NIEBP - Network Italiano Evidence Based Prevention

Formazione per le Antenne del NIEBP

Modulo 1
Cosa è la Evidence-based Prevention?

Firenze, 16 marzo 2023

Il programma formativo NIEBP

Che cos'è la Evidence Based Prevention	16 marzo 2023
La selezione delle priorità di intervento: l'esperienza del Laboratorio Prevenzione	4 Aprile 2023
EBP metodi – 2	18 Maggio 2023
Percorso di formazione specialistica per la realizzazione di Rapid Review	Date da definirsi
Percorso di affiancamento della progettazione degli studi di valutazione	

Programma del 1° modulo

Ora	Tipo	Titolo	Docenti
9:00	Lezione	Cosa è l'Evidence-based Prevention?	Fabrizio Faggiano
10:00	Lezione	Gli strumenti dell'EBP	Silvia Minozzi
11:00	Lezione	Le peculiarità della prevenzione	Fabrizio Faggiano
11:30	Lezione	Le fonti di evidenza	Patrizia Brigoni
12:10	Esercitazione		Marta De Vito, Federico Pagnoni
13:00		Termine della lezione e test ECM	

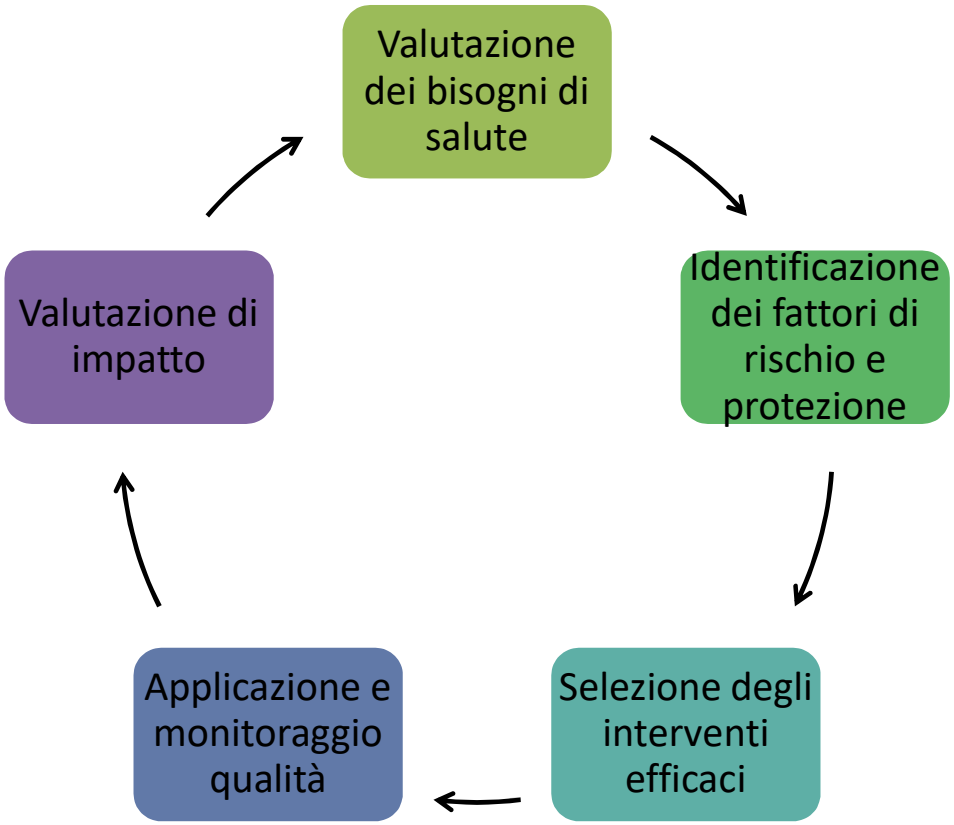
I docenti

Fabrizio Faggiano	Università del Piemonte Orientale
Silvia Minozzi	DEp Lazio, co-ed. Cochrane Drugs and Alcohol Review Group
Patrizia Brigoni	Documentalista UPO e Direttore BVS-P
Marta de Vito	Specializzandi Scuola di Igiene di UPO
Federico Pagnoni	Specializzandi Scuola di Igiene di UPO
Fabio Voller	ARS Toscana – Direttore corso

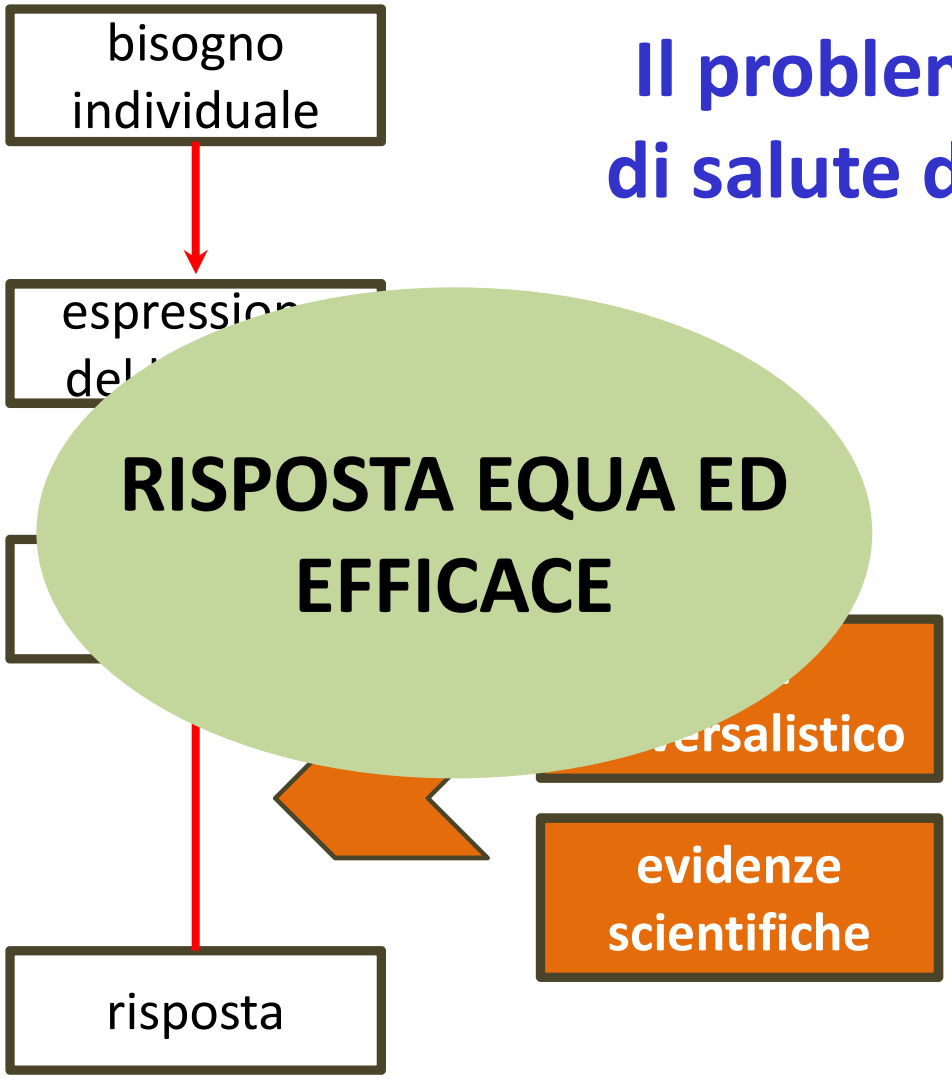
Indice di questa lezione

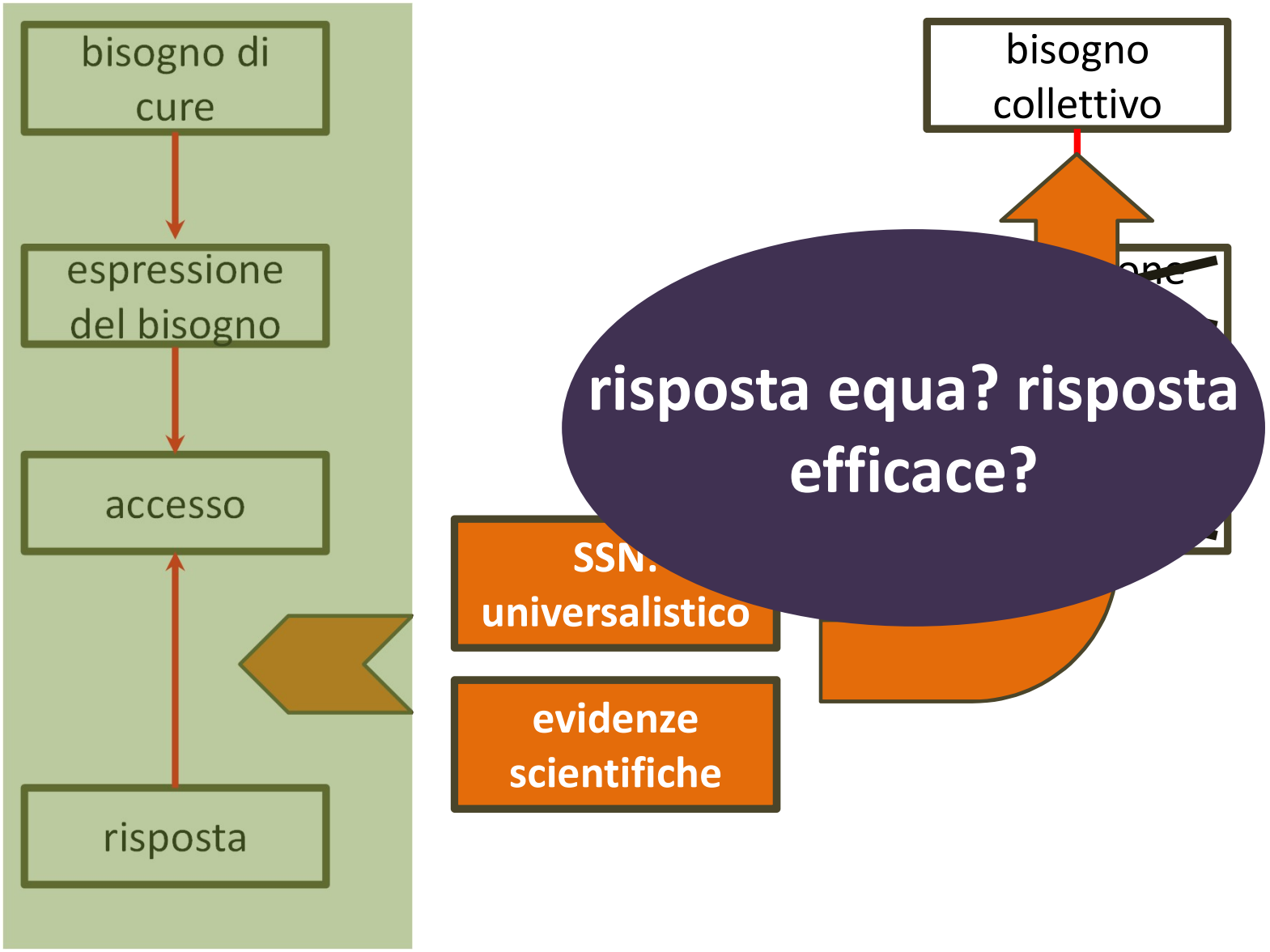
- Il ciclo della sanità pubblica
- Il bisogno di salute e il bisogno di prevenzione
- L'efficacia degli interventi
- Il concetto di efficacia
- La difficoltà della valutazione dell’efficacia
- I modelli di studio

Il processo ciclico della Sanità Pubblica



Il problema del bisogno di salute della collettività




bisogno di cure
espressione del bisogno
accesso
risposta
bisogno collettivo
risposta equa? risposta efficace?
SSN: universalistico
evidenze scientifiche

Health needs assessment

A systematic process … to assess the ***health problems*** facing a population. … It results in an agreed ***list of priorities*** to improve healthcare …. (*NICE*)

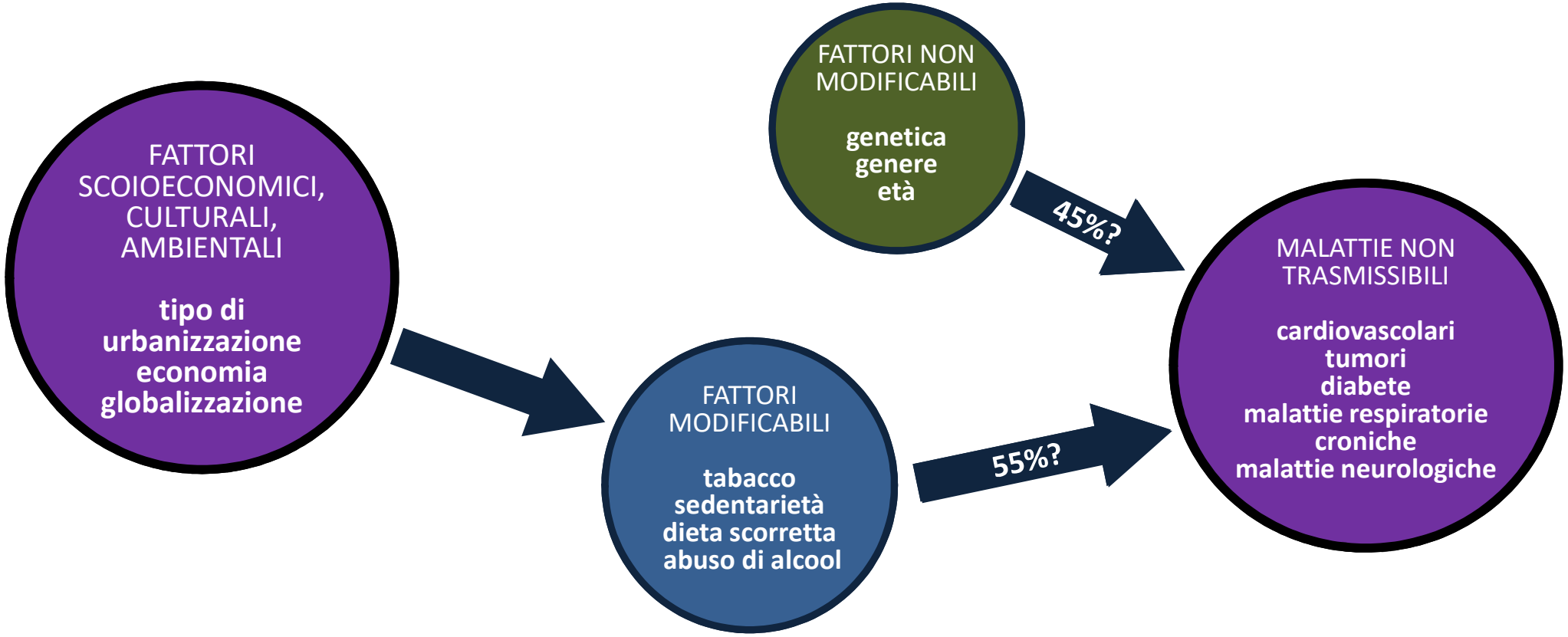
Il concetto di *Bisogno di salute* implica un *obiettivo di salute* (*goal*), un *difetto misurabile della realtà rispetto all'obiettivo* e un **mezzo per raggiungere l'obiettivo** (*Oxford handbook of PH*)

GBD Global Burden of Disease Project

	DALY	%
Malattie non-trasmissibili	16 313 740	90.2%
Incidenti	1 216 149	6.7%
Altre	552 868	3.1%
Totale	18 082 757	100%

Elaborazioni personalizzate accessibili su
http://vizhub.healthdata.org/gbd-compare

Ma ammalarsi è ineluttabile?



GBD Italy 2019 - Risks

Fattore di rischio	DALY	%
Tabacco	2 187 726	12.1%
Glicemia a digiuno elevata	1 848 809	10.2%
Ipertensione sistolica	1 661 664	9.2%
Sovrappeso	1 455 853	8.1%
Rischi dietetici	1 427 463	7.9%
Abuso di alcool	756 992	4.2%
Totale	9 338 507	51.8%

Il bisogno di prevenzione

- La presenza in una popolazione di fattori di rischio eliminabili configura un ***Bisogno di Prevenzione***
- Che interessa individui per lo più sani, e che non vengono espressi
- ***La valutazione dei bisogni di prevenzione*** di una popolazione è una azione attiva che il sistema sanitario deve effettuare con sistematicità

Efficacia degli interventi di prevenzione

EFFECT The result of a cause. In epidemiology, frequently a synonym for EFFECT MEASURE.

EFFECTIVENESS In the usage made standard among epidemiologists by A. L. Cochrane (1909–1988), effectiveness is a measure of the extent to which a specific intervention, procedure, regimen, or service, when deployed in the field in routine circumstances, does what it is intended to do for a specified population;[1] a measure of the extent to which a health care intervention fulfills its objectives[2] To be distinguished from EFFICACY and EFFICIENCY.

[1]Cochrane A L. *Effectiveness and Efficiency; Random Reflections on Health Services.* London: Nuffield Provincial Hospitals Trust, 1972.

[2]*Statistical Indicators for the Planning and Evaluation of Public Health Programmes*; 14th Report of the WHO Expert Committee on Health Statistics. WHO Technical Report Series No. 472. Geneva, 1971.

Efficacia degli interventi di prevenzione

- Primary prevention refers to actions aimed at avoiding the manifestation of a disease: this may include
  - actions to improve health through changing the impact of social and economic determinants on health;
  - the provision of information on behavioral and medical health risks, alongside consultation and measures to decrease them at the personal and community level;
  - nutritional and food supplementation;
  - oral and dental hygiene education;
  - and clinical preventive services such as immunization and vaccination of children, adults and the elderly, as well as vaccination or post-exposure prophylaxis for people exposed to a communicable disease).

www.emro.who.int/about-who/public-health-functions/health-promotion-disease-prevention.html

Il problema dell'efficacia degli interventi preventivi

Alcuni casi

1. Hormone replacement therapy
2. beta-carotene
3. Life education
4. Campagna mass media americana
5. Saint Luis Park Hearth health project

Hormone replacement therapy

- Rispetto all'uomo, la donna gode di una protezione importante nei confronti delle malattie cardiovascolari e dell'osteoporosi
- Questa protezione scompare dopo la menopausa, in corrispondenza del calo degli estrogeni
- Da decenni viene proposta alle donne in menopausa una terapia sostitutiva ormonale per mantenere la protezione pre-menopausale
- Gli studi di coorte hanno confermato questa teoria

Hrt: primi studi osservazionali

Postmenopausal estrogen therapy and cardiovascular disease. Ten-year follow-up from the nurses' health study
Stampfer, NEJM 1991

- RR for major CHD = 0.56 (0.40-0.80)
- RR for total mortality = 0.89 (0.78-1.00)
- RR for mortality from CVD = 0.72 (0.55-0.95)

La prima revisione sistematica

Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence[1,2]

By Meir J Stampfer, M.D.*,†,3 and Graham A Colditz, M.D.*,‡

Accepted July 19, 1990

Received May 21, 1990

Preventive Medicine, Stampfer, 1991

Conclusion

The preponderance of evidence from the epidemiologic studies strongly supports the view that postmenopausal estrogen therapy can substantially reduce the risk for coronary heart disease. The consistency of the findings is more apparent in the prospective cohort and angiographic studies. The summary relative risk from those studies was 0.50 (95% CI 0.43–0.56). This effect is unlikely to be explained by confounding factors or selection.

1. Hrt: le conferme recenti

Postmenopausal Estrogen and Progestin Use and the Risk of Cardiovascular Disease

Grodstein Ann Int Medicine 2000

- 16 year results from the Nurses health study
- RR of CHD estrogen+progestin = 0.39 (0.19-0.78)
- RR of CHD estrogen alone = 0.60 (0.43-0.83).

Hrt: 2002 - risultati di WHI

Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women

Principal Results From the Women's Health Initiative Randomized Controlled Trial

Writing Group for the Women's Health Initiative Investigators

Context Despite decades of accumulated observational evidence, the balance of risks and benefits for hormone use in healthy postmenopausal women remains uncertain.

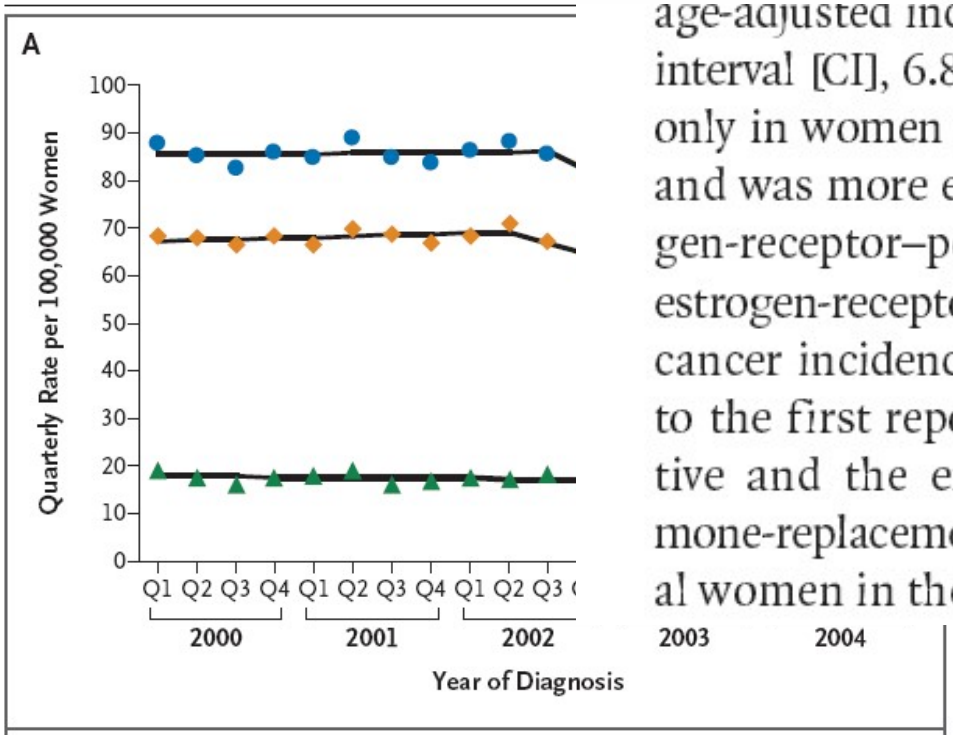
Objective To assess the maior health benefits and risks of the most commonly used

- 16608 postmenopausal women aged 50-79 years

Results On May 31, 2002, after a mean of 5.2 years of follow-up, the data and safety monitoring board recommended stopping the trial of estrogen plus progestin vs placebo because the test statistic for invasive breast cancer exceeded the stopping boundary for this adverse effect and the global index statistic supported risks exceeding benefits. This report includes data on the major clinical outcomes through April 30, 2002. Estimated hazard ratios (HRs) (nominal 95% confidence intervals [CIs]) were as follows: CHD, 1.29 (1.02-1.63) with 286 cases; breast cancer, 1.26 (1.00-1.59) with 290 cases; stroke, 1.41 (1.07-1.85) with 212 cases; PE, 2.13 (1.39-3.25) with 101 cases; colorectal cancer, 0.63

SPECIAL REPORT

The Decrease in Breast-Cancer Incidence



age-adjusted incidence was 8.6% (95% confidence interval [CI], 6.8 to 10.4). The decrease was evident only in women who were 50 years of age or older and was more evident in cancers that were estrogen-receptor–positive than in those that were estrogen-receptor–negative. The decrease in breast-cancer incidence seems to be temporally related to the first report of the Women's Health Initiative and the ensuing drop in the use of hormone-replacement therapy among postmenopausal women in the United States. The contributions

HRT 11 anni dopo…

ORIGINAL CONTRIBUTION

CLINICIAN'S CORNER

Estrogen Plus Progestin and Breast Cancer Incidence and Mortality in Postmenopausal Women

Rowan T. Chlebowski, MD, PhD
Garnet L. Anderson, PhD
Margery Gass, MD
Dorothy S. Lane, MD
Aaron K. Aragaki, MS
Lewis H. Kuller, MD
JoAnn E. Manson, MD, DrPH

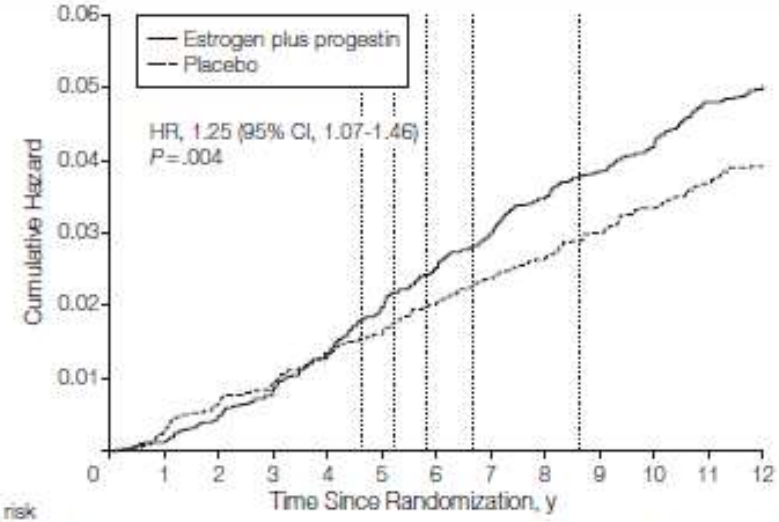
Context In the Women's Health Initiative randomized, placebo-controlled trial of estrogen plus progestin, after a mean intervention time of 5.6 (SD, 1.3) years (range, 3.7-8.6 years) and a mean follow-up of 7.9 (SD, 1.4) years, breast cancer incidence was increased among women who received combined hormone therapy. Breast cancer mortality among participants in the trial has not been previously reported.

Objective To determine the effects of therapy with estrogen plus progestin on cumulative breast cancer incidence and mortality after a total mean follow-up of 11.0 (SD, 2.7) years, through August 14, 2009.

Chlebowsky, JAMA 2010

HRT 11 anni dopo…

Figure 2. Incidence of Invasive Breast Cancer in the WHI Clinical Trial



No. at risk							
Estrogen plus progestin	8506	8329	8109	7796	7009	6189	2914
Placebo	8102	7914	7721	7466	6692	5889	2648

Intention-to-treat Kaplan-Meier cumulative hazard curves for incidence of invasive breast cancer by study group and time since randomization. The hazard ratio (HR), 95% confidence interval (CI), and *P* value are from Cox regression models, stratified by 5-year age intervals and randomization assignment in the Women's Health Initiative (WHI) dietary modification trial. All women stopped the intervention by 8.6 years. Quintiles of duration of follow-up are indicated by the dotted lines.

Chlebowsky, JAMA 2010

HRT: cosa è successo

- Una solida ***teoria eziopatogenetica*** (evidentemente sbagliata!)
- Gli ***studi osservazionali*** gravati da un importante ***confondimento*** (classe sociale-istruzione)
- La ***potenza dell'industria***…. e di alcune ***corporazioni mediche***

hanno sostenuto per decenni l'uso della terapia sostituiva ormonale nelle donne in post-menopausa

Prime conclusioni

- Le teorie eziopatogenetiche, ***in assenza di prove empiriche***, determinano decisioni che possono essere sbagliate

Il caso della chemioprevenzione dei tumori

- Nel 1981 Science pubblica il seguente articolo:

Peto R, Doll R et al. Can dietary beta-carotene materially reduce human cancer rates? Science 1981;290:201-8.

- Gli autori ipotizzano, a partire da una rassegna di studi, che gli alimenti contenenti retinolo e beta-carotene proteggano contro il cancro
- RR=3.0 per i bassi consumi
- Gli autori suggeriscono di studiare l'efficacia degli integratori dietetici a base di beta- carotene.

Il caso della chemioprevenzione dei tumori

La teoria dell'effetto protettivo era supportata da studi e esperimenti:

- con elevata concordanza
- RR=5.3 per i livelli più bassi di retinolo ematico
- provata capacità di reprimere colture cellulari malignizzate *in vitro*
- potente azione antiossidante

… dalla fine degli anni '80 il ß-carotene è presente in molti integratori vitaminici

Il caso della chemioprevenzione dei tumori

Studio ATBC (*Alpha-Tocopherol and Beta-Carotene cancer prevention study*) - Finlandia

- nel 1986: 29 133 fumatori maschi 50-69, randomizzati in 4 gruppi (combinazioni di ß-carotene e α-tocoferolo**)** e seguiti per 5-8 anni

Studio CARET (*Beta-Carotene and Retinol Efficacy trial*) - USA

- nel 1992: 18 314 soggetti, fumatori o esposti ad asbesto, randomizzati in 4 gruppi e seguiti fino al 1997

Il caso della chemioprevenzione dei tumori

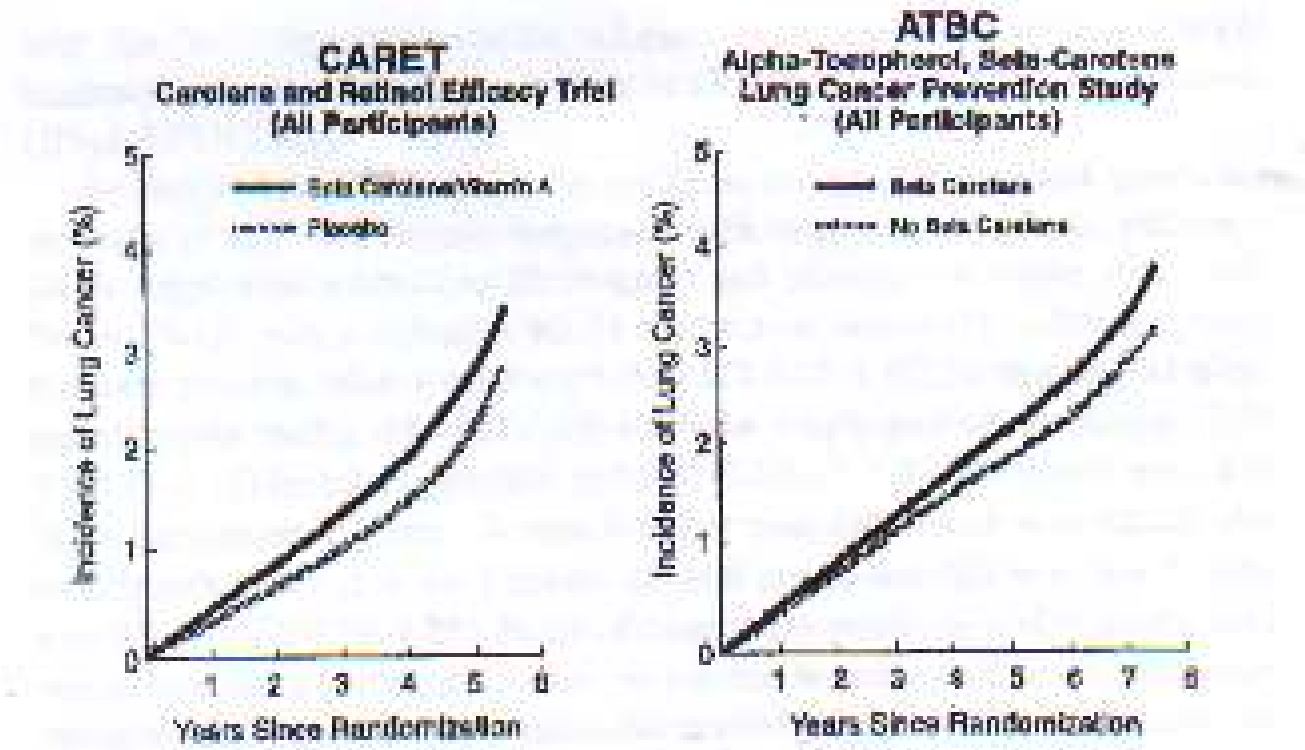


Figure 1 Kaplan-Meier curves of the cumulative incidence of lung cancer among participants receiving active vitamins and those receiving placebo. Data are shown only through 5.5 years of follow-up because of the small number of participants beyond that time.

Il caso della chemioprevenzione dei tumori

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CHEMOPREVENTION OF LUNG CANCER: The Rise and Demise of Beta-Carotene

Gilbert S. Omenn
Former address: School of Public Health & Community Medicine, University of Washington, Seattle, Washington 98195–7230 and Fred Hutchinson Cancer Research Center, Seattle, Washington 98109–1024; Current address: University of Michigan, Ann Arbor, Michigan 48109–0624; e-mail: gomenn@umich.edu

KEY WORDS: fruits/vegetables, carcinogenesis, vitamin-supplements, antioxidants, vitamin A

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Vol. 297 No. 8, February 28, 2007 TABLE OF CONT

Review

Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention

Systematic Review and Meta-analysis

Goran Bjelakovic, MD, DrMedSci; Dimitrinka Nikolova, MA; Lise Lotte Gluud, MD, DrMedSci; Rosa G. Simonetti, MD; Christian Gluud, MD, DrMedSci

JAMA. 2007;297:842-857.

Data Synthesis When all low- and high-bias risk trials of antioxidant supplements were pooled together there was no significant effect on mortality (RR, 1.02; 95% CI, 0.98-1.06). Multivariate meta-regression analyses showed that low-bias risk trials (RR, 1.16; 95% CI, 1.05-1.29) ...w-bias trials with 180 938 pa...). In low-bias risk trials, after exclus... .0-1.24), and vitamin E (RR, 1.04; ... no significant effect on mortality.

beta carotene (RR, 1.07; 95% CI, 1.02-1.11), vitamin A (RR, 1.16; 95% CI, 1.10-1.24), and vitamin E (RR, 1.04; 95% CI, 1.01-1.07), significantly increased mortality.

Conclusion ...s of vitamin C and selenium or

Author Affiliations: The Cochrane Hepato-Biliary Group, Copenhagen Trial Unit, Center for Clinical Intervention Research, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark (Drs Bjelakovic, L. L. Gluud, Simonetti, and C. Gluud and Ms Nikolova); Department of Internal Medicine, Gastroenterology and Hepatology, University of Nis, Nis, Serbia (Dr Bjelakovic); and Divisione di

Il caso della chemioprevenzione dei tumori

Goran Bjelakovic et al. **Antioxidant supplements for**

prev **nts**

β-carotene: RR=1.05 (95%CI 1.01-1.09)

Vitamine E: RR=1.03 (95%CI 1.00-1.05)

Vitamine A: RR=1.07 (95%CI 0.97-1.18) – Dose metaregression: RR=1.0006 (95%CI 1.0002-1.001)

Vitamine C: RR=1.02 (95%CI 0.98-1.07); Selenium: RR=0.97 (95%CI 0.91-1.03)

http://antlia.med.unipmn.it:2075/doi/10.1002/14651858.CD007176.pub2/full

Altre evidenze da CARET

Vol. 12, 350–358, April 2003 **Cancer Epidemiology, Biomarkers & Prevention**

Fruits and Vegetables Are Associated with Lower Lung Cancer Risk Only in the Placebo Arm of the β-Carotene and Retinol Efficacy Trial (CARET)[1]

Marian L. Neuhouser,[2] Ruth E. Patterson, Mark D. Thornquist, Gilbert S. Omenn, Irena B. King, and Gary E. Goodman

did not observe any statistically significant associations of fruit and vegetable intake with lung cancer risk among participants randomized to receive the CARET

Neuhouser, Cancer Epidemiology, Biomarkers & Preventio, 2003

Evidenze sperimentali

and has been used for studies of tobacco smoking and inhalation toxicology. In the first study, ferrets were given a high-dose beta-carotene supplement equivalent to 30 mg per day in humans, and exposed cigarette smoke or both for six months. A strong proliferative response in lung tissue and squamous metaplasia were observed in all beta-carotene-supplemented animals, and this response was enhanced by exposure to tobacco smoke. When compared to the control group, beta-carotene-supplemented animals (with or without smoke exposure) had statistically significantly lower concentrations of retinoic acid in lung tissue, and they exhibited reductions in RAR-beta gene expression (a tumor suppressor gene). Further, ferrets given a high-dose beta-carotene supplement and exposed to tobacco smoke had fourfold elevated expressions of *c-jun* and *c-fos* genes. In a second study, ferrets were given either physiological- or pharmacologic-dose beta-carotene supplementations, which were equivalent to 6 mg vs. 30 mg per day in humans, respectively. The animals were exposed to cigarette smoke for six months. The retinoic acid concentration and RAR beta-gene expression were reduced in the lung tissues, whereas the expression of AP1, cyclin D1, and proliferative cell nuclear antigen were greater in the high-dose, beta-carotene-supplemented animals with or without smoke, as well as the smoke-exposed, low-dose, beta-carotene-supplemented animals—but *not* in the low-dose, beta-carotene-supplemented animals alone, as compared with the control group. Squamous metaplasia was only observed in the lung tissues of high-dose,

Il caso della prevenzione dell'abuso di sostanze

- Life education: programma scolastico basato su modello di Moskovich

Valutazione di efficacia di "Life Education" in Australia 1991-1992:

- Cigarettes RR=1.6
- Alcohol RR=1.4
- Other substances RR=1.4

Il caso della prevenzione dell'abuso di sostanze

When the data are extrapolated to the state-wide ... estimates, ... of all smoking among year 6 schoolchildren,

25% of girls' and 19% of boys' smoking could be attributed to participation in Life Education

as could 22% of all boys' recent drinking

The program was extended to all Australia, UK, USA, … India, China, … South Africa….

The findings suggest that intervention programmes should be thoroughly evaluated prior to widespread implementation…

Hawthorne, Addiction 1995

American National Youth Anti-drug Media Campaign

- planned by the National Drug Control Policy (ONDCP)
- funded in 1997 by the United States Congress with ***$1.5 billion dollars***
- main objective: "***to educate and enable America's youth to reject illegal drugs as well as alcohol and tobacco***"
- alcohol and tobacco were omitted from the main focus of the campaign
- focused mainly on minimizing illegal drug use among young adolescents who have not yet become "regular" users of illegal substances
- televised antidrug public service announcements (PSAs) broadcasted 1998-2004

www.ojp.gov/pdffiles1/ondcp/171694.pdf

American National Youth Anti-drug Media Campaign

- Evaluation provides ***no evidence of positive effect in relation to teen drug use***, and shows some indications of a negative impact.
- the ***past month use of marijuana appeared significantly increased by 2.5% among 14-18 years*** (Orwin, GAO, 2006).
- Users of marijuana in past years: 24.5%
- RR of mariujana use in past year: ***1.21 (1.19;1.65)***
- Attitude belief scale: ***-2.7 (-6.8;-1.5)***
- Antimariujana Social Norms Scale: ***-6.3 (-10.4;-2.2)***

*www.**mediacampaign**.org/*

Hornik, AAAPSS, 2009

St-Louis du Parc Heart Health Project - Montreal

A five year programme targeting children in elementary schools aged 9–12 years in disadvantaged multiethnic neighbourhoods in Montreal.

Tobacco Control, Renaud, 2003

Risultati

Table 1 Comparison of outcomes by treatment in the condition in the longitudinal cohort sample surveys : Montreal, Quebec, 1994–97

	Intervention		Comparison¶		Intervention relative to comparison condition	
Outcome*	Number	%	Number	%	OR (95% CI)†	p Value
One year follow up						
Most intense intervention						
Initiated smoking‡	79/339	23.3	172/1233	13.9	1.87 (1.34 to 2.61)	0.0002
Continued smoking§	71/148	48.0	81/273	29.7	2.72 (1.71 to 4.33)	0.0001
Least intense intervention						
Initiated smoking‡	25/196	12.8	172/1233	13.9	0.73 (0.44 to 1.25)	0.2577
Continued smoking§	24/51	47.1	81/273	29.7	2.25 (1.18 to 4.30)	0.0135
Total						
Initiated smoking‡	104/535	19.4	172/1233	13.9	1.44 (1.06 to 1.95)	0.0188
Continued smoking§	95/199	47.7	81/273	29.7	2.59 (1.69 to 3.97)	0.0001
Two year follow up						
Most intense						
Initiated smoking‡	39/97	40.2	60/328	18.3	2.88 (1.65 to 5.01)	0.0002
Continued smoking§	26/45	57.8	17/57	29.8	3.19 (1.28 to 7.98)	0.0129
Least intense						
Initiated smoking‡	9/61	14.8	60/328	18.3	0.58 (0.25 to 1.35)	0.2050
Continued smoking§	5/13	38.5	17/57	29.8	3.14 (0.65 to 15.14)	0.1541
Total						
Initiated smoking‡	48/158	30.4	60/328	18.3	1.95 (1.17 to 3.23)	0.0100
Continued smoking§	31/58	53.4	17/57	29.8	3.03 (1.26 to 7.27)	0.0130

St-Louis du Parc Heart Health Project - Montreal

Explanations

- heightened sensitivity to smoking among children most exposed to the programme;
- defence mechanisms among children stimulated by cognitive dissonance or anxiety;
- intervention content inappropriately targeted to children's stages of cognitive development.

La prevenzione non è sempre efficace (a volte è dannosa)

	Int. Arms		Fav. Int.		Fav. Ctrl		NS Int.		
Issue	N.°	(%) col	N.°	(%) row	N.°	(%) row	N.°	(%) row	
ALC	124	24,65	48	38,71	4	3,23	72	58,06	
CVD	7	1,39	2	28,57	0	0	5	71,43	
IDU	90	17,89	32	35,56	5	5,56	53	58,89	
MH	62	12,33	19	30,65	0	0	43	69,35	
PE	30	5,96	8	26,67	0	0	22	73,33	
PRE	35	6,96	5	14,29	0	0	30	85,71	
TOB	155	30,82	57	36,77	7	4,52	91	58,71	
Tot	**503**	**100,00**	**171**	**34,00**	**16**	**3,18**	**316**	**62,82**	**100,00**

Int.: Intervention; **Fav.**: Favouring; **Ctrl**: Control; **NS**: Not significant; MH: **M**ental health; **TOB**: Tobacco; **CVD**: Cardiovascular Disease; **IDU**: Illicit Drugs Use; **ALC**: Alcohol; **PRE**: Pregnancy; **PE** : Physical exercise

Concina, UPO, 2013

Conclusioni preliminari

Because professionals sometimes do more harm than good when they intervene in the lives of other people, their policies and practices should be informed by rigorous, transparent, up-to-date evaluations.

Chalmers AAPPS 2003

Fiducia nelle teorie eziopatogenetiche

- Ma la ***complessità della biologia*** (e dell'interazione con le scienze sociali)
- ***e l'inadeguatezza degli strumenti di ricerca***
- rende ***la teorizzazione*** precaria e inaffidabile fino a che….
- ***…non sia confermata o refutata da una prova di efficacia (Popper)***

High quality scientific evidence is needed

la scelta di utilizzare un intervento di prevenzione implica una *pesante* responsabilità scientifica e etica

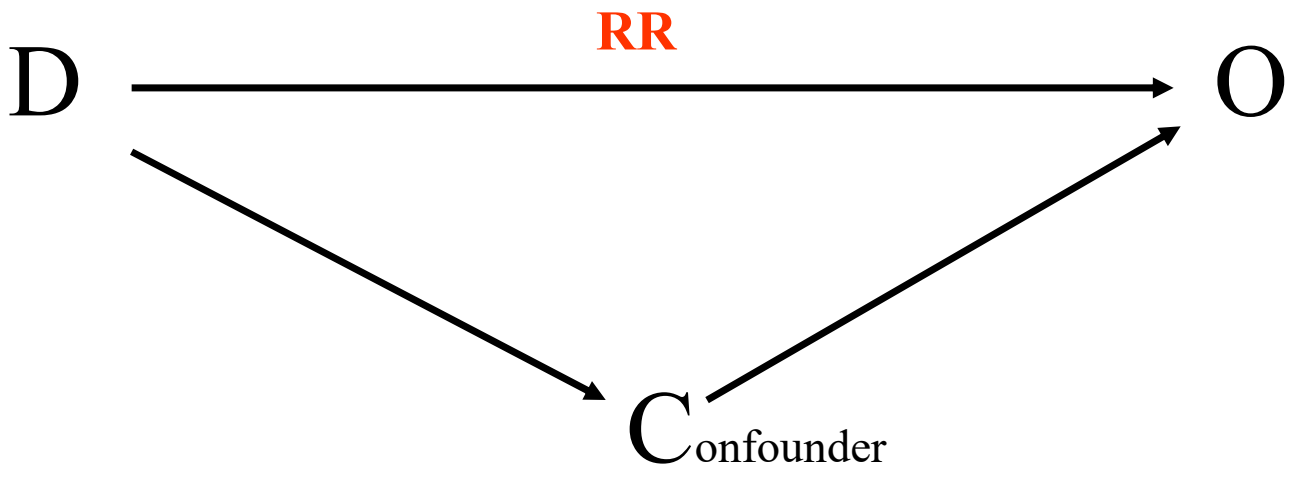
"High quality scientific evidence is needed when professionals intervene in the lives of other people"
(Ian Chalmers)

Cosa è la high quality scientific evidence?

- Studi capaci di misurare l'effetto di un intervento eliminando tutti i possibili bias associati
  - confondimento/bias di selezione
  - information/detection bias
  - suggestione (effetto placebo)
  - attrition bias
  - ….

Relazione causale

Confondimento



The confounder is a concurrent cause of the outcome, that correlates with the determinant.

Studi sperimentali vs osservazionali

- prevenzione della principale distorsione della valutazione:

IL CONFONDIMENTO

- richiede studi capaci di confrontare due popolazioni teoricamente identiche, ad eccezione dell'intervento da valutare
- situazione possibile solo con studi sperimentali

From evidence to practice

Primary studies (RCTs or other)

Systematic reviews (Cochrane reviews)

Guidelines

Point of care information services

Other local documents

Aspetti metodologici nelle prossime puntate del corso ….

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