



Journal Club
16 gennaio 2015
Aspetti di clinica geriatrica

Nuovi e vecchi farmaci “ricostituenti”

Marco Trabucchi

I motivi per un seminario sui “ricostituenti”

- rifiuto dell'intellettualismo
- ricerca di un perché del consumo
- la medicina dei sistemi o “personalizzata”
- la cura delle “non malattie”

La paura delle malattie, il dolore psichico che genera dolore somatico, la ricerca di certezze per il futuro.

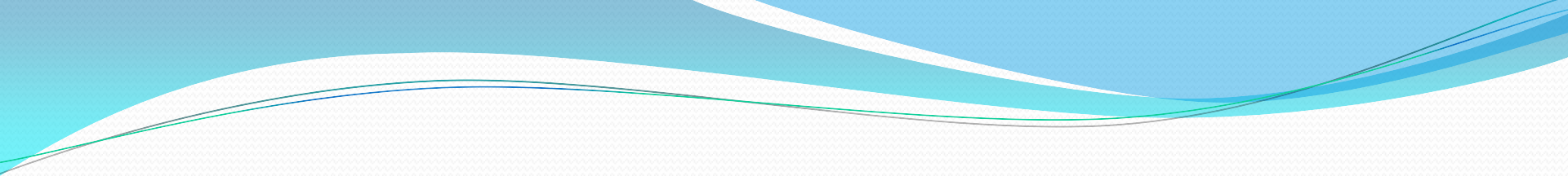
Perché negare un trattamento se atossico, costa poco ed è gradevole?

In alcune circostanze cliniche il “ricostituente” è lo strumento privilegiato per instaurare un rapporto medico-paziente.



“Ho paura del dolore”

Papa Francesco



**Le incertezze del medico:
il dibattito su organizzazione, prestazioni,
aspetti finanziari può allontanare il medico
dall'interesse per le grandi conquiste della
scienza e quindi rischia di diventare scettico ...
dalle nanotecnologie ai ricostituenti ...**

At the same time, the medical profession, responsible for delivering highest-quality care based primarily on the latest medical science (along with the art of medicine within the patient-physician relationship), has become, perhaps by necessity, somewhat preoccupied with the current transformation of the health care system and the emphasis on cost, quality, and population health. With the ongoing debate and rhetoric in the United States, the United Kingdom, and other countries regarding the organization, delivery, and financing of health care, as well as increased pressures to improve efficiency in clinical care, many physicians in practice and in training may be unaware of the extraordinary advances in basic and translational science and the novel discoveries in the biosciences, with the related implications for expanding medical knowledge and improving medical care—the magic of medicine.

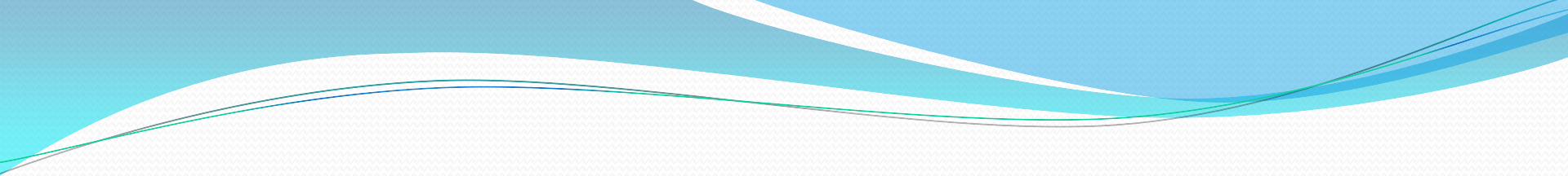
(Fontanarosa & Bauchner, JAMA 313(2):145-6, 2015)



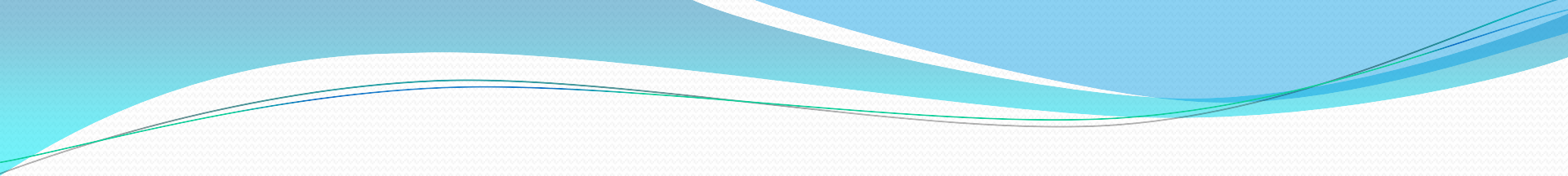
Nelle malattie croniche mix di relazioni ...

“Io ero gli occhi per il cieco, ero i piedi per lo zoppo” (Giobbe)

La ricchezza delle dinamiche d'aiuto non può trascurare il ruolo del farmaco come elemento (pseudo)tecnologico che integra e non si sostituisce ad altri “accompagnamenti”.



**Manca una sperimentazione clinica seria.
Si utilizzano acriticamente filoni di ricerca
teorica, senza studi nell'uomo (si vedano i
processi ossidativi dell'organismo o lo
sprouting del cronassial).**

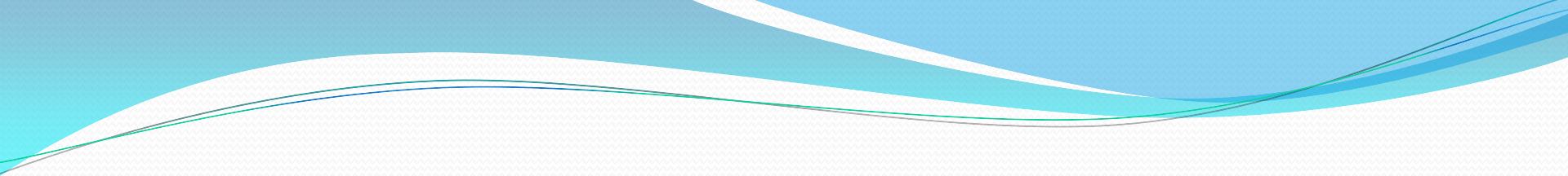


**Si ipotizza il deficit di una sostanza, considerando solo il valore assoluto e non il turnover, e senza valutarne i limiti di tolleranza (difficili da definire).
La questione tempo.**



Il famoso studio Physicians' Health Study II ha rappresentato il punto fermo negli USA sugli integratori

(Christen WG. et al, Ann. Epidemiol. 10(2):125-134, 2000).



Lo studio PHS II ha dimostrato come una supplementazione multivitaminica quotidiana sia in grado di ridurre, in maniera modesta ma statisticamente significativa, il rischio di cancro in soggetti adulti e, in particolare, negli anziani.

(Bernabei R., Martone AM. G Gerontol 62:500-5, 2014)

Rispetto al placebo, il gruppo sottoposto alla supplementazione multivitaminica non ha mostrato alcuna riduzione statisticamente significativa dell'incidenza di eventi cardiovascolari maggiori, ne alcuna riduzione degli endpoint secondari, quali IM totale e ictus totale. I risultati hanno suggerito una riduzione del rischio di IM fatale e una modesta riduzione degli eventi CV maggiori in uomini d'età pari o superiore a 70 anni. Non è emersa alcuna differenza nel confronto degli effetti del MVM nella prevenzione CV primaria rispetto a quella secondaria.

(Bernabei R., Martone AM. G Gerontol 62:500-5, 2014)

Multivitamins in the Prevention of Cardiovascular Disease in Men

The Physicians' Health Study II Randomized Controlled Trial

Howard D. Sesso, ScD, MPH

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J. Michael Gaziano, MD, MPH

Context Although multivitamins are used to prevent vitamin and mineral deficiency, there is a perception that multivitamins may prevent cardiovascular disease (CVD). Observational studies have shown inconsistent associations between regular multivitamin use and CVD, with no long-term clinical trials of multivitamin use.

Objective To determine whether long-term multivitamin supplementation decreases the risk of major cardiovascular events among men.

Design, Setting, and Participants The Physicians' Health Study II, a randomized, double-blind, placebo-controlled trial of a common daily multivitamin, began in 1997 with continued treatment and follow-up through June 1, 2011. A total of 14 641 male US physicians initially aged 50 years or older (mean, 64.3 [SD, 9.2] years), including 754 men with a history of CVD at randomization, were enrolled.

Intervention Daily multivitamin or placebo.

Conclusion Among this population of US male physicians, taking a daily multivitamin did not reduce major cardiovascular events, MI, stroke, and CVD mortality after more than a decade of treatment and follow-up.

Trial Registration clinicaltrials.gov Identifier: NCT00270647

JAMA. 2012;308(17):1751-1760

www.jama.com

I risultati preliminari non hanno mostrato un beneficio significativo in termini di performance cognitiva nella popolazione trattata rispetto al gruppo placebo.

Eventuali benefici risultanti dalla supplementazione multivitaminica potevano essere mascherati dal fatto che la popolazione arruolata comprendeva persone con livello di istruzione elevato e un regime alimentare completo e adeguato rispetto alla popolazione generale.

(Bernabei R., Martone AM. G Gerontol 62:500-5, 2014)

Studio PHS II: risultati endpoint neurodegenerative

- L'obiettivo dello Studio PHSII nell'endpoint funzione cognitiva era quello di valutare l'efficacia di un multivitaminico assunto su base quotidiana per un lungo periodo di tempo (oltre 10 anni) nella riduzione di patologie neurodegenerative
- I risultati non rilevano benefici a livello cognitivo tra la popolazione selezionata dello studio trattata con multivitaminici e quella trattata con placebo
- I risultati neutri possono essere ricondotti allo specifico disegno dello studio, infatti:
 - I partecipanti allo Studio PHSII hanno seguito un regime alimentare molto completo e adeguato rispetto alla popolazione generale o di altri studi condotti con integratori alimentari, dove i soggetti osservati avevano problemi di malnutrizione più significativi. Per questo i risultati dello studio PHS II possono essere sottostimati e meno significativi.
 - Inoltre la popolazione era unica perché tutti i partecipanti, medici, avevano un livello di istruzione elevato.

- Lo Studio è stato pubblicato su **Annals of Internal Medicine** a fine 2013

ORIGINAL RESEARCH | Annals of Internal Medicine

Long-Term Multivitamin Supplementation and Cognitive Function in Men

A Randomized Trial

Francine Codratt, ScD¹, Jacqueline O'Brien, ScD², Jia Hei Kang, ScD³, Binna Duhkes, PhD, Nancy R. Cook, ScD⁴, Olivia Okereke, MD, JoAnn E. Manson, MD, DrPH, Robert J. Glynn, PhD, Julia E. Buring, ScD¹, Michael Gaziano, MD, MPH, and Howard D. Sesso, ScD, MPH

Background: Despite widespread use of multivitamin supplements, their effect on cognitive health—a critical issue with aging—remains uncertain. To date, no long-term clinical trials have studied multivitamin use and cognitive decline in older persons.

Objective: To evaluate whether long-term multivitamin supplementation affects cognitive health in later life.

Design: Randomized, double-blind, placebo-controlled trial of a multivitamin from 1997 to 1 June 2011. The cognitive function already began in 1988. Up to 4 repeated cognitive assessments by telephone interview were completed over 12 years. (ClinicalTrials.gov NCT00206474)

Setting: The Physicians' Health Study II.

Patients: 8247 male physicians aged 65 years or older.

Intervention: Daily multivitamin or placebo.

Measurements: A global composite score averaging 5 tests of global cognition, verbal memory, and category fluency. The secondary end point was a verbal memory score combining 4 tests of verbal memory, which is a strong predictor of Alzheimer disease.

Results: No difference was found in mean cognitive change over time between the multivitamin and placebo groups or in the mean level of cognitive at any of the 4 assessments. Specifically, for the global composite score, the mean difference in cognitive change over follow-up was -0.01 SD (95% CI, -0.04 to 0.02 SD) when treatment was compared with placebo. Similarly, cognitive performance did not differ between the multivitamin and placebo groups on the secondary outcomes, verbal memory (mean difference in cognitive change over follow-up, -0.009 SD [CI, -0.04 to 0.03 SD]).

Limitation: Doses of vitamins may be too low or the population may be too well-nourished to benefit from a multivitamin.

Conclusion: In male physicians aged 65 years or older, long-term use of a daily multivitamin did not provide cognitive benefits.

Primary Funding Source: National Institutes of Health, BASF, Pfizer, and DSM Nutritional Products.

Ann Intern Med 2013;159:806-814.
DOI: 10.1093/ajph/103.11.1806

* Dr. Codratt and O'Brien contributed equally to the work.

See also:

Print	797, 824
Related articles	797, 824
Editorial comment	850
Summary for Patients	824

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METHODS
Study Design
The PHS II is a randomized, double-blind, placebo-controlled, 2 × 2 × 2 factorial trial testing β-carotene, vitamin E, ascorbic acid, and a multivitamin for their role in preventing chronic diseases among 14 641 male physicians aged 50 years or older. Cognitive function was a prespecified secondary outcome of PHS II.

Rischio malnutrizione nell'anziano

- Non è un effetto collaterale inevitabile dell'invecchiamento, ma molti cambiamenti associati all'invecchiamento possono indurre malnutrizione
- È una sindrome multifattoriale nella quale i fattori di rischio e i fattori causali spesso si sovrappongono
- Sono coinvolti fattori intrinseci e fattori esterni

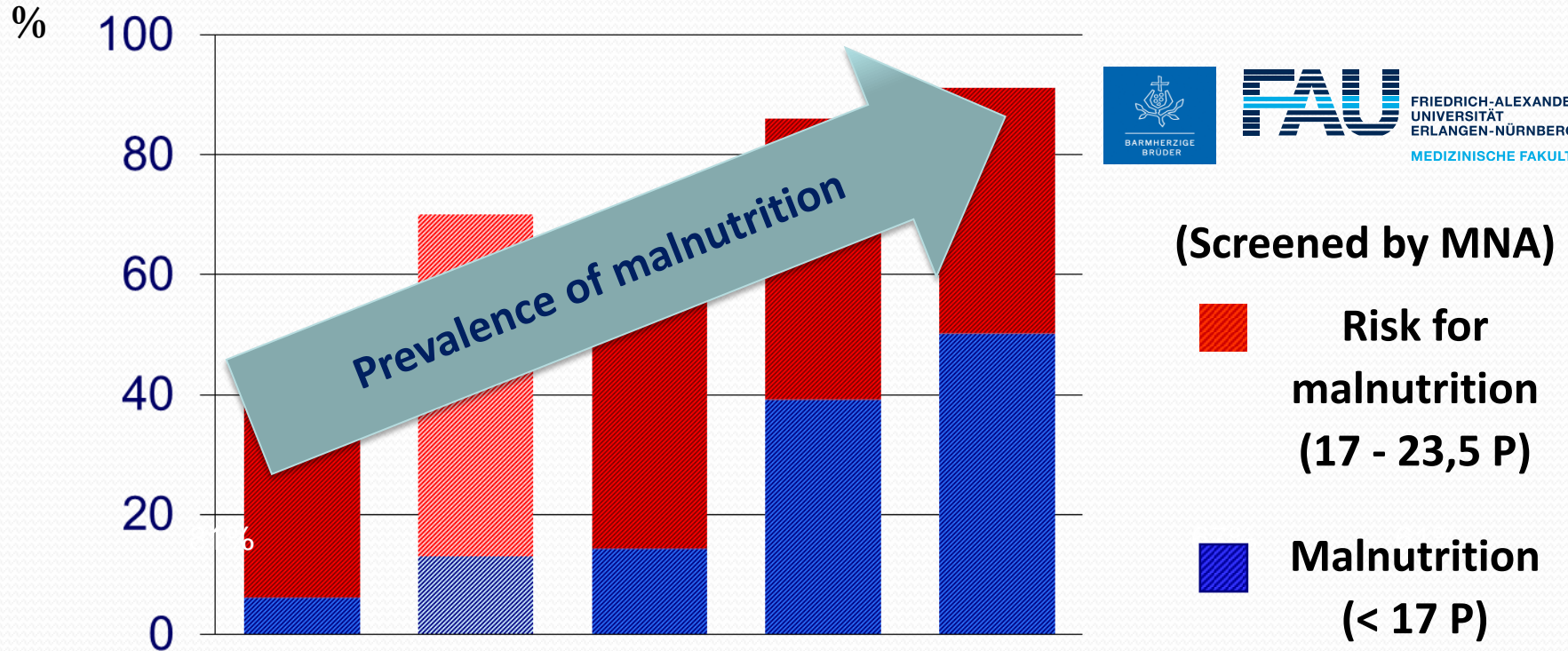
Epidemiologia

Prevalenza di malnutrizione in vari setting assistenziali

- Analisi di studi che hanno valutato la malnutrizione con MNA in vari ambiti (oltre 10.000 soggetti anziani)
- Prevalenza media di malnutrizione
 - ✓ 1% in soggetti sani in comunità
 - ✓ 4% in pazienti che ricevono assistenza domiciliare
 - ✓ 5% in pazienti con malattia di Alzheimer che vivono in casa
 - ✓ 20% in pazienti ospedalizzati
 - ✓ 37% in pazienti istituzionalizzati

BAPEN Nutrition Screening Week (NSW) 2012 data.

Prevalence of malnutrition in elderly persons depending on their living situations



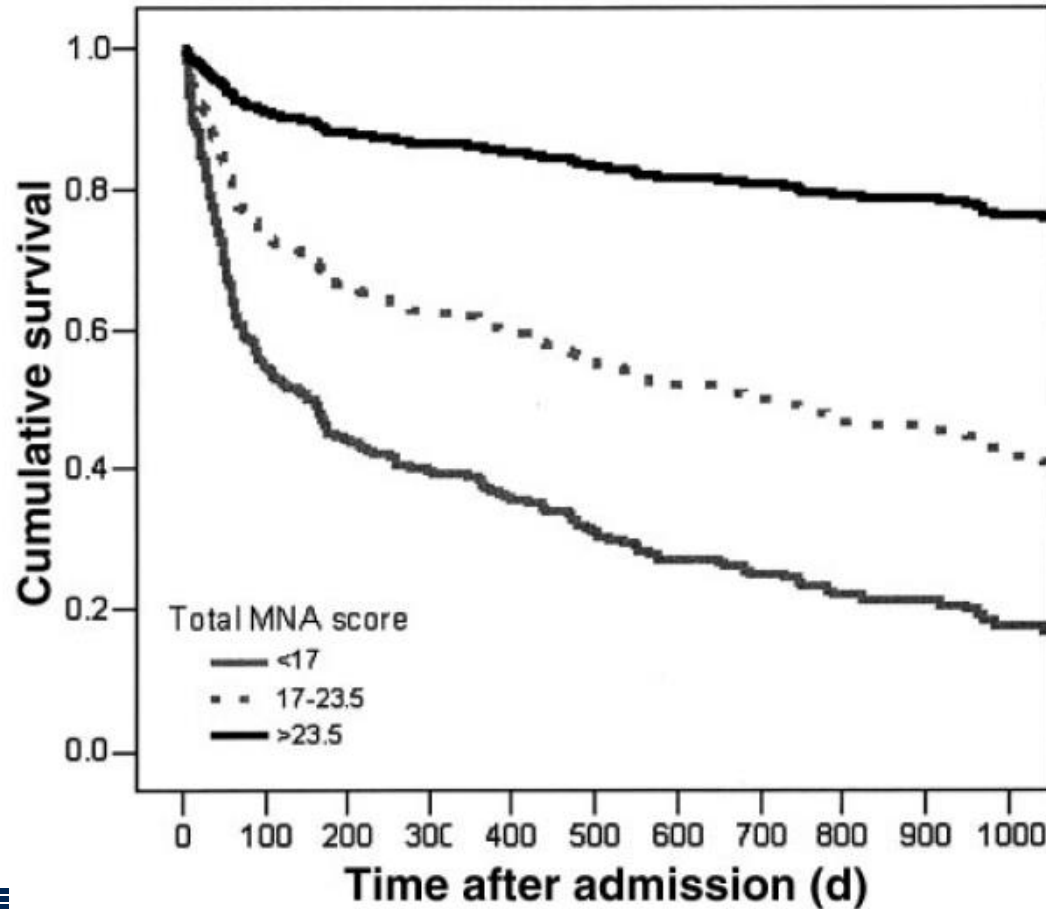
Comm.-dwelling NH Hospital Rehab
without need help
(n=964) (n=352) (n=1586) (n=1384) (n=340)

Loss of functionality

* ErnSIPP-Studie, Ernährungsbericht 2012

Survival of older persons in relation to nutritional state

N=414,
Age:
85 ± 6 J.



Good nutritional state

Risk for malnutrition

Malnutrition

Fattori di rischio di malnutrizione

➤ Fattori intrinseci

- ✓ Legati all'invecchiamento: perdita di appetito, modificazioni del cavo orale, alterazione del gusto e dell'olfatto, difficoltà di deglutizione
- ✓ Malattie e disabilità: patologie gastrointestinali, disturbi neurologici, psichiatrici, endocrini, insufficienza d'organo, altre condizioni cliniche (mal. infiammatorie, tumori), interventi chirurgici

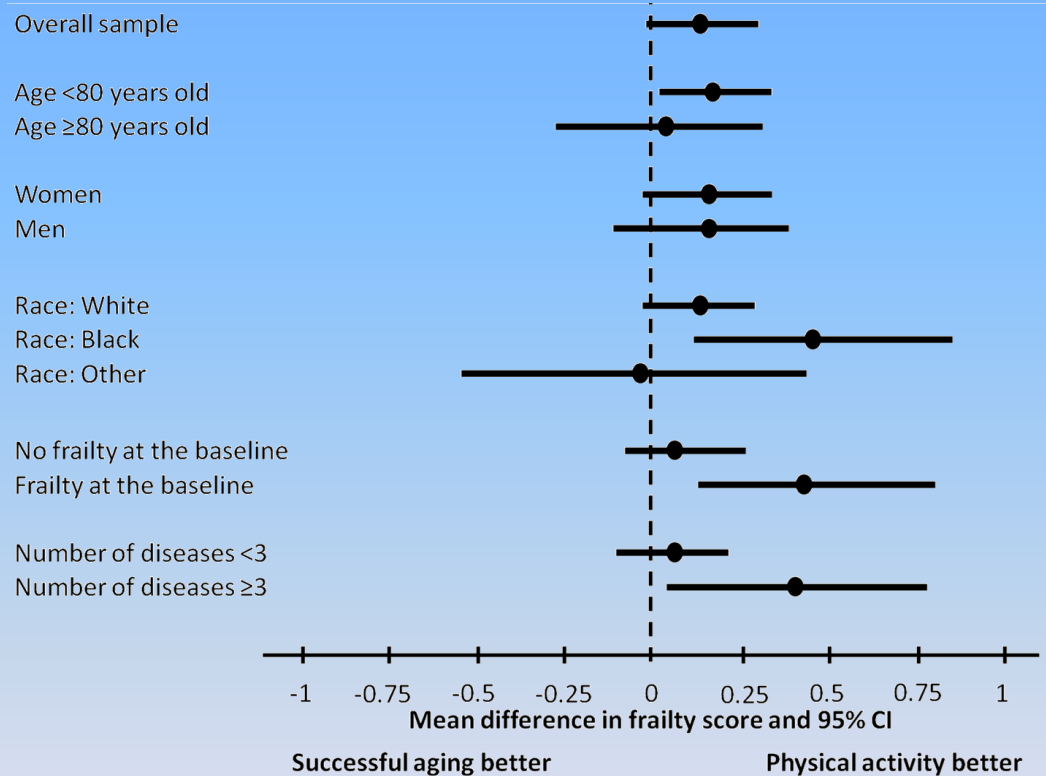
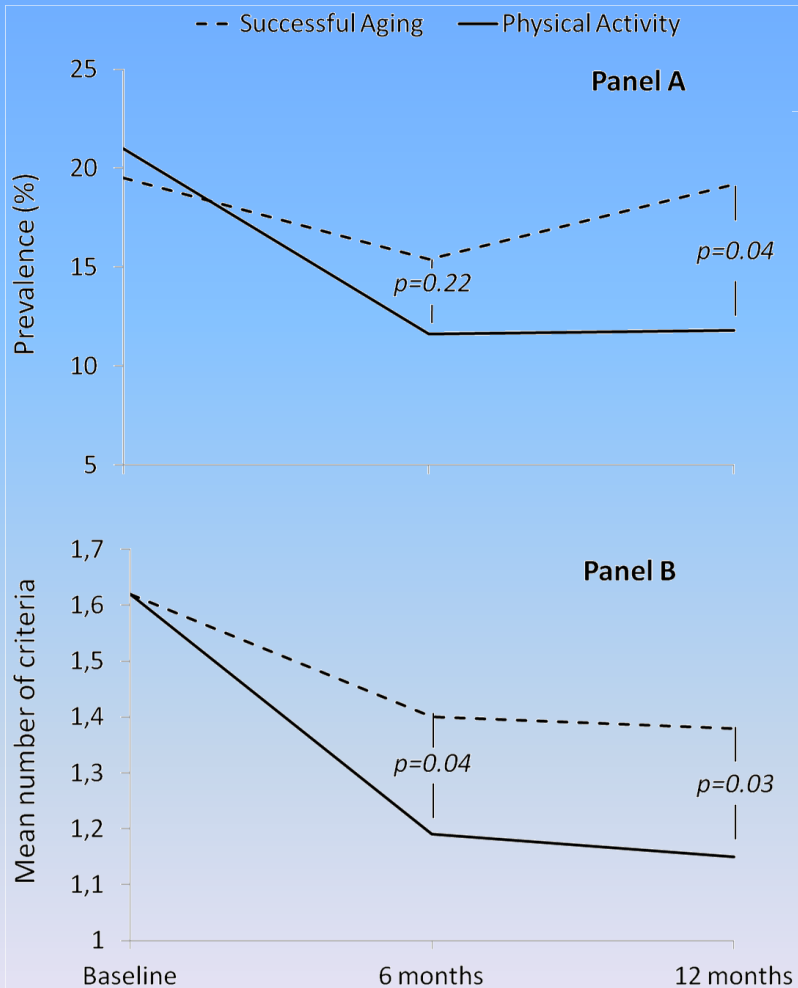
➤ Fattori esterni

- ✓ Marginalità sociale
- ✓ Istituzionalizzazione
- ✓ Farmaci
- ✓ Condizione economica

Conseguenze della malnutrizione

- ↓ massa e funzione muscolare
- ↓ risposta ventilatoria
- ↓ funzione intestinale
- alterazione della termoregolazione
- compromissione della capacità immunitaria
- ↑ tempi di cicatrizzazione delle ferite
- ↑ sensibilità alle infezioni
- ↑ tempi di guarigione e peggioramento del decorso delle malattie concomitanti

Preliminary results (LIFE database)



Cesari M et al. J Gerontol 2014 in press



VITAMINS ON TRIAL

After decades of study, researchers still can't agree on whether nutritional supplements actually improve health.

BY MELINDA WENNER MOYER

DATA DEFICIENCIES

For almost every claim about vitamins, studies have found at least some negative evidence. But most of the negative findings have some confounding variables.

462 | NATURE | VOL 510 | 26 JUNE 2014



So, back to the original question. Are supplements useless? The current state of research offers only an equivocal half-answer: ‘maybe yes’ for some individuals, nutrients and doses, and ‘maybe no’ for others. “Nutrition is complex, and I don’t think we’re necessarily going to find one formula that works for everybody,” says Mayne. But new tools in development could “really change the way we look at this”. The big question is whether, once scientists have all the pieces they need, they can put them together to create a clear and cohesive picture.

“CALCIUM AND VITAMIN D SUPPLEMENTATION REDUCES THE RISK OF BONE FRACTURES.”

The negative finding: The Women’s Health Initiative calcium and vitamin D trial¹¹ found no effect of supplementation on risk of hip fractures.

The confounder: Researchers had estimated that the control group was consuming less than 600 mg calcium per day, when actual intake was more than 1,000 mg.

“ANTIOXIDANT SUPPLEMENTATION REDUCES CANCER AND MORTALITY RISK.”

The negative finding: A meta-analysis¹⁹ of 21 clinical trials, covering a pooled sample of around 91,000 people and 8,800 deaths, found no evidence of an effect on mortality risk.

The confounder: The analysis did not stratify results by sex. Men may have been more likely than women to benefit from antioxidants²⁰.

“β-CAROTENE REDUCES THE RISK OF COLORECTAL ADENOMA, A PRECURSOR TO COLORECTAL CANCER.”

The negative finding: A 1994 clinical study¹⁷ assigning 864 patients to different treatment groups that included β-carotene supplementation found no evidence of benefit, and some evidence of harm.

The confounder: Among non-smokers and non-drinkers there was a significant decrease in the risk of adenocarcinoma, but smokers and drinkers had an increased risk¹⁸.

So, back to the original question. Are supplements useless? The current state of research offers only an equivocal half-answer: ‘maybe yes’ for some individuals, nutrients and doses, and ‘maybe no’ for others. “Nutrition is com-



Tra incertezze e imbrogli

UN BUON RICOSTITUENTE? PER LO STRESS E LA MEMORIA.

12 LUGLIO 2014 | DONNECULTURA | 1 COMMENTO

STRESS, STANCHEZZA CRONICA, PROBLEMI DI MEMORIA, AFFATICAMENTO, CAPELLI DEBOLI, UNGHIE DEBOLI ECC..

PER CHI HA PROBLEMI DI MEMORIA.

Se si hanno problemi di memoria per prima cosa è bene cercarne la causa.

Dopo i cinquant'anni quasi tutti registrano una leggera perdita della memoria; si tratta di un fatto assolutamente fisiologico legato all'età.

Anche durante o dopo un forte periodo di stress, anche psicologico, è normale avere dei vuoti di memoria. In questo caso si risolveranno appena ci si riprende. Provate a leggere più sotto cosa diciamo del ricostituente Sargenor che potrebbe fare al vostro caso, non avendo controindicazioni. Ma è bene chiedere la medico se si prendono altri medicinali.

• *Ginkgo biloba*: terapia preventiva?

Ginkgo biloba for Preventing Cognitive Decline in Older Adults

A Randomized Trial JAMA. 2009;302(24):2663-2670

Design, Setting, and Participants The Ginkgo Evaluation of Memory (GEM) study, a randomized, double-blind, placebo-controlled clinical trial of 3069 community-dwelling participants aged 72 to 96 years, conducted in 6 academic medical centers in the United States between 2000 and 2008, with a median follow-up of 6.1 years.

Results Annual rates of decline in z scores did not differ between *G biloba* and placebo groups in any domains, including memory (0.043; 95% confidence interval [CI], 0.034-0.051 vs 0.041; 95% CI, 0.032-0.050), attention (0.043; 95% CI, 0.037-0.050 vs 0.048; 95% CI, 0.041-0.054), visuospatial abilities (0.107; 95% CI, 0.097-0.117 vs 0.118; 95% CI, 0.108-0.128), language (0.045; 95% CI, 0.037-0.054 vs 0.041; 95% CI, 0.033-0.048), and executive functions (0.092; 95% CI, 0.086-0.099 vs 0.089; 95% CI, 0.082-0.096). For the 3MSE and ADAS-Cog, rates of change varied by baseline cognitive status (mild cognitive impairment), but there were no differences in rates of change between treatment groups (for 3MSE, $P = .71$; for ADAS-Cog, $P = .97$). There was no significant effect modification of treatment on rate of decline by age, sex, race, education, *APOE*E4* allele, or baseline mild cognitive impairment ($P > .05$).

Conclusion Compared with placebo, the use of *G biloba*, 120 mg twice daily, did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment.

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for the Ginkgo Evaluation of Memory (GEM) Study Investigators

• **Strategie A e B: quali raccomandazioni?**

Clinical practice with anti-dementia drugs: a revised (second) consensus statement from the British Association for Psychopharmacology

John T O'Brien and Alistair Burns

J Psychopharmacol published online 18 November 2010

DOI: 10.1177/0269881110387547

Intervention	Level of evidence	Recommendation
Dimebon for AD	There is preliminary level II evidence of a benefit of dimebon in AD, but further studies are awaited. Dimebon should not be prescribed for AD until further studies report.	B
Ginkgo biloba for dementia	There is level I evidence that <u>Ginkgo biloba is not beneficial</u> in improving cognitive symptoms in dementia.	A
Ginkgo biloba for prevention of dementia	There is level I evidence that <u>Ginkgo biloba is not effective</u> in the primary prevention of either all-cause dementia or Alzheimer's disease.	A
Hormone Replacement Therapy (HRT) in prevention and treatment of Alzheimer's disease in post-menopausal women	There is level I evidence that HRT is not effective either in treating cognition in Alzheimer's disease, or for the primary prevention of all-cause dementia or Alzheimer's disease. There is level I evidence that HRT is harmful. HRT should not be prescribed either as a prevention or treatment for dementia, including Alzheimer's disease.	A A
Folate and vitamin B12 for dementia	There is type I evidence that supplementation <u>with folic acid with or without vitamin B12 does not benefit cognition</u> in people with dementia. On current evidence, neither vitamin B12 nor folate, either singly or in combination, can be recommended as treatments for dementia, or for dementia prevention.	A
Statins for the treatment or prevention of dementia	There is level I evidence that statins do not prevent dementia. There is level II evidence that statins do not produce cognitive benefits in AD.	A B



Le grandi ambivalenze

Conclusion: In non-malnourished patients with very mild AD, lower levels of some micronutrients, a different fatty acid profile in erythrocyte membranes and a slightly but significantly lower MNA screening score were observed. This suggests that subtle differences in nutrient status are present already in a very early stage of AD and in the absence of protein/energy malnutrition.

Nutrition and neurodegeneration: epidemiological evidence and challenges for future research

Br J Clin Pharmacol. Mar 2013; 75(3): 738–755.

Sophie Gillette-Guyonnet, Marion Secher, and Bruno

Nearly all of the data linking nutrition to cognitive decline or dementia/AD comes from observational studies and results are sometimes conflicting because of methodologic issues. It seems necessary to develop further prospective studies of adequate duration, including subjects whose diet is monitored at a sufficiently early stage or at least before the onset of disease or cognitive decline. RCTs of dietary interventions have yielded mixed findings and need to be conducted that they focus on specific groups of subjects (middle-aged and elderly populations; subjects with vitamin deficiencies or normal and high levels). Such research identifying the role of specific nutrients, foods or dietary behaviors, is an indispensable step before we can propose specific recommendations in the future.

In the absence of curative treatment, even if it is difficult to change lifestyle habits, lifestyle factors (diet, social engagement, cognitive stimulation, physical exercise) seem the most reasonable candidates for prevention trials at the current time, in particular due to their safety. Due to the difficulties in conducting a multidomain intervention, RCTs may not represent the gold standard in this field, and large public health interventions at the population level may be required. However, such interventions would have to be feasible, cost-effective and easily transferable in order to have a real public health impact.

Mediterranean diet and cognitive decline

A **Mediterranean diet** might also have protective effects against cognitive decline in older individuals, because it **combines several foods and nutrients potentially protective** against cognitive dysfunction or dementia



- antioxidants (vitamin E, carotenoids, flavonoids),
- vitamins B12, folate
- PUFAs

Mediterranean Diet and Risk for Alzheimer's Disease

Nikolaos Scarmeas, MD^{1,2,3}, Yaakov Stern, PhD^{1,2,3}, Ming-Xin Tang, PhD^{1,4}, Richard Mayeux, MD^{1,2,3}, and Jose A. Luchsinger, MD^{1,5}

¹ Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University, New York, NY

Ann Neurol. 2006



- 2,258 community-based non demented individuals in New York were prospectively evaluated
- Compared with subjects in the lowest MeDi tertile
 - subjects in the middle MeDi tertile had 15 % less risk of developing AD
 - subjects in the highest tertile had a 40% less risk of developing AD

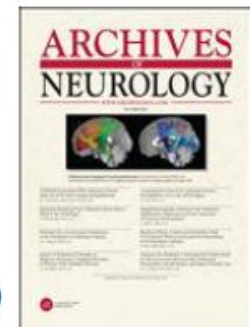
Higher adherence to the MeDi is associated with a reduction in risk for AD.

Mediterranean Diet and Mild Cognitive Impairment

Nikolaos Scarmeas, M.D.^{1,2,3}, Yaakov Stern, Ph.D.^{1,2,3}, Richard Mayeux, M.D.^{1,2,3}, Jennifer Manly, Ph.D.^{1,2,3}, Nicole Schupf, Ph.D.^{1,2}, and Jose A. Luchsinger, M.D.^{1,4}

¹ Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University Medical Center, New York, NY






Arch Neurol. 2009



- 1393 cognitively normal participants, 275 of whom developed MCI.
- Compared to subjects in the lowest MeDi adherence tertile,
 - subjects in the middle MeDi tertile had 17 % less risk of developing MCI,
 - Subjects the highest MeDi adherence tertile had 28 % less risk of developing MCI

Higher adherence to the MeDi is associated with a reduced risk for developing MCI

Single nutrient interventions in MCI and AD: No effect on cognitive functioning

Author	Journal	Nutrient	#Subjects/ Duration	Outcome
Stein 2011	J Alz Disease 	Vitamin D ₂	32 8 weeks	We conclude that high-dose vitamin D provides no benefit for cognition or disability over low-dose vitamin D in mild-moderate AD
DeKosky 2008	JAMA 	Ginkgo biloba	3069 median f-up 6.1 Y	Ginkgo biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI.
Aisen 2008	JAMA 	B-vitamins	409 18 months	This regimen of high-dose B vitamin supplements does not slow cognitive decline in individuals with mild to moderate AD.
McMahon 2006	N Eng J Med 	B-vitamins	276 24 months	The results of this trial do not support the hypothesis that homocysteine lowering with B vitamins improves cognitive performance.
Petersen 2005	N Eng J Med 	Vitamin E	769 36 months	Vitamin E had no benefit in patients with mild cognitive impairment.



Dai singoli nutrienti alle miscele: vi è una logica?



Per concludere ...



Associate editor: M.M. Mouradian

Mechanisms and therapeutic implications of the placebo effect in neurological and psychiatric conditions

Danielle Murray, A. Jon Stoessl

Abstract

The power of a placebo to effect clinically meaningful neurobiological change comparable to pharmacological therapies has been demonstrated, although the mechanisms are not fully understood. Predicting placebo responsiveness has only recently received more attention, but psychological disposition, contextual and biological factors are now known to dramatically affect a person's susceptibility to the placebo effect. The placebo effect depends upon expectancies that can be modified in a number of ways, including conditioning through explicit or implicit learned associations. Based on the dopaminergic response to anticipation of benefit in Parkinson's disease, it was suggested that the placebo effect can be seen as analogous to the expectation of reward. Dopaminergic pathways have since been implicated in the placebo response in pain and depression. Additionally, endogenous opioid release is known to mediate many forms of placebo analgesia.

We provide an overview of the mechanisms and the therapeutic implications of the placebo effect in neurological and psychiatric conditions. We include evidence for detrimental effects arising from seemingly inert interventions, termed the 'nocebo effect.' Neuroimaging has critically advanced the study of the placebo effect and provides some of the strongest evidence for the mechanisms of this phenomenon prevalent across an array of human health-related circumstances. This review specifically focuses on mechanisms of the placebo effect in the three conditions that have most significantly demonstrated this effect and for which a plausible physiological basis can be identified: pain, PD and depression. Other neurological and psychiatric diseases reviewed include multiple sclerosis, Huntington's disease, Alzheimer's disease, schizophrenia and epilepsy.



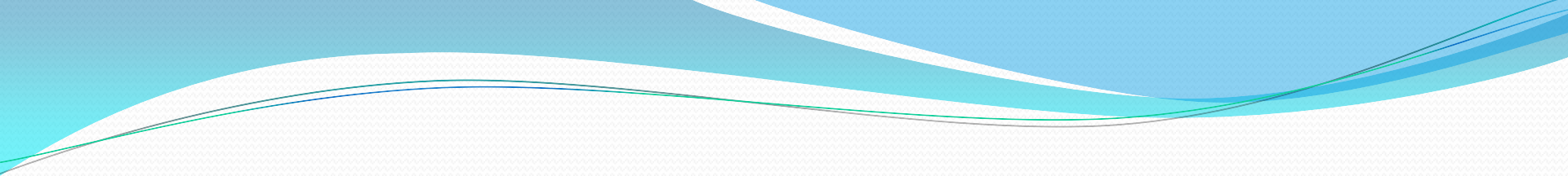
**Le alterne vicende dell'effetto placebo
nella recente storia della medicina.**



Una storia senza conclusione.

Sono necessari studi seri e controllati, partendo dal riconoscimento che talvolta non si tratta solo di placebo o di imbrogli.

Coerenza nel nostro atteggiamento di cura: non si può prescrivere un farmaco se non si ha il convincimento (soggettivo?) della sua efficacia.



**Un equilibrio tra l'atteggiamento scienziata, lontano dal sentire degli ammalati, e l'accettazione acritica di qualsiasi proposta.
C'è spazio ancora per molto lavoro.**