Soy-

- Botany-Glycine max-legume
- contains isoflavones that act as estrogen mimics (phytoestrogens), e.g genistein, daidzein, that bind to estrogen receptors in a competitive manner
  - Isoflavones are present in many plants but soy beans; soy milk and tofu are especially rich sources
  - other sources (mainly legumes):fennel seeds, red clover, yam, black beans, licorice
  - 1 cup of soybeans=about 300mg of isoflavones
  - consumption in Japan is ~50mg/d isoflavones

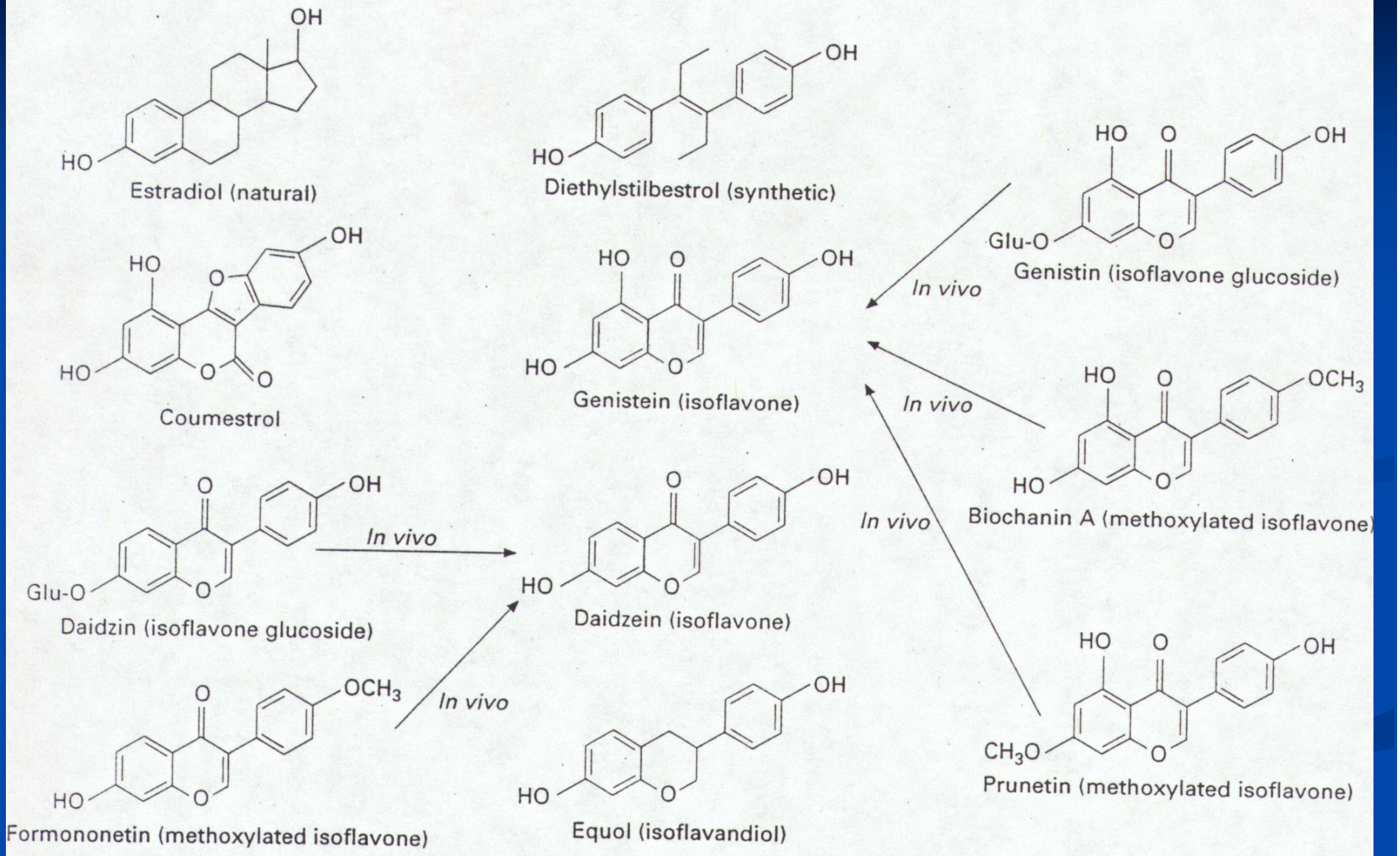
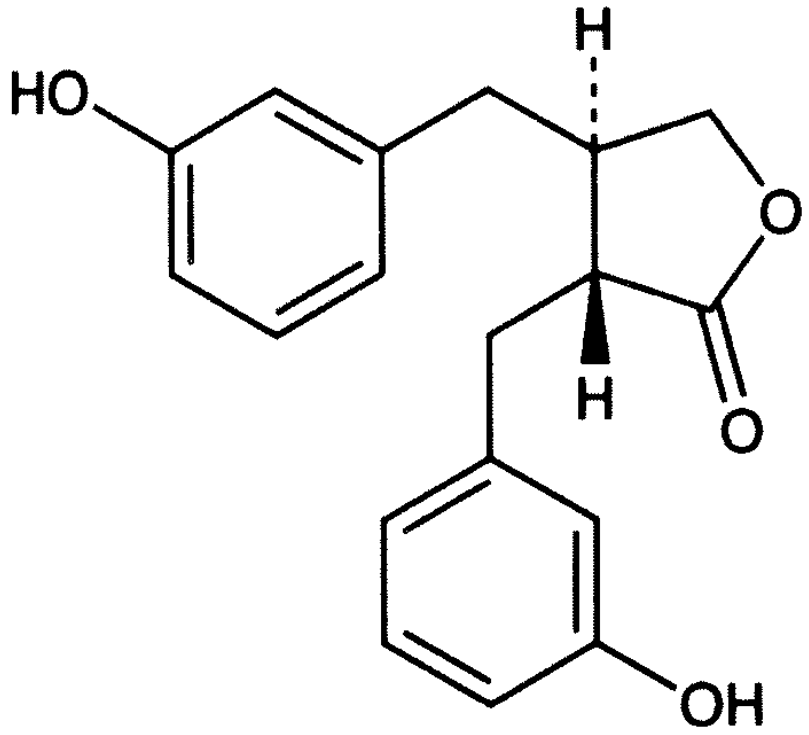


Fig. 5. Structural similarity of oestrogens and phytoestrogens.

Soy

- also contains lignans
  - are phenylpropanoid dimers with antioxidant and free radical scavanging properties
  - present in many plants but especially soy beans and flaxseed and red clover
  - Some evidence that ingestion of lignans may decrease risk of some cancers (breast)
  - act like phytoestrogens



Gum, mp 141-143°. uv max (ethanol): 227, 261 nm (log ϵ 4.66, 4.64).

Enterolactone (example of a lignan)

Isoflavone Pharmacology

- Isoflavones (IF) act a weak estrogenic compounds. Are essentially SERMs
- IF are competitive inhibitors of estrogen. If estrogen is high (premenopause), then will displace; if low (postmenopause) then will be an estrogen agonist.
- Bind to estrogen receptor B (bone,vascular) better than ER-A (reproductive)
- Have effects other than receptor action. Decrease aromatase, 3 B and17B-hydroxysteroid dehydrogenase, enzymes that convert precursor steroids to potent estradiol.
- Are antioxidants

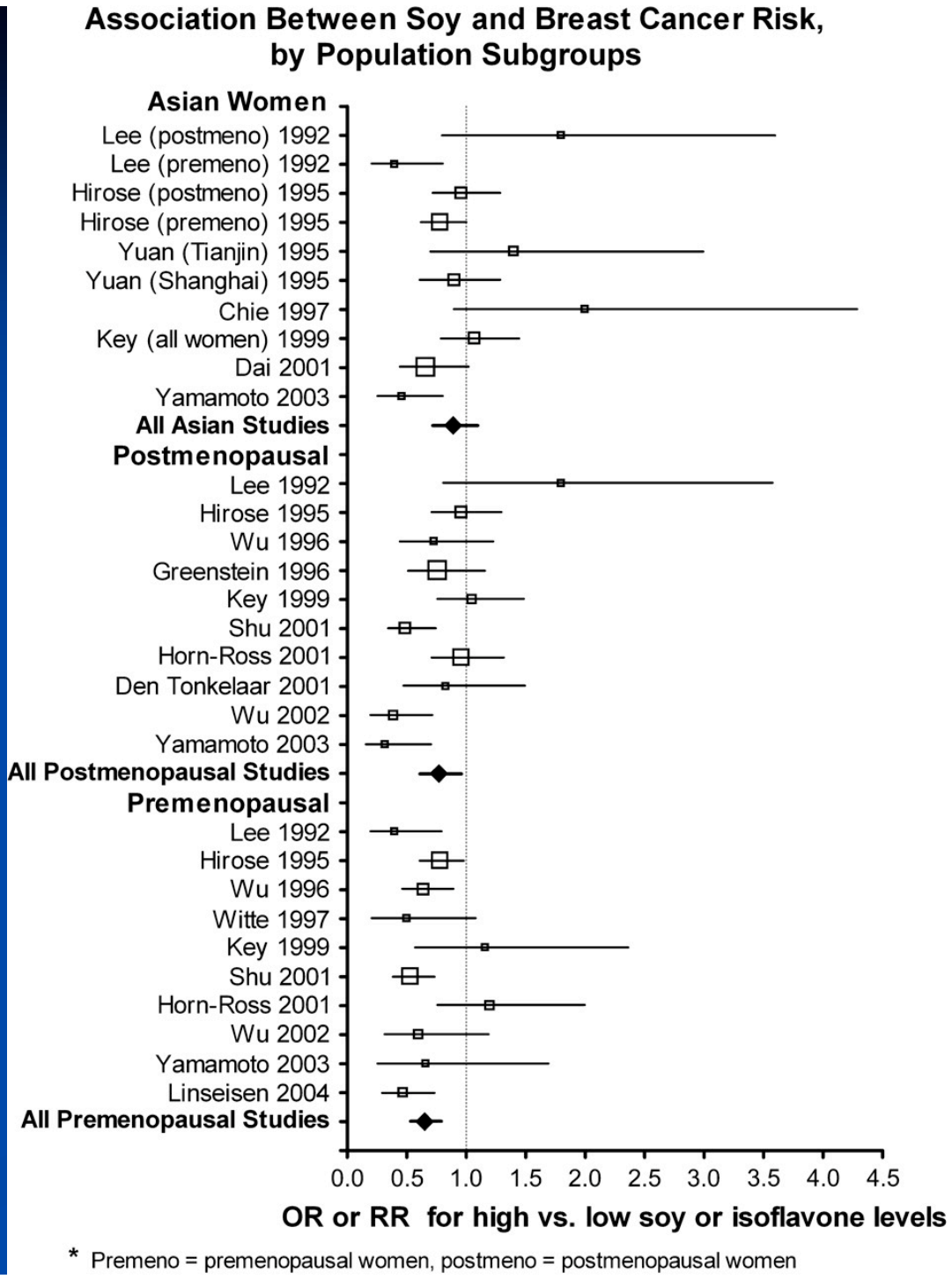
Isoflavones (continued)

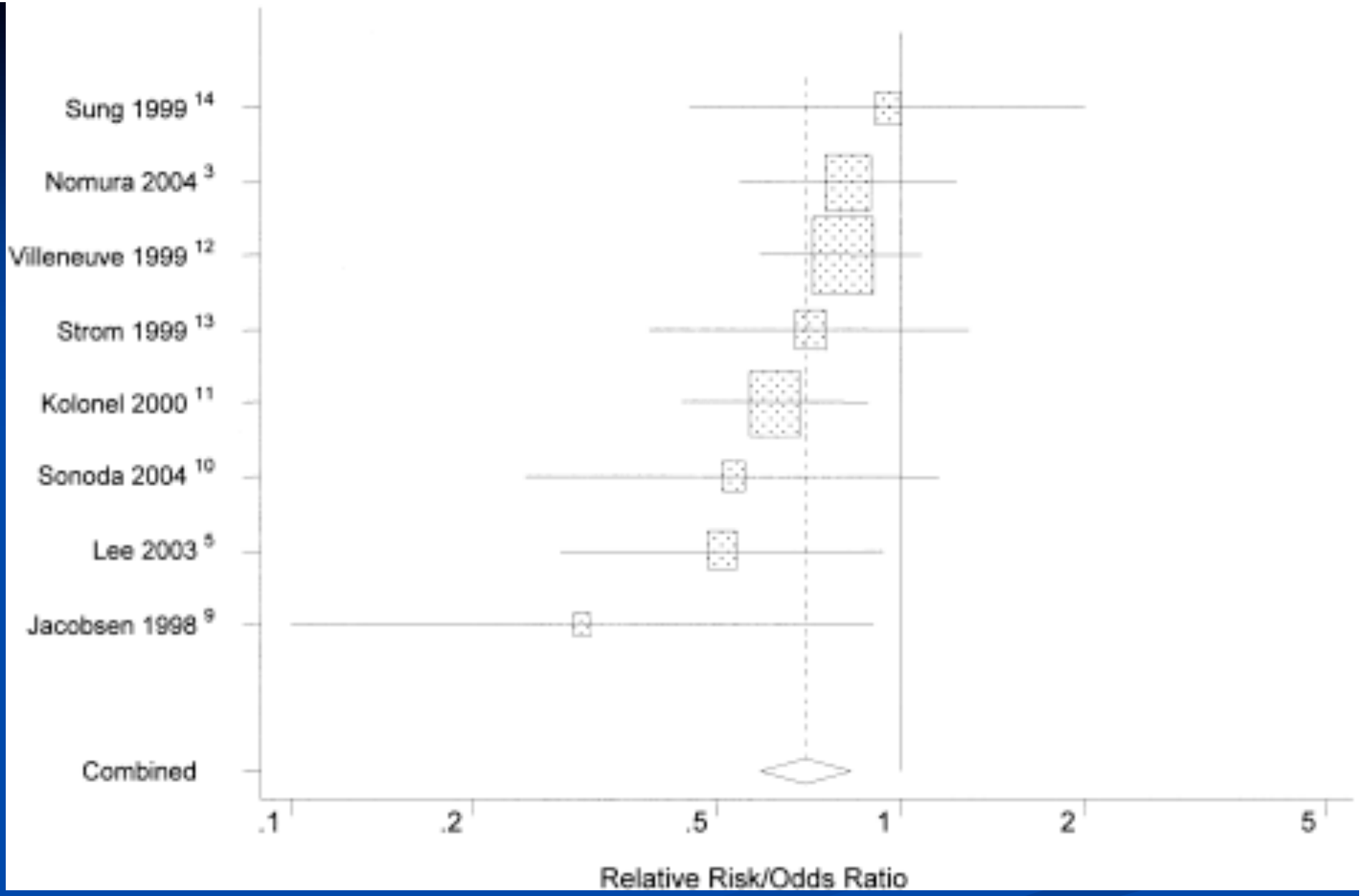
Product	mg isoflavones/100g
Raw soybeans	~100
Soy protein	100-300
Soy milk	10
Soy flour	199
Cooked soybeans	55
Tempeh	44
Tofu	31
Soy noodles	9

Soy Effects on **Cancers**

- Long consumption of soy associated with lower rates of breast, endometrial and prostate cancers.
- Animal studies show that high soy protein in diets will reduce incidence and development of several cancers
- Breast cancer
  - No long term prospective studies
  - In vitro, genistein and daidzein stimulate breast cancer growth in low conc but inhibit at high conc.
  - In mice, genistein increased growth rate of estrogen dependant and estrogen independent implanted tumors and antogonizes tamoxifen but at high concentrations the reverse was true.
  - In mice, genistein or soy given prior to the cancer will protect

Trock et al. J. Nat. Cancer Inst 2006;98:459-471





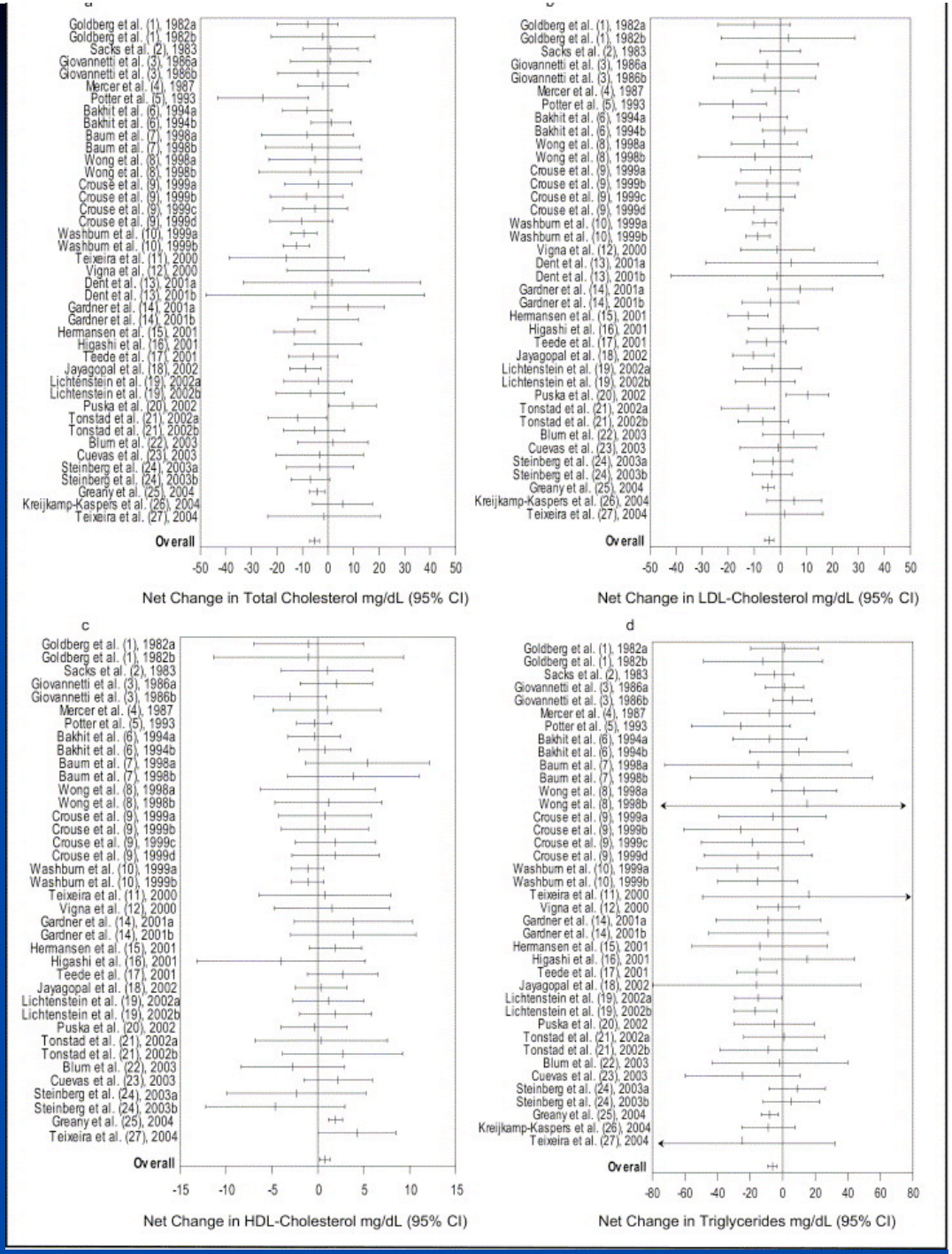
Yan and Sptiznagel, Int. J. Cancer 2005;117: 667-669
Prostate cancer risk vs intake

Soy Effects on **Heart Disease** Risks

- Soy diets associated with normalization of lipid profiles
  - Decreased total cholesterol (~9%), LDL (~13% decrease), increased HDL(small), triglycerides (~10% decrease) improved arterial dilation and compliance
- Soy modestly lowers BP
- In animal studies, soy without isoflavones did not affect lipids
- FDA now allows foods with 6.25g of soy protein per serving to state "consuming 25g of soy protein daily, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease"
- May need 20-50g/day of soy in diet for benefit; intake is low in Western countries and not correlated with cardio risk
- Isoflavones alone may not work as well

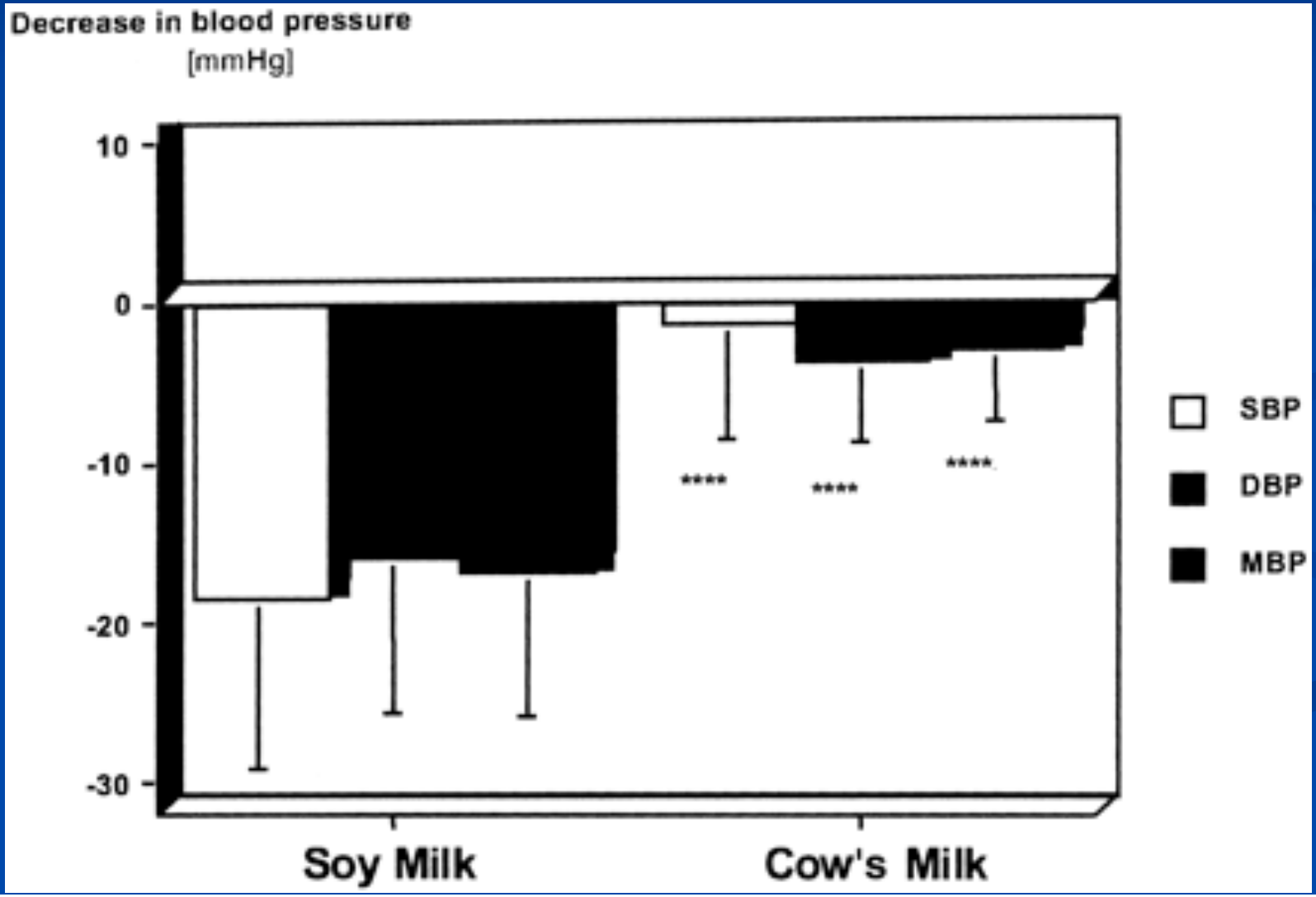
Reynolds et al. Am J Cardiol 2006;98:633-40.

47 studies included



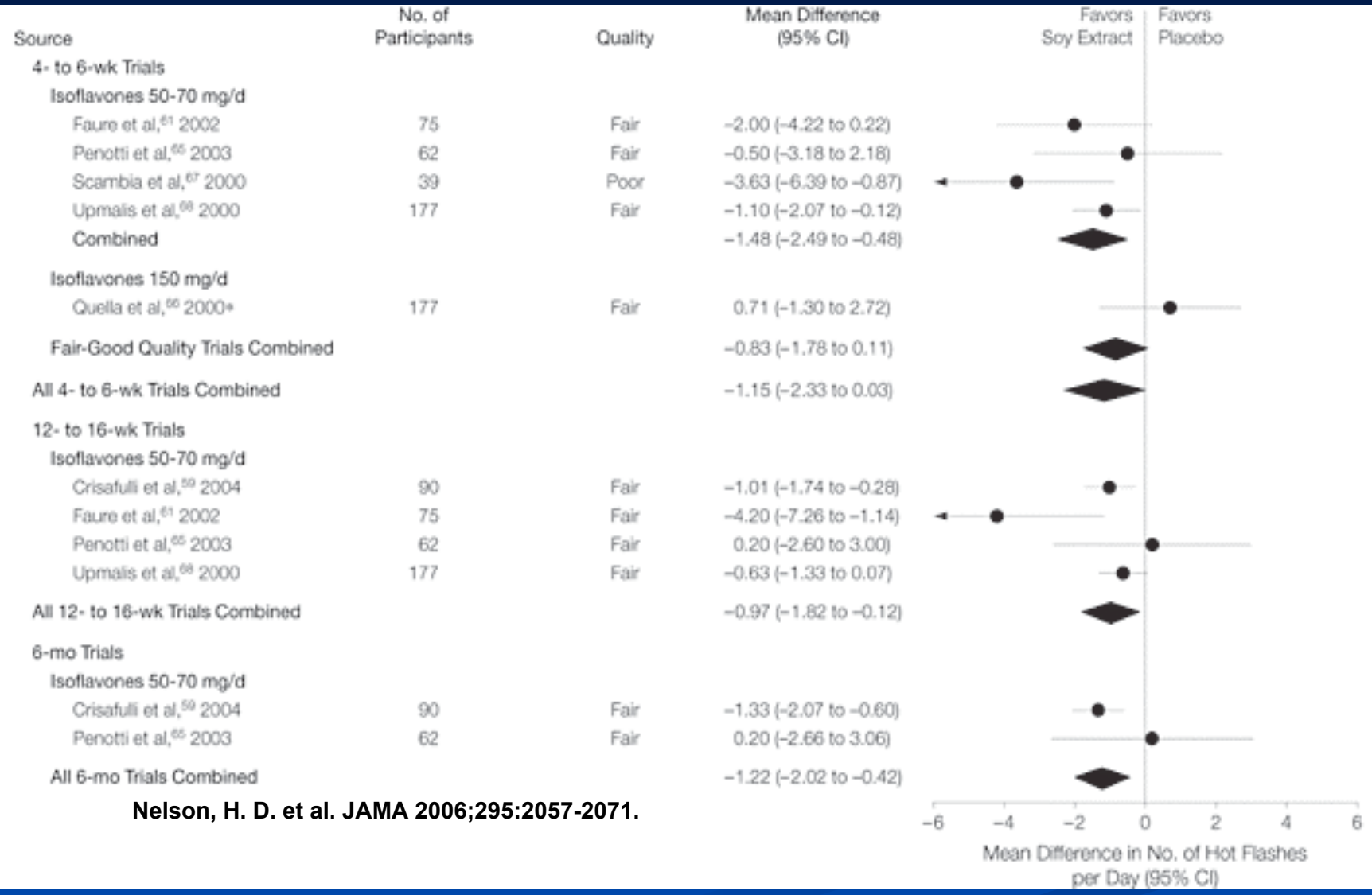
Rivas et al. J. Nutr 2002;132:1900-1902

Soy milk vs cow's milk for 3 mos; n=40



Soy and Menopausal and Postmenopausal problems

- can soy replace HRT?
- Hot flashes and other symptoms: soy flour as well as higher doses of soy isoflavones (100mg/d) have been tested. The results are generally positive for mild benefit. A big placebo effect is seen in the published studies.
- Osteoporosis- some studies using high isoflavone soy indicate decreased loss of bone mass in postmenopausal women

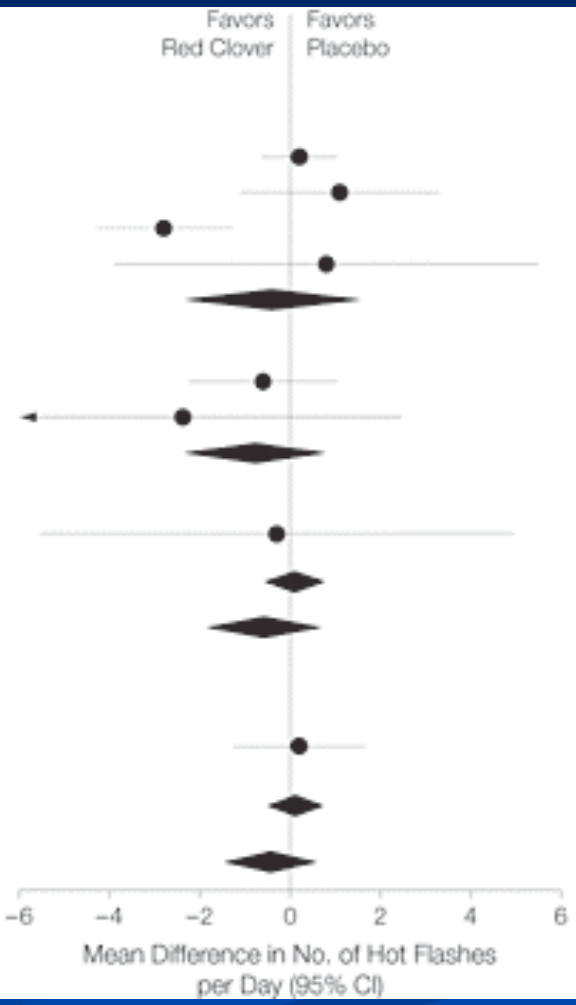


Nelson, H. D. et al. JAMA 2006;295:2057-2071.

Hot flashes in menopausal women

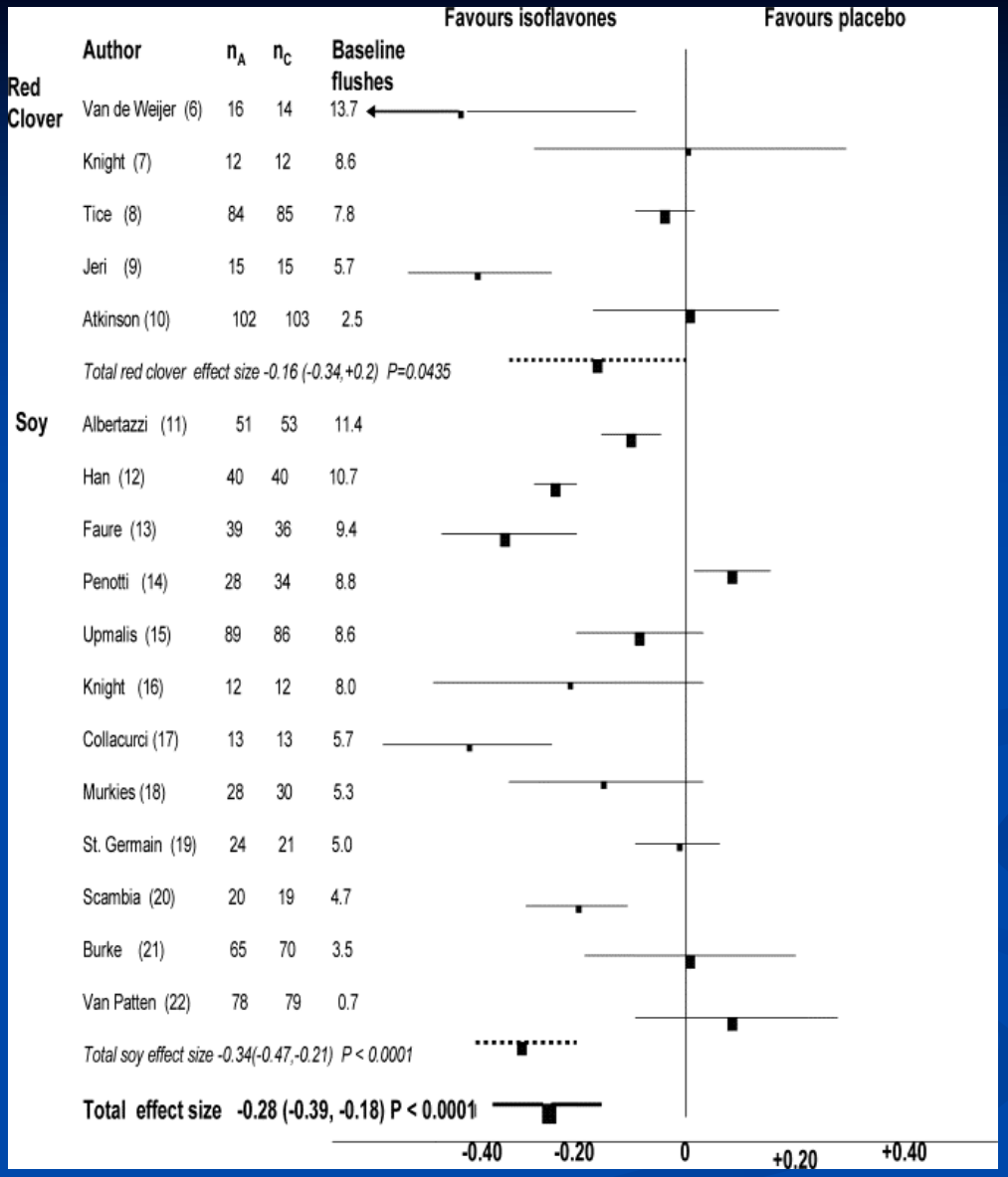
Trials of Red Clover Isoflavone Extracts

Source	No. of Participants	Duration of Trial	Quality	Mean Difference (95% CI)
Promensil Trials				
Promensil 40 mg/d				
Atkinson et al,[53] 2004	99	12 mo	Fair	0.20 (−0.63 to 1.03)
Baber et al,[54] 1999	51	12 wk	Fair	1.10 (−1.10 to 3.30)
Jeri,[55] 2002	30	16 wk	Poor	−2.80 (−4.31 to −1.29)
Knight et al,[56] 1999	24	12 wk	Poor	0.80 (−3.90 to 5.50)
Combined				−0.40 (−2.33 to 1.53)
Promensil 80-82 mg/d				
Tice et al,[57] 2003	169	12 wk	Good	−0.60 (−2.25 to 1.05)
van de Weijer and Barentsen et al,[58] 2002	30	12 wk	Fair	−2.37 (−7.20 to 2.46)
Combined				−0.79 (−2.35 to 0.78)
Promensil 160 mg/d				
Knight et al,[56] 1999	25	12 wk	Poor	−0.30 (−5.54 to 4.94)
Fair-Good Quality Promensil Trials Combined				0.10 (−0.60 to 0.79)
All Promensil Trials Combined				−0.59 (−1.84 to 0.67)
Rimostil Trial				
Rimostil 57 mg/d				
Tice et al,[57] 2003	168	12 wk	Good	0.20 (−1.26 to 1.66)
All Fair-Good Quality Trials Combined				0.11 (−1.51 to 0.74)
All Trials Combined				−0.44 (−1.47 to 0.58)



Nelson, H. D. et al. JAMA 2006;295:2057-2071.

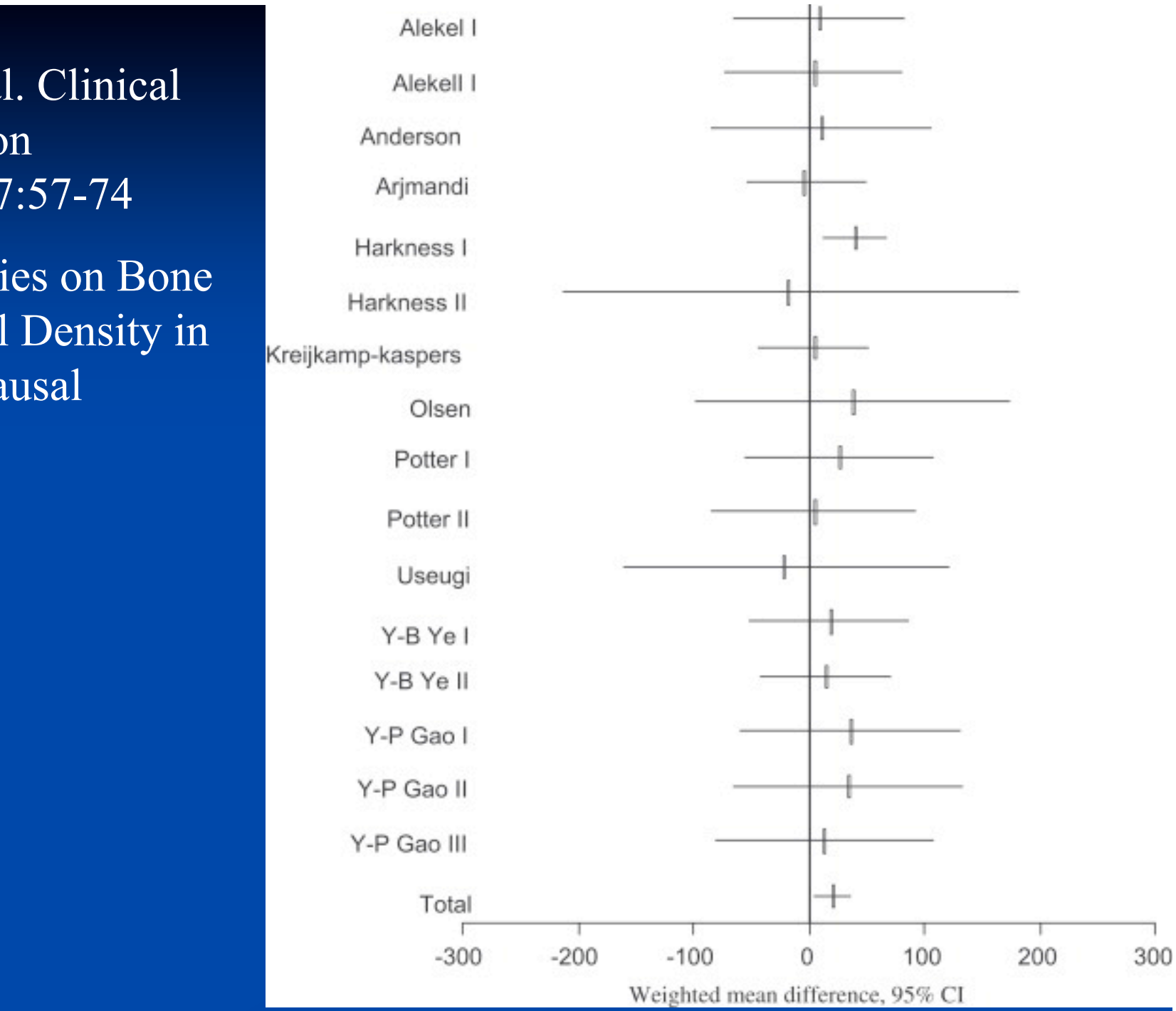
Red clover isoflavones (Promensil)



Howes et al. Maturitas. 2006;55:203-11

Ma et al. Clinical Nutrition 2008;27:57-74

10 studies on Bone Mineral Density in menopausal women



Data for Fracture by Quintile of Soy Protein Intake

Table 2. Data for Fracture by Quintile of Soy Protein Intake

Variable	Quintile of Soy Protein Intake, g/d					*P* Value for Trend
	<4.98 (n = 4880)	4.98-7.32 (n = 4882)	7.33-9.77 (n = 4880)	9.78-13.26 (n = 4880)	≥13.27 (n = 4881)	
No. of follow-ups	9559	9610	9649	9662	9616	NA
Person-years	21 635	22 091	22 232	22 234	22 052	NA
No. of cases	459	332	329	317	333	NA
RR (95% CI)						
Age and calorie (energy) adjusted	1.00	0.69 (0.60-0.80)	0.67 (0.58-0.77)	0.63 (0.54-0.73)	0.63 (0.54-0.74)	<.001
Multivariate*	1.00	0.72 (0.62-0.83)	0.69 (0.59-0.80)	0.64 (0.55-0.76)	0.63 (0.53-0.76)	<.001

Abbreviations: CI, confidence interval; NA, data not applicable; RR, relative risk.
*Adjusted for age, body mass index, hours of exercise per week, cigarette smoking, alcohol consumption, history of diabetes mellitus, level of education, family income, season of recruitment, and intakes of total calories, calcium, nonsoy protein, fruits, and vegetables.

Zhang, X. et al. Arch Intern Med 2005;165:1890-1895.

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Data for Fracture by Quintile of Soy Isoflavone Intake

Table 3. Data for Fracture by Quintile of Soy Isoflavone Intake

Variable	Quintile of Soy Isoflavone Intake, mg/d					*P* Value for Trend
	<21.16 (n = 4881)	21.16-32.39 (n = 4881)	32.40-44.31 (n = 4880)	44.32-60.26 (n = 4880)	≥60.27 (n = 4881)	
No. of follow-ups	9564	9624	9648	9658	9602	NA
Person-years	21 654	22 147	22 288	22 136	22 018	NA
No. of cases	450	340	312	340	328	NA
RR (95% CI)						
Age and calorie (energy) adjusted	1.00	0.72 (0.63-0.83)	0.65 (0.56-0.75)	0.70 (0.60-0.81)	0.65 (0.56-0.76)	<.001
Multivariate*	1.00	0.75 (0.65-0.87)	0.67 (0.58-0.78)	0.72 (0.61-0.84)	0.65 (0.55-0.78)	<.001

Abbreviations: See Table 2.
*Adjusted for age, body mass index, hours of exercise per week, cigarette smoking, alcohol consumption, history of diabetes mellitus, level of education, family income, season of recruitment, and intakes of total calories, calcium, nonsoy protein, fruits, and vegetables.

Zhang, X. et al. Arch Intern Med 2005;165:1890-1895.

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Risks and Interactions

- Can be allergenic for some
- Soy isoflavones can inhibit thyroid synthesis
- Soy use in breast cancer patients
  - Dietary soy may be OK but probably best to avoid supplements.
  - Studies generally show no benefit of soy vs placebo in hot flashes associated with breast cancer therapy with tamoxifen (e.g., Van Patten et al. J Clin Oncol 2002;20:1449-1455).
- Drug Interactions- not to be given with tamoxifen; isoflavones inhibit CYP in vitro but probably not in vivo

Other Effects of Soy

- Diabetes- may improve glucose tolerance
- Diabetes- may improve neuropathy and kidney function
- Memory – may see improvement
- Men-prostate- may be slightly protective; no effect on PSA
- Women-may improve immune function

Other herbals used for menopausal symptoms

Red clover- contains lignans and isoflavones; some studies show benefit for menopausal symptom relief, others no benefit

Black cohosh- does not affect endometrium but may relieve hot flushes and other menopausal symptoms; may build bone; may not be contraindicated in breast cancer and treatment regimens. More later

Flaxseed and Flaxseed oil – some evidence for benefit

Evening primrose oil- not consistent evidence for benefit

Chasteberry- helps in PMS but ? for menopause

Dong quai- no observed benefit in one good study

Yam- is a scam

Topical progesterone- works but risks same as HRT?

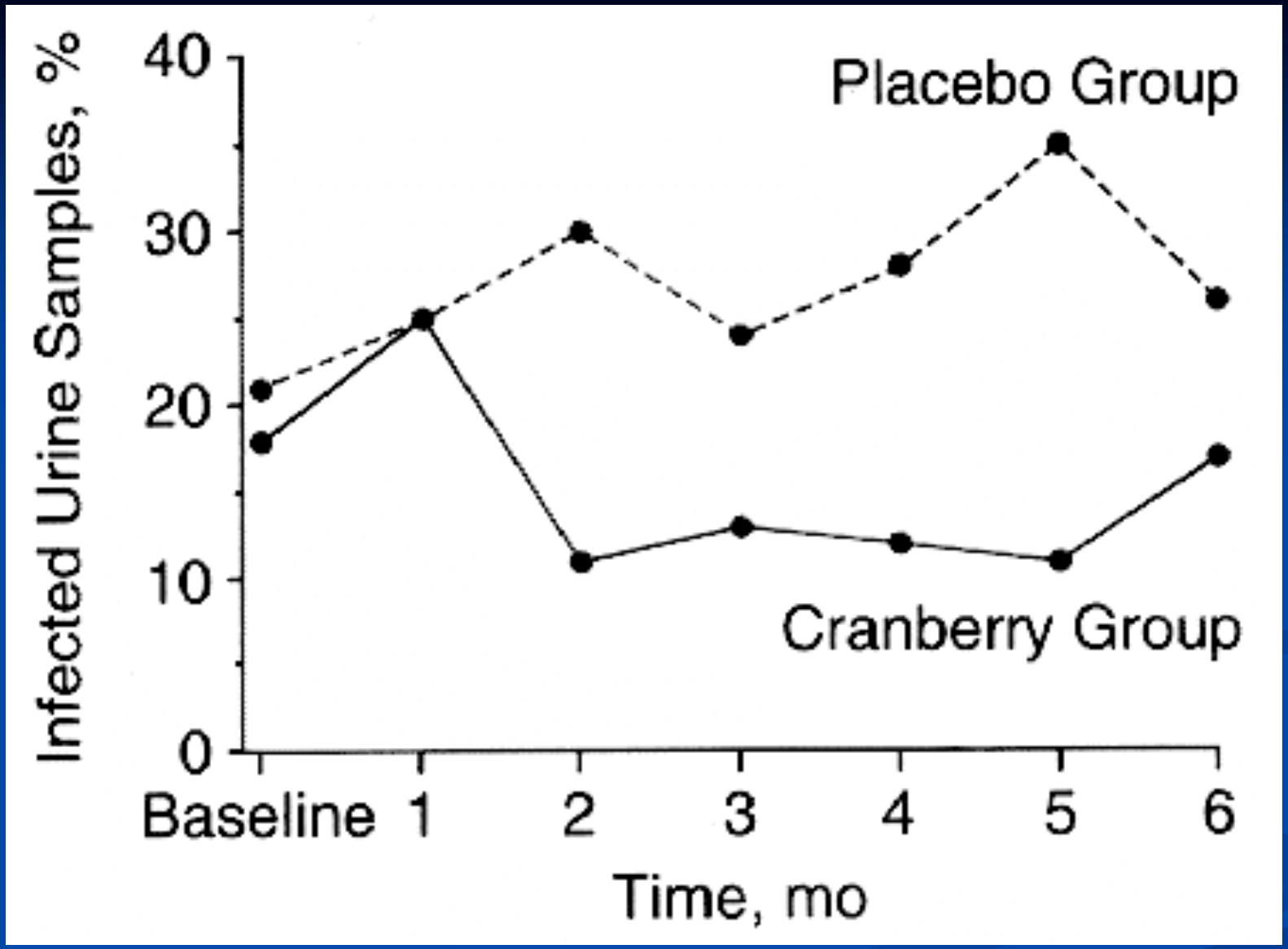
Soy

- **Summary**
  - **Efficacy**: increased soy ingestion may decrease hot flashes and other postmenopausal symptoms; Soy has cardiovascular and cancer prevention benefits. Isoflavones probably are the active components.
  - **Safety**: good but use in breast cancer may be risky; for infants is OK but low in vitamins
  - **Drug interactions**: not with tamoxifen
  - **Product selection**: Soy=best; Isoflavones OK
  - **Dose**: about 20-40g of soy protein. This contains 30-50mg of isoflavones.
  - **Questions remaining** include
    - *How much benefit? Safety in breast cancer?*

Cranberry

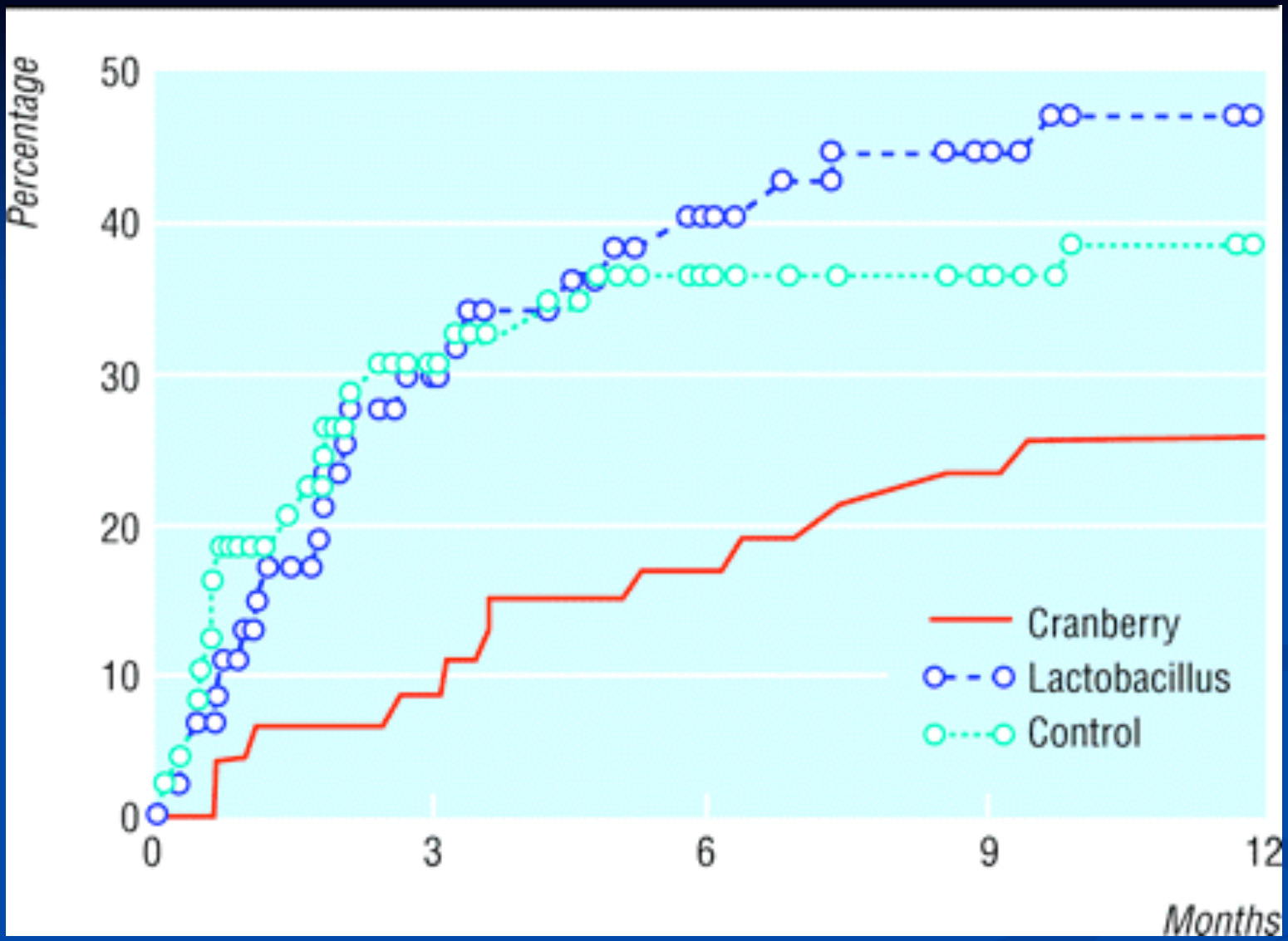
- Vaccinium macrocarpon-cultivated in Washington
- Long history of use
- The mechanism was thought to be urine acidification
- Now E. coli (other pathogens also) adhesion inhibitors are known to be present but not in other juices. An unidentified, high mol wt material may be responsible
- Need about 8-16 oz (240-480ml) of juice (not drink or cocktail)
- Much less evidence for efficacy of cranberry capsules

- Evidence for effectiveness in UTI **treatment** is weak
- Will acidify urine and contains high oxalic acid levels so that kidney stones could be a risk
- Cranberry juice will also reduce urine pH and ammonia odor.
- One study showed enhanced eradication of H. pylori when added to an antibiotic regimen.



N=153; 300ml/d of juice; Avorn et al. JAMA 1994;271:751-754.

First UTI in 12 months



Kontiokari et al. BMJ 2001;322:1571 n=150 50ml (7.5g) of cranberry concentrate (diluted)(also had some loganberry juice)

Cranberry

- Summary
  - **Efficacy**: reasonable evidence for benefit for PREVENTION of UTI.
  - **Safety**: good but could be risky for those that form kidney stones easily. Has salicylates.
  - **Drug interactions**: little effect on CYP or warfarin INR
  - **Product selection**: need the juice; capsules work?
  - **Questions remaining** include
    - *Does cranberry juice help with Helicobacter pylori?*
    - *Other infections?*
    - *Help in dental caries?*

•Garlic

- History
- Chemistry
  - organosulfur compounds
    - alliin
    - allicin
    - Ajoene
    - S-allylcysteine
    - interconversions and odor

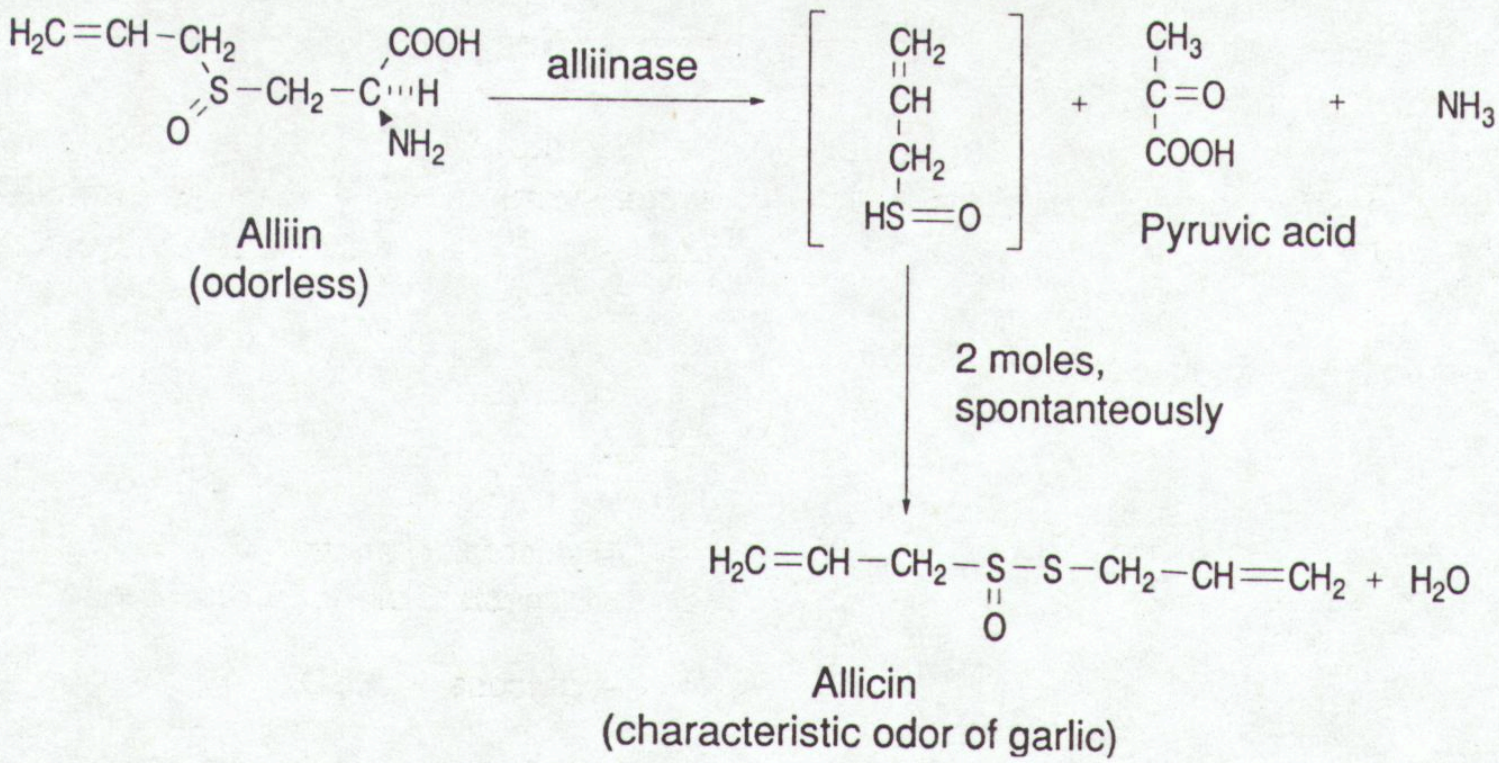


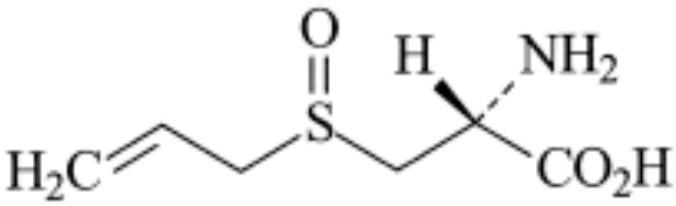
Fig. 4–6. Formation of allicin in *Allium* species.

Alliin is a major component found in fresh and dried (carefully) garlic. Allicin is odiferous and pharmacologically active

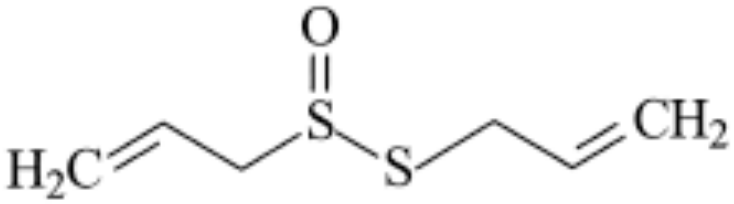
(*Z*)-Ajoene

2-Propenyl 3-(2-propenylsulfinyl)-1-propenyl disulfide

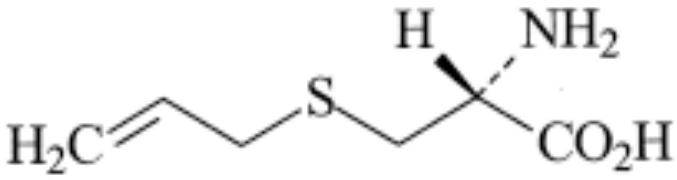
Ajoene and like allylsulfides are major components of garlic oil



Alliin



Allicin



S-Allyl-L-Cysteine

S-allylcysteine and like compounds are major components of aged garlic

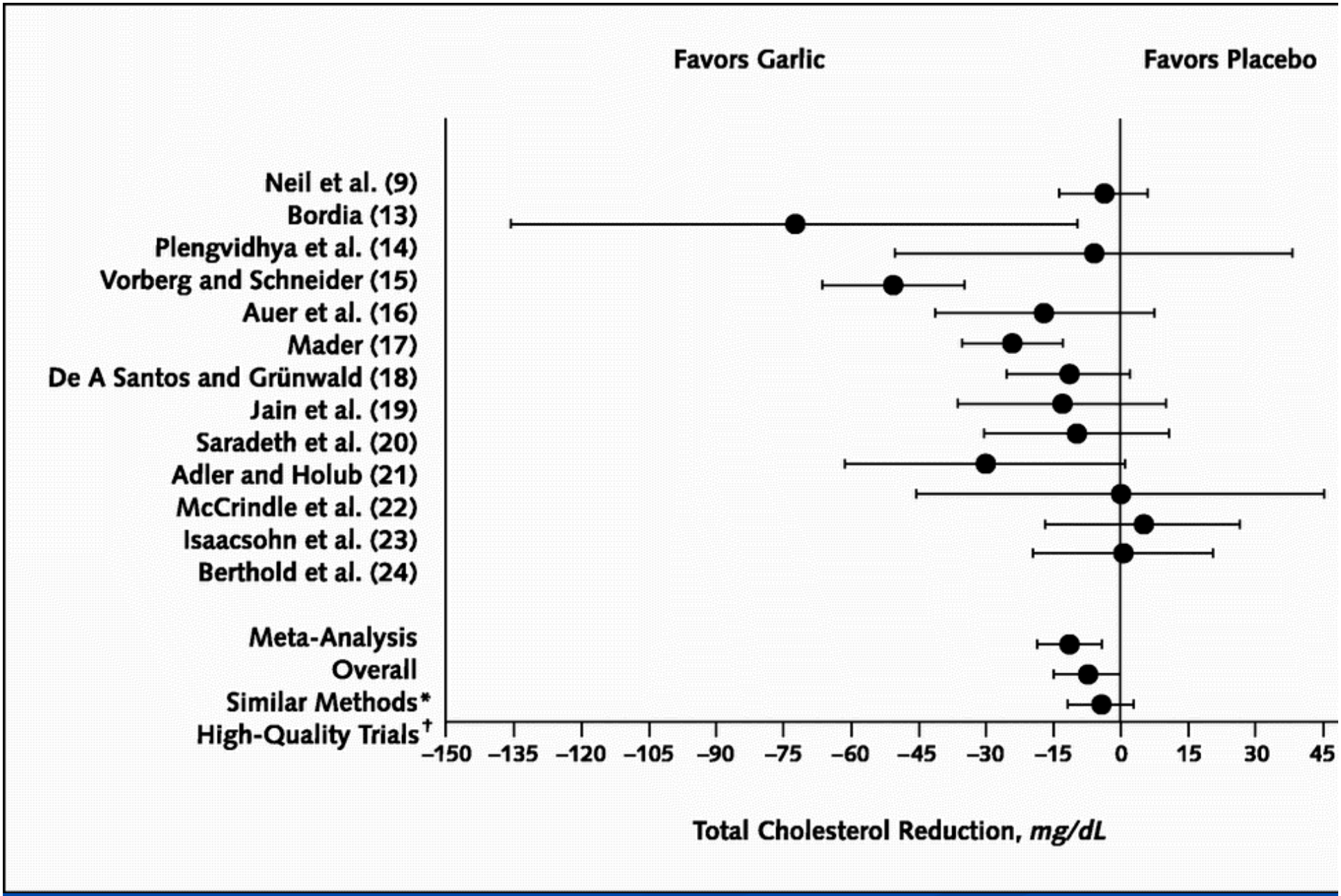
•Pharmacology

- cholesterol lowering
- decease atherosclerosis
- triglyceride lowering
- antihypertensive
- antimicrobial
- insecticide
- increased fibrinolysis
- decreased plaque size
- decreased platelet aggregation
- increased catalase and glutathione peroxidase
- decreased cancer induction (animal studies)

cholesterol lowering

- most early studies (>40) show lowering effects but studies are often not of high quality

- Meta-analyses have shown a cholesterol lowering effect of 10%, triglycerides of 10% and LDL of 11%. (Ann Int Med 119:599-605,1993;J R Coll Physicians-London 28:39-45,1994, Ann Int Med 133:420-429, 2000, J Am Acad Nurse Prac 2003;15:120-128) but studies are lacking in quality

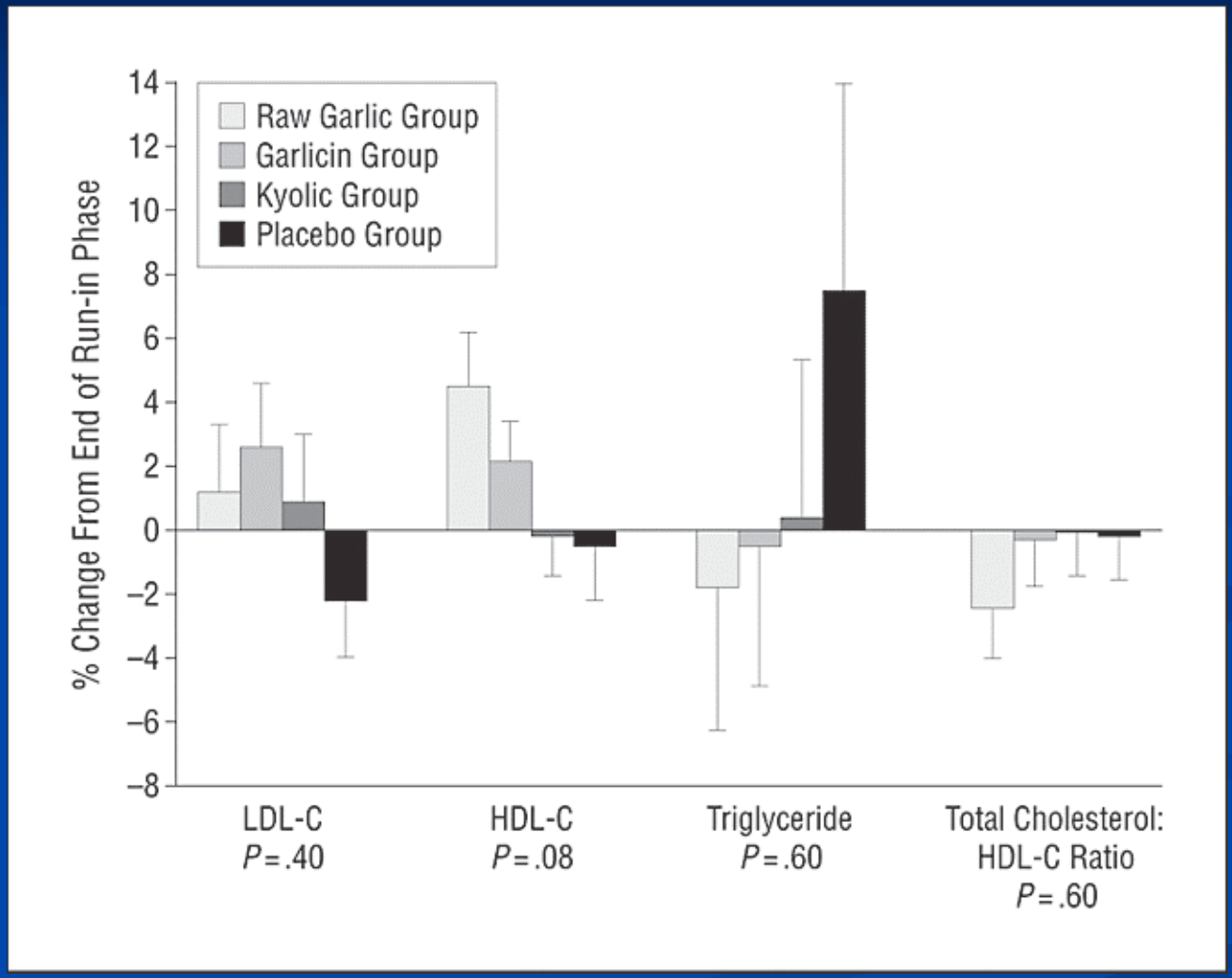


Stevinson et al. Ann Int Med 133:420-429, 2000

lipid lowering

- Some recent well designed studies show no effect on cholesterol lowering (see next slide)
- Kwai story
- Kanner et al (J Am Coll Nutr 2001;20:225-231) used a high potency, enteric coated garlic powder prep for 12 weeks to lower total and LDL cholesterol (n=46, 9.6mg/d allicin)

Six-month percent change (mean and SE) relative to the end of the run-in phase in participants with available data



Gardner, C. D. et al. Arch Intern Med 2007;167:346-353.

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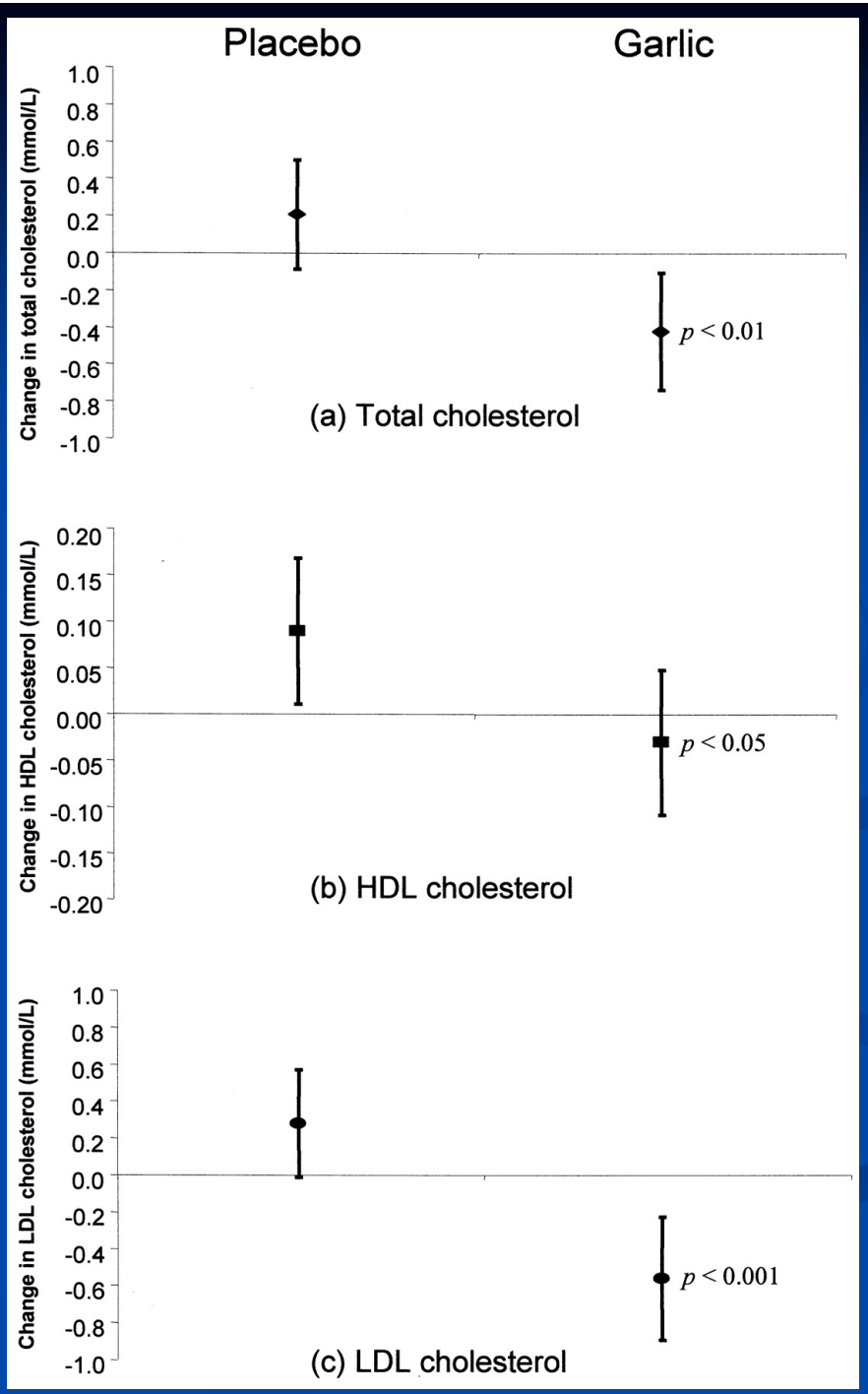
Kanner et al. J Am College Nutr 2001;20:225-231.

N=42

EC garlic powder tab standardized to 2.4mg allicin/tab

Dose:2 BID or 9.6mg allicin/d for 12 weeks

Diet modification run-in period of 1-2 weeks prior to study

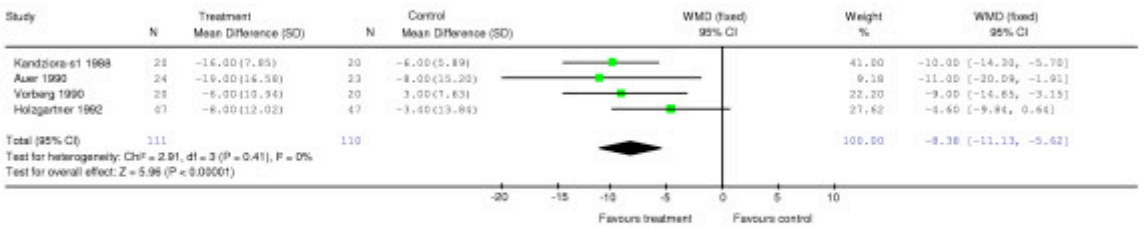


Other beneficial garlic effects in heart and vascular disease

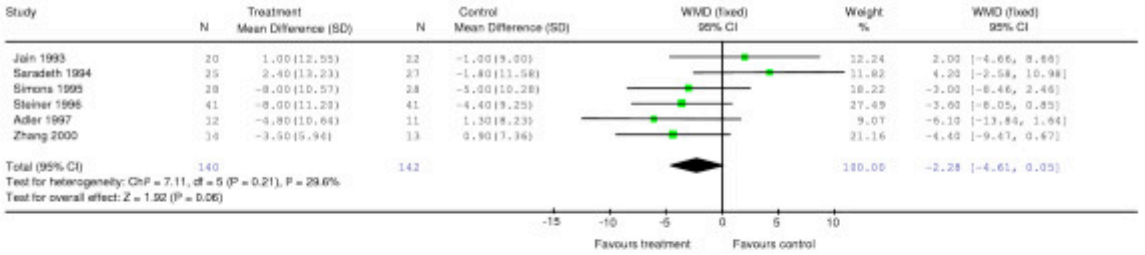
- One study showed decrease in plaque size (n=152, 48mos) compared to placebo (Koscielny et al. Atherosclerosis 144:237-249,1999)
- Another study indicated that chronic garlic intake increased the elasticity of the aorta (Circulation 1997;96:2649-2655
- Small reduction in systolic and diastolic blood pressure
- Garlic has modest platelet adhesion inhibition effects

Ried et al. BMC Cardiovasc Disord 2008;8:13

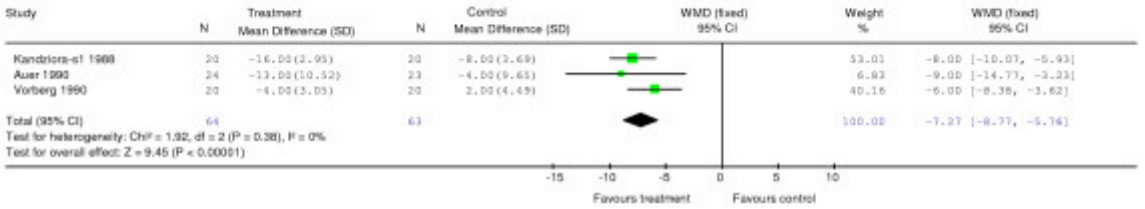
A) SBP hypertensive subgroup



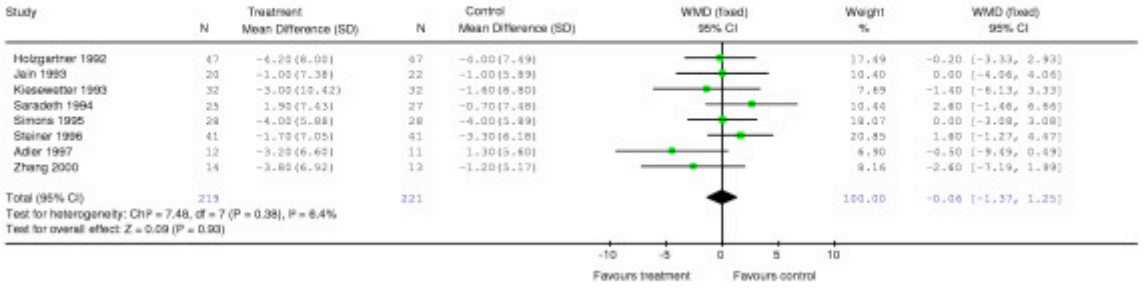
B) SBP normotensive subgroup



C) DBP hypertensive subgroup



D) DBP nomotensive subgroup



Other garlic benefits?

- **Evidence - cancer**
  - A meta-analysis showed modest protective effects for diet intake for colorectal RR=0.69 and stomach cancers (RR=0.53) Fleischauer et al. Am J Clin Nutr 2000 Oct;72(4):1047-52.
  - However, supplements did not reduce precancerous lesions. Yu, YC et al. J Natl Cancer Inst. 2006 Jul 19;98(14):945-6.
- **Evidence - infections**
  - A 12 weeks use of a potent garlic supplement reduced the incidence of the common cold compared to placebo (n=146); Rx 24 colds vs placebo 65 colds. Recovery was faster in the Rx. Josling P. Advances in Therapy 2001;18:189-193.
  - 0.6% cream of ajoene may help with tinea infections.
- **Insect Repellent**
  - Lab studies no (Rajan et al. Med Vet Entomol 2005;19:84-89.) ; field studies maybe (RR=0.7, 1.2g/d in crossover study in Swedish military) Stjernberg et al. JAMA 2000;248:831.

Garlic

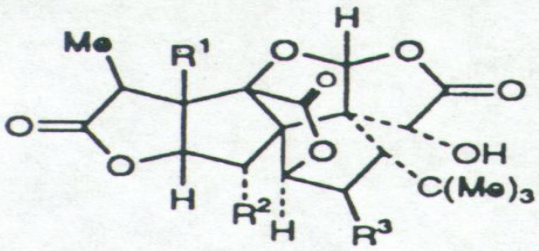
- Adverse effects
  - Nothing special
- Drug interactions:
  - platelet anti-adhesion effects; careful with aspirin and warfarin
  - Reduced AUC of saquinavir in volunteers. May induce p-glycoprotein (more later) but effect may be product dependant. Avoid garlic use with anti HIV therapies

Garlic

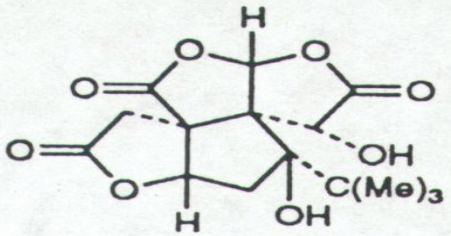
- **Summary**
  - **Efficacy**: the literature is conflicting for use in hyperlipidemia and hypertension; maybe mild benefit if excellent product is used; other cardiovascular benefits are possible.
  - **Safety**: good
  - **Drug interactions**: warfarin; possibly aspirin and other antiplatelet adhesion drugs; not with HIV drugs
  - **Product selection**: avoid Kwai? Suggest enteric coated garlic powder tablets standardized to about 2mg allicin/tab.
  - **Dose**: equivalent of about 4g (2-4 cloves) of fresh garlic per day (~8-12mg allicin). Want >4mg allicin delivered past the stomach
  - **Questions remaining** include
    - *Who can benefit from use; Other uses?*

Ginkgo biloba

- Botanical Aspects
- History
- Chemistry
  - *bioflavonoid glycosides*
    quercetin, kaempherol, isorhamnetin
  - *terpenoids*
    Ginkgolides A,B,C,J
    bilobalide

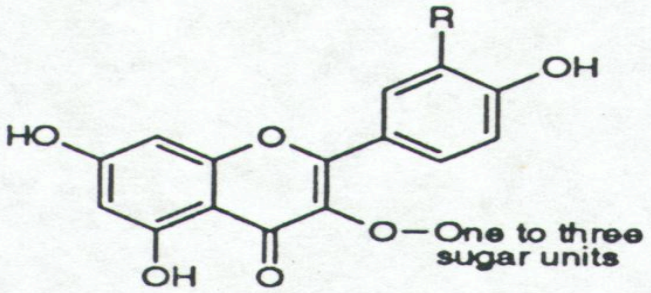


Ginkgolide structures

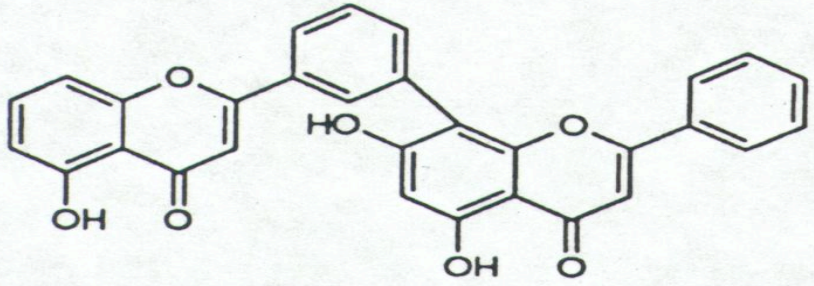


Bilobalide

	R^1	R^2	R^3
Ginkgolide A;	OH	H	H
Ginkgolide B;	OH	OH	H
Ginkgolide C;	OH	OH	OH
Ginkgolide J;	OH	H	OH
Ginkgolide M;	H	OH	OH



Flavonol structures
Kaempferol derivatives; R = H
Quercetin derivatives; R = OH
Isorhamnetin derivatives; R = OMe



Amentoflavone

Fig. 23.5. Some constituents of *Ginkgo biloba* leaves

•*Ginkgo biloba*

- **Pharmacology**
  - Antioxidant/antiinflammatory
  - Free radical scavenger
  - Anti PAF (ginkgolide B)- but may not occur in vivo in humans
    - Decreased platelet activation by collagen (ex-vivo human study)
  - Complex effects on insulin responses to glucose load (increased in normals but decreased in diabetics)
  - Vasodilation
  - Lower blood pressure
  - Increased capillary blood flow, decreased blood viscosity
  - Stimulation of endothelium-derived relaxing factor
  - Increased nitric oxide and decreased endothelin-1 in vivo
  - Neuroprotective effects and neurotransmitter modulations (animal and in vitro studies)

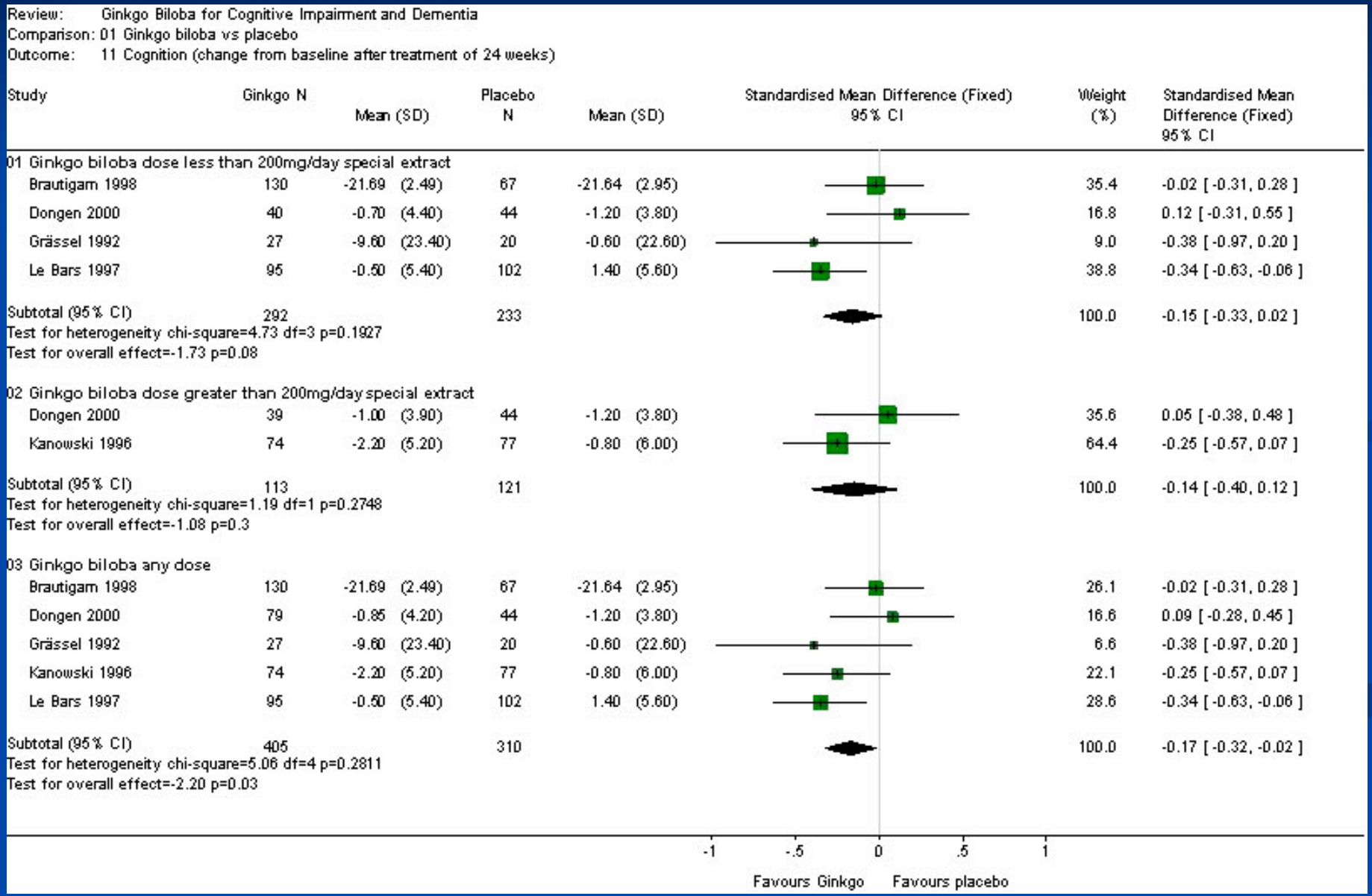
Common Uses

- Claudication (peripheral vascular disease)
- Dementia treatment (multi-infarct and Alzheimer's)
- Cerebral insufficiency
- Age-associated memory impairment
- Memory enhancement (in healthy patients)
- Tinnitus
- Altitude (mountain) sickness
- Vertigo
- Macular degeneration
- Premenstrual syndrome (PMS)
- Decreased libido and erectile dysfunction
- Depression and seasonal affective disorder (SAD)
- Chemotherapy adjunct (reduce adverse vascular effects)
- Multiple sclerosis
- Glaucoma
- Acute ischemic stroke

Ginkgo and Dementia, Alzheimer's Disease

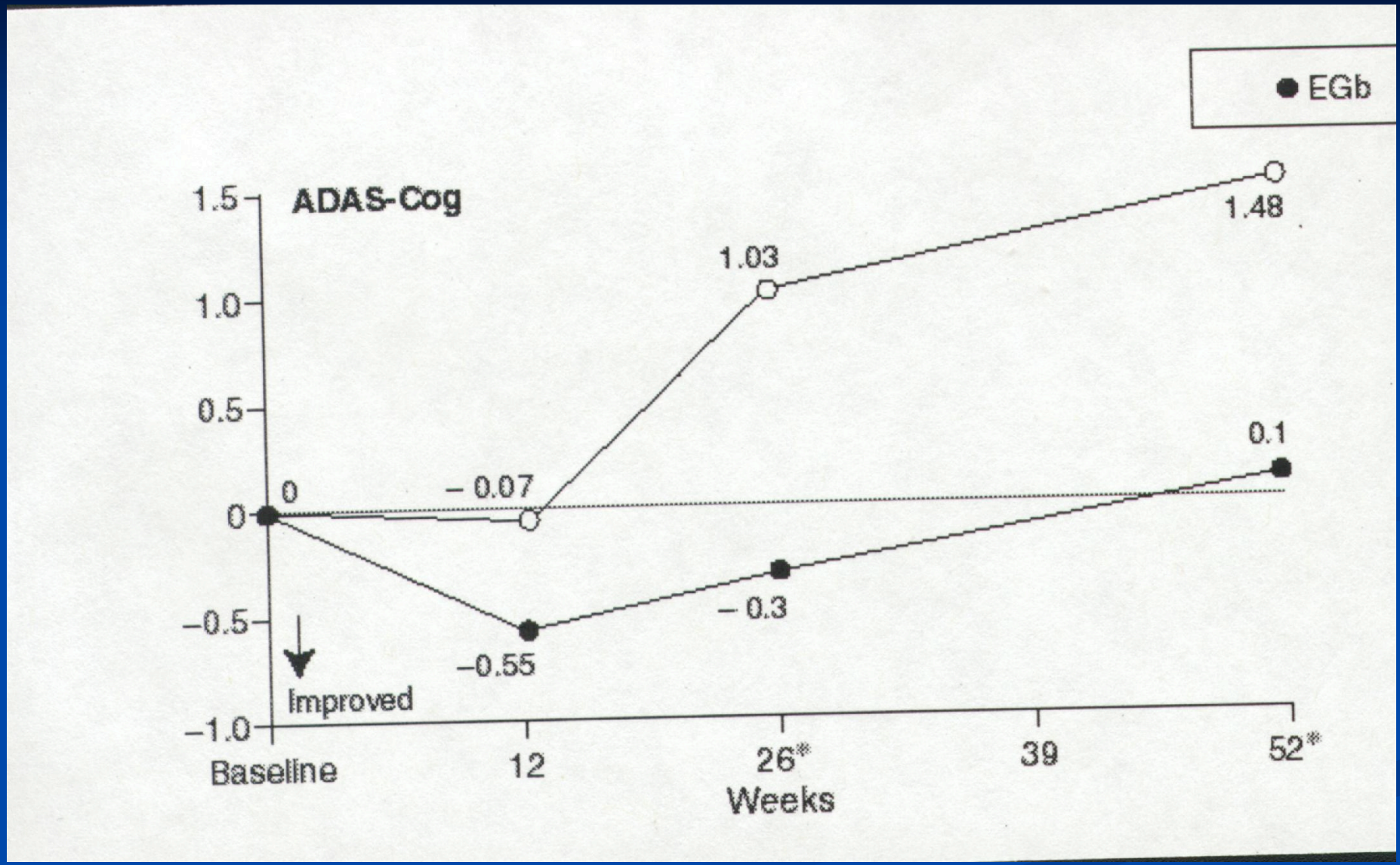
• >30 double blind, placebo controlled trials evaluating ginkgo have been published. Most show ginkgo to be better than placebo. The benefits have been modest, however.

Pittler MH, Ernst E. Ginkgo biloba extract for the treatment of cognitive impairment and dementia: a meta-analysis of randomized trials. Am J Med 2000;108(4):276-281.



Ginkgo - JAMA article

- LaBars et al., JAMA 278:1327-1332, 1997 (Oct 22)
  - USA study 6 research centers
  - N=309 1 year
  - 202 evaluable at 52 weeks
    - In ginkgo group 24% had 4 point improvement on ADAS-Cog vs 14% in placebo group
    - adverse effects: same as placebo
  - conclusions: modest improvement, improvement recognized by caregivers


EGb
ADAS-Cog
1.5
1.0
0.5
0
−0.5
−1.0
0
− 0.07
1.03
1.48
0.1
− 0.3
−0.55
Improved
Baseline
12
26*
39
52*
Weeks

A new study in the Journal of the American Medical Association shows that Ginkgold helps with age-related mental function.*†

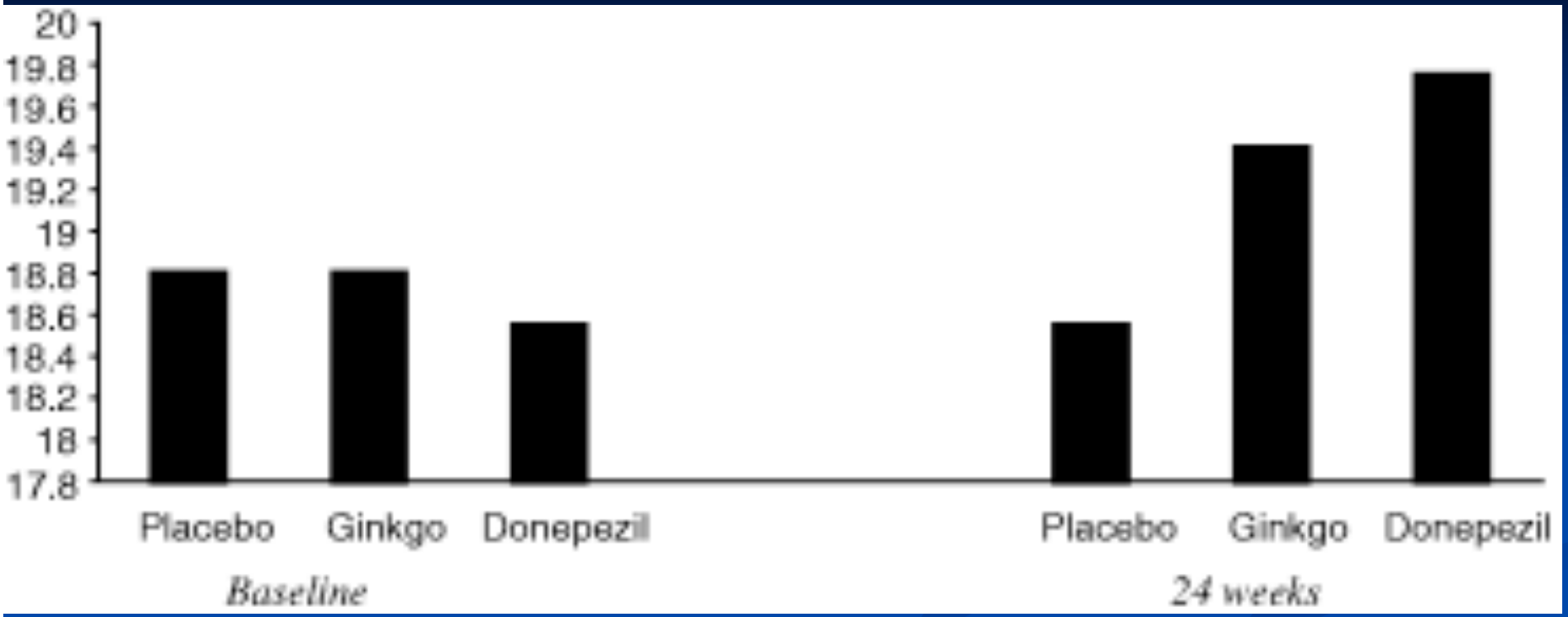
For the benefits of this breakthrough study choose the extract actually used, patented Ginkgold.® Other brands may claim to be similar, or perhaps cost less. But don't be fooled: In head-to-head research, only the Ginkgold® extract was shown to increase activity in all areas of the brain.*†† So, for better mental sharpness, choose the better ginkgo extract—Ginkgold® from Nature's Way.

Trust The Leaf™ Nature's Way

*This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

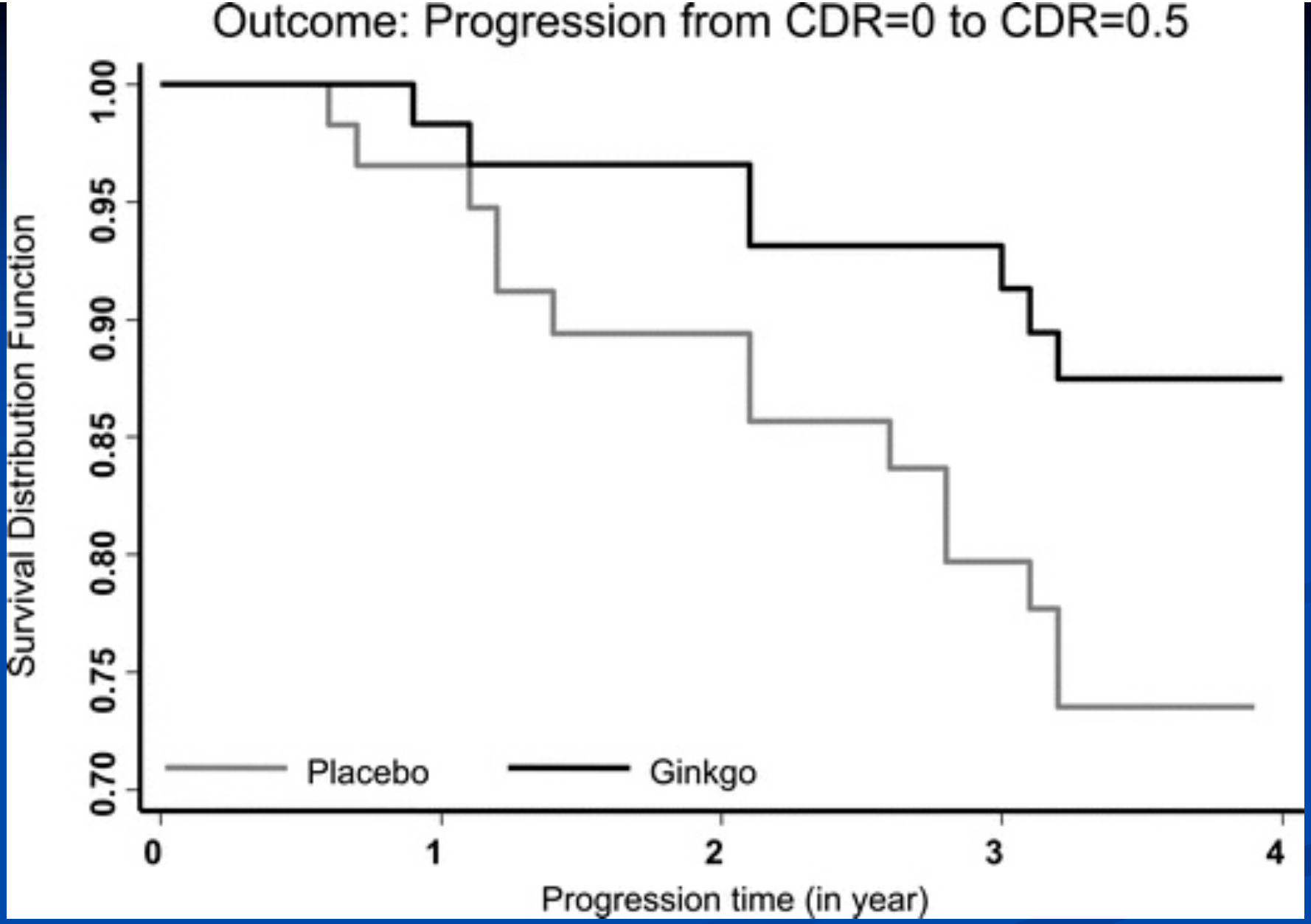
†Le Bars et al "A Placebo-Controlled, Double-blind, Randomized Trial of an Extract of Ginkgo Biloba for Dementia" Journal of the American Medical Association 278(16):1327-1332. 1997

††Itil, T.M. and Martorano, D. Psychopharmacology Bulletin 31:147-158. 1995.



- Mini-mental state exam scores EGb761 160mg/d n=76

- Mazza, M., Capuano, A., Bria, P. & Mazza, S.
  Ginkgo biloba and donepezil: a comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study.
  European Journal of Neurology 2006;**13** (9): 981-985.



Dodge et al. Neurology 2008;70:1809-1817 n=118 2yr (used Thorne Research GBE 80mg TID; all over 85 years of age

Ginkgo and Memory Enhancement in Healthy Adults

Crews et al. HerbalGram 2005;67:43-62

6/7 acute studies show improvement in memory tests

7/9 long term studies show improvement in memory tests

N=203 >60 years old, 40mg Ginkoba TID x 6 weeks

ORIGINAL CONTRIBUTION

Ginkgo for Memory Enhancement
A Randomized Controlled Trial

Paul R. Solomon, PhD
Felicity Adams, BA
Amanda Silver, BA
Jill Zimmer, BA
Richard DeVeaux, PhD

Context Several over-the-counter treatments are marketed as having the ability to improve memory, attention, and related cognitive functions in as little as 4 weeks. These claims, however, are generally not supported by well-controlled clinical studies.

Objective To evaluate whether ginkgo, an over-the-counter agent marketed as enhancing memory, improves memory in elderly adults as measured by objective neuropsychological tests and subjective ratings.

Design Six-week randomized, double-blind, placebo-controlled, parallel-group trial.

Setting and Participants Community-dwelling volunteer men (n=98) and women (n=132) older than 60 years with Mini-Mental State Examination scores greater than 26 and in generally good health were recruited by a US academic center via newspaper advertisements and enrolled over a 26-month period from July 1996 to September 1998.

Intervention Participants were randomly assigned to receive ginkgo, 40 mg 3 times per day (n=115), or matching placebo (n=115).

Main Outcome Measures Standardized neuropsychological tests of verbal and nonverbal learning and memory, attention and concentration, naming and expressive language, participant self-report on a memory questionnaire, and caregiver clinical global impression of change as completed by a companion.

Results Two hundred three participants (88%) completed the protocol. Analysis of the modified intent-to-treat population (all 219 participants returning for evaluation) indicated that there were no significant differences between treatment groups on any outcome measure. Analysis of the fully evaluable population (the 203 who complied with treatment and returned for evaluation) also indicated no significant differences for any outcome measure.

Conclusions The results of this 6-week study indicate that ginkgo did not facilitate performance on standard neuropsychological tests of learning, memory, attention, and concentration or naming and verbal fluency in elderly adults without cognitive impairment. The ginkgo group also did not differ from the control group in terms of self-reported memory function or global rating by spouses, friends, and relatives. These data suggest that when taken following the manufacturer's instructions, ginkgo provides no measurable benefit in memory or related cognitive function to adults with healthy cognitive function.

JAMA. 2002;288:835-840 www.jama.com

SOME OVER-THE-COUNTER TREATments are marketed as having the ability to improve memory, attention, and related cognitive functions. These claims are generally not supported by well-controlled clinical studies. Ginkoba claims to "enhance mental focus and improve memory and concentration."[1] Several published studies reported beneficial effects of ginkgo on cognition. These studies, however, either report cognitive improvement in only 1 of many memory tests administered[2,3] or report cognitive enhancement in cognitively impaired clinical populations such as patients with cerebrovascular or Alzheimer disease.[4,5] In contrast, advertising claims imply that the compound is broadly beneficial to those both with and without clinically significant cognitive impairments. Specific advertising claims cite more than 50 clinical trials that demonstrate benefit centered around concentration and memory. These studies were conducted for periods ranging from 14 days to 2 months. The manufacturer claims benefit with "at least 4 weeks of uninterrupted use."[6]

The purpose of the present study was to evaluate ginkgo in healthy elderly volunteers in a randomized, double-blind, placebo-controlled trial using standardized tests of memory, learning, attention and concentration, and expressive language as well as subjective ratings by participants and family.

METHODS

Participants

Following approval by the Williams College institutional review board, participants were recruited from newspaper advertisements that solicited individuals who would participate in a study designed to improve memory. An initial telephone interview was conducted to determine if the participant was likely to meet entry criteria for the study. Those who passed the screen provided informed consent and a medical history including current medications, neurologic or psychiatric

Author Affiliations: Department of Psychology (Dr Solomon and Ms Zimmer), Program in Neuroscience (Dr Solomon and Mss Adams, Silver, and Zimmer), Department of Mathematics and Statistics (Dr DeVeaux), Williams College, Williamstown, Mass; and The Memory Clinic, Southwestern Vermont Medical Center, Bennington (Dr Solomon).
Corresponding Author and Reprints: Paul R. Solomon, PhD, Bronfman Science Center, Williams College, 33 Hoxsey St, Williamstown, MA 01267 (e-mail: psolomon@williams.edu).

N=262
Ginkgold
60mg BID
x 6 weeks

HUMAN PSYCHOPHARMACOLOGY
Hum Psychopharmacol Clin Exp 2002; **17**: 267–277.
Published online 5 July 2002 in Wiley InterScience (www.interscience.wiley.com). **DOI**: 10.1002/hup.412

A double-blind, placebo-controlled, randomized trial of *Ginkgo biloba* extract EGb 761® in a sample of cognitively intact older adults: neuropsychological findings

Joseph A. Mix[1]* and W. David Crews, Jr.[2,3]

[1]*Liberty University, Lynchburg, Virginia, USA*
[2]*Virginia Neuropsychology Associates, Inc., Lynchburg, Virginia, USA*
[3]*Virginia Polytechnic Institute and State University, Blacksburg, Virginia, USA*

There appears to be an absence of large-scaled clinical trials that have examined the efficacy of *Ginkgo biloba* extract on the neuropsychological functioning of cognitively intact older adults. The importance of such clinical research appears paramount in light of the plethora of products containing *Ginkgo biloba* that are currently being widely marketed to predominantly cognitively intact adults with claims of enhanced cognitive performances. The purpose of this research was to conduct the first known, large-scaled clinical trial of the efficacy of *Ginkgo biloba* extract (EGb 761®) on the neuropsychological functioning of cognitively intact older adults. Two hundred and sixty-two community-dwelling volunteers (both male and female) 60 years of age and older, who reported no history of dementia or significant neurocognitive impairments and obtained Mini-Mental State Examination total scores of at least 26, were examined via a 6-week, randomized, double-blind, fixed-dose, placebo-controlled, parallel-group, clinical trial. Participants were randomly assigned to receive either *Ginkgo biloba* extract EGb 761®($n = 131$; 180 mg/day) or placebo ($n = 131$) for 6 weeks. Efficacy measures consisted of participants' raw change in performance scores from pretreatment baseline to those obtained just prior to termination of treatment on the following standardized neuropsychological measures: Selective Reminding Test (SRT), Wechsler Adult Intelligence Scale-III Block Design (WAIS-III BD) and Digit Symbol-Coding (WAIS-III DS) subtests, and the Wechsler Memory Scale-III Faces I (WMS-III FI) and Faces II (WMS-III FII) subtests. A subjective Follow-up Self-report Questionnaire was also administered to participants just prior to termination of the treatment phase. Analyses of covariance indicated that cognitively intact participants who received 180 mg of EGb 761® daily for 6 weeks exhibited significantly more improvement on SRT tasks involving delayed (30 min) free recall ($p < 0.04$) and recognition ($p < 0.01$) of noncontextual, auditory-verbal material, compared with the placebo controls. The EGb 761® group also demonstrated significantly greater improvement on the WMS-III FII subtest assessing delayed (30 min) recognition ($p < 0.025$) of visual material (i.e. human faces), compared with the placebo group. However, based on the significant difference ($p < 0.03$) found between the two groups' pretreatment baseline scores on the WMS-III FII, this result should be interpreted with caution. An examination of the participants' subjective ratings of their overall abilities to remember by treatment end on the Follow-up Self-report Questionnaire also revealed that significantly more ($p = 0.05$) older adults in the EGb 761® group rated their overall abilities to remember by treatment end as 'improved' compared with the placebo controls. Overall, the results from both objective, standardized, neuropsychological tests and a subjective, follow-up self-report questionnaire provided complementary evidence of the potential efficacy of *Ginkgo biloba* EGb 761® in enhancing certain neuropsychological/memory processes of cognitively intact older adults, 60 years of age and over.

KEY WORDS — *Ginkgo biloba* extract; neuropsychological; cognitive; memory; elderly; clinical trial

Ginkgo biloba – peripheral circulation

Adapted from Vasa 27:106-110,1998

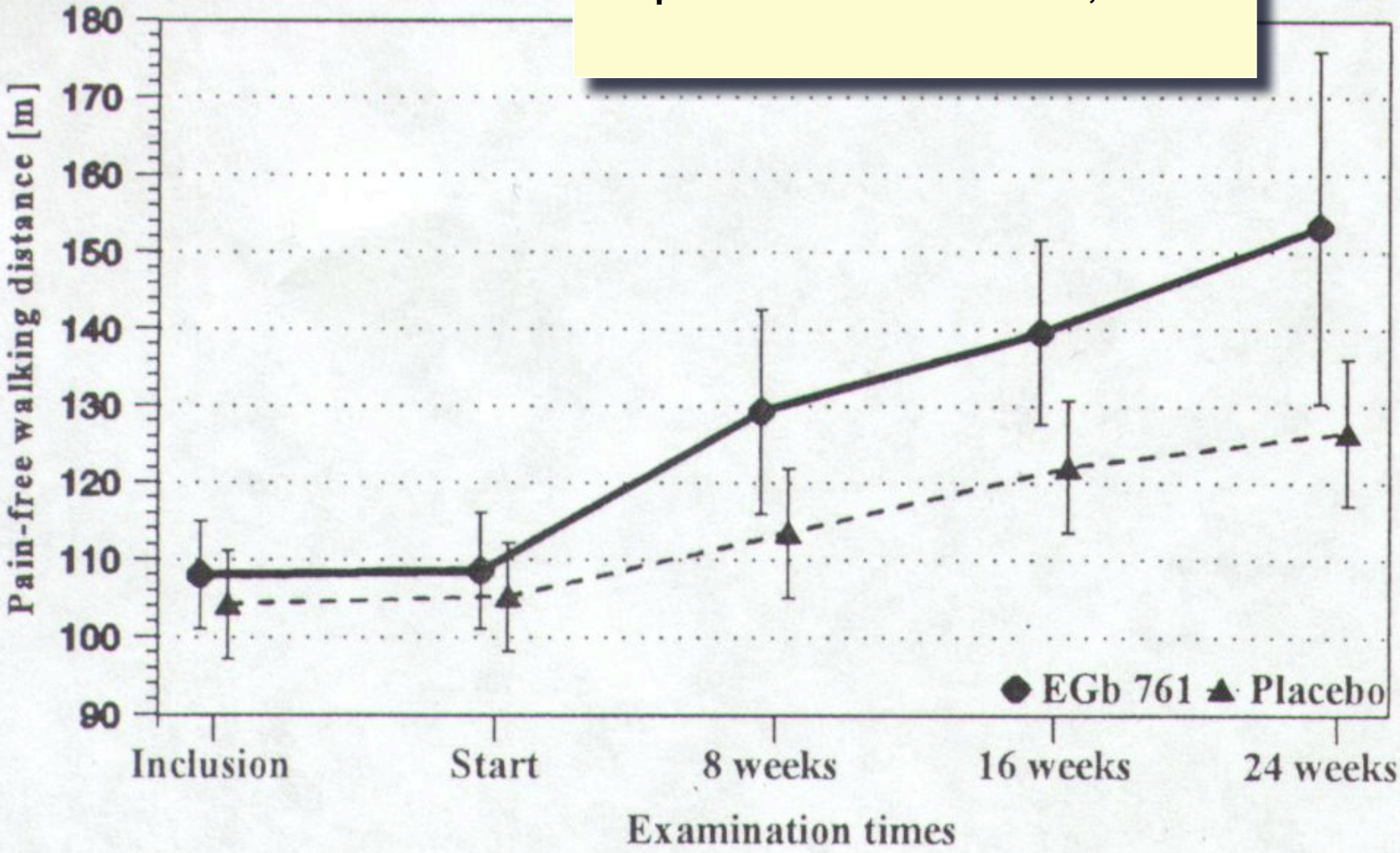
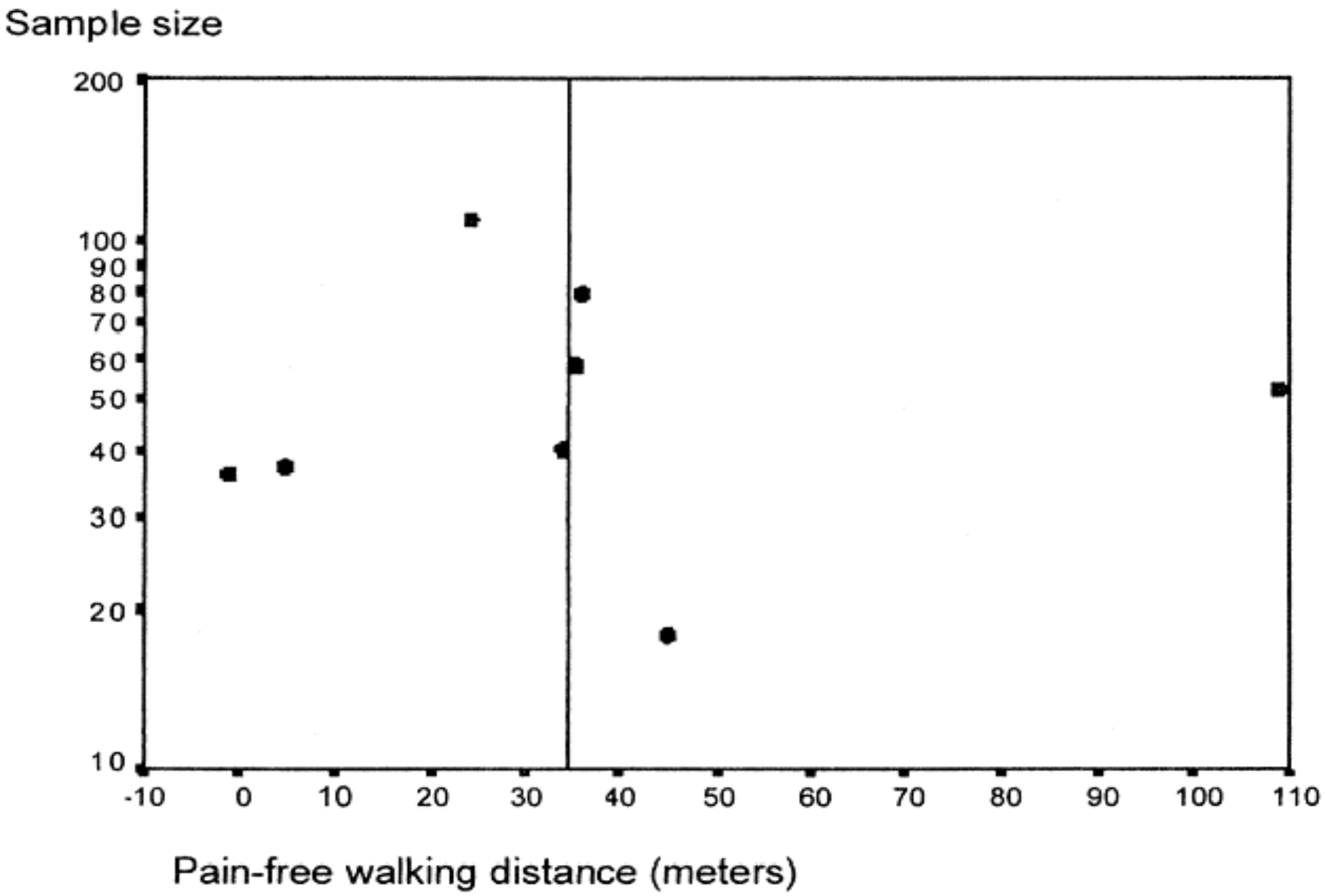


Fig. 1: Course of pain-free walking distance (m) at baseline, after 2 weeks placebo treatment and after 8, 16, and 24 weeks treatment with EGb 761 or placebo (arithmetic means with 95% confidence intervals)



Pittler and Ernst. Am J Med 108:276-281, 2000

•*Ginkgo biloba*

Other Uses (much less well studied)

- Impotence (associated with SSRI antidepressants) – several small studies show some improvement but others do not
- Tinnitus- (recent studies indicated no help, e.g. n=1121, BMJ 2001;322:73)
- Vertigo- several small studies showed improvement
- PMS- a study in France (n=165) indicated improvement
- prevent altitude sickness- (most but not all studies show benefit; start 1-2d prior and continue during trip)
- Macular degeneration-one study showed improvement
- A fixed combination of ginkgo and ginseng shows promise for beneficial effects on memory and (one study) attention deficit hyperactivity disorder

•*Ginkgo biloba*

Other Uses (much less well studied)

- Raynaud's Syndrome – one study showed decreased attacks
- Diabetic Retinopathy – one study showed improved color vision
- Glaucoma – one study showed improvement
- SAD – no benefit
- Activities of Daily Living in Older Adults – one study showed improvement
- Anxiety- one study showed improvement in young adults with anxiety
- MS- one study showed improvement in functionality in adults with MS

Ginkgo

Safety

Rare bleeds

Ginkgo seeds contain 4-methoxypyridoxine and can cause seizures. Two cases of seizure episodes associated with ginkgo extracts (contamination?)- maybe avoid ginkgo in the seizure prone

Ginkolic acids are toxic but removed during extract prep

Drug interactions

Seems not to have effects on CYP in vivo (more later)

Possible additive effects with antiplatelet adhesion drugs

Effects on insulin are complex-careful in diabetes

Bleeds associated with ginkgo use

Patient age	Ginkgo use	Other therapy	Bleed	ref
70	1 week	Aspirin	Iris	1
78	2 mos	Warfarin	Intracerebral	2
33	2 years	None	Subdural	3
61	6 mos	None	Subarachnoid	4

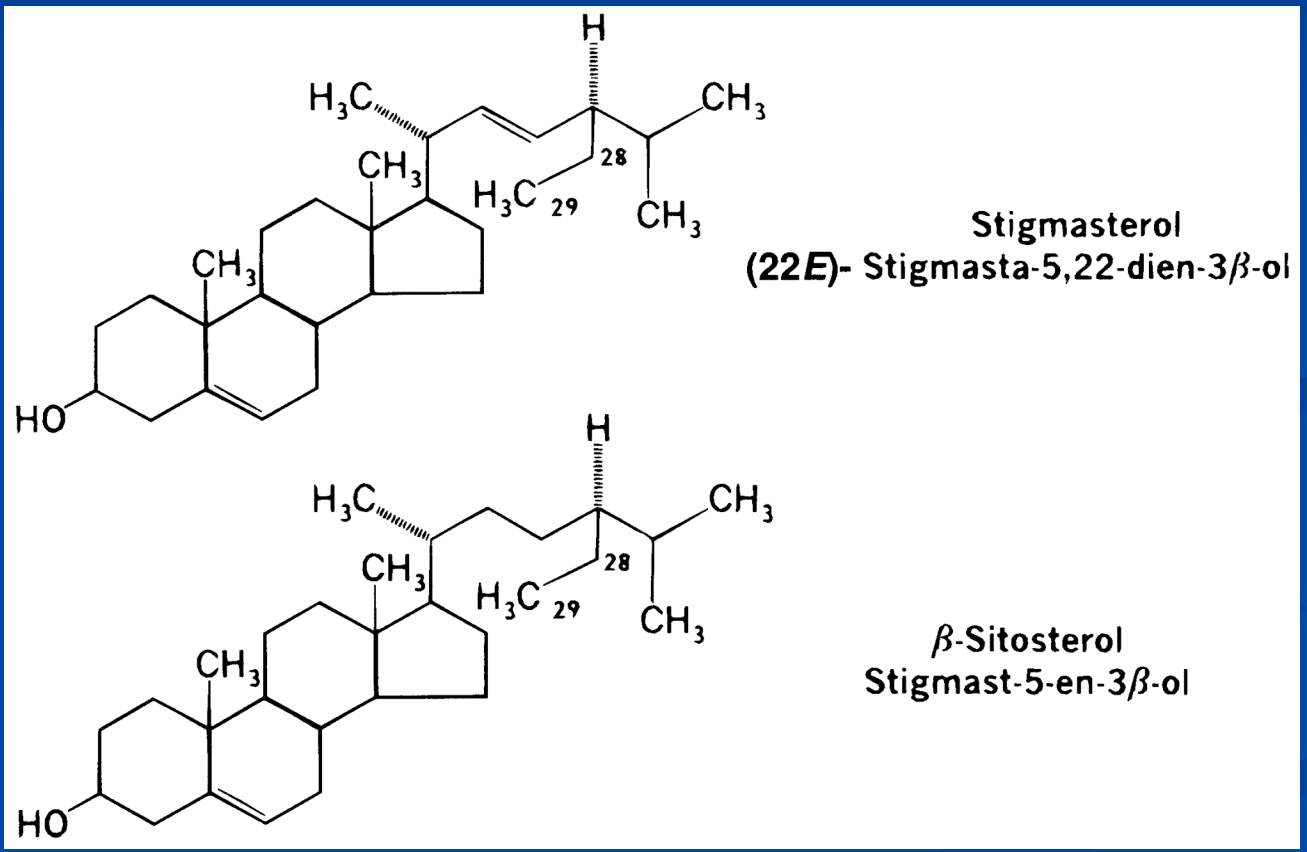
1. NEJM 336:1108,1997
2. Neurology 50:1933-1934,1998
3. Lancet 352:36-37,1998
4. Neurology 46:1775-1776,1996

Ginkgo biloba

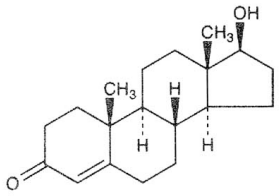
- **Summary**
  - **Efficacy**: evidence for benefit in dementia, poor memory and poor peripheral circulation
  - **Safety**: good but watch for rare bleeding episodes, seizures?
  - **Drug interactions**: possibly warfarin, antiplatelet adhesion drugs; CYP 3A4 interactions are uncertain
  - **Product selection**: look for EGb761 or LI 1370 extracts; these are the best studied; 24% flavone glycosides and 6% terpene lactones
  - **Dose**: 1-2 60mg tabs, BID
  - **Questions remaining** include
    - *Extent of memory improvement in younger patients?*
    - *Delay Alzheimer's and dementia?*
    - *Help in other circulatory disorders?*
    - *Synergistic with other drugs and treatments?*
    - *Optimum dose and treatment time?*

Saw palmetto

- Botany
  - Serenoa repens, Sabal, American dwarf palm tree, cabbage palm
- History
- Chemistry
  - fatty acids
  - sitosterols
  - flavones, isoflavones, coumestrans[#]
- Pharmacology
  - lipid extracts of berry inhibit testosterone 5α-reductase and therefore conversion of testosterone to dihydrotestosterone



9322. Testosterone. *(17β)-17-Hydroxyandrost-4-en-one;* Δ^4-androsten-17β-ol-3-one; *trans*-testosterone; Andi Mertestate; Oreton; Testoderm; Testolin; Testro AQ; Vir sterone. $C_{19}H_{28}O_2$; mol wt 288.43. C 79.12%, H 9.78%, 11.09%. Principal hormone of the testes, produced by t interstitial cells. Major circulating androgen; convert by 5α-reductase in androgen-dependent target tissues *5α-dihydrotestosterone* which is required for normal ma sexual differentiation. Also converted by aromatization estradiol, *q.v.* Isoln from bull testes: David *et al., Z. Ph siol. Chem.* **233,** 281 (1935). Prepn from cholesterol a confirmation of structure: A. Butenandt, G. Hanisch, *B* 68, 1859 (1935); *eidem, Z. Physiol. Chem.* **237,** 89 (193 from dehydroandrosterone: L. Ruzicka, A. Wettstein, *He Chim. Acta* **18,** 1264 (1935); from mixed esters: L. Ruzic *et al., ibid.* 1478. Crystal structure: P. J. Roberts *et al., Chem. Soc., Perkin Trans. II* **1973,** 1978. Historical revie J. M. Hoberman, C. E. Yesalis, *Sci. Am.* **272,** 76-81 (F 1995). Review of role in aging males: F. E. Kaiser, J. Morley, *Neurobiol. Aging* **15,** 559-563 (1994); of clinical re vance in females: R. S. Rittmaster, *Am. J. Med.* **98,** Sup 1A, 17S-21S (1995).



Needles from dil acetone, mp 155°. $[\alpha]_D^{24}$ +109° (c = 4 alc). uv max: 238 nm. Insol in water. Sol in alcol ether, and other organic solvents.

Acetate, $C_{21}H_{30}O_3$, mp 140-141°.

17β-Cyclopentanepropionate, $C_{27}H_{40}O_3$, *testosterone cyp nate, depAndro, Depotest, Depo-Testosterone, Depovirin, I testis, Virilon.* Pharmacology: A. C. Ott *et al., J. C Endocrinol. Metabol.* **12,** 15 (1952). Crystals, mp 101-1($[\alpha]_D^{25}$ +87° ($CHCl_3$). Sol in oils.

Enanthate, $C_{26}H_{40}O_3$, *Andro LA, Androtardyl, Delatest Everone, Primoteston, Testinon, Testo-Enant.* Prepn: Ju mann *et al.,* **U.S.** pat. **2,840,508** (1958 to Schering A Comprehensive description: K. Florey, *Anal. Profiles D*

Saw palmetto

- Pharmacology (continued)
  - block binding of DHT to receptors
  - block nuclear not cytosolic estrogenic, progestogenic and androgenic receptors in prostate
  - inhibit cyclooxygenase (one report of a bleed) and 5-lipooxygenase thereby decreasing inflammation
  - inhibit prolactin at receptor level
  - inhibit testosterone metabolism in prostate tissues in vitro
  - observations: no big plasma changes in hormones. No PSA changes. Favorable cytological changes occur in the prostate.

•Saw palmetto

Evidence for efficacy in BPH

- Vs Active control
  - Carraro et al (Prostate 1996;29:231-240)
    - multicentered European randomized trial of 1098 patients
    - compared Permixon (hexane extract of saw palmetto) vs. finasteride (Proscar)
  - Debruyne et al. Comparison of a phytotherapeutic agent(Permixon) with an alpha-blocker (Tamsulosin) in the treatment of benignprostatic hyperplasia: a one-year randomized international study. *Eur Urol.* 2002;41:497-507. same
- Vs placebo
  - Most studies but not all (see recent Bent study) have showed benefit vs placebo, e.g. study by Gerber et al. (Urology 2001;58:960-5)

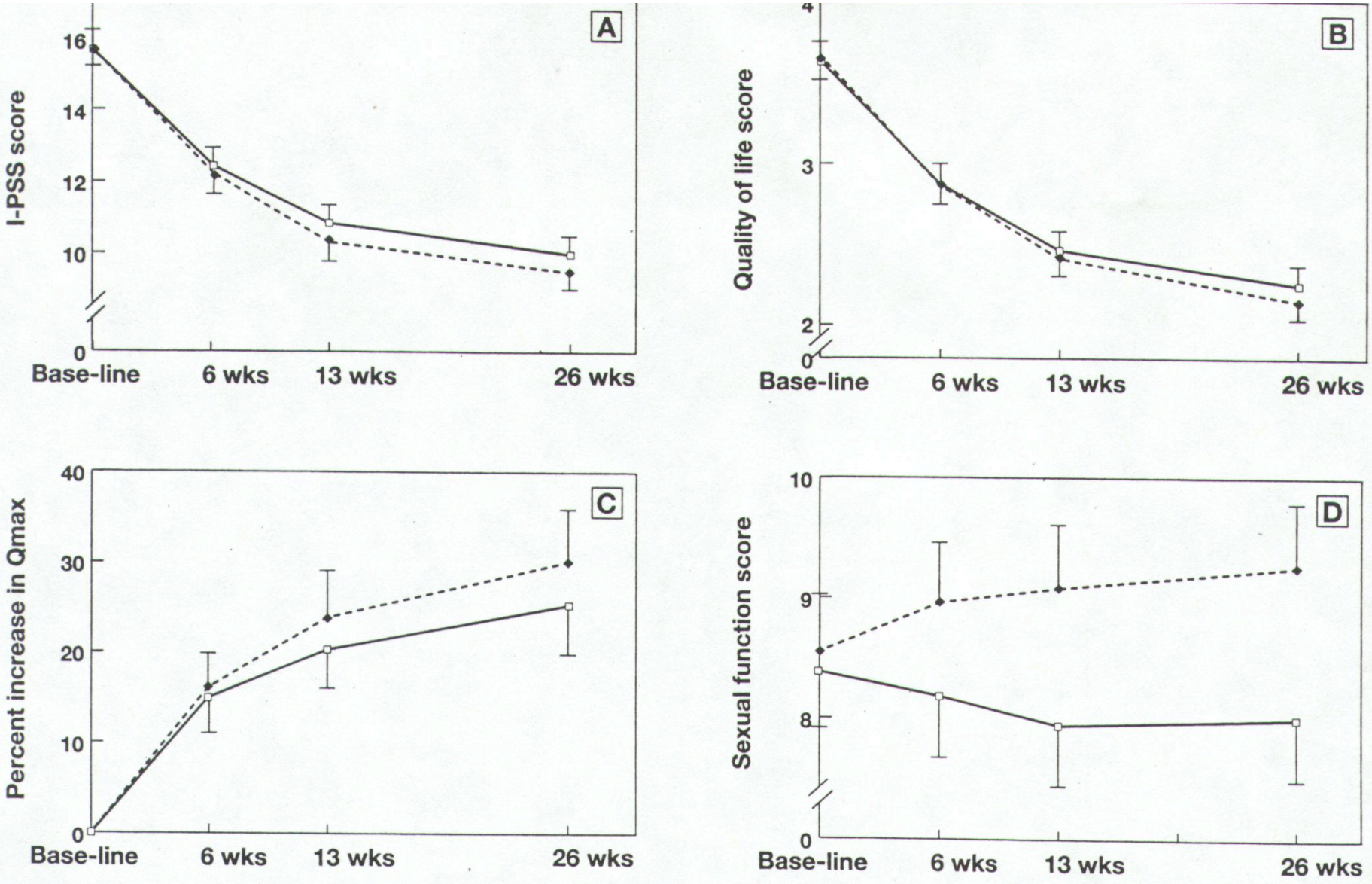
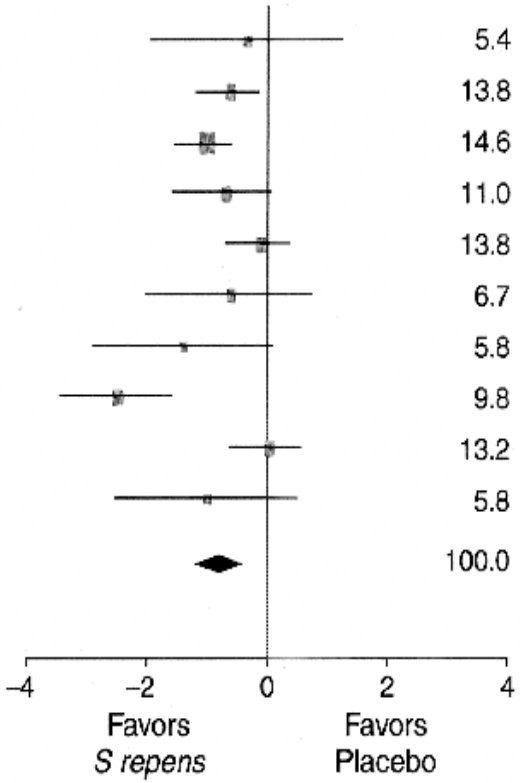


Fig. 1. Mean total IPSS (**A**), mean quality of life score (**B**), percentage of increase in mean peak urinary flow (**C**), and mean sexual function score (**D**), in men with BPH receiving either 320 mg Permixon® (open squares) or 5 mg finasteride (solid diamonds) (±0.95 confidence intervals).

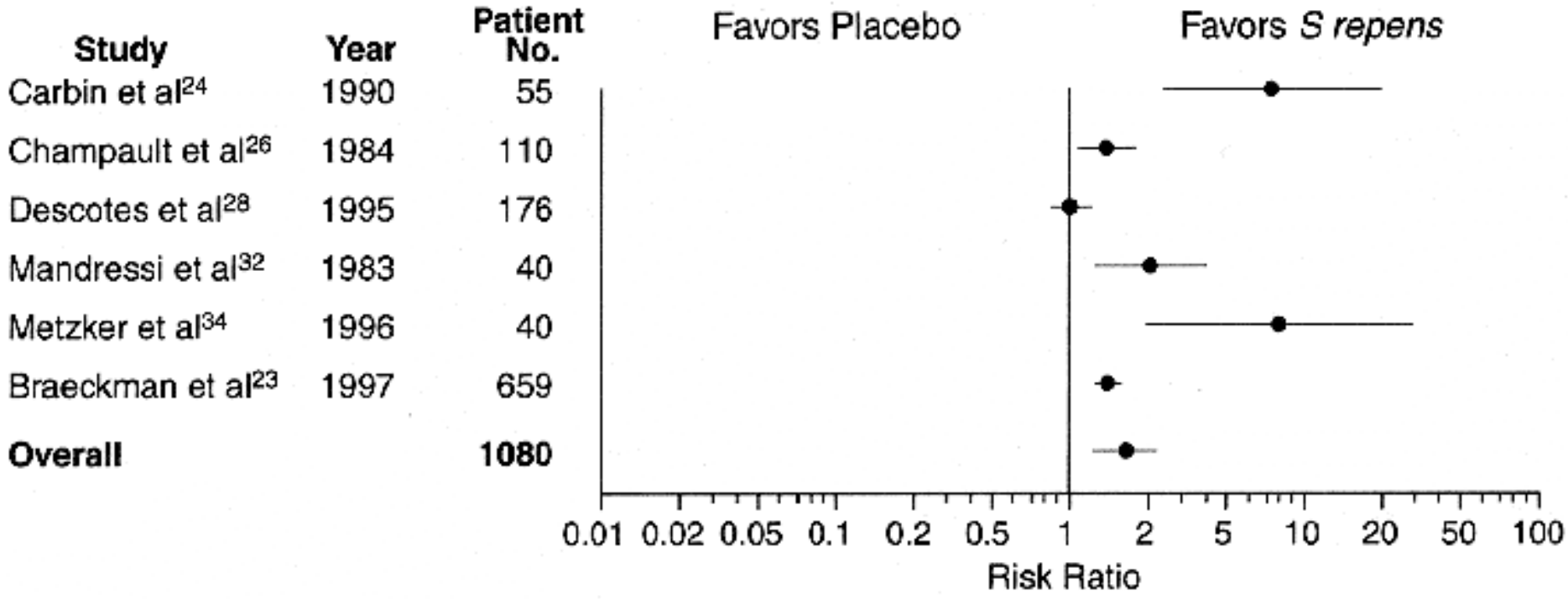
Carraro et al., Prostrate 29:231-240, 1996

Study	Expected, No.	Expected, Mean (SD)	Control, No.	Control, Mean (SD)	Weighted Mean Difference (95% CI Random)	Weight, %	Weighted Mean Difference (95% CI Random)
Boccafoschi and Annoscia[22]	11	1.80 (2.01)	11	2.10 (1.79)		5.4	−0.300 (−1.891 to 1.291)
Carbin et al[24]	26	1.40 (1.02)	27	2.00 (1.04)		13.8	−0.600 (−1.155 to −0.045)
Champault et al[26]	47	1.70 (1.16)	41	2.70 (1.09)		14.6	−1.000 (−1.470 to −0.530)
Cukier et al[27]	43	2.20 (1.97)	47	2.90 (1.99)		11.0	−0.700 (−1.519 to 0.119)
Descotes et al[28]	82	1.40 (1.81)	94	1.50 (1.94)		13.8	−0.100 (−0.654 to 0.454)
Emili et al[29]	15	1.70 (1.90)	15	2.30 (1.90)		6.7	−0.600 (−1.960 to 0.760)
Mandressi et al[32]	20	1.70 (2.41)	20	3.10 (2.46)		5.8	−1.400 (−2.909 to 0.109)
Mattei et al[33]	19	1.50 (1.48)	19	4.00 (1.48)		9.8	−2.500 (−3.441 to −1.559)
Reece Smith et al[36]	33	1.90 (1.20)	37	1.90 (1.40)		13.2	0.000 (−0.609 to 0.609)
Tasca et al[39]	14	0.90 (2.02)	13	1.90 (1.99)		5.8	−1.000 (−2.513 to 0.513)
Total	**310**		**324**			100.0	−0.762 (−1.210 to −0.315)

$\chi^2_9 = 26.49$, $Z = 3.34$



From Wilt et al. JAMA 280:1604-1609, 1998



From Wilt et al. JAMA 280:1604-1609, 1998

TABLE I. *Changes in International Prostate Symptom Score and quality-of-life score in men treated with saw palmetto and placebo for 6 months*

	Initial	2 Months	4 Months	Final	Change
Symptom score					
Saw palmetto	16.7 ± 4.9	13.1 ± 4.6	12.0 ± 5.1	12.3 ± 5.5	−4.4 ± 5.9
Placebo	15.8 ± 4.8	12.4 ± 5.2	13.3 ± 5.4	13.6 ± 6.6	−2.2 ± 5.4
					$P = 0.038$
Quality-of-life score					
Saw palmetto	3.3 ± 1.1	3.0 ± 1.4	2.6 ± 1.2	2.6 ± 1.5	−0.7 ± 1.5
Placebo	3.1 ± 1.3	2.8 ± 1.1	2.8 ± 1.3	2.8 ± 1.2	−0.3 ± 1.1
					$P = 0.20$

Data presented as the mean ± SD.

Gerber et al. Urology 2001;58:960-965

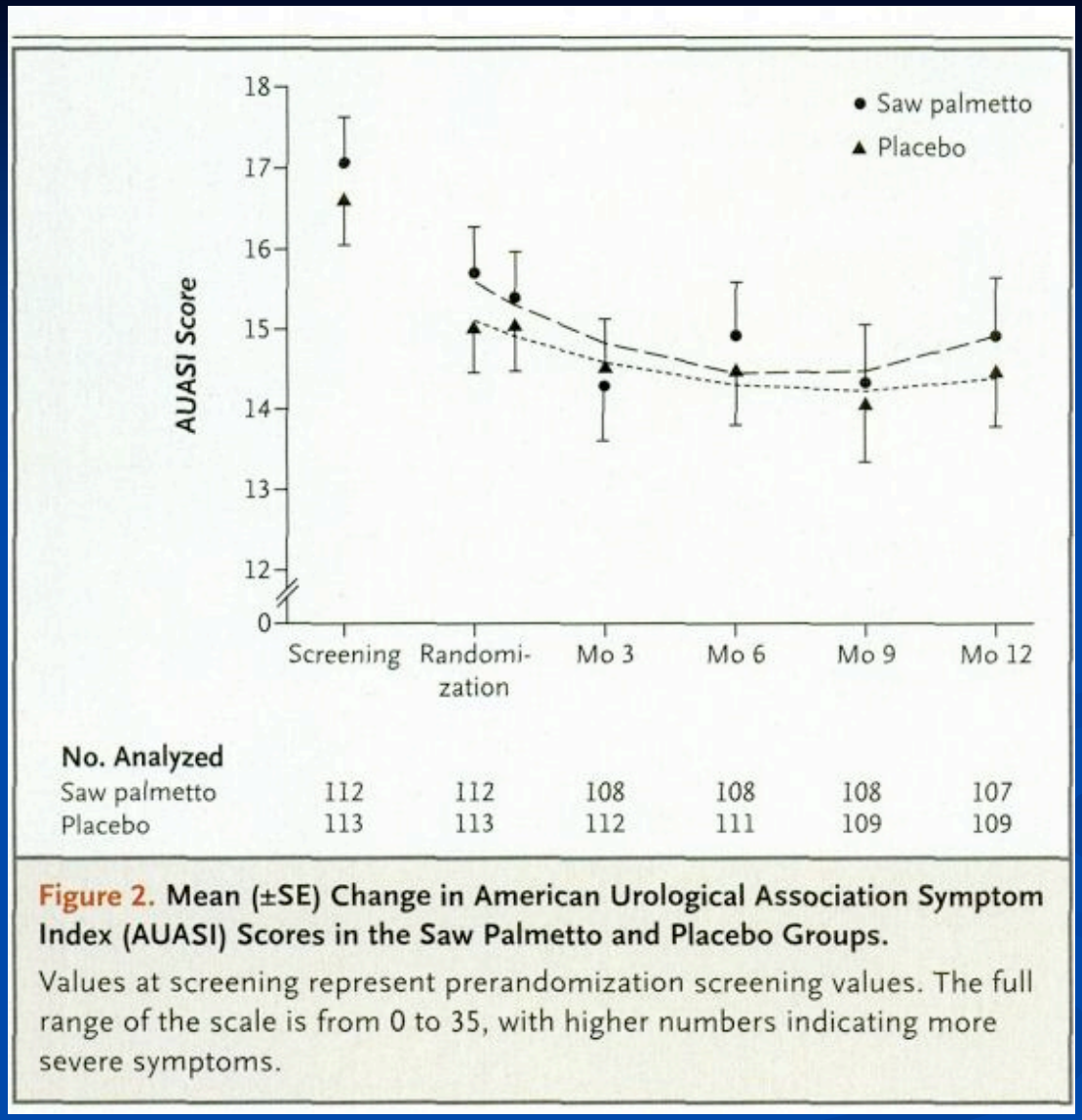


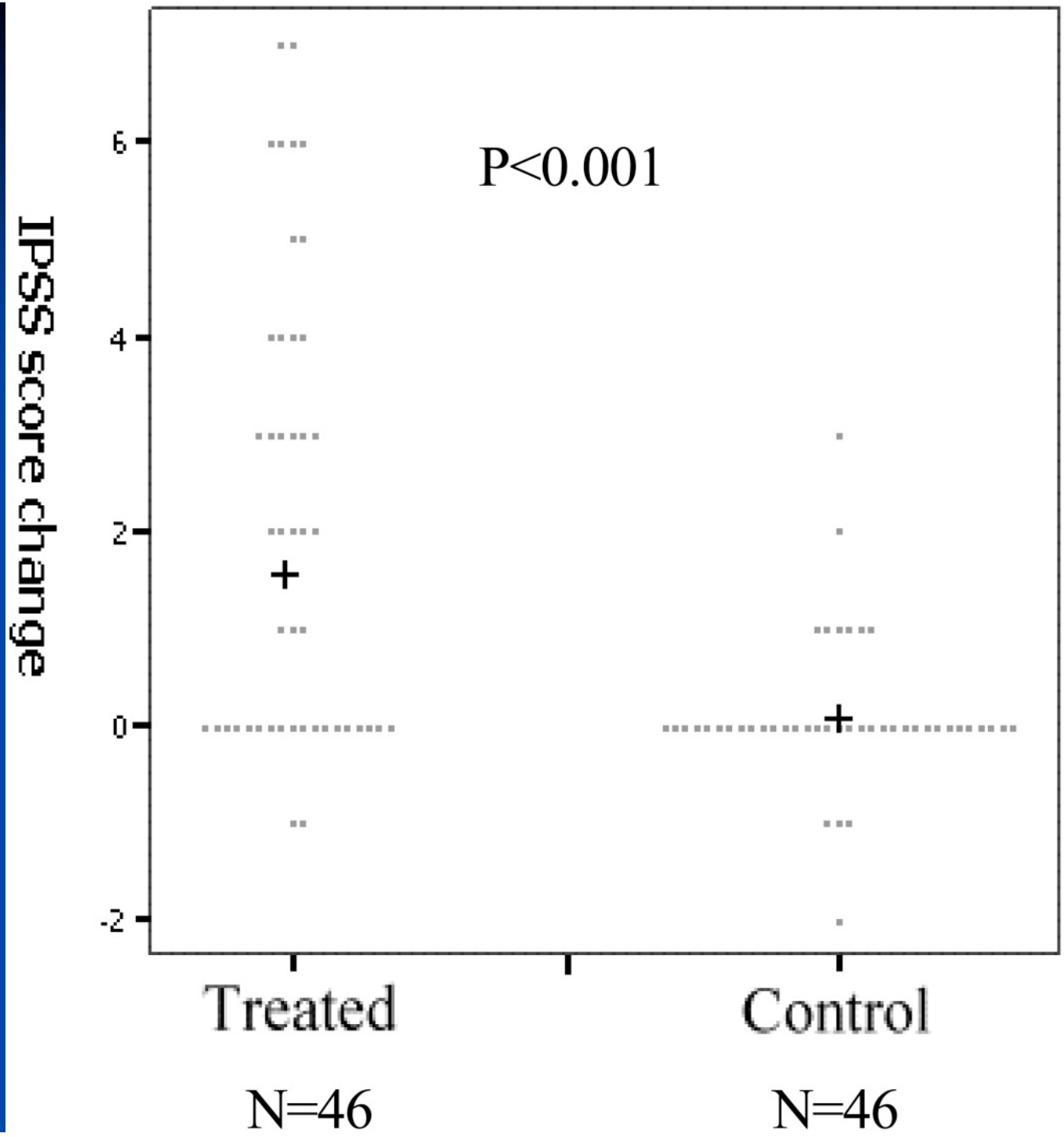
Figure 2. Mean (±SE) Change in American Urological Association Symptom Index (AUASI) Scores in the Saw Palmetto and Placebo Groups.

Values at screening represent prerandomization screening values. The full range of the scale is from 0 to 35, with higher numbers indicating more severe symptoms.

Bent et al. NEJM 2006;354:557-566 n=255 Rx for 12 mos. Used Indena carbon dioxide extract product yielding 160mg/capsule (91% fatty acids). One BID.

Shi et al. J Urol. 2008;179:610-5.

N=92 3 months



- **Chronic noninfective protatitis**-no benefit

- **Adverse effects**:
  - –one report of hemorrhage during surgery
  - –due to prolactin inhibition and some isoflavone content, avoid in pregnancy and lactation

- **Dose**: 160mg twice a day or 320mg q d of a 85-95% lipid extract

Saw Palmetto

- **Summary**
  - **Efficacy**: overall evidence in reducing symptoms of BPH
  - **Safety**: good; one report of hemorrhage during surgery; avoid in pregnancy
  - **Drug interactions**: none noted so far
  - **Product selection**: want standardized extract containing 85-95% fatty acids and sterols
  - **Dose**: about 160mg of extract BID for treatment; some use 320mg q d
  - **Questions remaining** include
    - *Will saw palmetto prevent BPH and even prostate cancer? Maybe avoid CO2 extract?*

Pygeum and BPH

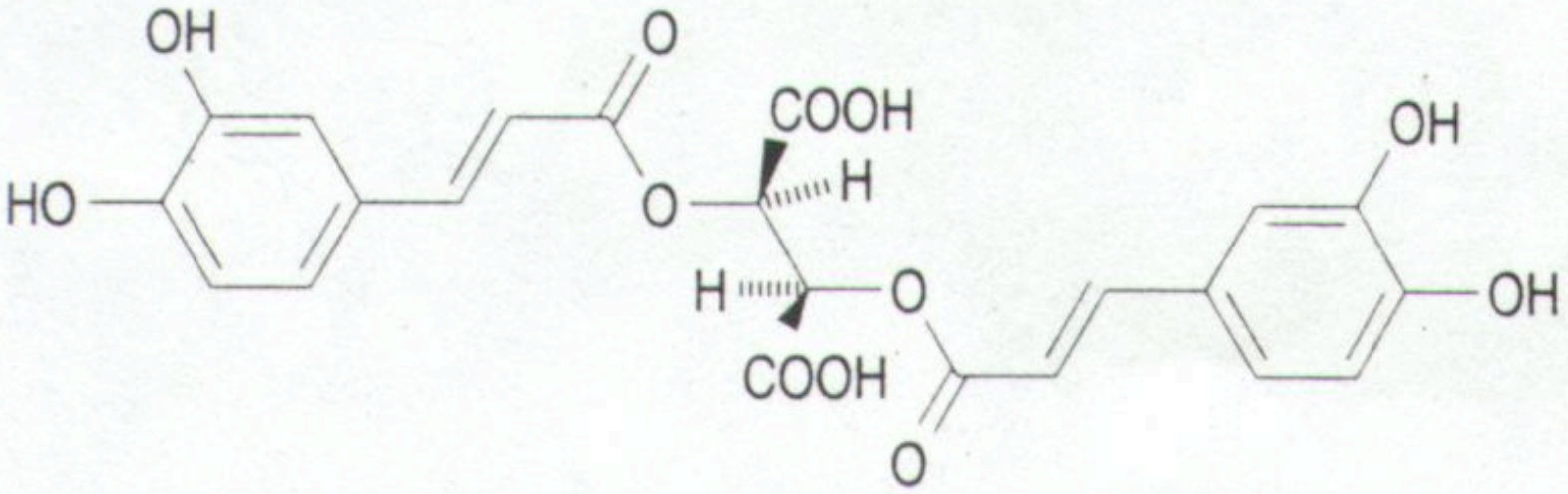
- not as well studied as saw palmetto
- extract of the bark of an evergreen tree (Prunus africana) found in Africa
- tree nearly endangered so use is not to be encouraged
- saw palmetto is cultivated
- studies support its use for BPH (e.g. Wilt et al. Cochrane Database Syst Rev. 2002;(1):CD001044); takes a few months to work
- products should be standardized to contain 14% triterpenes and 0.5% docosanol
- dose: 100mg qd is therapeutically equivalent to 50mg BID
- no special safety problems; better than Saw palmetto?? Combination products with Saw palmetto better??

Echinacea

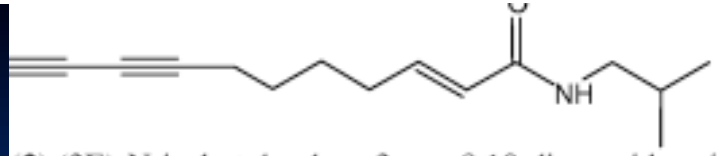
- **Botany**
  - Echinacea purpurea, E. augustifolia, E. pallida
- **History**
  -

Echinacea

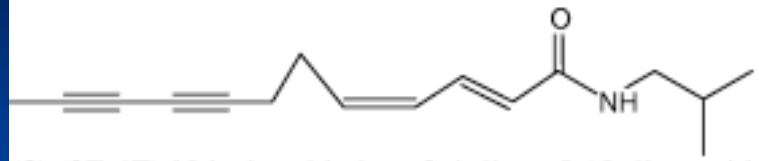
-
- Chemistry
  - high molecular weight polysaccharides
    - heteroxylan
    - arabinogalactan
  - phenylpropanoid - chicoric acid
  - alkylamides
  - flavonoids
- Pharmacology
  - phagocyte activation
  - release of TNF, interleukin-1 and B2
  - increase immune response
  - local anesthesia
  - antimicrobial
  - antioxidant



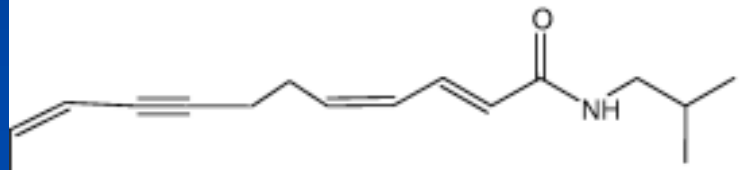
Chicoric acid



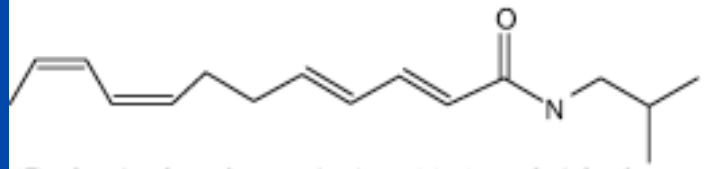
(2) (2E)-N-isobutylundeca-2-ene-8,10-diynamide m/z = 231



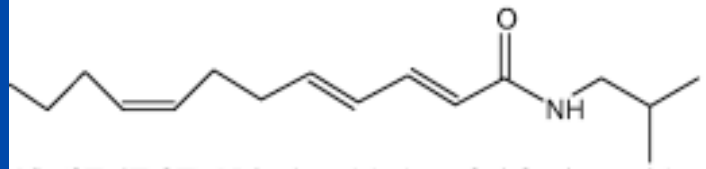
(3) (2E,4Z)-N-isobutyldodeca-2,4-diene-8,10-diynamide m/z = 243



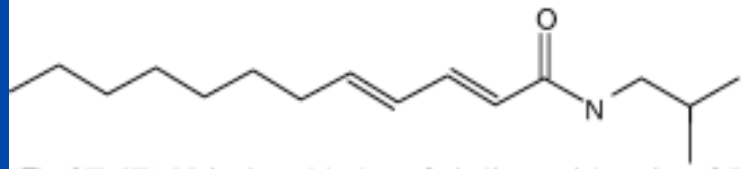
(4) (2E,4Z,8Z)-N-isobutyldodeca-2,4,10-triene-8 -ynamide m/z = 245



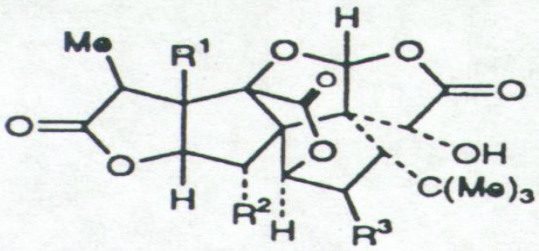
(5) (2E,4E,8Z,10Z)-N-isobutyldodeca-2,4,8,10-tetraenamide m/z = 247



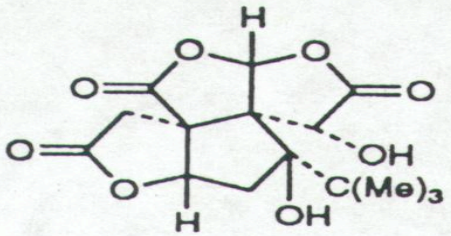
(6) (2E,4E,8Z)-N-isobutyldodeca-2,4,8-trienamide m/z = 249



(7) (2E,4E)-N-isobutyldodeca-2,4-dienamide m/z = 251

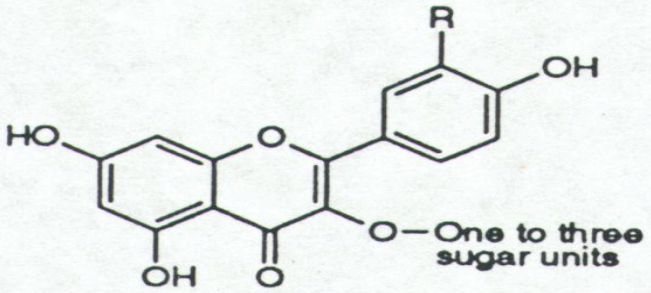


Ginkgolide structures

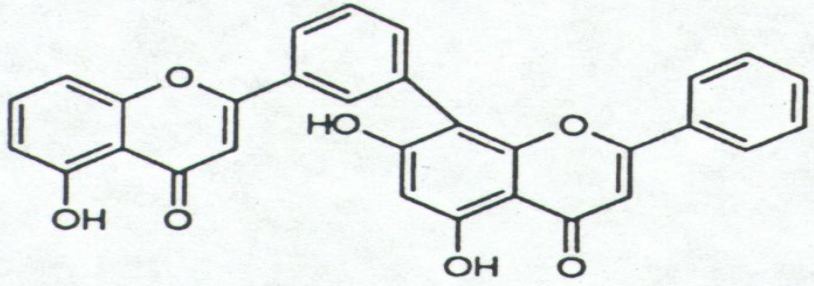


Bilobalide

	R^1	R^2	R^3
Ginkgolide A;	OH	H	H
Ginkgolide B;	OH	OH	H
Ginkgolide C;	OH	OH	OH
Ginkgolide J;	OH	H	OH
Ginkgolide M;	H	OH	OH



Flavonol structures
Kaempferol derivatives; R = H
Quercetin derivatives; R = OH
Isorhamnetin derivatives; R = OMe



Amentoflavone

Fig. 23.5. Some constituents of *Ginkgo biloba* leaves

Prevention of colds/flu

- Melchart et al., Archives of Family Medicine 7:541-545,1998
  - n=302, double blind, placebo controlled, randomized prevention trial in Germany
  - no difference in time to first cold (t=66 vs t-65 in the placebo (patients believed they had more benefit from echinacea, however)($p<.04$)
- Grimm and Muller, Am J Med 106:138-143, 1999
  - similar prevention trial and results as above
- Turner et al., Antimicrob Agents Chemother 44:1708-1709, 2000
  - experimental cold prevention - no effect
- Bastyr study in Seattle

Popular echinacea may make you sick

Study disputes herbal aid's preventive value

By TOM PAULSON
P-I REPORTER

A study done at one of the nation's leading research and teaching institutions for naturopathic medicine has shown that taking the popular herbal supplement echinacea as a preventive measure might make you sick.

EDITORIALS

Doubts about echinacea

HERBAL hounds beware. Echinacea, the purported Holy Grail of cold cures, may actually cause more sickness than it prevents.

Preliminary findings by local researchers at Bastyr University indicate that echinacea users had more symptoms of respiratory infection than people who took placebos over a six-month study period. The results, which were presented at a medical conference in Seattle, have yet to be printed in a peer-reviewed medical journal. But they're similar to recently published studies on echinacea's lack of preventative powers.

A study published in the March issue of the American Journal of Medicine concluded that the world's most popular herbal supplement had no impact on the duration or severity of respiratory infections.

Serious scientific inquiry is demonstrating that echinacea use may be no better — or actually worse — than doing nothing at all.

The sniffle-prone should be free, of course, to gobble down eye of newt or root of purple coneflower if they believe it clears their stuffy noses. They should be free to hang garlic around their necks, on their earlobes, or from their window sills if they think it will ward off germs. They should even be free to undergo strange procedures such as "sham surgery," outlined in gruesome detail in The New York Times this week, if they are fully informed of the risks, benefits and incomplete scientific evidence of bona fide effectiveness.

The freedom to heal — whether physically, psychologically or psychosomatically — is only truly free when patients are fully informed.

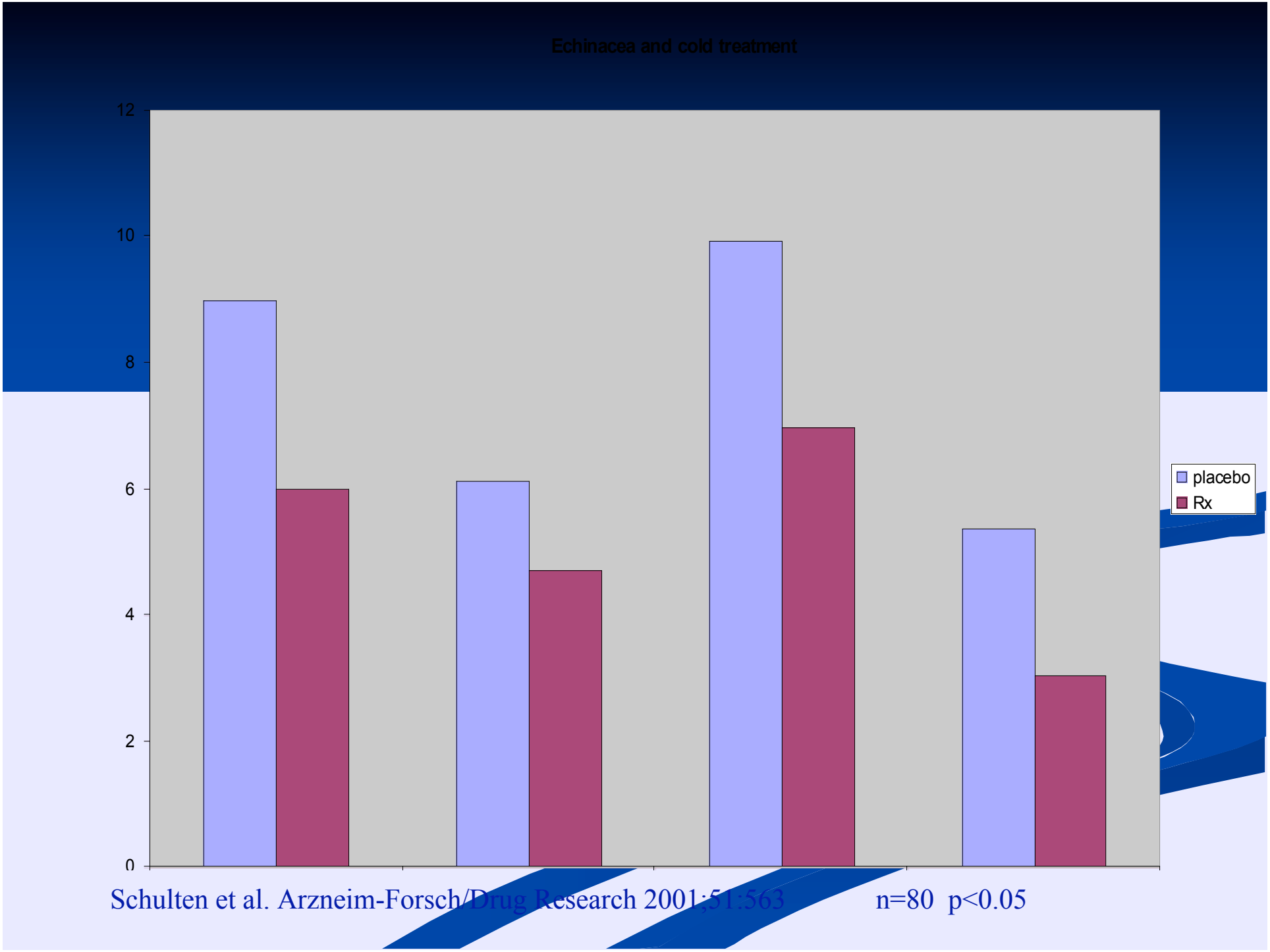
Bastyr University earns kudos for subjecting alternative therapies to rigorous scientific research and publicizing the results regardless of special-interest opposition. Proponents as well as skeptics of alternative medicine must agree on age-old principles: Methodical testing and full disclosure are the best antidotes to health quackery.

•Echinacea-Treatment of Colds/Flu

- In a recent review, Linde et al. concluded that there is some evidence that preparations based on the aerial parts of Echinacea purpurea might be effective for the early treatment of colds in adults but results are not fully consistent. Linde K, Barrett B, Wolkart K, et al. Echinacea for preventing and treating the common cold. Cochrane Database Syst Rev 2006;(1):CD000530.
  .

- A study evaluated the pressed juice (5ml BID) of E. purpurea in 80 subjects. Days of illness in treated = 6 vs 9 in placebo (p=0.01). Cold symptoms were less severe in Rx group. (Schulten et al, Arzneim.-Forsch./Drug Research 2001;51:563-568

- Brinkeborn et al (Phytomedicine 1999;6:1-5) reported a reduction in symptoms in treated compared to placebo in a large (n=246) study. Used E. purpurea extract (95% herb, 5% root) or a concentrate of same or E. purpurea root extract. The aerial parts-based products showed benefit. The root extract did not.



Schulten et al. Arzneim-Forsch/Drug Research 2001;51:563 n=80 $p<0.05$

More recent studies

- Taylor et al. JAMA 2003;290:2824-2830. UW study in treating URI in children n= 407 no benefit (used pressed juice product)
- Yale and Liu Arch Intern Med 2004;164:1237-1241. Rx for colds in adults N=128 no benefit (used pressed juice)
- Goel et al. J Clin Pharm Ther 2004;29:75-83 N=282 adults. Used potent product (Echinilin) and high loading dose. Echinilin, a water/ethanol extract of E. purpurea plants contained alkamides/chicoric acid/polysaccharides in a concentration of 0.25/2.5/25 5 mg/ml in 40% ethanol. Got big benefit from treatment.
- Turner et al. N Engl J Med 2005;353:341-8. Used 3 different E. augustifolia root extracts. N=399 BUT only ~50/group. Low dose used. All given rhinovirus 39.

The Seattle Times
seattletimes.com

Thursday, July 28, 2005 - 12:00 AM

Study says Echinacea is not cold remedy

By Karen Kaplan
Los Angeles Times

Echinacea, the popular herbal remedy for fighting the common cold, does not ward off runny noses, sore throats or headaches, nor does it help speed recovery from cold symptoms, according to the results of a broad clinical trial published in today's New England Journal of Medicine.

The federally funded research was undertaken because more than 200 smaller studies had provided inconclusive and conflicting results about the benefits of the herbal remedy, which is derived from the purple coneflower.

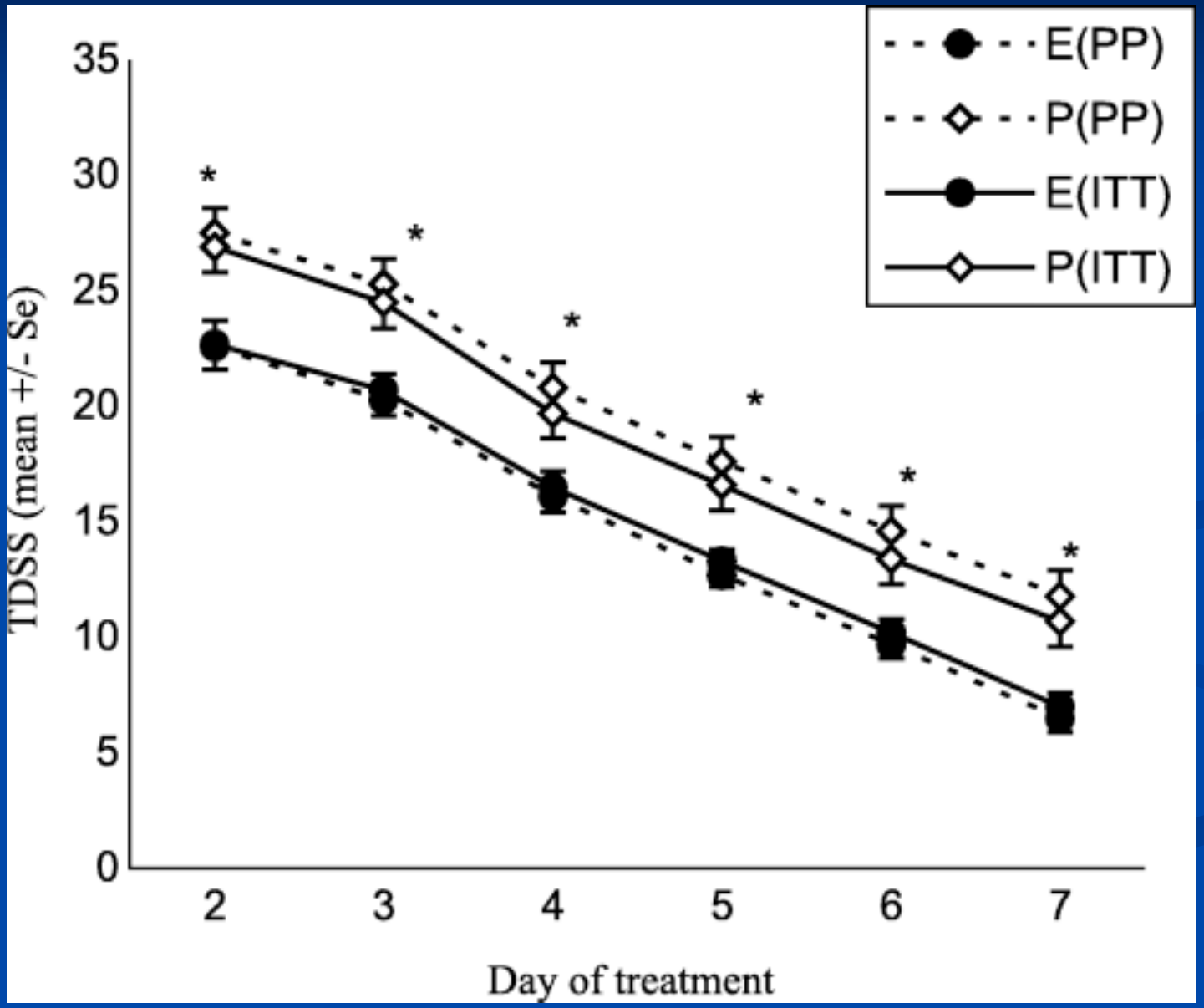
"We find no evidence that it actually does anything to common cold symptoms," said Dr. Ronald Turner, a professor of pediatrics at the University of Virginia School of Medicine and the study's lead author. "If that's the reason you're buying it, then you're wasting your money."

Echinacea enthusiasts said they do not think the results of the study merit such a clear-cut conclusion. They noted that Turner and his colleagues used only the root of one type of the plant and said the dosage given was too low.

Echinacea, a member of the same plant family as sunflowers and daisies, was used for hundreds of years by more than a dozen American Indian tribes to treat snakebites, toothaches, coughs and other ailments.

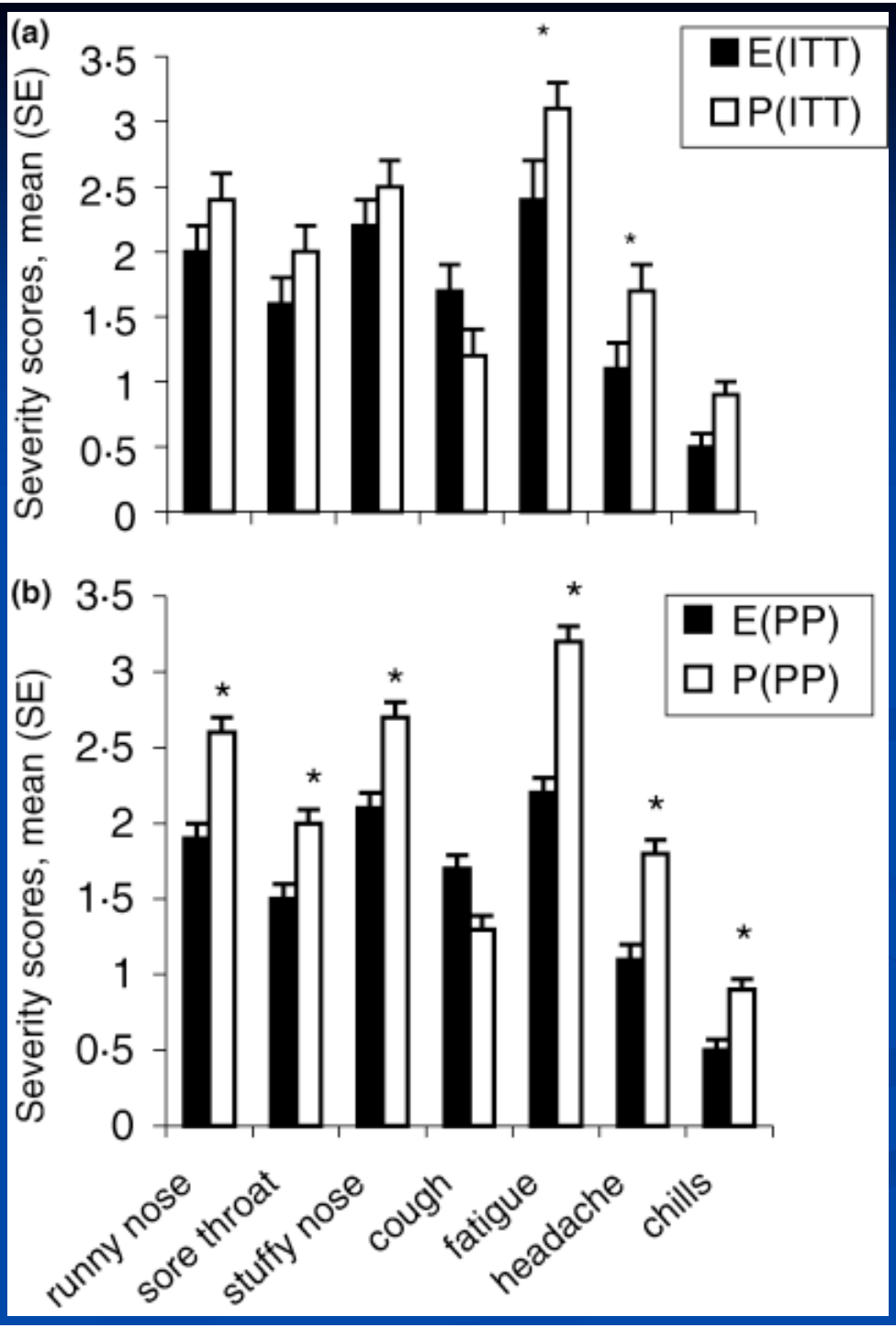
Americans spent $153 million on echinacea products last year, making it one of the five best-selling herbs in the country, according to the Nutrition Business Journal, an industry publication.

Goel et al. J Clin Pharm Ther 2004;29:75-83 N=282 echinilin standardized; 10 stat then 1 qid



Goel et al. J Clin Pharm Ther 2004;29:75-83

N=282 echinilin standardized; 10 stat then 1 qid



- Other immune stimulant uses?
  - Cancer
  - AIDS
  - bacterial and fungal infections
- Products (which is best??)
  - tablets 250mg
  - tincture
  - root extract or extract of tops or pressed juice

Echinacea

- **Summary**
  - **Efficacy**: evidence for treatment not prevention; take at first sign of cold/flu; reduce severity and duration about 25%
  - **Safety**: good; rare allergy; not where immunostimulation would be undesirable (e.g. lupus, rheumatoid arthritis); outcomes in 206 pregnant women taking echinacea were OK but-----
  - **Drug interactions**: not documented but don't give to patients taking immunosuppressive drugs
  - **Product selection**: standardized extracts usually contain about 4% phenolics
  - **Dose**: use loading dose (2x) then 1 QID
  - **Questions remaining** include
    - *Which product? Tincture? Tablets? Root extract? Flowering tops? Pressed juice? E. purpurea? E. augusifolia? E. pallida? (GWE recommends Echinamide in 2008)*