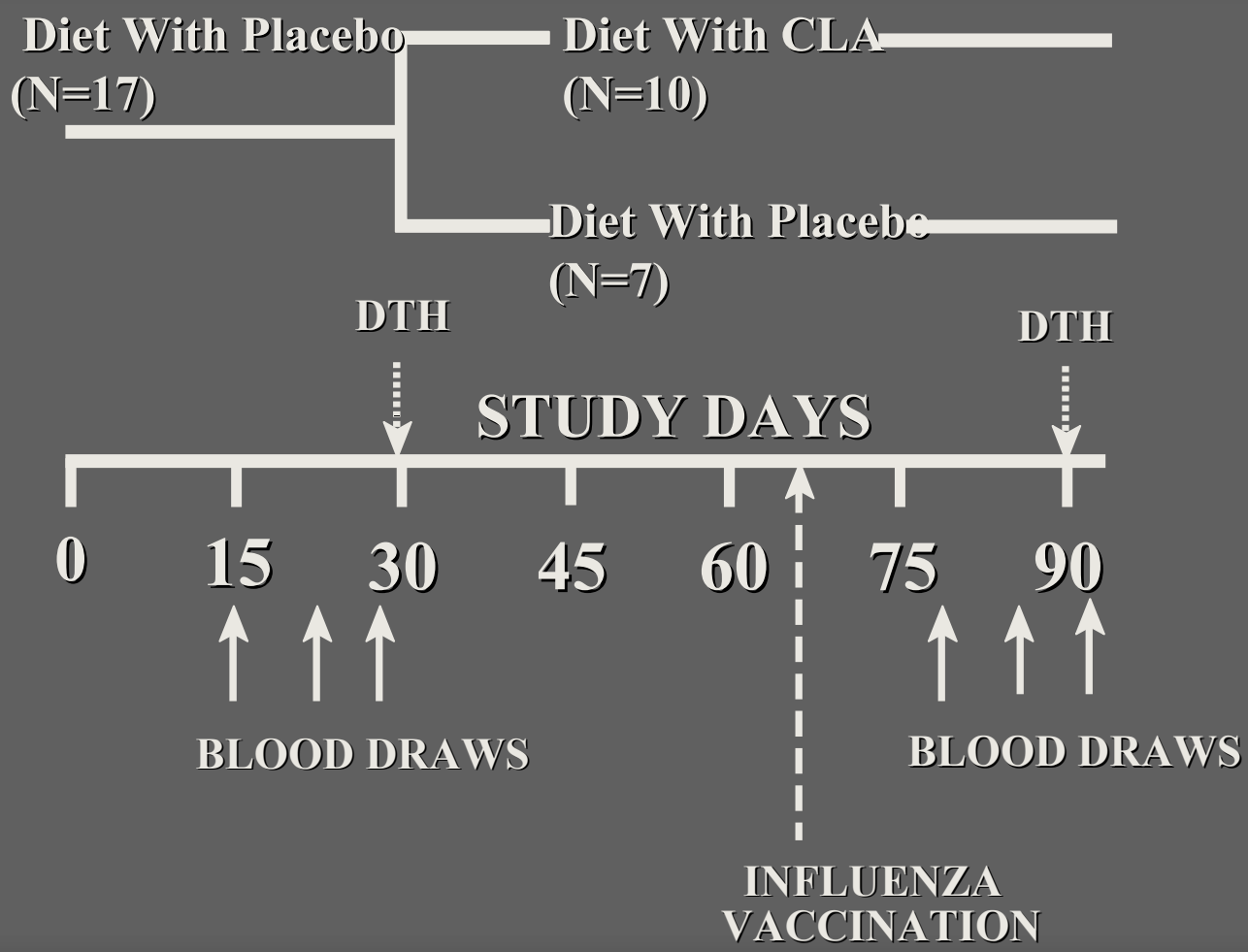
Health Effects of CLA

- Anti-carcinogenic
- Anti-atherogenic
- Anti-diabetogenic
- Decreases body fat
- Increases lean body mass
- Improves immune response

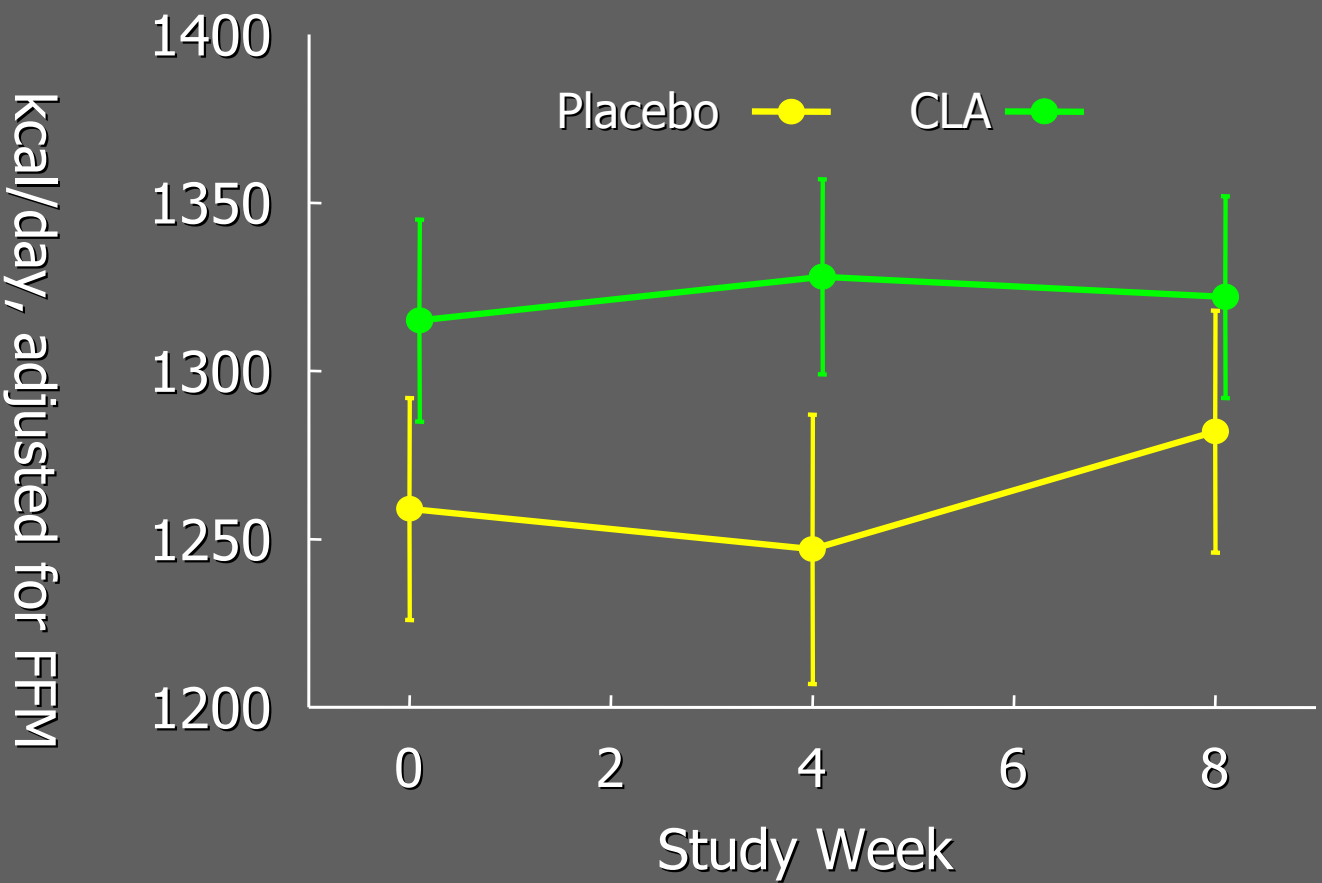
Summary of Animal Studies

Author	Sps	Fat	LBM	Risks
Pariza, 97	Mice	⇓	⇑	----
Delany, 99	Mice	⇓	=	Liver, Spleen, Insulin, Leptin
Kasaoka, 00	Mice	⇓	NE	Liver, Spleen, Insulin, Leptin
Riera, 00	Pigs	⇓	NE	----
Ostrowaska, 99	Pigs (A)	⇓	⇑	----
Stangl, 00	Rats	⇓	⇑	----

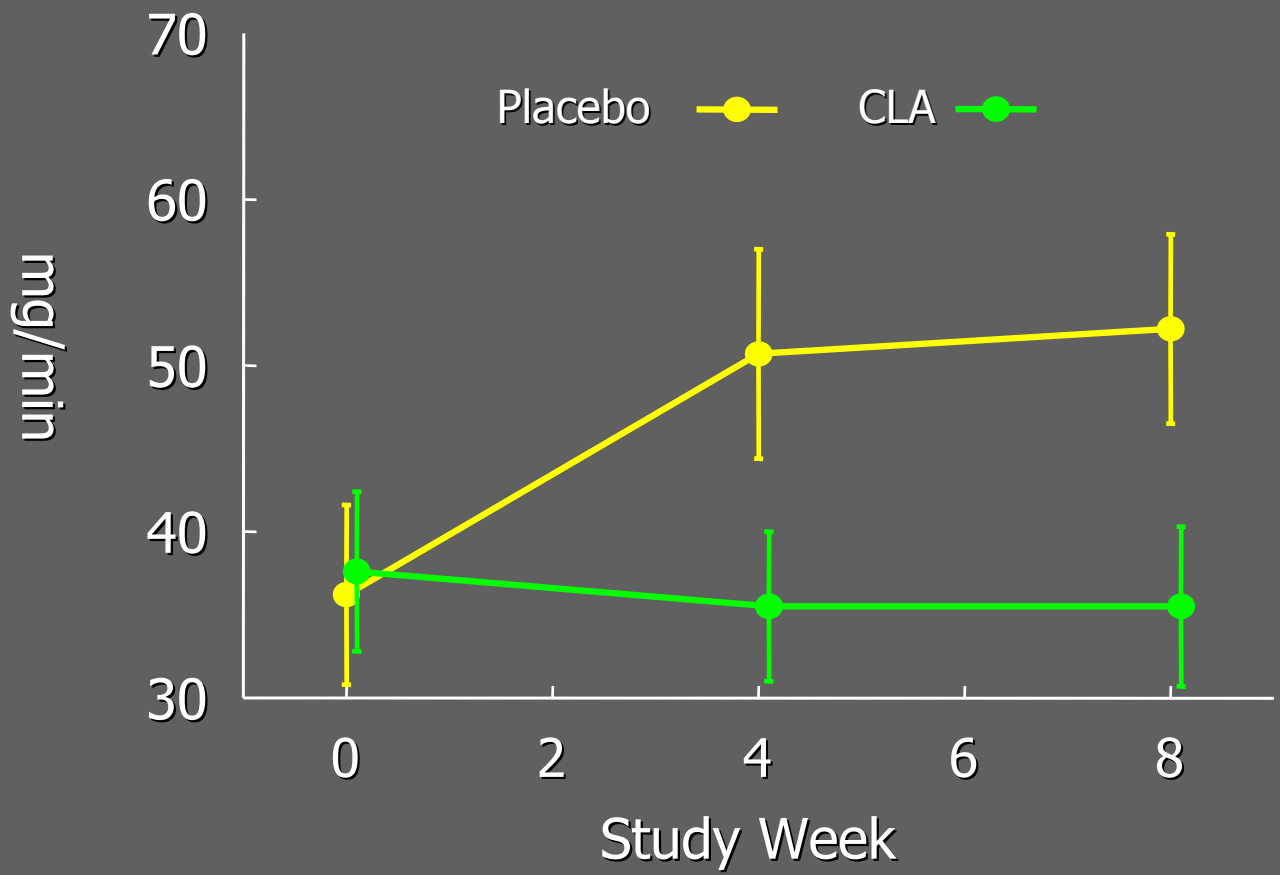
Study Design



Effect of CLA on Resting Energy Expenditure



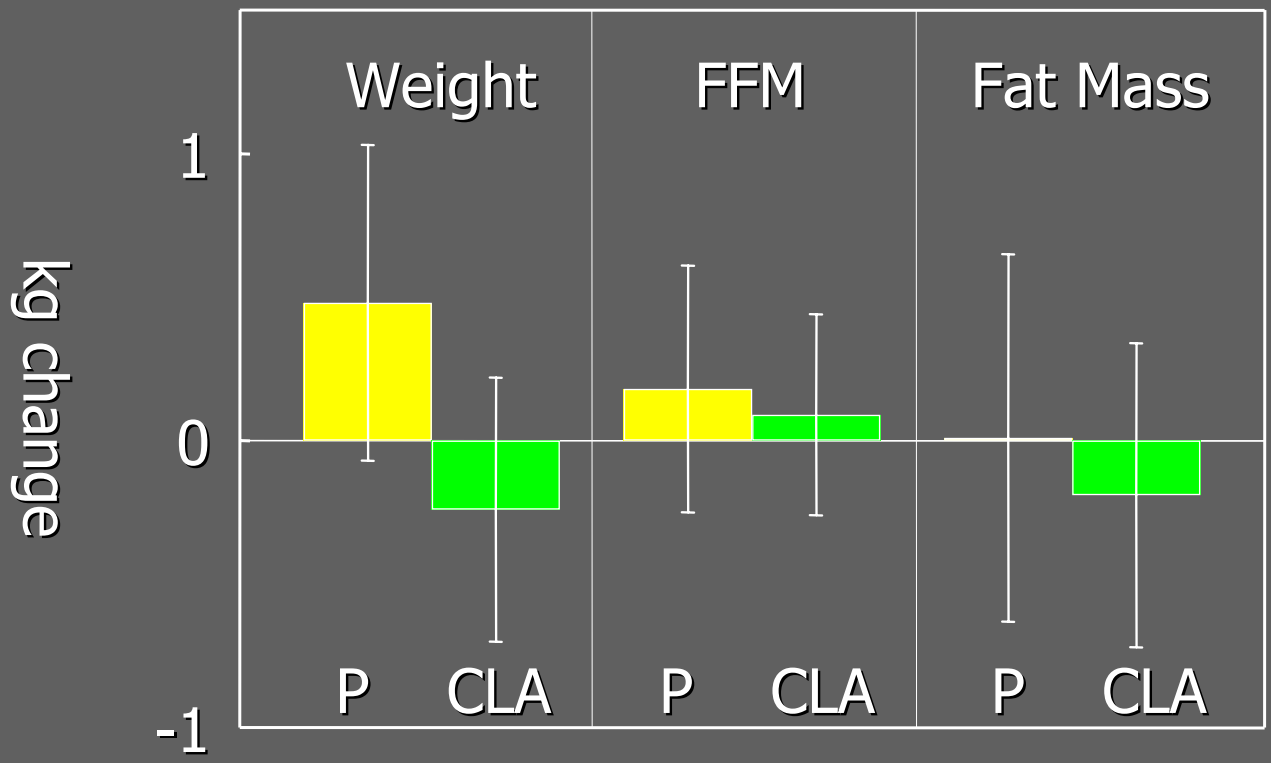
Effect of CLA on Fat Oxidation at Rest



CLA & Rate of Glycerol Appearance

CLA & Fatty Acid Re-esterification

Effect of CLA on Weight and Body Composition



Summary of Results

After 4-8 wks of supplementation, no effect of CLA on:

- Energy expenditure
- Respiratory quotient, fat oxidation
- Lipolysis
- FFA re-esterification
- Body weight, body composition

CLA Has No Effect on Body Fat Change in Obese Humans During Weight Reduction

- Subjects:
  - 80 obese adults
- CLA (2.7 g/d) or placebo for 6 months
- All decreased caloric intake and increased exercise
- Body fat decreased by 1 kg in both groups

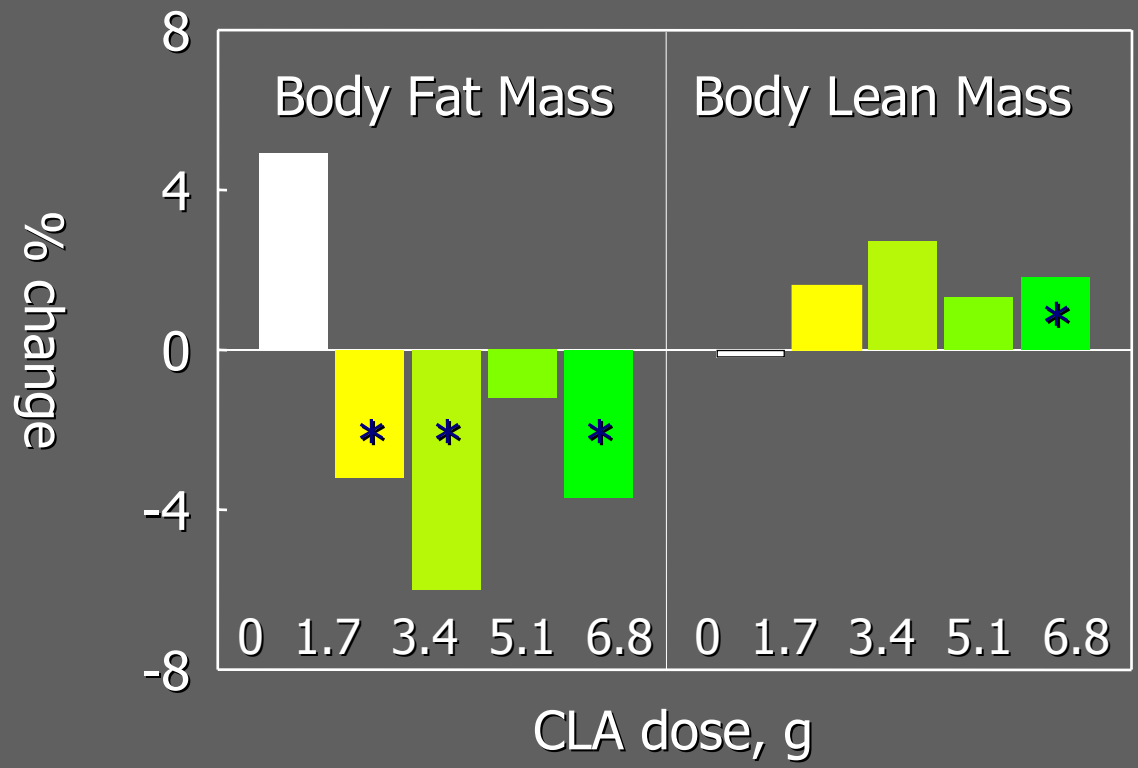
Atkinson. In Advances in CLA Research 1999;1:328-353.

CLA Reduces Body Fat in Humans

- Subjects:
  - Mean age = 45 years
  - 53 healthy adults
- CLA (4.2 g/d) or placebo for 3 months
- % body fat decreased by -1.2% ($p<0.0001$) (determined by BIA & skin fold thickness)

Vessby and Smedman. Chem Phys Lipids 1999;101:152.

CLA Affects Body Composition of Overweight and Obese Subjects



Adapted from Blankson et al. J. Nutr 2000;130:2943-8.

Summary of Human Studies

- In contrast to the results from animal models, supplementation with a mixture of CLA isomers failed to reduce body fat, except in the Norwegian study
- In most studies food intake and activity levels were not controlled
- Generally safe but some undesirable effects found in several studies

Contrasting Results: CLA and Body Composition

- Sensitivity and error in body composition measures, prediction errors 1.5-2 Kg fat
- Amount and type of food & activity level
- CLA dose and isomer composition
- Duration of supplementation period
- Type subjects, age, BMI (obese vs normal)
- Other confounding variables

Discrepancies Between Animal and Human Studies

- CLA dose per Kg body weight
- Species differences
- CLA isomer composition
- Growing animals vs adult humans
- Methods to determine body composition and their prediction errors
- Composition, amount and storage of the diets
- Other confounding variables

CLA Alteration of Immune Response in Animals

- Splenocyte or lymphocyte proliferation (mitogen) ↑or no effect
- CD4+/CD8+ ↑ or did not change
- IL-2 ↑ or did not change
- DTH ↑ or did not change
- Listeria resistance, NK activity & lymphocyte cytoxicity no effect
- IL-6, TNFα ↓
- IgA, IgG, IgM ↑
- IgE ↓

Conclusion : Modest and variable effects only

Summary of WHNRC Study

- 8-Fold increase in PBMC CLA concentration; no significant changes in other fatty acids.
- No change in lymphocyte proliferation & phenotypes, DTH, antibody production, secreted PGE_2, LTB_4, IL-1β, TNFα, or IL-2.
- No change in intracellular concentration of IL-2, IFNγ, TNFα, and % of cells producing them.
- No change in platelet activation, serum lipids

Effect of Dietary CLA on Serum Influenza Antibody Titers

Viral strain	Study day	CLA	Control
AH1N1	65	53	47
	92	520	510
AH3N2	65	70	37
	92	149	144
B/Habrin	65	46	72
	92	160	290

CLA Stimulates Antigen Specific Antibody

- Unilever study, supplemented CLA 1.7 g/d for 84 d to healthy men (30-70 yr, 25/group); two different mixtures of CLA, containing the c9,t11 and t10,c12 isomers in a ratios of 50:50 or 80:20, were used
- DTH and other indices did not change
- Serum antibody against Hep B and PBMC proliferation not different, however twice the number of subjects in 50:50 group attained antibody titers > 10 IU/L
- Authors suggest that t10, c12 isomer of CLA enhanced humoral response
- Mohede et al 2001, AOCS Annual Meeting Absts

Summary Human Studies Re Effects of CLA on Immune Fx

- Most indices of immune fx (DTH, number circulating WBC & their sub-sets, lymphocyte proliferation and phenotypes, secretion of cytokines & eicosanoids, etc) not changed
- Serum antibody titer against influenza not altered but increased against Hep B?

Safety Issues Regarding CLA

- Animals: increased liver and spleen weights, decreased leptin & increased insulin
- Humans: Benefits are questionable
- Some adverse effects noted in human stds WHNRC std elevated insulin decreased leptin
- Sweden std decreased glucose disposal, insulin sensitivity & serum HDL
- Norwegian std decreased HDL
- Other side effects in individual subjects

Safety Issues Continued

- Individuals taking CLA on their own:
- Subj 1 taking adderall for ADHD, developed nausea, insomnia, rapid heart beat, hungry even after a full meal
- Subj 2 MS patient, developed optic neuritis and loss of balance
- Symptoms disappeared in both within a week of discontinuation

Areas for Future Research

- Safety vs benefits; relevance to improve human health
- Isomer specific effects on body composition, immune fx, lipid and CHO metabolism, minimum amount needed
- What is the best model to study health effects of CLA, Primates vs humans, obese, dislipidemic, immune compromised, other disease conditions, normal
- Long-term studies with controlled food intake and activity level at more than one labs; the effects should be greater than the prediction errors.
- Mechanisms by which CLA isomers alter physiologic fx