

# Fruits, Vegetables and Health: Overview



*Fruits, Vegetables, and Health:*  
A Scientific Overview, 2011



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# Causes of Death in the United States

Cause of Death	Percent of Total
1. Diseases of the heart	28.5 (World 12.2)
2. Malignant tumors	22.8 (World lung 2.1)
3. Cerebrovascular diseases	6.7 (World 9.7)
<b>Dietary factors play a role in top 3</b>	<b>3 causes = 58% of all deaths in USA</b>
4. Chronic lower respiratory diseases	5.1 (World 7.7)
5. Accidents (unintentional injuries)	4.4
6. Diabetes mellitus	3.0
7. Influenza and pneumonia	2.7
8. Alzheimer's disease	2.4

CDC/NHS, National Vital Statistics System, WHO



# Global Burden

# Global Resource

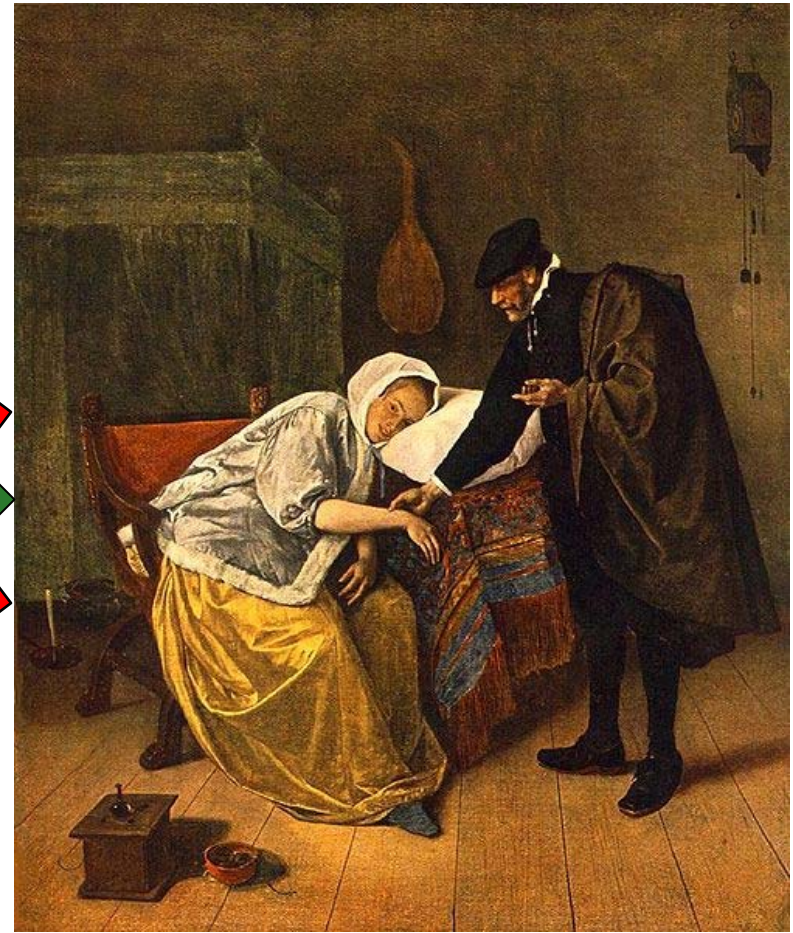
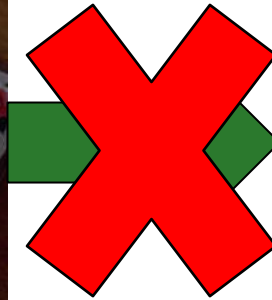


Textscience.org

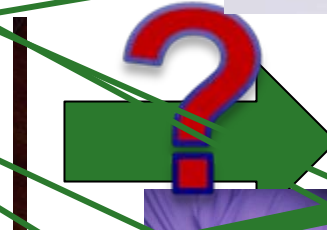
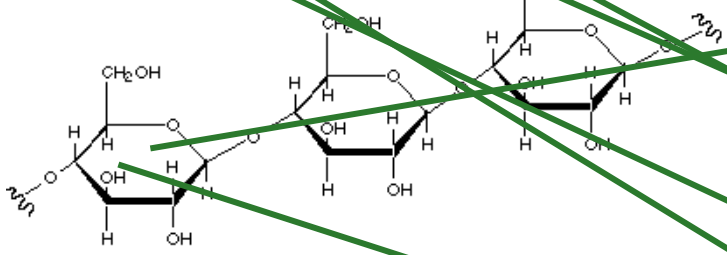
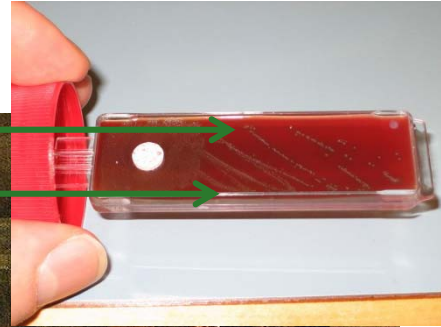
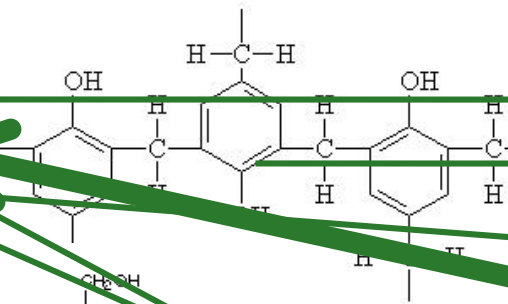
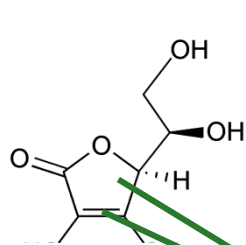




# Examining the Link: FV Intake and Disease



# Examining the Link: FV Intake and Disease





40 healthy adults

- No conditions present that may produce hair loss or gain
- Provided informed consent



Baseline (before treatment) measurement of normal hair loss

Subjects randomized into vitamin X supplement and placebo groups

The perfect study....in a fairytale world!



20 subjects receive a placebo for 3 months



Pills distributed to subjects by double-blind procedure



20 subjects receive 25,000 IU vitamin X for 3 months

Hair loss measured

Hair loss measured



Difference in hair loss between groups tested for statistical significance

# Study Approach 101 – Refer to appendix

- Plan for power and applicability
  - Can't generalize findings
- Need to quantify FV intake/intervention
  - Challenge!
- Decide duration of exposure
- Assess outcomes
  - Which ones?
- Avoid bias at all levels

# Grades of Evidence Based on Study Design

U.S. Preventive Services Task Force 1996

- **Level I** - Evidence from at least one properly conducted randomized, controlled trial
- **Level II (1)** - Evidence from well-designed controlled trials without randomization
- **Level II (2)** - Evidence from well designed cohort or case control analysis (preferably from more than one center)
- **Level II (3)** - Evidence from multiple time series with or without intervention (penicillin)
- **Level III** - Opinion of respected authorities based on clinical experience or reports of expert committees



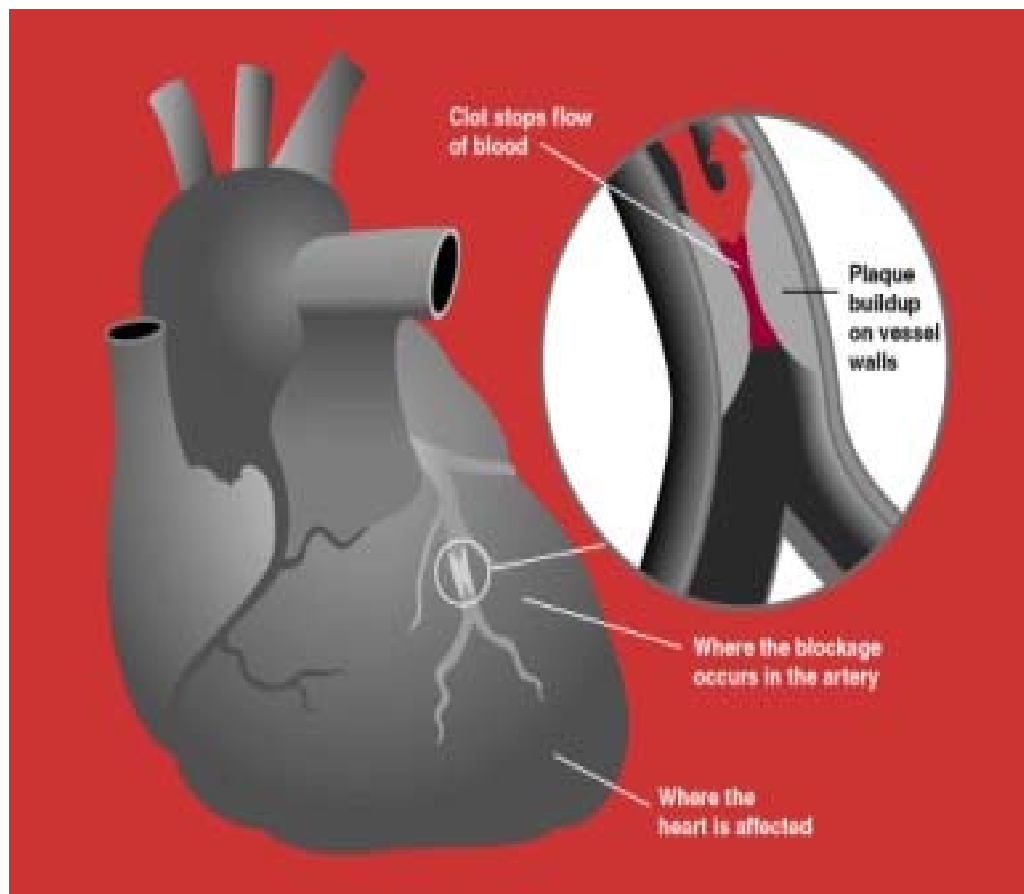
# Fruit and Vegetable Intake and Health

- Arthritis
- Bone Health
- **Cancer**
- **Cardiovascular Disease**
  - Stroke, Blood pressure, related processes
- **Cognition**
- **Diabetes**
- **Pulmonary Health** –
  - Asthma, COPD
- Skin Health
- **Weight and Obesity**

# Cardiovascular Disease

- Includes diseases of the blood vessels supplying the heart (coronary heart disease, CHD), brain, and periphery, among other disorders
- 29% of world deaths, top killer globally

WHO Fact sheet No. 317 Jan 2011

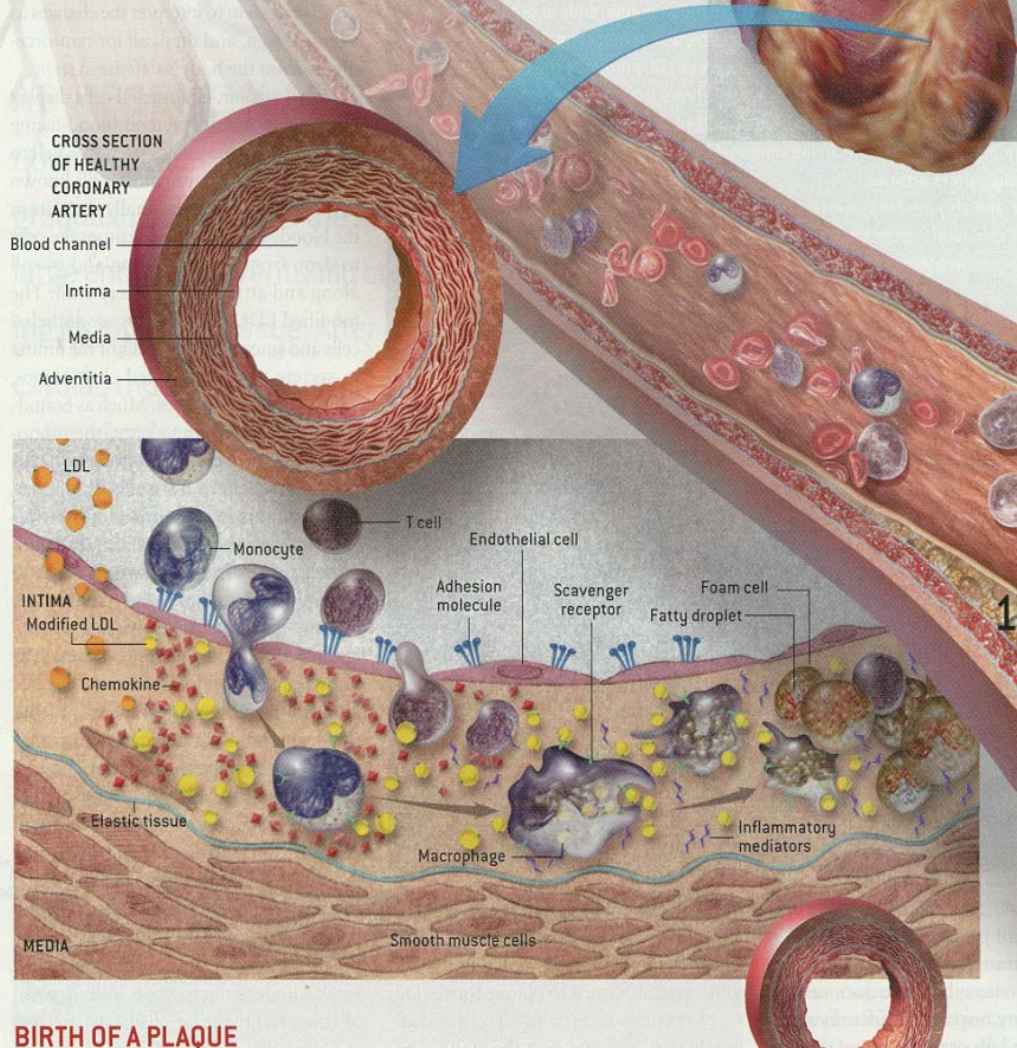


U.S. Government (public domain)



# Inflammation's Many Roles

INFLAMMATION—now recognized as a central player in atherosclerosis—occurs when certain white blood cells (those that normally constitute the first line of defense against infection) invade and become active in a tissue. These diagrams depict the growth of an atherosclerotic plaque in a coronary artery; the three close-up views highlight some of the inflammatory processes that can ensue when someone's blood carries too much low-density lipoprotein (LDL).



**BIRTH OF A PLAQUE**

# How Might Fruits and Vegetables Help?



**Many diseases  
have shared  
mechanisms**

- Antioxidant activity
- Anti-inflammatory effects
- Modulate production/uptake of cholesterol
- Regulate blood pressure
- Promote healthy endothelial function
- Reduce platelet aggregation and
- Affect cell signals associated with cell growth or cell death, proliferation
- Stimulate immune responses, scavenging responses and more
- Detoxification effects
- Antibacterial, anti-viral

# Coronary Heart Disease Risk Reduction

- Consumption of more than 5 servings of FV/day (>391 g) associated with a 17% reduced risk of CHD (P<0.001)

- Based on 2007 meta-analysis of 13 cohorts published between 1992 and 2004

*J Human Hypertension. 2007;21:717-728.*

- Analysis published a year earlier included 6 cohort studies and showed a 4% reduction in CHD risk for each additional portion/day of FV intake

*J Nutr. 2006;136:2588-2593*



# Coronary Heart Disease Risk Reduction

- **Jan 2011!**
- 8 servings of fruits and vegetables per day (80 g/portion) was associated with a significant 22% reduction in CHD mortality compared to <3 servings per day

European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart study. 2010 *Eur Heart J*: doi:10.1093/eurheartj/ehq465.

- 313,074 men and women
- Followed for an average of 8.4 years



# Quantifying Intake



Source: CafeMom  
Images via Adriana  
Velez

# Coronary Heart Disease Risk Reduction

- Other new prospective data from 7-10 year follow up cohorts in The Netherlands, Denmark, Japan, Italy; case study Serbia
  - each show inverse association between FV intake and CHD
- Caution regarding absolute estimates of risk reduction from case control and observational trials but collective data are promising

# Stroke Risk Reduced by FV Intake

- 3-5 servings of FV day reduced risk of stroke by 11% compared to < 3/day;
  - 26% reduction if more than 5 FV/day\*
- Supported by recent data from cohort of Finnish men and women (n=3932) followed for 24 years
  - Br J Nutr. 2009;102:1075-1083*
  - Cruciferous, citrus, legumes, root vegetables
- Consume more than 5 servings of FV each day to reduce risk of stroke
  - \*Lancet. 2006;367:320-326*



# Blood Pressure

- Fruit intake may be particularly beneficial in overweight subjects
  - BMI >25 = 79% lower odds of being hypertensive if consuming highest quartile of fruit intake (P=0.005)

*J Human Hypertension advance online publication. 2010:1-8*

- Inconsistent results in studies with subjects of variable ages and duration
  - more work needed

# FV and Risk of All Cancers

- Prospective analysis (n=25,623, 851 cases) of Greek cohort of the EPIC study, 7.9 years
  - Intake of FV (median intake of 837 g/day) reduced risk of overall cancer

*Cancer Epidemiol Biomarkers Prev. 2008;17(2):387-392*

- Other studies null effect of FV on overall cancer risk
- Issues: complex and long term etiology of cancer, some studies limited variety of FV, low median intake of FV (as low as 204 g/day)



# Site Specific Cancers: Digestive Tract

- Vegetable intake protective particularly for **cancers of the digestive tract**
- Multi-center case-control studies in Italy (n=10,000 subjects and 17,000 controls)
- 20-70% lower risk between the highest and lowest levels of vegetable intake

*Nutr and Cancer. 2009;61(6):756-766*



# Site Specific Cancers: Breast

- Risk of breast cancer may be reduced in association with vegetable intake
- Prospective report (USA); 2 case studies (China, Korea) published in 2009-2010 suggested potential benefit
- Individual FV, cruciferous, China: green leafy vegetables, tomatoes, and bananas, associated with lower risk

*Am J Epidemiol.* 2010;172:1268-1279

*Int J Cancer.* 2009;125:181-188

*Nutr and Cancer.* 2010;62(4):443-453



# Site Specific Cancers: Lung

- New analysis of the EPIC cohort (n=452,187, followed for 8.7 years)
  - inverse association between lung cancer and increased variety of vegetable consumption, mainly in current smokers

*Cancer Epidemiol Biomarkers Prev. 2010;19(9):2278-2286*

- Cruciferous vegetables may be modestly but inversely associated with lung cancer risk.

*Cancer Epidemiol Biomarkers Prev. 2009;18(1):184-195*



# Site Specific: Esophageal and Gastric

- Reduced risk in case-control studies
- Prospective studies less conclusive
- Oropharyngeal cancer approximate 50% risk reduction associated with FV

*Nutr Clin Prac. 2009;24(2):250-260*

- Duration of exposure and the type of FV are important
  - Citrus strongest inverse association



# Processes Associated With Aging



# Cognitive Function Linked to FV Intake

- FV may attenuate decline of normal aging
- Fewer than 2 servings FV per day associated with decline in at least two prospective trials
  - Risk of poor function on tests of reasoning, verbal fluency, memory associated with  $< 2$  FV/day
    - 60% risk after 11 year follow-up
    - 85% after 17 years

*Am J Epidemiol. 2009;170(4):428-437*

- Animal work suggests possible benefit of FV on degenerative diseases
  - e.g. Alzheimer's



# Promising Observational Data: Cognition

## Cross-sectional studies:

- Norway, dose-dependent effect of FV intake\* = improved function on 4 of 6 tests of cognitive function

- \*FV up to 500 g/day, V up to 150-200 g/day

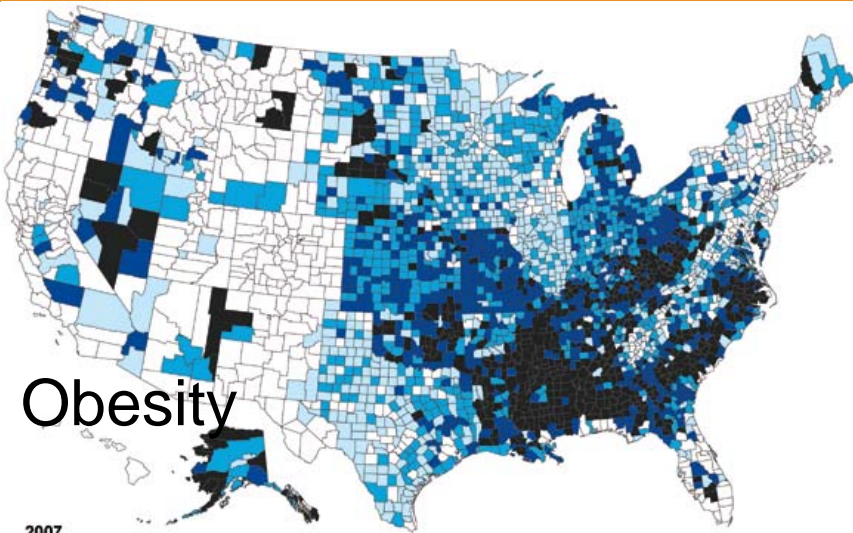
*The Hordaland Study. Br. J Nutr. 2010;104:1190-1201*

- Germany, FV intake >350 g/day linked to better neuropsychological testing vs. intake of 0-100 g/day

- Independent of age! *J Alzheimer's Disease. 2009;17:921-927*



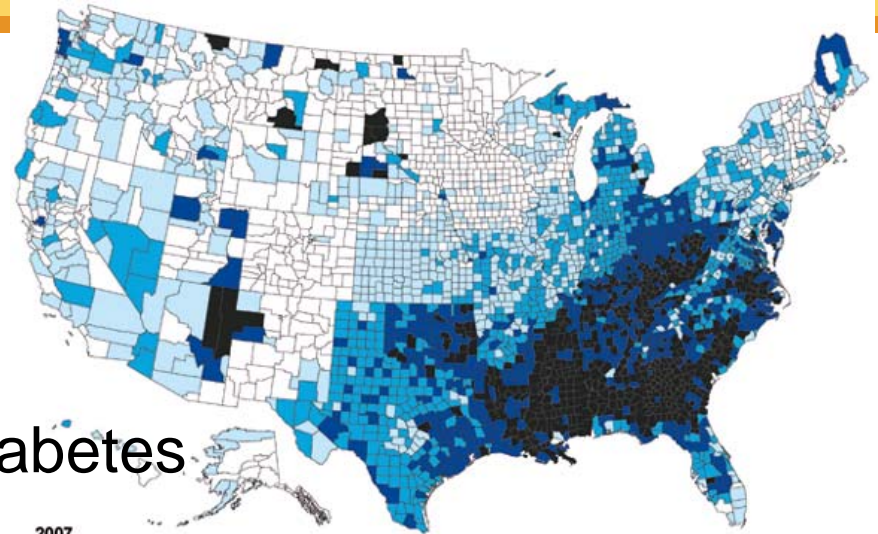
# The Epidemic of Diabetes and Obesity



Obesity

2007  
Age-adjusted percent of adults  $\geq 20$  years old who are obese

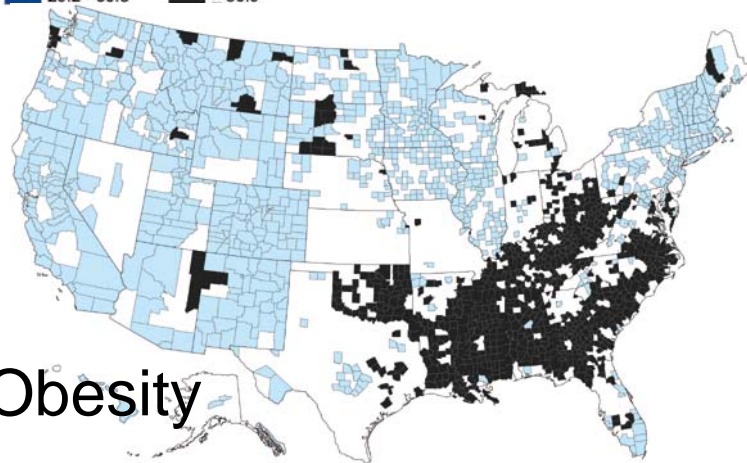
0 - 26.2	26.3 - 27.7	27.8 - 29.1	29.2 - 30.8	$> 30.9$
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Diabetes

2007  
Age-adjusted percent of adults  $\geq 20$  years old with diabetes

0 - 7.0	7.1 - 8.1	8.2 - 9.0	9.1 - 10.5	$\geq 10.6$
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Diabetes and Obesity

2007  
Counties in top 2 quintiles for both diabetes and obesity  
Counties in bottom 2 quintiles for both diabetes and obesity

Source: CDC



# Diabetes: Worldwide Increase

## кръвна захар проба

Препоръчва се да не се взима кръв от палеца или показалеца поради чувствителността на тези пръсти и честота им употреба.



# Reduced Risk of Diabetes Linked to FV

- EPIC – Norfolk cohort, middle-aged subjects moderately overweight
- 12 year follow-up data
  - 22% reduced risk of diabetes for highest versus lowest quintile of FV intake
  - 30% reduced risk associated with fruit alone
  - 20% for vegetables

*Arch Intern Med* 2008;168(14):1493-1499



# Reduced Risk of Diabetes Linked to FV

- **Nurses' Health Study** - 18 year follow-up = 18-26% lower risk associated with a 3-serving-per-day increase of fruit ( $P < 0.001$ ) *Diabetes Care. 2008;31(1311-1317)*
- 9-12% reduction with a 1-serving-per-day increase in green leafy vegetables (spinach, kale, and lettuces).
- Meta-analysis of 6 studies
  - Trend analysis: 1.35 servings of green leafy vegetables compared to 0.2 servings per day was associated with risk reduction of 14% ( $P = 0.01$ ) *BMJ. 2010;341*
  - However, significant heterogeneity, fewer men



# Lung Function and Pulmonary Health

- Healthy function and asthma - recent focus on adolescents, children
  - FV intake below recommended even at highest percentile of intake
- <0.25 servings/day linked to lower lung capacity; more self-reported bronchial symptoms *Chest. 2007;132:238-245*



# Lung Function and Pulmonary Health

- FV intake may be more protective if oxidant/inflammatory stressors are present
  - e.g. children with asthma
  - higher ozone areas in Mexico
- FV associated with reduced inflammatory markers, improved lung function

*Resp Res.* 2009;10:122

- Maternal FV intake less likely to influence pulmonary function in offspring



# FV Intake Reduces Predicted Weight Gain

- EPIC data - 5 European sites
  - Median FV intake 324 g/day in women
  - 377 g/day in men
    - wide range between countries.
- Over 6.5 year follow-up each 100 g of fruit consumed reduced predicted weight gain by 14 grams
  - Small but cumulative benefit
- More pronounced benefit in ex-smokers
  - Weight attenuated by 37 g/100 g fruit



# FV and Body Weight Regulation

- Brazil, 6 month intervention
  - FV included, n=80 middle age subjects, mainly women
- Reduced BMI and FV intake correlated
  - Total vegetables (P=0.002), fruits (P=0.011), and dark or yellow fruit/vegetables (P=0.035).
- Each 100 g increase in fruit intake associated with 500 g lower weight
  - Vegetable intake = 300 g lower weight
  - Compliance; 20% study drop out

# Other Potential Benefits of FV Intake

- **Osteoarthritis:** 10 year follow-up, fruit intake (vitamin C)
  - inversely associated with MRI bone measures including tibial bone area (P=0.04) and bone marrow lesions (28%) (P=0.05)
  - predictive of reduction in risk of future osteoarthritis
- **Bone Health:** bone mineral density, markers of bone metabolism, risk and/or fractures in postmenopausal women
  - some promising but inconsistent data, more work to be done
- **Glaucoma:** Reduced risk associated with 2 servings/week vegetables vs. fewer than 1/week
  - 64% reduction in risk associated with carrots (P=0.009)
  - Peaches, collard and kale also protective
- **Skin Health?** Indirect link through anti-oxidant processes; maternal intake of citrus linked to reduced eczema in infants



# Final Considerations

- Growing number of studies
- Many investigators cite that benefits of whole exceed the “the sum of the parts”
- Still many unanswered questions related to quantity, variety, duration
- Studies of worldwide populations important
- Mechanistic studies important

# The Future

- Well controlled randomized clinical trials warranted
  - Focus on accurate and detailed quantitation
- Further define importance of FV intake related to quantity, variety, duration
- Emphasis on applicability of the research outcomes
  - Strategies to increase FV intake needed