[연수강좌]

미세영양소의 임상적 적용

조 비 룡

서울의대 가정의학교실

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
  - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

1. Homocysteine associated Vitamins

- Vitamin B_6 (pyridoxin)
- Vitamin B_9 (folacin)
- Vitamin B_{12} (cobalamin)
- Betaine, Cholin

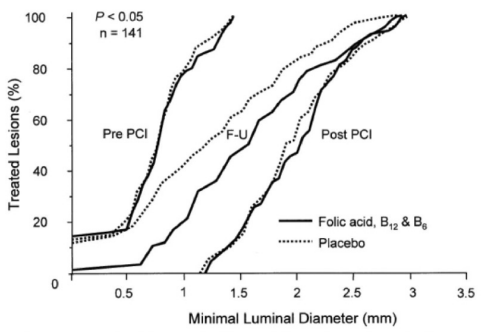
Effect of Homocysteine-Lowering Therapy on Restenosis After Percutaneous Coronary Intervention for Narrowings in Small Coronary Arteries

Guido Schnyder, MD, Marco Roffi, MD, Yvonne Flammer, MD, Riccardo Pin, MD, Franz R. Eberli, MD, Bernhard Meier, MD, Zoltan G. Turi, MD, and Otto M. Hess, MD

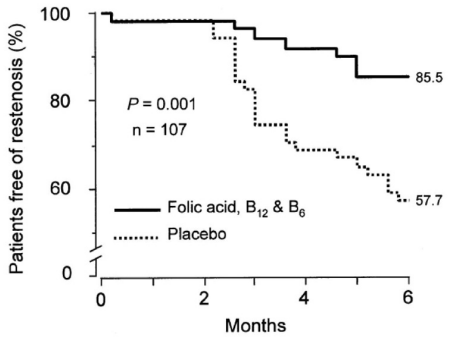
(2003, AJC)

- **58/55 RCT**
- **Homocysteine-lowering** 치료가 **PCI** 이후의 **Small Coronary A.**의 협착을 유의하게 줄인다.
  - RR = 0.34

6개월 후의 MLD의 변화 비교



Freedom from Restenosis



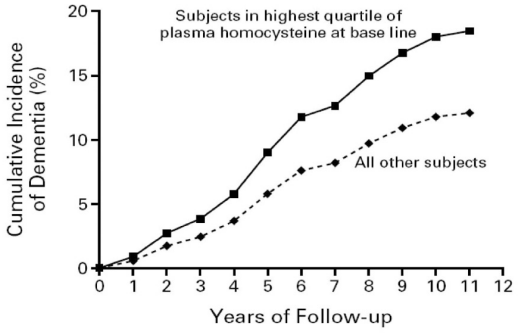
The New England Journal of Medicine (2000, 2)

PLASMA HOMOCYSTEINE AS A RISK FACTOR FOR DEMENTIA AND ALZHEIMER'S DISEASE

Sudha Seshadri, M.D., Alexa Beiser, Ph.D., Jacob Selhub, Ph.D., Paul F. Jacques, Sc.D., Irwin H. Rosenberg, M.D., Ralph B. D'Agostino, Ph.D., Peter W.F. Wilson, M.D., and Philip A. Wolf, M.D.

- **1092명 (평균 76세) Retrospective 관찰**
- **Framingham Study**
- **높은 Homocysteine 농도는 AD의 강력한 위험 인자**
- **OR 1.4/SD/8 year**
- **Hyperhomocysteinemia (>14umol/L)**
- **Risk Double**

Crude Cumulative Incidence of Dementia



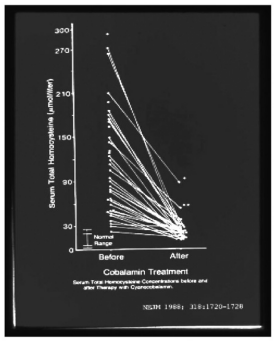
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 13, 2004 VOL. 350 NO. 20

Homocysteine Levels and the Risk of Osteoporotic Fracture

Joyce B.J. van Meurs, Ph.D., Rosalie A.M. Dhonukshe-Rutten, M.Sc., Saskia M.F. Pluijm, Ph.D., Marjolein van der Klift, M.D., Ph.D., Robert de Jonge, Ph.D., Jan Lindemans, Ph.D., Lisette C.P.G.M. de Groot, Ph.D.,

'Marginal' B12 deficiency can result in neurodegenerative diseases

- 141 subjects with a variety of neurodegenerative diseases whose disease significantly improved with administration of B12
- A significant minority of these subjects had 'low-normal' B12 levels of 200-350 pg/mL



Homocystein의 기대 기능

- 동맥 경화 방지
  - 심혈관계 질환 예방
- 치매 예방
- 말초 신경질환 예방
- 골절 예방

Vit B Treatment Protocol

- Folic acid (0.4 -5 mg)
  - 4주 투여 시 약 25% 감소
- Vitamin B_{12} (200-1000 μg)
  - 7% 추가 감소
- Pyridoxine (10 – 250 mg)

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
  - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

2. Vitamin D levels diminish with age and disability

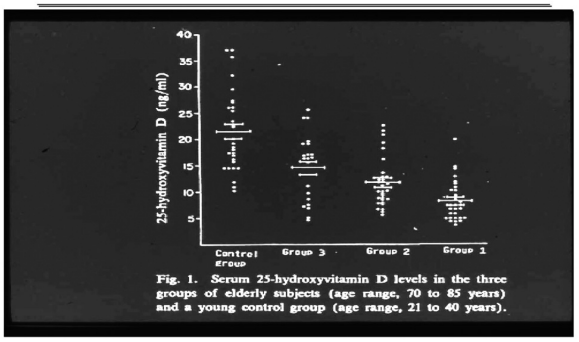
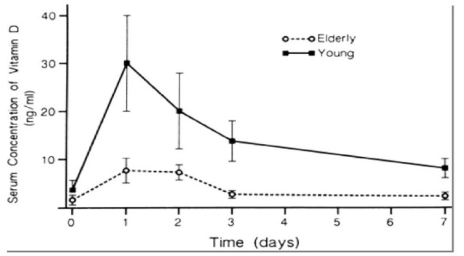


Fig. 1. Serum 25-hydroxyvitamin D levels in the three groups of elderly subjects (age range, 70 to 85 years) and a young control group (age range, 21 to 40 years).

Causes of diminished D levels in the elderly

- habitually low dietary intake (120 I.U./d)
- impaired synthesis in senile skin (see below)
- little sun exposure in homebound and institutionalized elders



From Holick et al. Lancet;2:1104–1105,1989.

Vit. D effects on Fall

Moderate protective effect on Fracture Risk

– **Bone Mineral Density** change

JBMR
June 2000, Volume 15, Number 6
Page 1113

Effects of a Short-Term Vitamin D and Calcium Supplementation on Body Sway and Secondary Hyperparathyroidism in Elderly Women

MICHAEL PFEIFER,[1] BETTINA BEGEROW,[1] HELMUT W. MINNE,[1] CHRISTINE ABRAMS,[2] DETLEF NACHTIGALL,[3] and CORINNA HANSEN[3]

[1]Institute of Clinical Osteology "Gustav Pommer" and Clinic "DER FORSTENHOF," Bad Pyrmont, Germany.
[2]Department of Public Health and Primary Care, University of Hull, Hull, U.K.
[3]Strathmann Company, Hamburg, Germany.

- 148 women (mean [±SD] age, 74 ± 1 years)
  - •25-hydroxycholecalciferol level below 50 nmol/liter
- Supplementation : 8주간 시행
  - 1200 mg of calcium plus 800 IU of vitamin D
  - 1200 mg of calcium
- 결과
  - a decrease in the serum PTH of 18% ($p = 0.0432$)
  - a decrease in body sway of 9% ($p = 0.0435$)
  - mean number of falls per subject during a 1-year follow-up period
    - 0.45 for the calcium mono group
    - 0.24 for the calcium and vitamin D group ($p = 0.0346$).

JBMR
February 2003, Volume 18, Number 2
Page 343

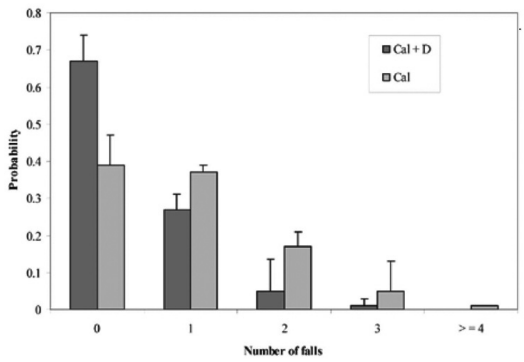
Effects of Vitamin D and Calcium Supplementation on Falls: A Randomized Controlled Trial

HEIKE A BISCHOFF,[1,2] HANNES B STÄHELIN,[3] WALTER DICK,[1] REGULA AKOS,[1] MARGRITH KNECHT,[3] CHRISTIAN SALIS,[1] MATTHIAS NEBIKER,[1] ROBERT THELER,[4] MICHAEL PFEIFER,[5] BETTINA BEGEROW,[5] ROBERT A LEW,[2] and MARTIN CONZELMANN[6]

[1]Department of Orthopaedics, University of Basel, Basel, Switzerland. orsid0911951
[2]Division of Rheumatology, Immunology and Allergy, The Robert B. Brigham Multipurpose Arthritis Center, Brigham and Women's Hospital, Boston, Massachusetts, USA.
[3]Department of Geriatrics, University of Basel, Basel, Switzerland.
[4]Department of Rheumatology, University of Basel, Basel, Switzerland.
[5]Institute for Clinical Osteology, Bad Pyrmont, Germany.
[6]Department of Geriatrics, Felix Platter Spital, Basel, Switzerland.

- 122 elderly women (mean age, 85.3 years) in long-stay geriatric care.
  - 1200 mg calcium plus 800 IU cholecalciferol ($n = 62$)
  - 1200 mg calcium ($n = 60$)
- 12-week treatment period.
- 비교
  - Falls per person (0, 1, 2-5, 6-7, >7 falls)
  - Musculoskeletal Function
    - TUG test, knee flexor/extensor strength, grip strength.

Vitamin D & Fall



Vitamin D on Musculoskeletal Function

TABLE 5. MUSCULOSKELETAL FUNCTION AT BASELINE AND PERCENTAGE DIFFERENCE FROM BASELINE AFTER 3 MONTHS OF FOLLOW-UP IN THE TWO TREATMENT GROUPS

	Baseline (n = 60 in Cal-group and n = 62 in Cal + D-group)		*Change (n = 29 in Cal-group and n = 33 in Cal + D-group)*	
Characteristics	*Median (IQR)*	*p Value (1)*	*Percentage change*	*p Value (2)*
Knee flexor strength (kp)*				
Cal-group	8.0 (5.5–10.0)		−3.9%	
Cal + D-group	7.5 (6–9.9)	NS	+3.7%	
Knee extensor strength (kp)*				
Cal-group	11.75 (9.25–15.5)		+1.4%	
Cal + D-group	12.5 (9.63–15.5)	NS	+8.6%	
Grip strength (bar)†				
Cal-group	0.190 (0.155–0.263)		+0%	
Cal + D-group	0.205 (0.130–0.265)	NS	+5.5%	
Timed up & go test(s)				
Cal-group	23 (17–39.5)		−3.2%	
Cal + D-group	25 (19.5–40.5)	NS	−11.1%	
Overall musculoskeletal function				0.0094

p value (1) represents the probability of the difference of the median baseline values between the two treatment groups in 122 subjects. IQR represents interquartile range. Change shows difference from baseline in percent (based on median changes) among 62 subjects who had complete data set at base-line and follow-up for single measurements. *p* Value (2) represents the probability of the difference of change between the two treatment groups over time for overall summed musculoskeletal function.
* To convert kilopond into Newton multiply by 10.
† One bar equals 10^5 pascal, which is equivalent to 1 N/m^2.

Vit. D effects on Fall

Moderate protective effect on Fracture Risk

– **Bone Mineral Density** change

– Directly improve **Muscle Strength**

- Reducing Fx. Risk through fall prevention
- Reduced Fx. within 8 to 12weeks

Effect of Vitamin D on Falls
A Meta-analysis

Heike A. Bischoff-Ferrari, MD, MPH
Bess Dawson-Hughes, MD
Walter C. Willett, MD, DrPH
Hannes B. Staehelin, MD
Marlet G. Bazemore, MD
Robert Y. Zee, MD
John B. Wong, MD

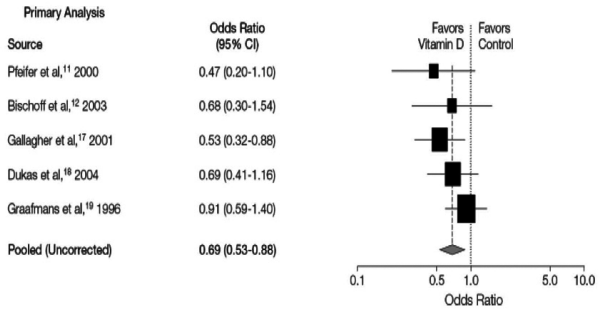
Context Falls among elderly individuals occur frequently, increase with age, and lead to substantial morbidity and mortality. The role of vitamin D in preventing falls among elderly people has not been well established.

Objective To assess the effectiveness of vitamin D in preventing an older person from falling.

Data Sources MEDLINE and the Cochrane Controlled Trials Register from January 1960 to February 2004, EMBASE from January 1991 to February 2004, clinical experts, bibliographies, and abstracts. Search terms included trial terms: *randomized-controlled trial* or *controlled-clinical trial* or *random-allocation* or *double-blind method*,

- *JAMA 2004;291:1999-2006*
- Vit D의 낙상에 대한 효과에 대한 Meta-analysis

Results
Primary Analysis



Comment

- 22% reduction in the risk of falling
  - compared with Calcium or placebo
  - NNT = 15
- Muscular Effect of Vitamin D
  - Type II muscle fiber hypertrophy after 3 mos.
  - Nuclear Vit D receptor 가 근육에 풍부하게 존재

JAMA
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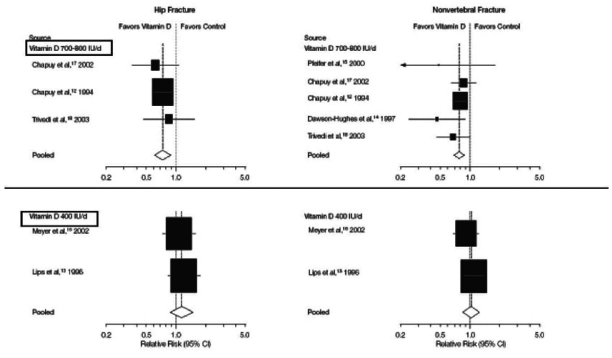
Volume 293(18) 11 May 2005 p 2257–2264

Fracture Prevention With Vitamin D Supplementation: A Meta-analysis of Randomized Controlled Trials
[Review]

Bischoff-Ferrari, Heike A. MD, MPH; Willett, Walter C. DrPH; Wong, John B. MD; Giovannucci, Edward ScD; Dietrich, Thomas MPH; Dawson-Hughes, Bess MD

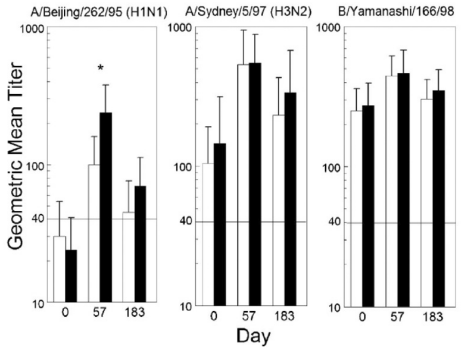
- SR
  - 5 RCT for Hip Fx(9294), 7 RCT for nonvertebral Fx (9820)
- Results
  - Vit D 전체적인 효과는 없다
    - 700IU – 800IU : RR (Hip Fx) = 26%
      RR (NonV Rx) = 23%

Forest Plots Comparing the Risk of Hip and Nonvertebral Fractures

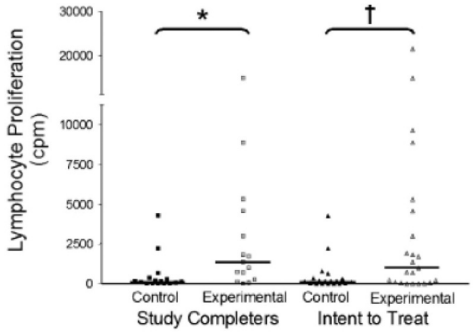


Hip and Nonvertebral Fracture Efficacies by

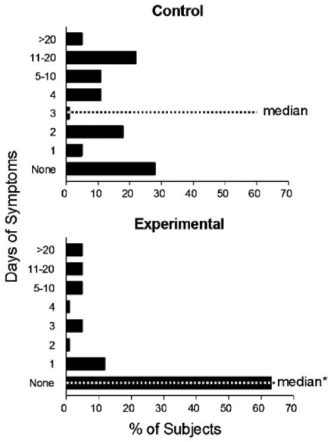
Geometric mean Ab titier



Lymphocyte proliferation to vaccine components



Reduced Days of Symptoms of Upper Respiratory Tract Infection



bmj.com

Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials

Alia El-Kadiki and Alexander J Sutton

BMJ 2005;330;871-; originally published online 31 Mar 2005;
doi:10.1136/bmj.38399.495648.8F

- Systematic Review
- 8 Clinical Trials were included
- Results
  - 연중 평균 감염 일수 = 17.5% 감소 (11 – 24)
  - OR (감염수/연구) = 1.10 (0.81 – 1.50)
  - 감염률 = 0.89 (0.78 – 1.03)

Table 1 Characteristics of the trials included in the meta-analyses

Study (location)	Age of trial participants in years	Duration of follow-up	Infections assessed	No of subjects in placebo group	No of subjects in treatment group	Jadad score	Comments
Chavance et al 1992 (France)[21]	60+	4 months	Respiratory, nose, throat, ear, skin, mouth, urinary, and gynaecological infections	106 (of which 7 were lost to follow-up, leaving an effective sample size of 101)	110 (of which 7 were lost to follow-up, leaving an effective sample size of 103)	3	Double blind
Girodon et al 1999 (France)[22]	65+	2 years (maximum)	Respiratory and symptomatic urogenital infections	182 (of which 4 withdrew and 51 died during the study, but all were included in analysis)	181 (of which 3 withdrew and 55 died during the study, but all were included in analysis)	4	A double blind, 2×2 factorial trial (arms multivitamin only and minerals only excluded from meta-analyses) Population was from nursing homes
Chandra 1992 (United States)[23]	65+	12 months	Any infection (diagnosis was based on clinical features and laboratory tests included blood count, radiography of the chest and sinuses, bacterial and fungal cultures of sputum, urine and blood, C reactive protein, and erythrocyte sedimentation rate)	48	48	4	Double blind
Barringer et al 2003 (United States)[24]	65+	12 months	Upper respiratory tract infection, lower respiratory tract infection, influenza-like syndrome, gastrointestinal infection, and urinary tract infection	17	18 65 (2 dropped out and were lost to follow-up leaving an effective sample size of 16)	4	People aged <65 years were excluded from the analysis. A large proportion of subjects had diabetes Double blind
Graat et al 2002 (Netherlands)[25]	60+	15 months (maximum)	Acute respiratory tract infections	230	240	3	A double blind, 2×2 factorial trial. Arms of vitamin E only and multivitamin-mineral + vitamin E have been excluded from meta-analyses
Chandra 2002 (location not specified)[26]	50-65	12 months	Common adult infection illnesses diagnosed by fever, cough, elevated erythrocyte sedimentation rate and C reactive protein, x ray of the sinuses and chest, blood culture, sputum culture, and urine culture	22 (three lost to follow-up, leaving an effective sample size of 19)	22	4	Double blind
Jain 2002 (India)[27]	51-78	12 months	Respiratory infections	18	18	2	Blinding unclear
Girodon et al 1997 (France)[28]	65+	2 years	Respiratory and symptomatic urogenital infections	29 (of which 7 dropped out before and but were included in analysis)	21 (of which 7 dropped out before and but were included in analysis)	4	A double blind, 2×2 factorial trial (arms multivitamin only and minerals only excluded from meta-analysis) Population was from nursing homes

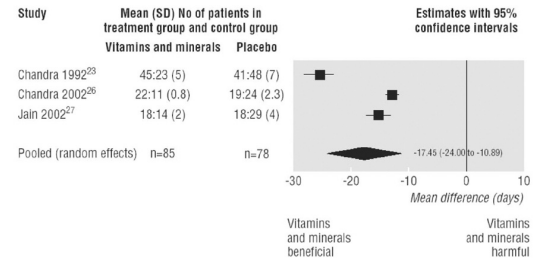
Table 2 Details of composition of multivitamin and mineral supplements given in each trial

Study (location)	Details	Daily intake of supplements
Chavance et al 1993 (France)[21]	Commercial Product	Vitamins A (retinol 5000 IU), B1 (thiamine) 2.25 mg, B2 (riboflavin) 2.6 mg, B6 (pyridoxine) 3 mg, B12 (cyanocobalamin) 9 µg, C 90 mg , D2 400 IU, E 90 IU, nicotinamid 20 mg, biotin 45 µg, pantothenic acid 10 mg Calcium 162 mg, iron 27 mg, zinc 22.5 mg, folic acid 0.4 mg, phosphorus 125 mg, iodine 150 µg, magnesium 100 mg, copper 3 mg, manganese 7.5 mg, potassium 7.5 mg
Girodon et al 1999 (France)[22]	Commercial Product	Vitamins A (β carotene 6 mg), C 120 mg, E 15 mg Zinc 20 mg, selenium 100 µg
Chandra 1992 (United States)[23]	Commercial Product	Vitamins A (retinol 400 µg), B1 (thiamine) 2.2 mg, B2 (riboflavin) 1.8 mg, niacin 16 mg, B6 (pyridoxine) 3.0 mg, B12 4.0 µg, C 80 mg, D 4 µg, E 44 mg Calcium 200 mg, iron 16 mg, zinc 14 mg, copper 400 µg, copper 1.4 mg, selenium 20 µg, iodine 0.2 mg, magnesium 100 mg
Barringer et al 2003 (United States)[24]	Commercial Product	Vitamin A 4000 IU (β carotene 1000 IU), B1 (thiamine) 4.5 mg, B2 (riboflavin) 3.4 mg, niacin 20 mg, B6 (pyridoxine) 6 mg, B12 (cyanocobalamin) 30 µg, C (ascorbic acid) 120 mg, D 400 IU, E 60 IU, K 20 µg, biotin 0.09 mg, pantothenic acid 19 mg Calcium 120 mg, iron 16 mg, folic acid 400 µg, zinc 22.5 mg, selenium 105 µg, magnesium 100 mg, copper 2 mg, iodine 150 µg, manganese 4 mg, chromium 180 µg
Graat et al 2002, (Netherlands)[25]	Commercial Product	A capsule contained: Vitamins A (retinol 600 µg, β carotene 1.2 mg), B1 (thiamine) 1.4 mg, B2 (riboflavin) 1.6 mg, niacin 18 mg, B6 (pyridoxine) 2.0 mg, B12 (cyanocobalamin) 1 µg, biotin 150 µg, C 60 mg, E 10 mg, D (cholecalciferol) 5 µg, K 30 µg, pantothenic acid 6 mg Calcium 74 mg, iron 4.9 mg, folic acid 200 µg, zinc 10 mg, selenium 25 µg, magnesium 30 mg, copper 1.0 mg, iodine 100 µg, phosphorus 49 mg, manganese 1.0 mg, chromium 25 µg, molybdenum 25 µg, silicium 2 µg Each participant received 2 capsules per day
Chandra 2002 (location not specified)[26]		Vitamins A (retinol 400 µg), B1 (thiamine) 2.2 mg, B2 (riboflavin) 1.5 mg, niacin 16 mg, B6 (pyridoxine) 3.0 mg, B12 4.0 µg, C 80 mg, D 4.0 µg, E 44 mg Calcium 200 mg, iron 16 mg, zinc 14 mg, copper 1.4 mg, selenium 20 µg, iodine 200 µg, magnesium 100 mg, folate 400 µg
Jain 2002 (India)[27]		Vitamins A (retinol 400 µg), B1 (thiamine) 2.2 mg, B2 (riboflavin) 1.5 mg, niacin 16 mg, B6 (pyridoxine) 3.0 mg, B12 4.0 µg, E 44 mg Calcium 200 mg, iron 16 mg, zinc 14 mg, copper 1.4 mg, selenium 20 µg, iodine 200 µg, magnesium 100 mg, folate 400 µg
Girodon et al 1997 (France)[28]		Vitamins A (β carotene 6 mg), C 120 mg, E 15 mg Zinc 20 mg, selenium 100 µg

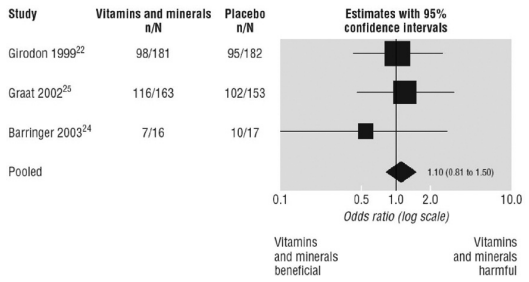
Table 3 Reporting of infections by different definition of outcome (binary)

Study (location)	Mean days of infection	At least one infection	Infection rate
Chavance et al 1993 (France)[21]			X
Girodon et al 1999 (France)[22]		X	
Chandra 1992 (United States)[23]	X		
Barringer et al 2003 (United States)[24]		X	
Graat et al 2002, (Netherlands)[25]		X	X
Chandra 2002 (location not specified)[26]	X		
Jain 2002 (India)[27]	X		X
Girodon et al 1997 (France)[28]			X
Total instances reported	3	3	4

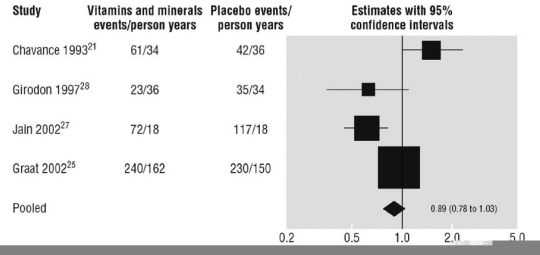
Number of Days of Infection



OR for at least One Infection during the Study Periods



Incidence Rate Ratio for Infection



Different Forms of Vitamin E

- 4종 Tocopherol + 4종 Tocotrienol
  - α, β, γ, δ
  - α-tocopherol; 인체 활성화 형태
    - Natural form : RRR-AT
      - α TTP에 훨씬 친화적임
    - Synthetic form : all-rac-AT
- RRR-AT > 800 IU + Vit C regimen

Table 1. Summary of studies relating antioxidant intake and risk of AD

Reference	Setting	Design	Participants	Exposure	Outcome	Results
Masaki et al[82]	Honolulu-Asia Aging Study	Cohort	3385 men, age 71–93 years	Use of supplements of vitamins C and E	AD, mixed dementia, vascular dementia. Cognitive function	Intake of supplements of both vitamins related to low risk of vascular dementia but not related to risk of AD; intake of either related to better cognitive function
Grodstein et al[83]	Nurses' Health Study	Cohort	14 968 women, age 70–79 years	Use of supplements containing vitamins C and E	TICS, delayed recall of TICS ten-word list, delayed recall of EBMT, verbal fluency, digit span backwards test	Current users of supplements had better global scores than non-users
Zandi et al[84]	Cache County Study	Cohort	4740, 90% age ⩾65 years	Use of vitamin C and E supplements	Incident AD	Reduction in risk of AD in users of combination of vitamin C and E supplements, but not in users of those supplements alone
Engelhart et al[85]	Rotterdam Study	Cohort	5395, age ⩾55 years	Intake of vitamins C and E, carotenes, and flavonoids measured by SFFQ		Dietary vitamins C and E inversely related to risk of dementia
Morris et al[86]	Chicago Health and Aging Project	Cohort	2889 community residents, age 65–102 years	Intakes of vitamins E and C and carotenes from food	Cognitive change of EBMT, MMSE, symbol digit modalities test (baseline and 3 years)	Vitamin E is inversely related to cognitive decline
Morris et al[87]	Chicago Health and Aging Project	Cohort	815 community dwelling people age ⩾65 years	Intake of dietary and supplement vitamins C and E, and β carotene measured by SFFQ	Incident AD	Dietary vitamin E intake inversely related with lower risk of AD. No association for intake of vitamin E supplement, vitamin C, or carotenoids
Luchsinger et al[88]	Washington Height Columbia Aging Project	Cohort	980 community dwelling individuals age ⩾65 years	Intake of dietary and supplement vitamins C and E and carotenes measured by SFFQ	Incident AD	No relation between antioxidants with AD

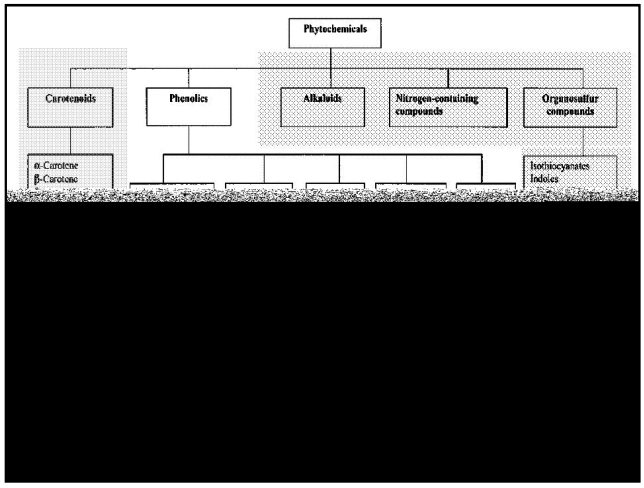
TICS=telephone interview of cognitive status; EBMT=East Boston Memory Test; SFFQ=semiquantitative food frequency questionnaire.

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
  - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

5. 'Phyto-chemical'

- **Phyto-**
  - Greek word for 'plants'
- **Bioactive non-nutrient** plant compound
  - may help prevent diseases like cancer and heart disease
  - *Anti-oxidant effect,* Metabolic effect
- Phyto-nutrient
  - 5대 영양소의 포함 여부
- 5,000종류 이상이 알려짐
  - 계속 증가하고 있음



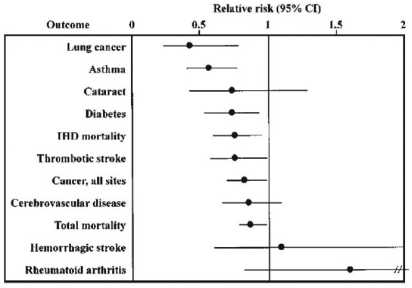


FIGURE 1. Relative risks (●) and 95% CIs (horizontal bars) of chronic diseases between the highest (>47 g/d) and lowest (0 g/d) quartiles of apple intake. The relative risks were adjusted for sex, age, disease-specific nondietary confounding factors, and intakes of vegetables and fruit other than apples. IHD, ischemic heart disease.

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ORIGINAL RESEARCH COMMUNICATION

Flavonoid intake and the risk of cardiovascular disease in women[1,2,3]

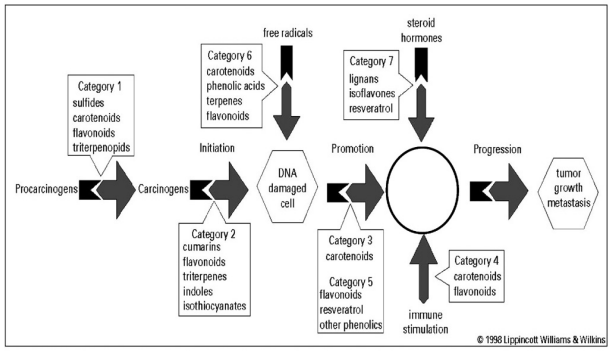
Howard D Sesso, J Michael Gaziano, Simin Liu and Julie E Buring

[1] From the Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School,

- The Women's Health Study
- **39,876** female US health professionals
- 6.9 yr FU
- Results
  - Not significant

	Category of intake[2]				
	1st (Lowest)	2nd	3rd	4th (Highest)	*P* for trend
Tea	None	<1 cup/d	1–3 cups/d	≥4 cups/d	
No. of women	12383	15862	8472	1185	
No. of CVD cases	240	303	162	17	
Age- and treatment-adjusted RR[3]	1.00 (ref)	1.05 (0.88, 1.24)	1.06 (0.87, 1.30)	0.85 (0.52, 1.40)	0.64
Multivariate-adjusted RR[4]	1.00 (ref)	1.14 (0.95, 1.36)	1.15 (0.93, 1.42)	0.74 (0.44, 1.25)	0.36
No. of important vascular events	178	205	126	6	
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.95 (0.78, 1.16)	1.12 (0.89, 1.40)	0.41 (0.18, 0.92)	0.16
Multivariate-adjusted RR[4]	1.00 (ref)	1.02 (0.83, 1.26)	1.18 (0.93, 1.51)	0.33 (0.14, 0.80)	0.07
Broccoli	None	≤1 serving/wk	2–4 servings/wk	≥5 servings/wk	
No. of women	2173	23201	10960	1900	
No. of CVD cases	67	444	183	32	
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.65 (0.51, 0.85)	0.59 (0.45, 0.79)	0.58 (0.38, 0.89)	0.027
Multivariate-adjusted RR[4]	1.00 (ref)	0.75 (0.57, 0.99)	0.70 (0.51, 0.96)	0.71 (0.44, 1.15)	0.21
No. of important vascular events	49	307	138	23	
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.62 (0.46, 0.84)	0.61 (0.44, 0.85)	0.58 (0.35, 0.95)	0.18
Multivariate-adjusted RR[4]	1.00 (ref)	0.73 (0.53, 1.01)	0.73 (0.51, 1.06)	0.72 (0.41, 1.27)	0.56
Apples	None	≤1 apple/wk	2–6 apples/wk	≥1 apple/d	
No. of women	3557	17697	13670	3130	
No. of CVD cases	90	323	245	52	
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.73 (0.57, 0.92)	0.68 (0.53, 0.86)	0.58 (0.41, 0.81)	0.015
Multivariate-adjusted RR[4]	1.00 (ref)	0.82 (0.64, 1.04)	0.87 (0.66, 1.14)	0.78 (0.52, 1.16)	0.74
No. of important vascular events	63	228	182	31	
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.73 (0.55, 0.97)	0.72 (0.54, 0.96)	0.49 (0.32, 0.76)	0.015
Multivariate-adjusted RR[4]	1.00 (ref)	0.83 (0.62, 1.11)	0.96 (0.69, 1.32)	0.66 (0.40, 1.08)	0.56
Onions	None	≤1 serving/wk	2–4 servings/wk	≥5 servings/wk	
No. of women	16309	16029	3722	1978	
No. of CVD cases	291	311	78	39	
Age- and treatment-adjusted RR[3]	1.00 (ref)	1.03 (0.88, 1.21)	1.08 (0.84, 1.39)	1.03 (0.73, 1.44)	0.73
Multivariate-adjusted RR[4]	1.00 (ref)	1.00 (0.85, 1.19)	1.18 (0.91, 1.54)	1.00 (0.68, 1.46)	0.50
No. of important vascular events	200	227	55	30	
Age- and treatment-adjusted RR[3]	1.00 (ref)	1.10 (0.91, 1.33)	1.11 (0.82, 1.51)	1.17 (0.79, 1.72)	0.45
Multivariate-adjusted RR[4]	1.00 (ref)	1.04 (0.85, 1.28)	1.21 (0.89, 1.66)	1.15 (0.75, 1.78)	0.28
Tofu	None	1–3 servings/mo	≥1 serving/wk		
No. of women	34756	2142	1058		
No. of CVD cases	655	35	23		
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.89 (0.64, 1.25)	1.18 (0.78, 1.79)		0.76
Multivariate-adjusted RR[4]	1.00 (ref)	1.09 (0.77, 1.55)	1.17 (0.71, 1.91)		0.45
No. of important vascular events	467	24	16		
Age- and treatment-adjusted RR[3]	1.00 (ref)	0.86 (0.57, 1.29)	1.15 (0.70, 1.89)		0.95
Multivariate-adjusted RR[4]	1.00 (ref)	1.03 (0.67, 1.57)	1.16 (0.65, 2.08)		0.64

4) Anti-carcinogenesis Effects



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Resveratrol and breast cancer risk
[Research papers: Breast Cancer]

Levi, F[1,2]; Pasche, C[2]; Lucchini, F[1]; Ghidoni, R[3]; Ferraroni, M[4]; La Vecchia, C[1,4,5]

- Resveratrol
  - French Paradox
  - Grape Skin(속성되면서 증가), Mulberry, Peanut
- Case-Control Study
  - Case : 369
  - Control : 602
- Results
  - Odds Ratio
    - Intermediate : 0.5
    - The highest : 0.39
    - Significant only for 'Grape'

Odds Ratios for Breast Cancer

Table 1 Distribution of 369 cases of breast cancer and 602 controls according to various sources of dietary resveratrol intake, and corresponding odds ratios (OR) and 95% confidence intervals (CI). Vaud, Switzerland, 1993–2003

	1st tertile[a]		2nd tertile		3rd tertile		
	Cases:controls	OR[b] (95% CI)	Cases:controls	OR (95% CI)	Cases:controls	OR (95% CI)	χ^2, trend
Total (wine & grapes)	133:208	1.0	84:191	0.50 (0.34–0.72)	152:203	0.39 (0.25–0.62)	18.80 (P<0.001)
Wine, total	184:406	1.0	69:92	1.05 (0.18–6.25)	116:104	1.60 (0.28–9.28)	1.95 (P = 0.25)
Grape	168:213	1.0	79:151	0.64 (0.44–0.93)	122:238	0.55 (0.39–0.76)	12.79 (P<0.001)

[a]Reference category: tertile of total resveratrol determined on controls distribution. The upper cut-points for the tertile of total resveratrol intake (μg/day) ranged between 0.0 and 73.0 for the 1st tertile (lowest), 73.1 and 160.7 for the 2nd tertile, >160.7 for the 3rd tertile (highest); intake from wine was 0.0 for the 1st tertile, ranged between 0.1 and 176.8 for the 2nd tertile, >176.8 for the 3rd tertile; intake from grapes ranged between 0.0 and 72.2 for the 1st tertile, 72.3 and 126.4 for the 2nd tertile, >126.4 for the 3rd tertile.

[b]OR adjusted for age, education, body mass index, hormone replacement therapy, menopausal status, parity, energy intake, and total alcohol consumption.

Odds Ratios for Breast Cancer in strata of various covariates

	2nd tertile[a] OR[b] (95% CI)	3rd tertile OR (95% CI)	μ^2, trend
Age at menopause			
Pre-peri	0.58 (0.29–1.16)	0.46 (0.20–1.05)	3.72 (P = 0.054)
<50 years	0.42 (0.21–0.87)	0.38 (0.15–0.91)	5.88 (P = 0.015)
≥ 50 years	0.46 (0.24–0.86)	0.41 (0.18–0.93)	6.32 (P = 0.012)
Parity			
0	0.45 (0.20–1.04)	0.29 (0.10–0.86)	5.50 (P = 0.019)
≥ 1	0.51 (0.33–0.78)	0.40 (0.24–0.68)	13.77 (P = 0.000)
HRT			
Never	0.52 (0.34–0.81)	0.46 (0.27–0.77)	10.65 (P = 0.01)
Ever	0.26 (0.11–0.61)	0.16 (0.05–0.52)	11.85 (P = 0.001)
BMI (kg/m)^2			
<25	0.52 (0.31–0.87)	0.37 (0.18–0.73)	9.84 (P = 0.02)
≥ 25	0.41 (0.23–0.73)	0.40 (0.21–0.77)	8.80 (P = 0.003)

Table 3. Odds ratios* (95% confidence intervals) for lung cancer cell types by quantile of intake of onions, apples, white grapefruit, quercetin, and naringin

Cell type†	Odds ratio (95% confidence interval) by Q_1 (low)	Q_2	Q_3	Q_4 (high)	Two-sided P for trend‡
Onions					
SCC	1.0 (referent)	1.6 (0.4–5.6)	0.7 (0.2–2.8)	0.1 (0.0–0.6)	.003
ADC	1.0 (referent)	1.0 (0.5–2.0)	0.7 (0.4–1.5)	0.6 (0.3–1.2)	.24
Other	1.0 (referent)	1.0 (0.4–3.0)	0.8 (0.3–2.2)	0.3 (0.1–0.7)	.005
Apples					
SCC	1.0 (referent)	0.6 (0.2–1.8)	0.6 (0.2–1.9)	0.5 (0.2–1.8)	.42
ADC	1.0 (referent)	0.8 (0.4–1.5)	1.2 (0.6–2.4)	0.7 (0.3–1.3)	.23
Other	1.0 (referent)	1.0 (0.5–2.1)	0.5 (0.2–1.1)	0.6 (0.3–1.4)	.26
White grapefruit					
SCC	1.0 (referent)	0.2 (0.0–2.0)	0.3 (0.1–1.6)		.16
ADC	1.0 (referent)	1.4 (0.6–3.5)	0.6 (0.3–1.5)		.39
Other	1.0 (referent)	0.2 (0.0–1.2)	0.3 (0.1–1.5)		.09
Quercetin					
SCC	1.0 (referent)	0.9 (0.3–3.1)	1.6 (0.4–5.4)	0.5 (0.2–1.9)	.44
ADC	1.0 (referent)	1.2 (0.6–2.2)	0.7 (0.4–1.4)	0.9 (0.4–2.0)	.65
Other	1.0 (referent)	0.8 (0.4–1.8)	0.8 (0.4–1.7)	0.5 (0.2–1.2)	.13
Naringin					
SCC	1.0 (referent)	0.2 (0.1–1.1)	0.2 (0.1–1.0)		.06
ADC	1.0 (referent)	0.9 (0.5–1.7)	1.4 (0.7–2.5)		.32
Other	1.0 (referent)	0.7 (0.2–1.8)	0.3 (0.1–0.9)		.03

Table 4. Odds ratios* for lung squamous cell carcinoma by CYP1A1 genotype and onion intake

Onion intake	CYP1A1	n†	Odds ratio (95% confidence interval)
≤median	*1/*1	22/124	1.0 (referent)
>median	*1/*1	6/126	0.2 (0.1–0.5)
≤median	*1/*2 or *2/*2	24/86	1.7 (0.7–4.0)
>median	*1/*2 or *2/*2	20/117	1.0 (0.4–2.4)
Two-sided P for interaction‡ = .07			

*Adjusted for age, sex, ethnicity, smoking status, duration, (duration)^2, number of cigarettes smoked per day, and β-carotene and saturated fat intakes.
†No. of case patients/No. of control subjects.
‡*See* "Statistical Methods" section for further details.

5) 항산화 작용

- 가장 활발히 연구되는 분야
- 대표적 작용 기전
  - Free radical quenching
  - LDL oxidation 저하
- Mixture 연구가 활발

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
  - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical