations (eg, the National Health and Nutrition Education Survey [NHANES]) to create simulated populations that match the real populations, person by person.**
- **For the study, 11 prevention activities relating to CVD and combinations of these activities were analyzed**

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Kahn R. et al., The Impact of Prevention on Reducing the Burden of Cardiovascular Disease. *Circulation. 2008;118:576-585.*

Table 1. Interventions Studied

Intervention	Total Eligible Population ×1000, %	Treatment Goals	Feasible Performance, % Achieved*
Baseline (without interventions)	200 000 (100)	. . .	. . .
Provide aspirin if 10-year MI risk ≥10%	12 315 (6.2)†	81 mg aspirin/day	50
Lower LDL cholesterol to <160 mg/dL in low-risk individuals‡	15 445 (7.7)	<160 mg/dL	75
Lower LDL cholesterol to <130 mg/dL in high-risk individuals§	17 857 (8.9)	<130 mg/dL	70
Lower LDL cholesterol to <100 mg/dL in people with CAD	3212 (1.8)	<100 mg/dL	70
Lower blood pressure to 140/90 mm Hg in nondiabetic individuals	30 820 (15.4)	<140/90 mm Hg	75
Lower A1C to <7.0% in diabetic individuals	5739 (2.9)	<7.0%	60
Lower blood pressure to 130/80 mm Hg in diabetic individuals	11 498 (5.8)	<130/80 mm Hg	60
Lower LDL cholesterol to <100 mg/dL in diabetic individuals	13 000 (6.5)	<100 mg/dL	65
Reduce FPG to <110 mg/dL	16 392 (8.2)	FPG <110 mg/dL	60
Smoking cessation	49 265 (24.6)	Stop immediately	30
Reduce weight to BMI <30 kg/m^2	60 257 (30.1)	BMI <30 kg/m^2	20

Effect of Interventions Over 30 Years on Outcomes and Costs (Thousands) in the US Population (Assuming 100% Performance)

	MI Total	Stroke Total	Life-Years Total	QALYs	Cost of Prevention Interventions	Cost of All Medical Activities Except Prevention Interventions	Cost of Total Medical	Cost/QALY
Baseline (without interventions)	43 208±736	33 138±665	4 870 695	4 459 603	—	$9 504 964 366	$9 504 964 366	NA
Difference caused by prevention activities (thousands)								
Do everything, 100% performance	−27 429 (−63%)	−10 212 (−31%)	220 710 (5%)	243 926 (5%)	8 530 159 750	−904 118 726 (−10%)	7 626 041 025 (80%)	$36 380
Aspirin to high-risk individuals	−3409 (−8%)	331 (1%)	17 417 (0%)	17 005 (0%)	50 094 774	604 823 (0%)	50 699 597 (1%)	$2779
BMI <30 kg/m^2	−7133 (−17%)	−1083 (−3%)	55 200 (1%)	65 779 (1%)	1 204 091 934	−192 856 223 (−2%)	1 011 235 711 (11%)	$18 941
Blood pressure <140/90 mm Hg in nondiabetic individuals	−2851 (−7%)	−4574 (−14%)	39 124 (1%)	38 737 (1%)	1 973 968 837	−185 029 283 (−2%)	1 788 939 554 (19%)	$52 983
CAD: LDL cholesterol <100 mg/dL	−2246 (−5%)	−176 (−1%)	14 052 (0%)	10 985 (0%)	367 637 668	22 827 810 (0%)	390 465 478 (4%)	$39 130
Diabetes: blood pressure <130/80 mm Hg	−3355 (−8%)	−2337 (−7%)	30 984 (1%)	32 626 (1%)	824 447 730	−100 554 813 (−1%)	723 892 917 (8%)	$25 317
Diabetes: A1C <7%	−1086 (−3%)	263 (1%)	25 282 (1%)	38 389 (1%)	1 780 231 248	−231 969 165 (−2%)	1 548 262 083 (16%)	$48 759
Diabetes: LDL cholesterol <100 mg/dL	−4434 (−10%)	−760 (−2%)	18 036 (0%)	18 350 (0%)	1 077 255 101	−24 148 005 (0%)	1 053 107 096 (11%)	$67 199
High-risk CAD: LDL cholesterol <130 mg/dL	−3094 (−7%)	−1636 (−5%)	21 525 (0%)	21 222 (0%)	1 549 184 577	−17 874 128 (0%)	1 531 310 449 (16%)	$83 327
Low-risk CAD: LDL cholesterol <160 mg/dL	−924 (−2%)	−553 (−2%)	3707 (0%)	3990 (0%)	736 032 166	−53 235 769 (−1%)	682 796 396 (7%)	$272 061
Pre-diabetes: FPG <110 mg/dL	−3686 (−9%)	−322 (−1%)	25 443 (1%)	42 617 (1%)	819 873 408	−231 927 737 (−2%)	587 945 671 (6%)	$17 478
Smoking: stop	−3311 (−8%)	−1387 (−4%)	28 142 (1%)	27 597 (1%)	25 279 854	−72 490 798 (−1%)	−47 210 943 (0%)	−$1755

Data are means±SEM or n (%) unless otherwise indicated. FPG, fasting plasma glucose.

Effect of Interventions Over 30 Years on Outcomes and Costs (Thousands) in the US Population (Assuming Maximum Feasible Performance)

	MI Total	Stroke Total	Life-Years Total	QALYs	Cost of Prevention Intervention(s)	Cost of All Medical Activities Except Prevention Interventions	Cost of Total Medical	Cost/QALY
Baseline (without interventions)	43 208±736	33 138±665	4 870 695	4 459 603	—	$9 504 964 366	$9 504 964 366	NA
Difference caused by prevention activities (thousands)								
Do everything, feasible performance	−15 527 (−36%)	−6718 (−20%)	131 543 (3%)	147 161 (3%)	5 848 702 328	−495 593 170 (−5%)	5 353 109 158 (56%)	$42 249
Aspirin to high-risk individuals	−1705 (−4%)	166 (0%)	8708 (0%)	8503 (0%)	25 047 387	302 412 (0%)	25 349 799 (0%)	$2779
BMI <30 kg/m^2	−1427 (−3%)	−217 (−1%)	11 040 (0%)	13 156 (0%)	240 818 387	−38 571 245 (0%)	202 247 142 (2%)	$18 941
Blood pressure <140/90 mm Hg in nondiabetic individuals	−2138 (−5%)	−3431 (−10%)	29 343 (1%)	29 053 (1%)	1 480 476 628	−138 771 963 (−1%)	1 341 704 665 (14%)	$52 983
CAD: LDL cholesterol <100 mg/dL	−1572 (−4%)	−123 (0%)	9837 (0%)	7689 (0%)	257 346 368	15 979 467 (0%)	273 325 835 (3%)	$39 130
Diabetes: blood pressure <130/80 mm Hg	−2013 (−5%)	−1402 (−4%)	18 591 (0%)	19 576 (0%)	494 668 638	−60 332 888 (−1%)	434 335 750 (5%)	$25 317
Diabetes: A1C <7%	−652 (−2%)	158 (0%)	15 169 (0%)	23 034 (1%)	1 068 138 749	−139 181 499 (−1%)	928 957 250 (10%)	$48 759
Diabetes: LDL cholesterol <100 mg/dL	−2882 (−7%)	−494 (−1%)	11 723 (0%)	11 927 (0%)	700 215 816	−15 696 203 (0%)	684 519 612 (7%)	$67 199
High-risk CAD: LDL cholesterol <130 mg/dL	−2166 (−5%)	−1145 (−3%)	15 068 (0%)	14 855 (0%)	1 084 429 204	−12 511 890 (0%)	1 071 917 314 (11%)	$83 327
Low-risk CAD: LDL cholesterol <160 mg/dL	−693 (−2%)	−415 (−1%)	2780 (0%)	2993 (0%)	552 024 124	−39 926 827 (0%)	512 097 297 (5%)	$272 061
Pre-diabetes: FPG <110 mg/dL	−2212 (−5%)	−193 (−1%)	15 266 (0%)	25 570 (1%)	491 924 045	−139 156 642 (−1%)	352 767 402 (4%)	$17 478
Smoking: stop	−993 (−2%)	−416 (−1%)	8443 (0%)	8279 (0%)	7 583 956	−21 747 239 (0%)	−14 163 283 (0%)	−$1755

Data are means±SEM and n (%) unless otherwise indicated. FPG, fasting plasma glucose.

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Special Report

The Impact of Prevention on Reducing the Burden of Cardiovascular Disease

Richard Kahn, PhD; Rose Marie Robertson, MD, FAHA; Robert Smith, PhD; David Eddy, MD, PhD

Conclusions—Aggressive application of nationally recommended prevention activities could prevent a high proportion of the CAD events and strokes that are otherwise expected to occur in adults in the United States today. **However, as they are currently delivered, most of the prevention activities will substantially increase costs.** If preventive strategies are to achieve their full potential, ways must be found to reduce the costs and deliver prevention activities more efficiently.

(Circulation. 2008;118:576-585.)

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AHA Policy Statement

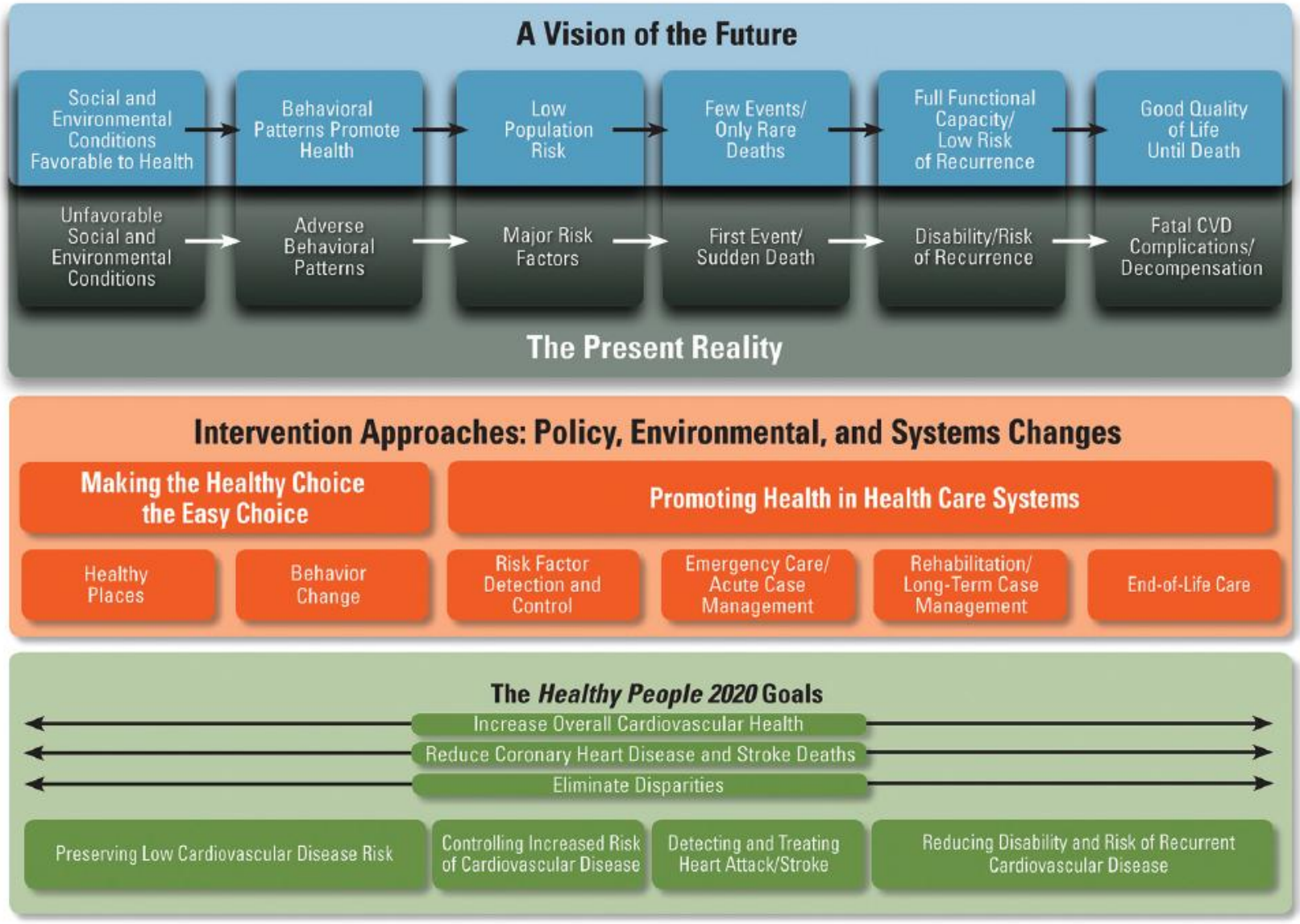
Value of Primordial and Primary Prevention for Cardiovascular Disease

A Policy Statement From the American Heart Association

William S. Weintraub, MD, FAHA, Chair; Stephen R. Daniels, MD, PhD, FAHA, Co-Chair; Lora E. Burke, PhD, MPH, FAHA; Barry A. Franklin, PhD, FAHA; David C. Goff, Jr, MD, PhD, FAHA; Laura L. Hayman, PhD, RN, FAHA; Donald Lloyd-Jones, MD, ScM, FAHA; Dilip K. Pandey, MBBS, PhD; Eduardo J. Sanchez, MD, MPH; Andrea Parsons Schram, DNP, CRNP; Laurie P. Whitsel, PhD; on behalf of the American Heart Association Advocacy Coordinating Committee, Council on Cardiovascular Disease in the Young, Council on the Kidney in Cardiovascular Disease, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Clinical Cardiology, and Stroke Council

Circulation. 2011;124:967-990.

ACTION FRAMEWORK FOR A COMPREHENSIVE PUBLIC HEALTH STRATEGY TO PREVENT HEART DISEASE AND STROKE



A framework for a comprehensive health strategy to prevent cardiovascular diseases (CVD), including policy, environmental, and systems changes to achieve Healthy People 2020 goals. Reprinted from Labarthe et al69 with permission of the publisher.

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AHA Policy Statement

Value of Primordial and Primary Prevention for Cardiovascular Disease

A Policy Statement From the American Heart Association

- Cardiovascular disease prevention can be achieved not only through drug interventions aimed at reducing major cardiovascular risk factors but also with appropriate life style modifications
- While the impact of drug therapies on CVD can be assessed with cost-benefit assessments, the impact of prevention measures is more difficult to assess also due to their time duration (life-long?)

Thus cardiovascular disease prevention does not only pertain to the individual state health systems, but it is a societal issue, linked to a correct and productive development.

Circulation. 2011;124:967-990.

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Needs:

- Technological developments to facilitate and sustain population-based interventions based on changes in lifestyle, with particular attention to nutrition and physical activity

- Development of motivational techniques in order to increase behavioral changes, including motivational strategies carried out during primary prevention

- Assessment of independent and adjunctive benefits of actions aimed at modifying lifestyle in comparison to the effect of cardioprotective therapies and viceversa.

- Assessment of the effects of moderate physical activity compared to strenous one, with particular attention to benefits, risks, and long term compliance

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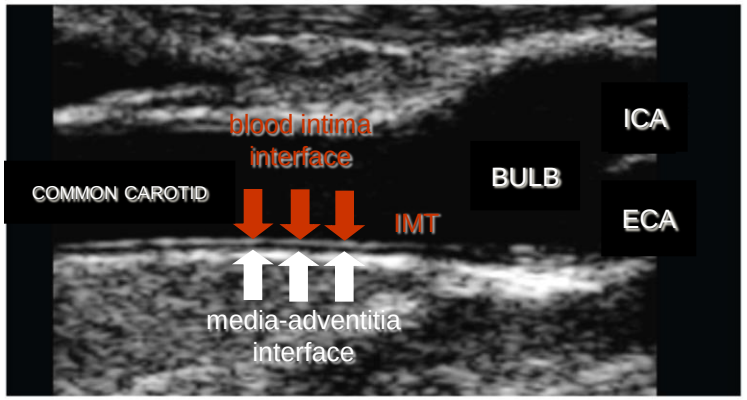
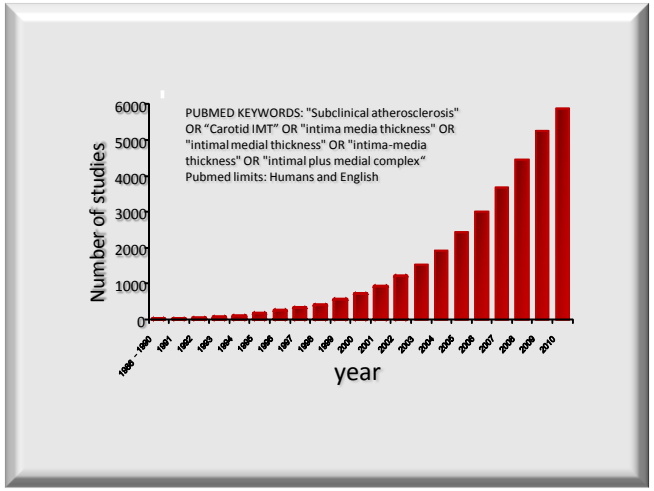
What we should discuss:

- Limits and advantages of places where to carry out preventive interventions (home, community, workplace, school, hospitals etc.)
- Potential impact of taxes on the consumption of junk food, sweeteneed drinks, and tabacco products)
- Potential impact of starting treatment of major CV risk factors early in life
- Role of genetic tests to develop personalized approaches to prevention
- Identify the best imaging or biochemical biomarker to assess the effect of preventive interventions

Carotid IMT: a biomarker of CV events

Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging
P Pignoli, E Tremoli, A Poli, P Oreste and R Paoletti
***Circulation* 1986, 74:1399-1406**





By the year 2012 we know that Carotid IMT correlates

With:

- **Cardiovascular risk factors**
- **Coronary disease assessed by angiography**
- **The prevalence of cardiovascular events**
- **The incidence os associated with new CV events**

European Heart Journal (2007) 28, 2094–2101
doi:10.1093/eurheartj/ehm244

Clinical research
Coronary heart disease

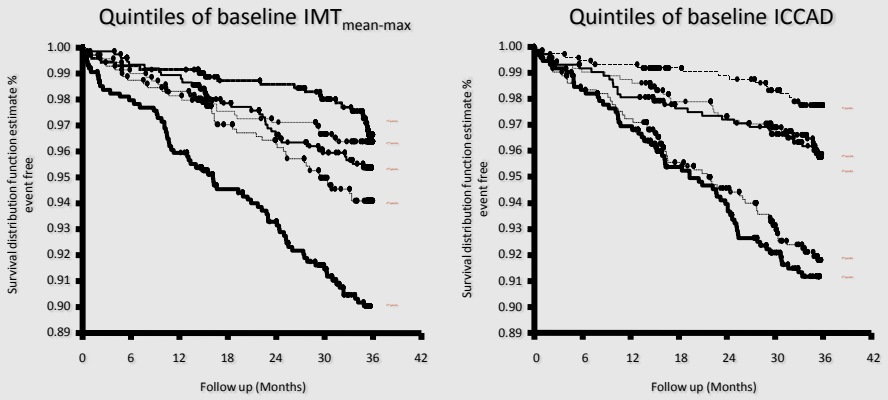
Carotid intima-media thickness by B-mode ultrasound as surrogate of coronary atherosclerosis: correlation with quantitative coronary angiography and coronary intravascular ultrasound findings

Mauro Amato[1], Piero Montorsi[1,2], Alessio Ravani[1], Elisa Oldani[1], Stefano Galli[1,2], Paolo M. Ravagnani[1,2], Elena Tremoli[1,3], and Damiano Baldassarre[1,3]*

Carotid IMT: a biomarker of CV events

THE IMPROVE STUDY
Carotid Intima Media Thickness (IMT) and IMT-Progression as Predictors of Vascular Events in a High Risk European Population

Kaplan-Meier event-free curves and the combined endpoint according to quintiles of $IMT_{mean-max}$ and ICCAD



Overall the studies indicate that Carotid IMT is a surrogate marker:

- to study the determinants of atherosclerotic disease
- to predict atherosclerotic dIsease in vascular districts other than carotids
- to estimate the risk to develop new CV events
- to increase the predictivity of cardiovascular risk chart
- to help clinicians in therapeutic decisions