

Herbal Remedies and HIV Risks and Benefits

**John J. Faragon PharmD, BCPS, AAHIVE
Regional Pharmacy Director
New York/New Jersey AIDS Education and
Training Center**

Overview

- **Discuss the role of the FDA in regulating herbal treatments**
- **Discuss common herbal therapies used by patients regardless of HIV status**
- **List common uses of herbal therapies**
- **Review herbal therapies to be avoided in patients receiving HIV treatment**

Herbal Therapy and the FDA

FDA Regulation of Dietary Supplements – The Problem...

- **Manufacturer does not have to prove the safety and effectiveness before it is marketed to consumers**
 - **No claims about efficacy are evaluated by the FDA**
- **Only until the product is on the market does the FDA monitor the herbal for safety**
- **Warning statements issued as needed to the public only after the safety issues is identified**

FDA Alert Examples

- **Kava – used for anxiety stress, tension, insomnia**
 - **Hepatic Toxicity Possibly Associated with Kava-Containing Products (CDC MMWR Report, November 29, 2002)** The FDA advised consumers of the potential risk of severe liver injury associated with the use of kava-containing dietary supplements.
 - **Letter to Health Care Professionals: FDA Issues Consumer Advisory That Kava Products May be Associated with Severe Liver Injury* March 25, 2002**
 - **Letter to Health Care Professionals about FDA Seeking Information on Liver Injury and Kava products* December 19, 2001**

FDA Alert Examples

- **LipoKinetix:**
 - **FDA Warns About Weight Loss Product**
FDA alerts consumers and health care professionals about LipoKinetix, a dietary supplement weight loss product. This product has been implicated in a number of serious adverse reactions related to several cases of liver injury.
 - **FDA Warns Consumers Not to Use the Dietary Supplement LipoKinetix* November 19, 2001**
 - **Letter to Health Care Professionals on Hazardous Dietary Supplement LipoKinetix* November 19, 2001**
 - **Letter to Distributor on Hazardous Dietary Supplement LipoKinetix* November 19, 2001**

FDA Alert Examples

- **St. John's Wort and Indinavir**
 - **FDA Public Health Advisory: Risk of Drug Interactions with St. John's Wort and Indinavir and Other Drugs February 10, 2000**

Other Risks of Herbal Therapy

- **Herbal products are not required to meet quality control standards prior to marketing**
- **Most have undergone limited or no safety and efficacy research**
- **Patients may delay conventional medical treatment**
- **May have a false sense of the safety of natural products**

What's really in there?

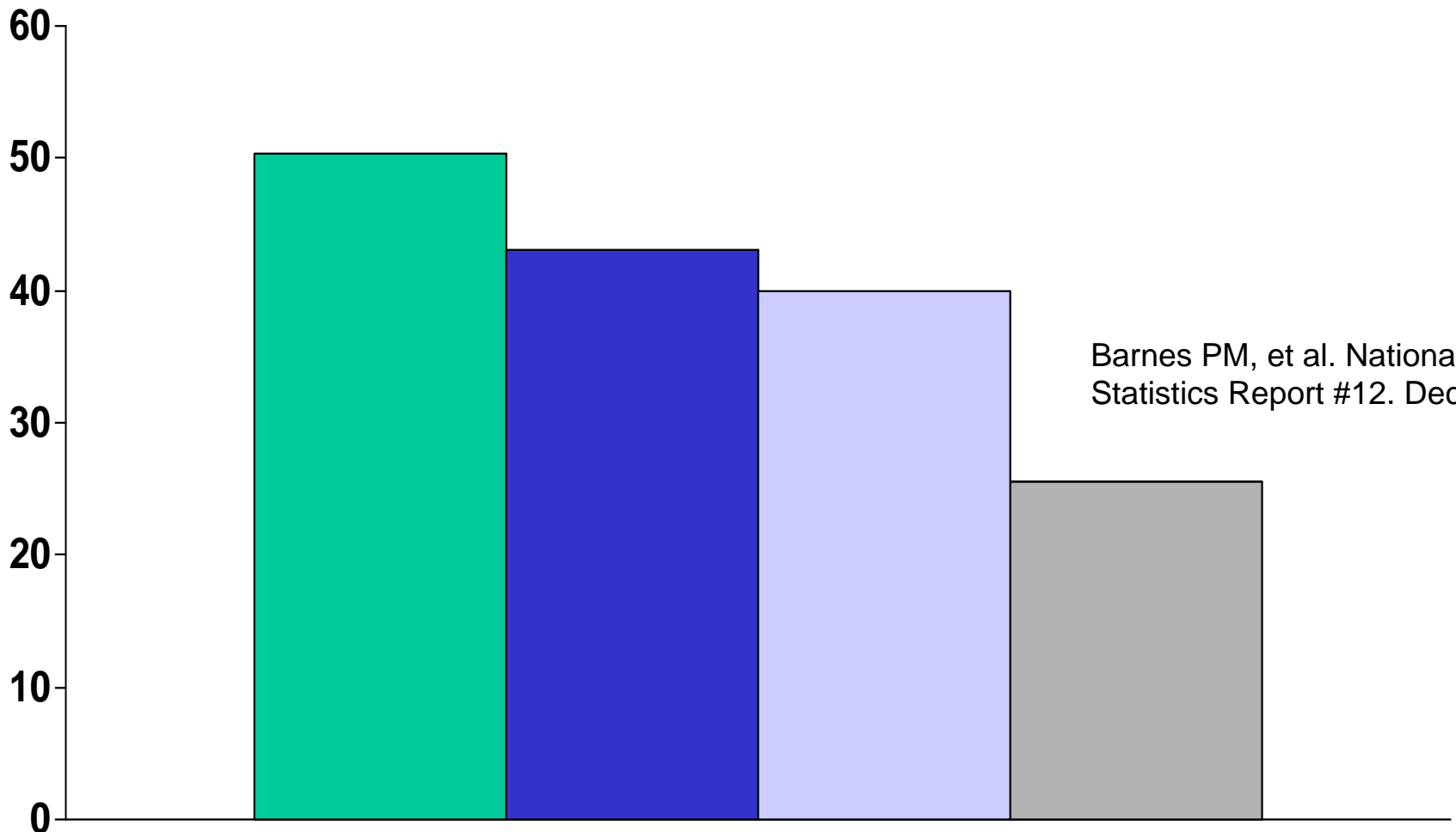
- An herbal supplement may not contain the correct plant species
- The amount of the active ingredient may be lower or higher than the label states
- The dietary supplement may be contaminated with other herbs, pesticides, or metals, or even adulterated with unlabeled ingredients

Herbal Therapy Use and the General Population

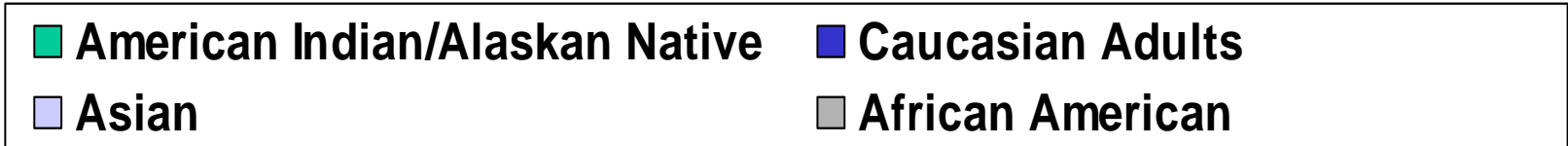
National Health Statistics Report #12 – December 2008

- **Data from the National Health Information Survey**
- **Over 23,000 persons 18 and older**
- **Complimentary therapy rates nearly 4/10 in past 12 months**
- **Most common was use of non vitamin, non mineral, natural products (18%)**
- **Results also include chiropractic care, meditation, yoga, breathing exercises, etc.**

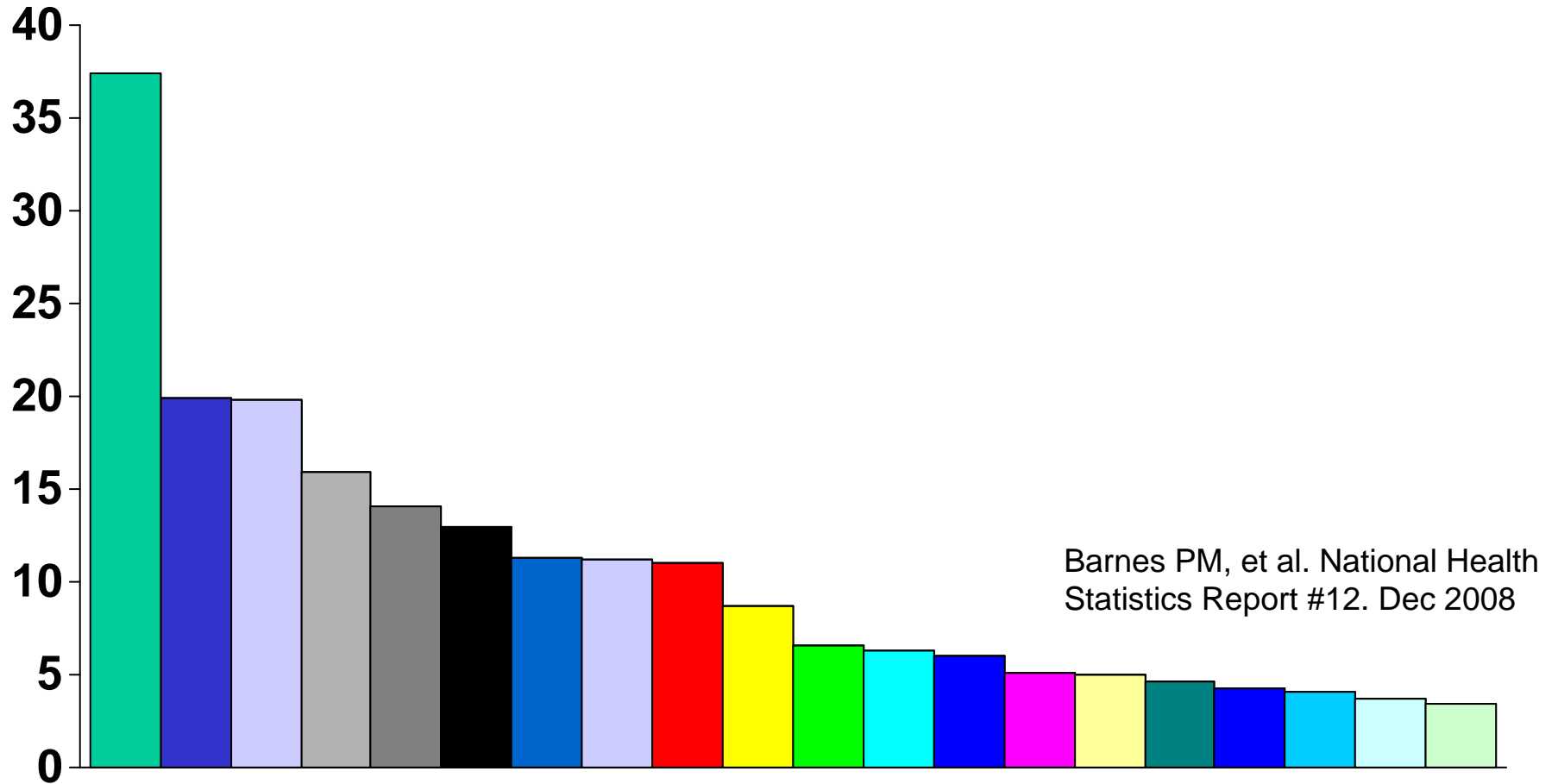
Who uses Complimentary Therapy?



Barnes PM, et al. National Health Statistics Report #12. Dec 2008

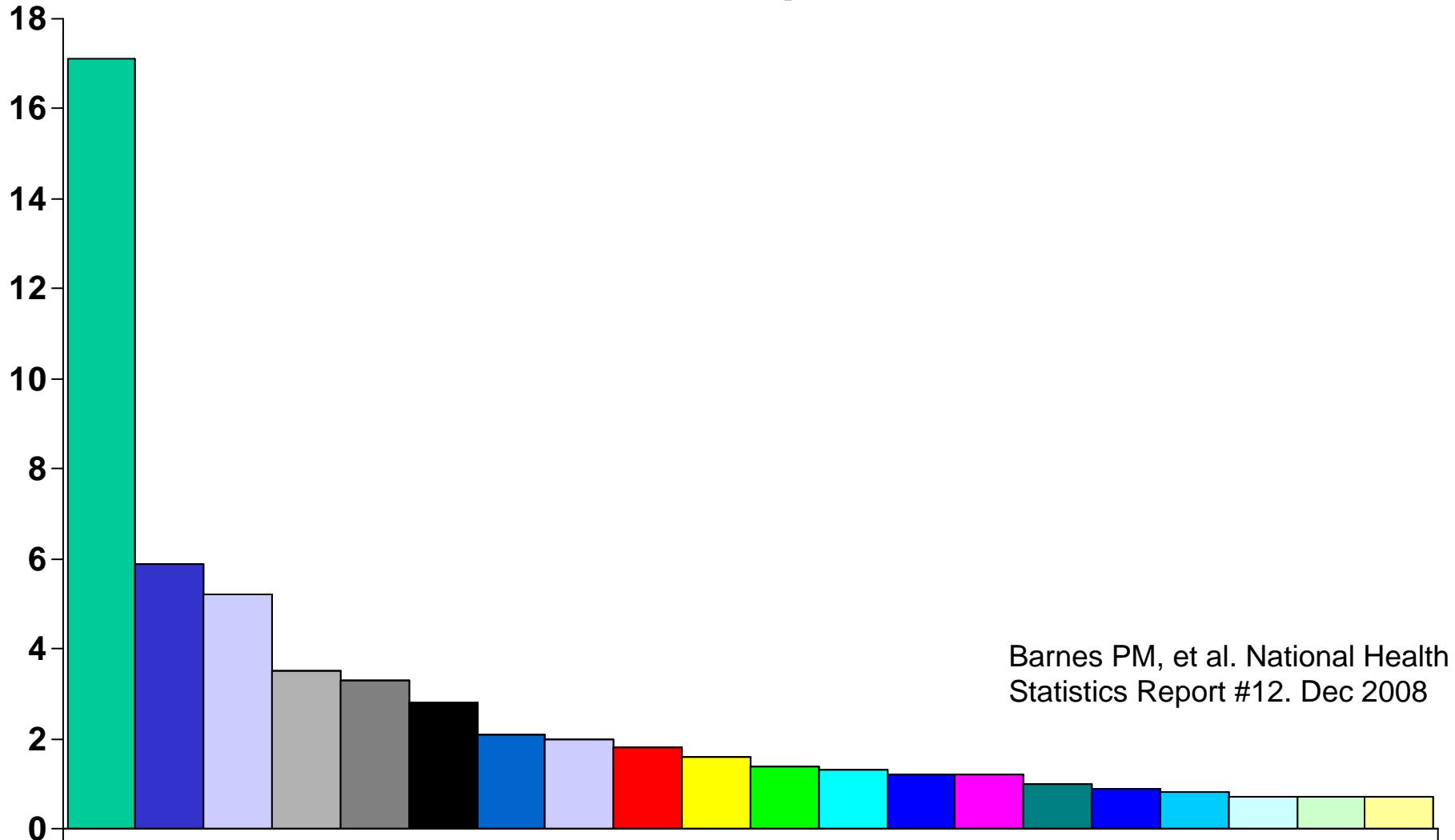


Common Herbal Therapies Used in the United States



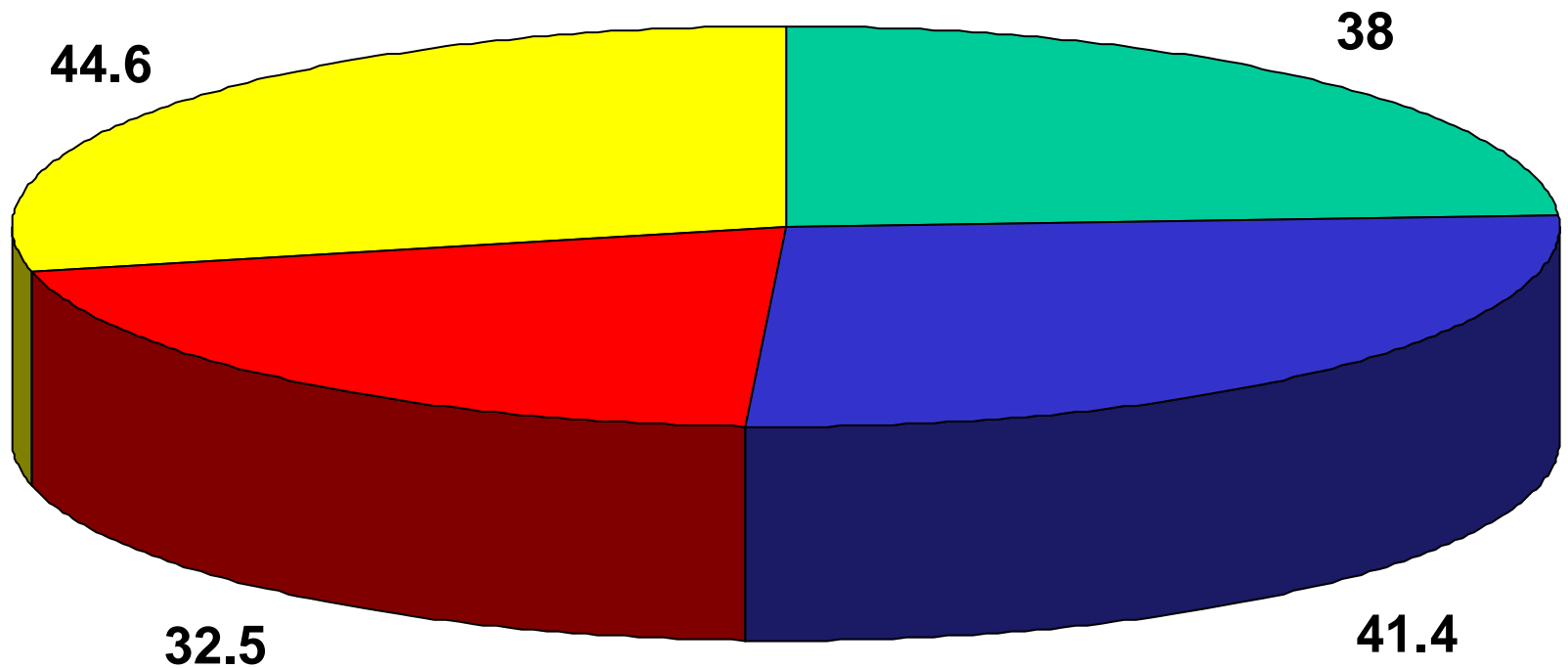
- | | | | |
|------------|------------------|--------------|-------------|
| Fish Oil | Glucosamine | Echinacea | Flaxseed |
| Ginseng | Combination herb | Ginkgo | Chondroitin |
| Garlic | CoQ10 | Fiber | Green tea |
| Cranberry | Saw Palmetto | Soy | Melatonin |
| Grape Seed | MSM | Milk Thistle | Lutein |

Common Uses of Herbal Therapies in the Unites States



Back Pain	Neck Pain	Joint Pain	Arthritis	Other
Anxiety	Cholesterol	Head cold	Other MS	Mig Headache
Insomina	Stress	Stomach	Depression	Reg Headaches
HTN	Fibromyalgia	DM	Sprain	CHD

Where Does Herbal Therapy Use Occur?



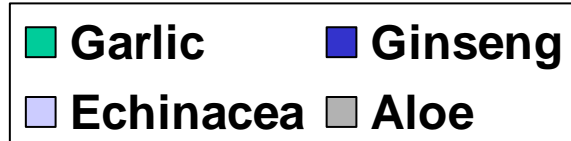
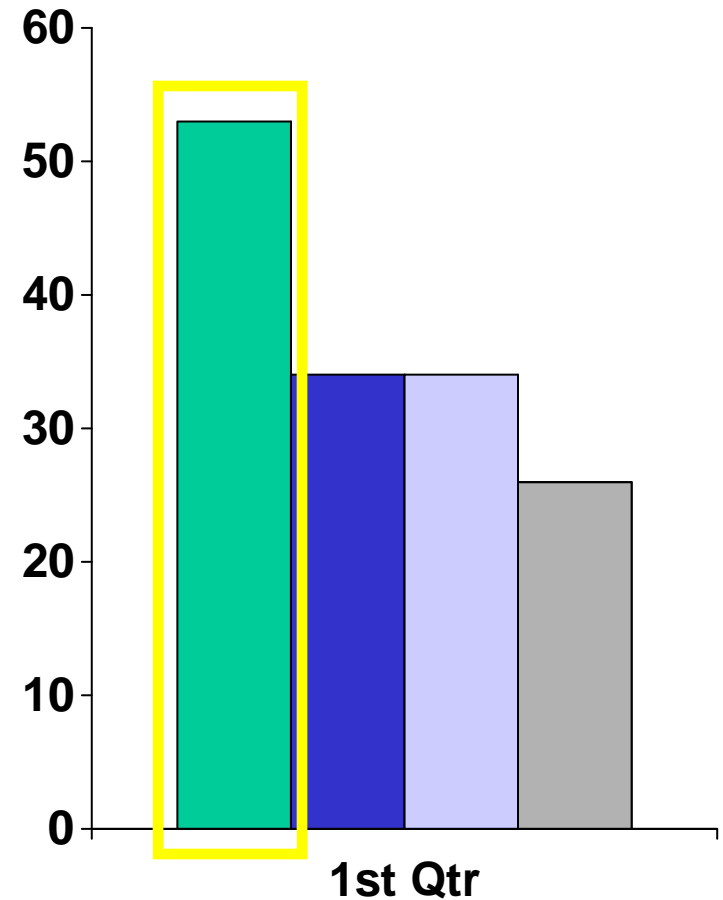
Barnes PM, et al. National Health
Statistics Report #12. Dec 2008

■ Northeast ■ Midwest ■ South ■ West

Herbal Therapy Use and HIV

Herbal Therapy with HIV is Common

- **AMCOA Study – Alternative Medicine Care Outcomes in AIDS study**
- **1675 patients**
- **63% reported using alternative medicine while on ARV therapy**



Herbal Therapy Usage

– Fairfield et al

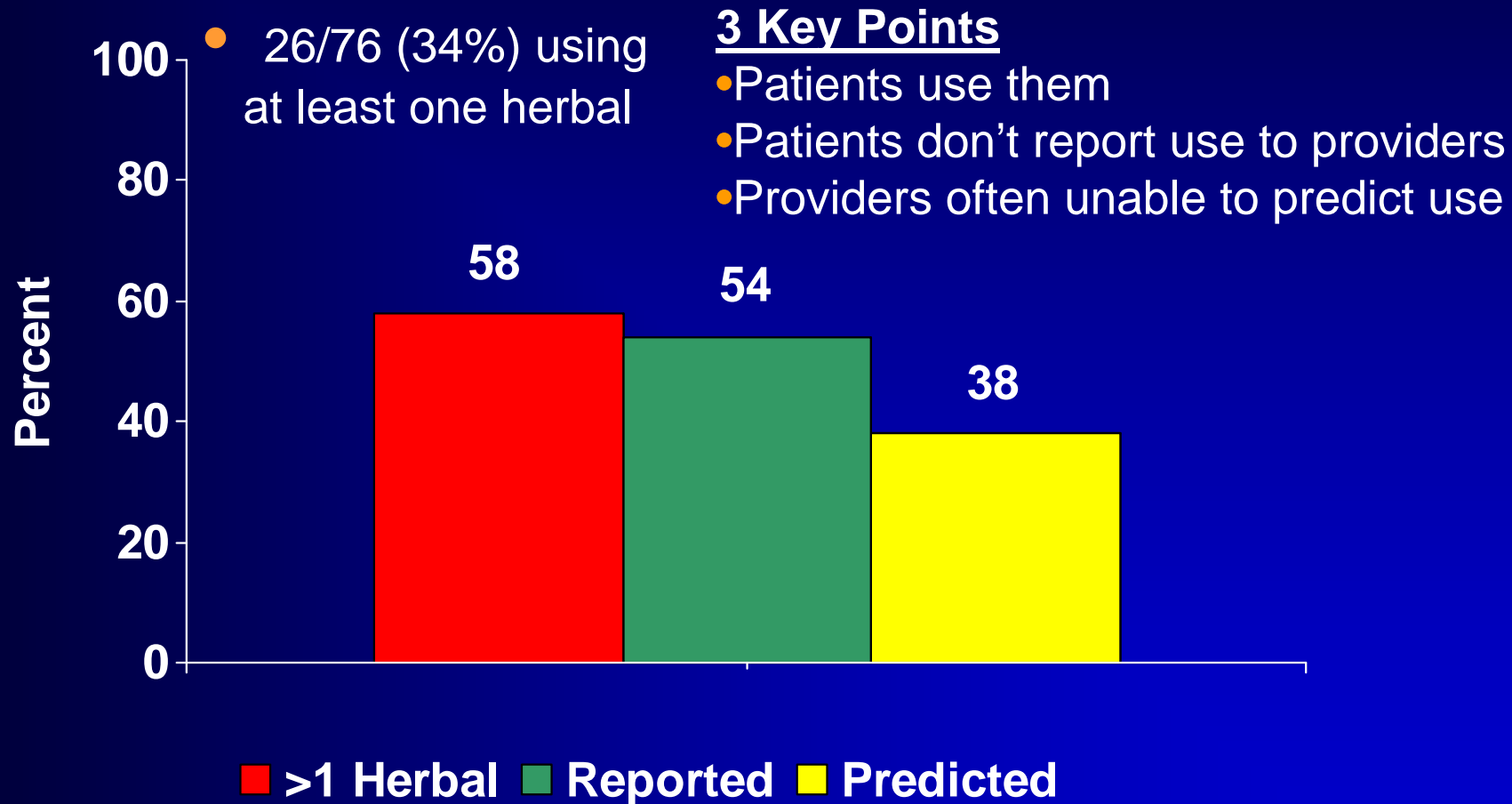
- Surveyed 180 HIV-infected patients
- 68% reported using vitamins, herbals, or dietary supplements
- Most used to fight HIV or boost immunity

Herbal Therapy Usage

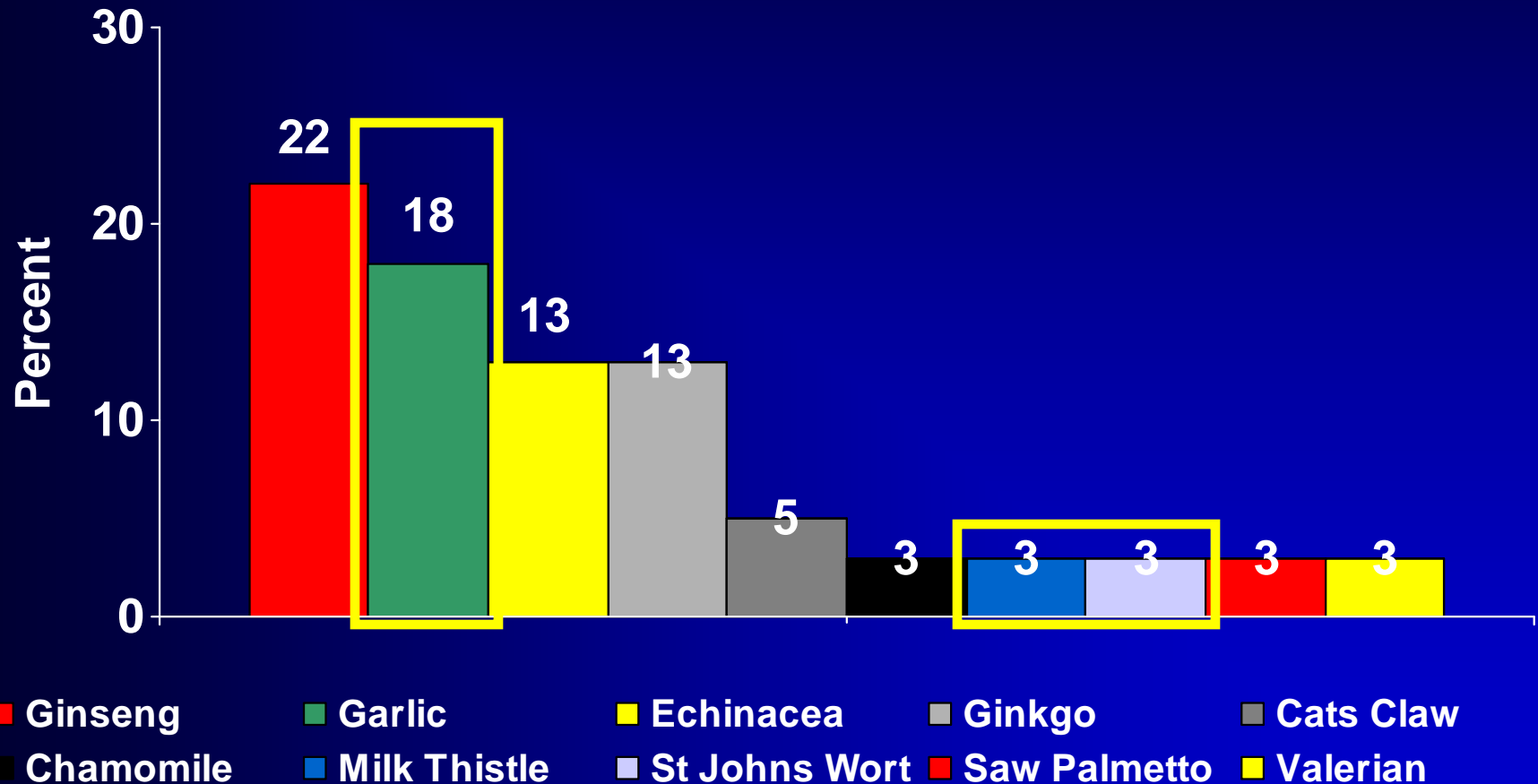
– Anderson et al

- Surveyed 184 HIV-infected patients from 3 clinics in Philadelphia region
- 40% taking at least one alternative therapy
 - 15% taking Chinese herbs
- Immune enhancing agents most common (83%)

Herbal Therapy Use at Albany Medical Center – HIV Medicine



Herbal Therapy Use at Albany Medical Center – HIV Medicine



Select Herbal Therapies

Cats Claw

- **Widely promoted to enhance immune function**
- **?? increase in CD4 counts, results never published in medical journals**
- **No reported side effects in HIV, though metabolized the same way as PI and NNRTIs**
- **Potential risk exists with HIV meds**

Lactic Acidosis

NRTI Class Side Effect

- **DNA polymerase γ**
 - responsible for mtDNA replication
- **NRTI's inhibit polymerase γ**
 - potential for mitochondrial toxicity
- **DNA polymerase γ inhibited, mtDNA synthesis decreased, lactic acid production increases.**

Glucose/Glycogen

ATP

Pyruvate

CO₂ + H₂O

Lactate

Mitochondria

Acetyl-CoA

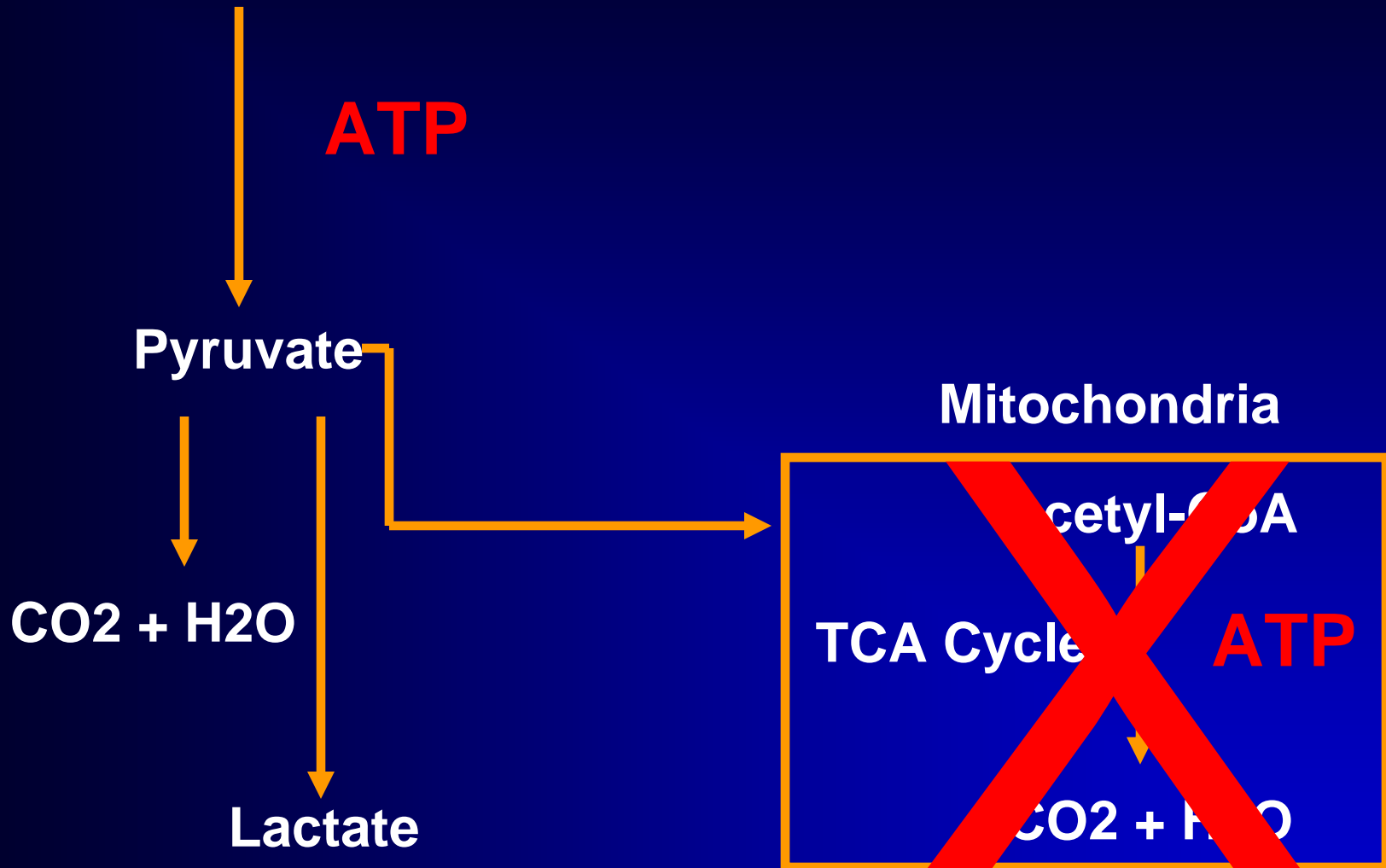
TCA Cycle

ATP

CO₂ + H₂O

GLYCOLYSIS

OXIDATIVE PHOSPHORYLATION



Coenzyme Q10

- Also known as ubiquinone
- Assists with energy production in mitochondria
- Can be used to treat lactic acidosis from ARV therapy
- Riboflavin and levocarnitine may also be used for treatment

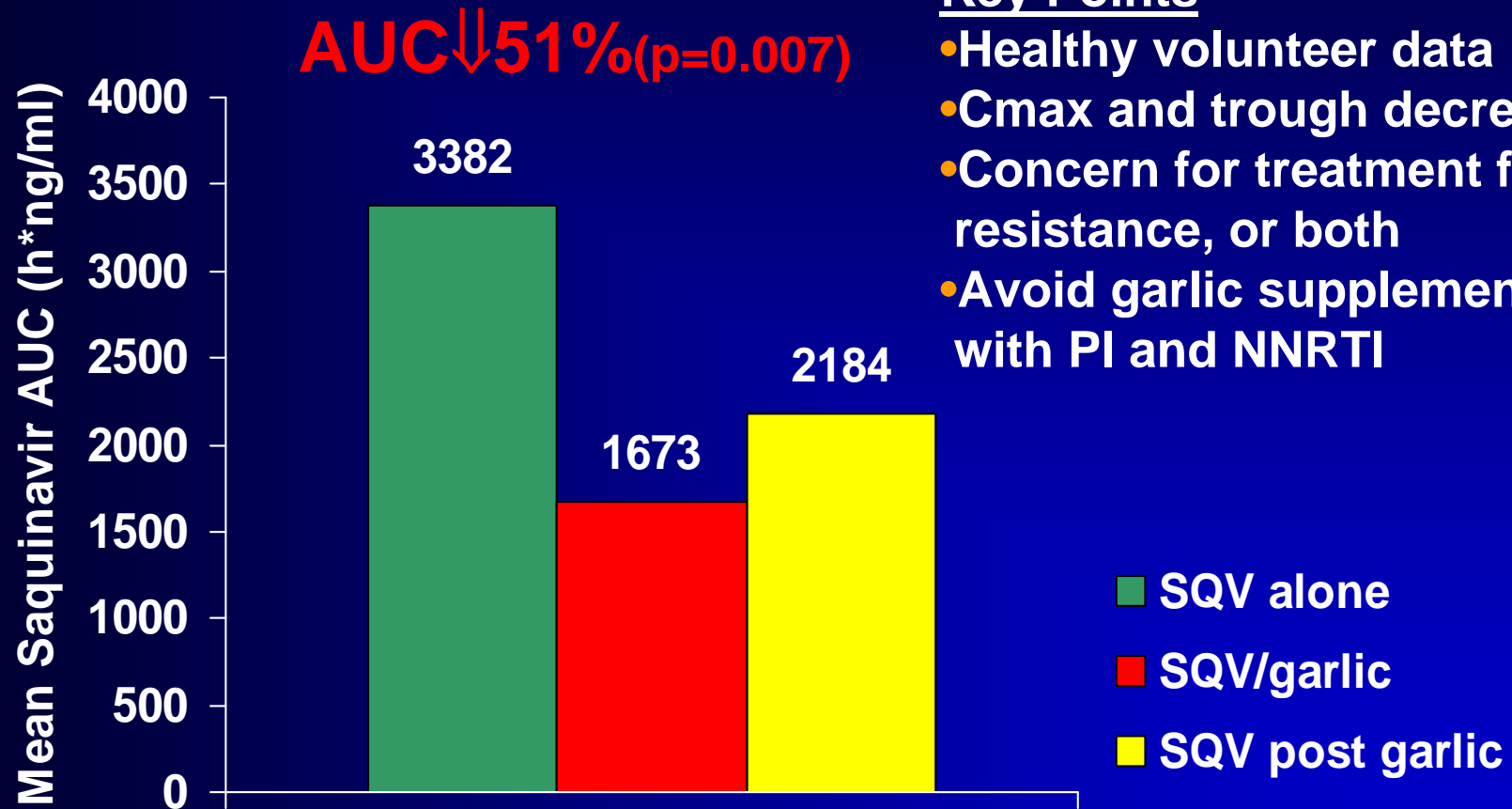
Echinacea

- Promoted to treat the common cold and enhance the immune system
- Risk of enhancing HIV replication has been suggested with long term use
- Often contained in herbal mixtures
- **AVOID** long term use in HIV

Garlic

- **Promoted to treat fungal infections**
- **May also lower cholesterol**
- **Interacts with protease inhibitors and likely NNRTIs as well**
- **Dietary garlic probably OK**
- **AVOID in HIV**

Garlic and Fortovase®



Key Points

- Healthy volunteer data
- C_{max} and trough decreased
- Concern for treatment failure, resistance, or both
- Avoid garlic supplements with PI and NNRTI

Ginger

- **Used to combat nausea, and maybe for morning sickness**
- **Used in HIV to combat nausea from HIV medications**
- **Strong antioxidant properties**
- **Inhibits platelet aggregation, increases bleeding risk, caution if low platelet counts**

Gingko Biloba

- **May help with memory loss in elderly, has antioxidant properties**
- **Used in HIV to treat memory loss or in AIDS related dementia, though not studied**
- **Some data in Alzheimers showing minimal efficacy**
- **Inhibits platelet aggregation**
- **Avoid with anticoagulants**

Ginseng

- **May help with stress**
- **Potential benefit to immune system,
? Increase in CD4 cells**
- **Avoid with anticoagulants**
- **May be OK, though no studies with
HIV medications**

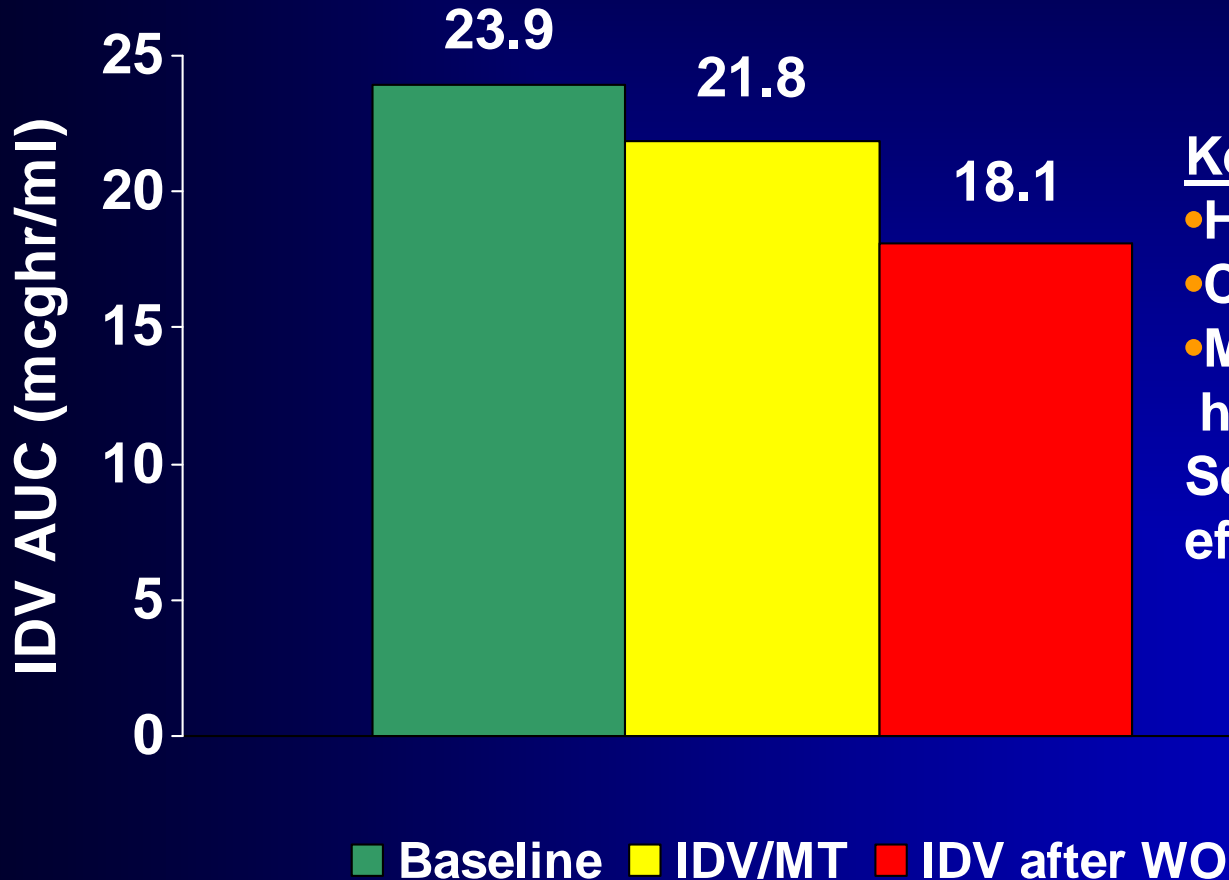
Goldenseal

- **May be used to treat diarrhea**
- **Avoid in pregnancy**
- **High doses can cause nausea, vomiting and neuropathy**
- **Interferes with Vitamin B metabolism**
- **Misconception that it speeds up THC metabolism and interferes with urine drug screens**

Milk Thistle

- **Used to reverse liver damage, sometimes used in liver related diseases ie HCV/HBV**
- **Studies lacking for efficacy**
- **Reduces drug levels of HIV medications, but not to same degree as other herbal therapies**

Milk Thistle and Crixivan®



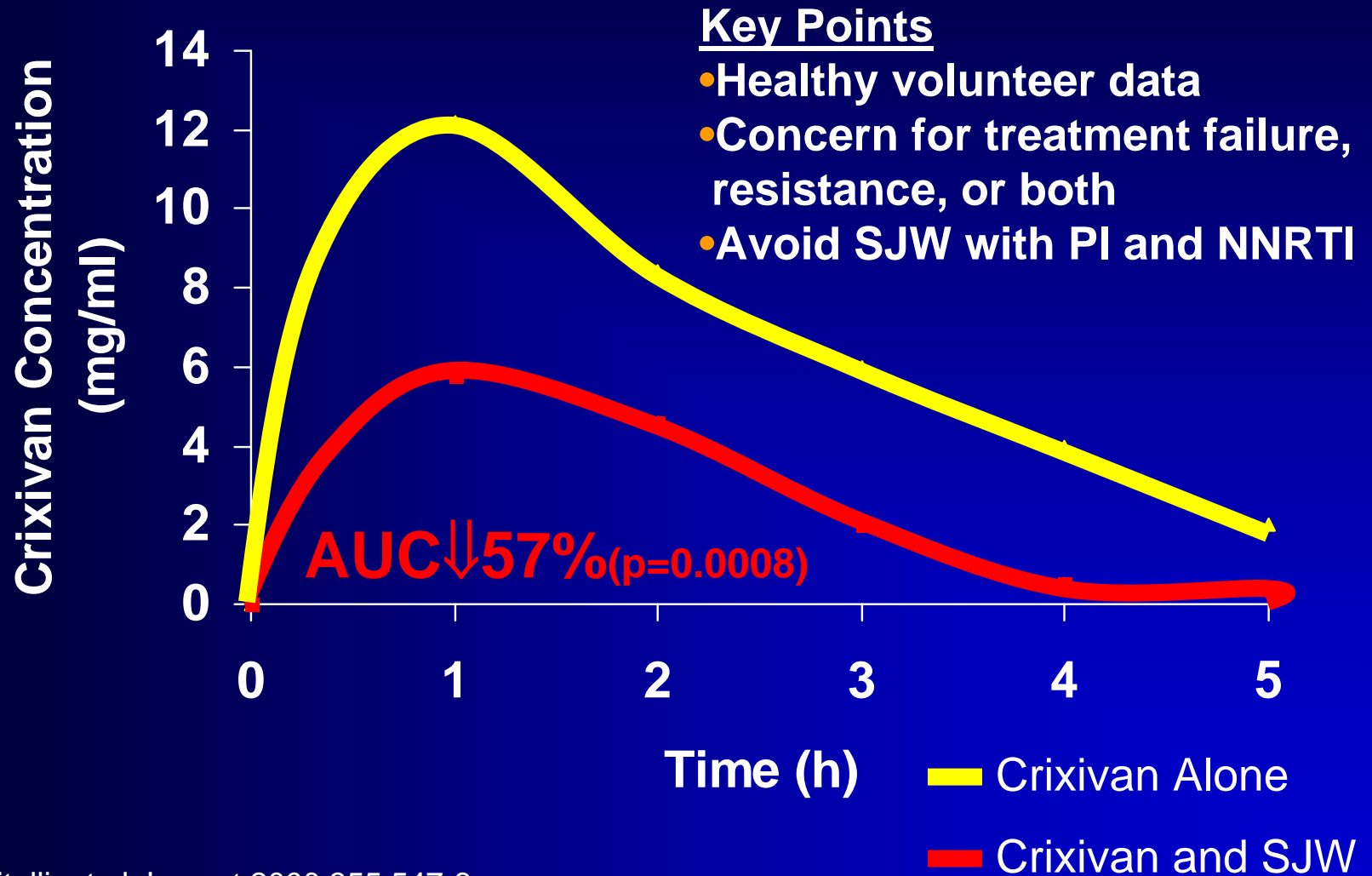
Key Points

- Healthy volunteer data
 - Crixivan levels reduced
 - MT used as an hepatoprotectant
- Second study showed no effect

St Johns Wort

- **Limited data demonstrating efficacy in depression**
- **Known CYP450 inducer, therefore reduces drug levels of many medications**
- **Avoid with oral contraceptives, anticoagulants, antidepressants, and transplant medications**
- **AVOID in HIV, contraindicated on guidelines and in product labels**

St. John's Wort and Crixivan®



Herbal Therapy and HIV Follow Up Survey – Albany Medical Center

- **173 patients surveyed**
- **41% receiving PI-based regimen**
- **28% receiving NNRTI-based regimen**
- **31% antiretroviral-naïve**
- **6% currently taking either garlic or St. John's Wort on a regular basis while receiving PI- or NNRTI-based HAART**
- **18% reported PAST use of either St. John's Wort or garlic on a regular basis while taking HAART**
- **Did the previous education work?**

Herbal Therapy and HIV Medications

- **Potential issues when combining herbal therapy and HIV medications**
 - increased toxicity of the herb
 - decreased efficacy of the herb
 - increased toxicity of the antiretroviral
 - decreased efficacy of the antiretroviral
 - greatest concern is the potential change in the efficacy of HAART
 - Often limited to no data to support use

Herbal Therapy Use and and HIV

My Recommendations

- **AVOID Garlic supplements**
- **AVOID Echinacea (short term use may be OK)**
- **AVOID St. Johns Wort**
- **Consider avoiding milk thistle**
- **If on anticoagulants or antiplatelets ie: warfarin, aspirin, clopidogrel, etc – avoid ginger, ginkgo, ginseng**
- **Other herbs – Consider avoiding if no data exists with HIV medications OR at least separate from ARV therapy to avoid interactions**
- **Consult physician prior to starting herbal therapy**

Overview

- **Discuss common herbal therapies used by patients regardless of HIV status**
- **List common uses herbal therapies**
- **Discuss the role of the FDA in regulating herbal treatments**
- **Review herbal therapies to be avoided in patients with HIV infection**

Resources

- **NIH National Center for Complimentary and Alternative Medicine located at <http://nccam.nih.gov>**
- **National Health Statistics Report #12, December 2008 located at <http://www.cdc.gov>**
- **A Practical Guide to Herbal Therapies for People Living with HIV located at <http://www.catie.ca>**