Helseeffekter av oksidert fiskeolje. En intervensjonsstudie på friske personer.

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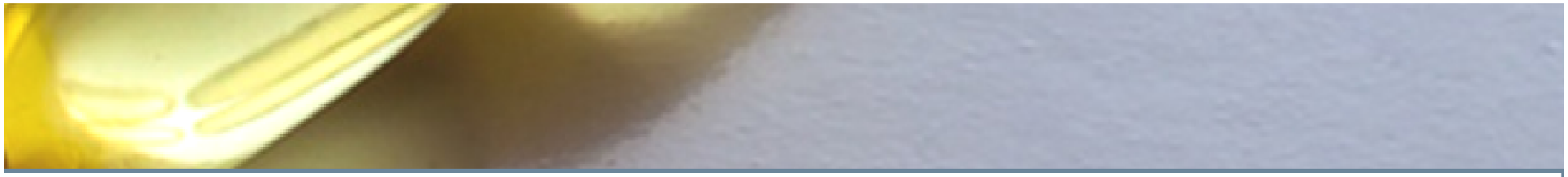
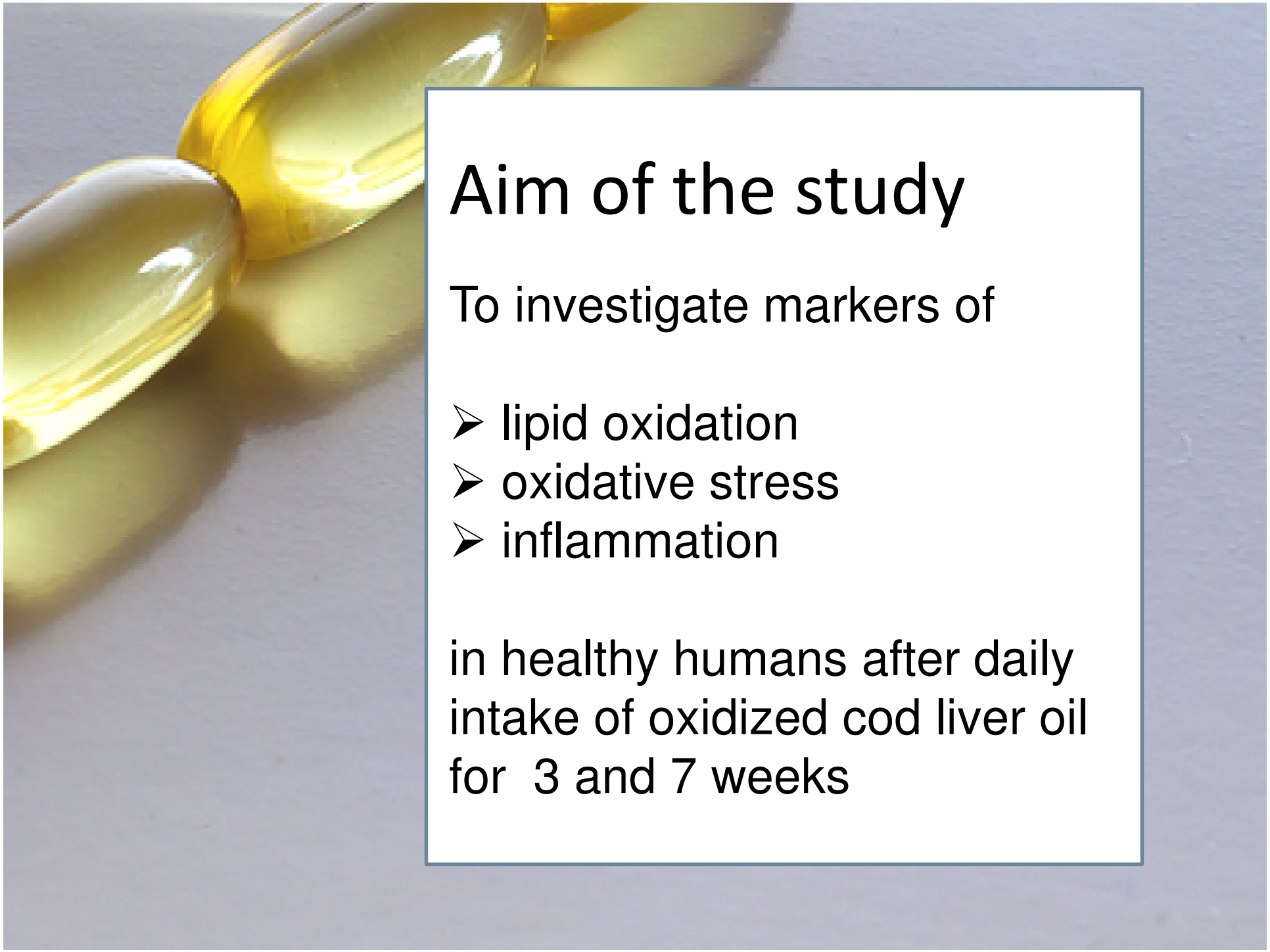
Outline of the presentation

- introduction
- design and analysis
- results
- discussion
- conclusion



Background

- n-3 protect against CVD
- n-3 are susceptible for oxidation
- Oxidation products in omega-3 supplements
- Oxidized vegetable oil increase lipid peroxides
- Data on intake of oxidized fish oil not available



Aim of the study

To investigate markers of

- lipid oxidation
- oxidative stress
- inflammation

in healthy humans after daily intake of oxidized cod liver oil for 3 and 7 weeks

Study protocol

Inclusion criteria:

- Healthy, none smokers men and women 18-50 years
- CRP < 10 mg/L
- Tot-chol < 7.5 mmol/L, triglycerides < 4.5 mmol/L
- Blood pressure (≤ 160/110 mmHg)
- Normal serum level of: glucose, insulin, TSH, T3 and T4
- BMI < 30 kg/m^2
- Willing to avoid fish, fish products, dietary supplements and omega-3 enriched food during the study period
- Wiiling to take 16 capsules/day for 7 weeks

Ethics:

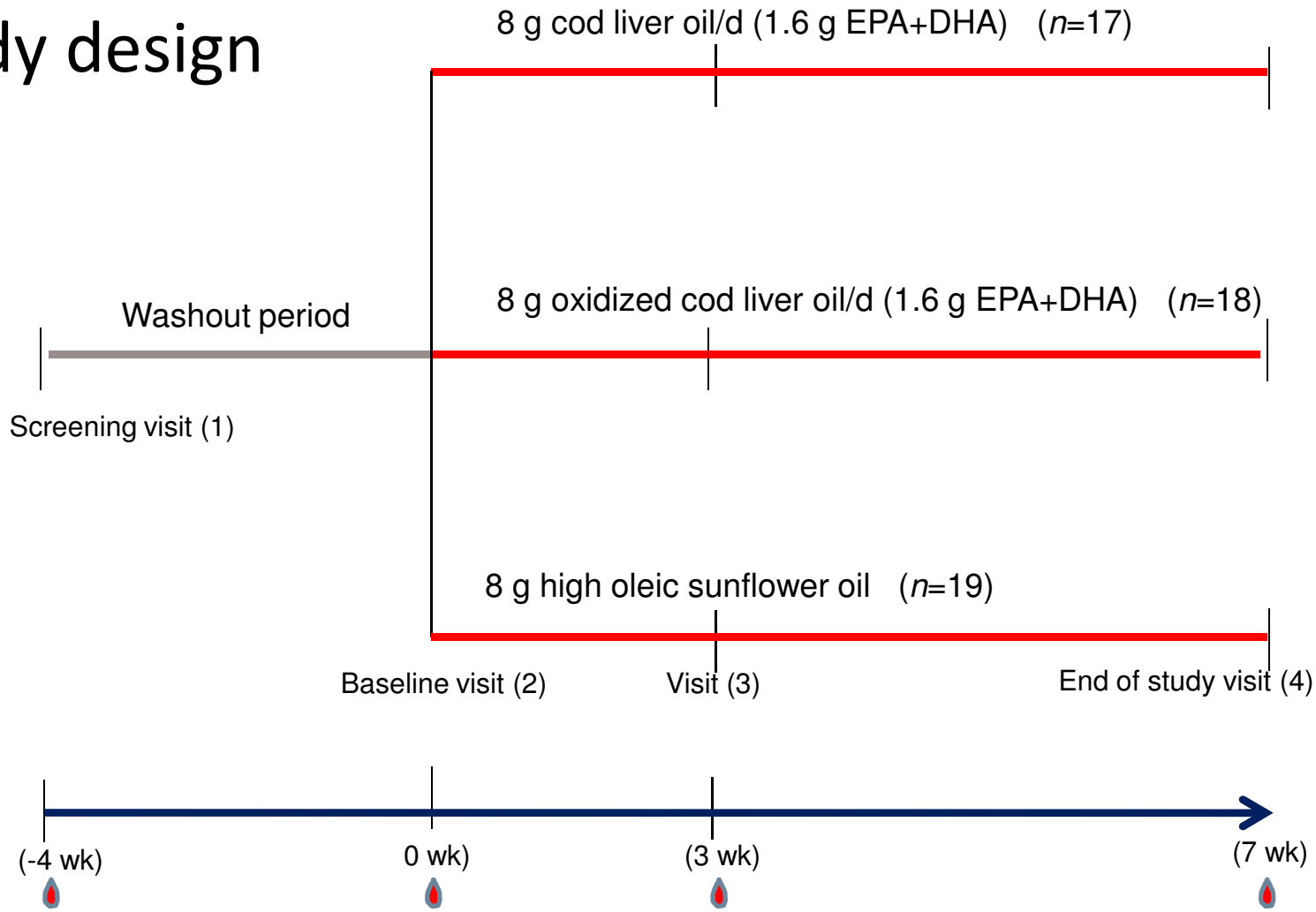
Appoved by Regional Committee of Medical Ethics and by the Norwegian Social Science Data Service

Registered at www.clinicaltrial.gov

Study design:

- Double-blinded, randomized controlled trial
- Stratified by gender
- Capsule compleance < 70% → exclusion

Study design



Lipid oxidation products and fatty acids were measured in food and capsules

Content of volatile oxidation products were analyzed by Dynamic headspace/GC-MS

Fatty acid composition and lipid oxidation products in the intervention oils

	Cod liver oil[1]	Oxidized Cod liver oil[1]	High oleic sunflower oil
Fatty acids:			
SFA (g/100g)	16	16	7
MUFA (g/100g)	47	46	76
PUFA (g/100g)	28	28	9
EPA (C20:5, n-3) (g/100g)	9.0	9.1	0
DHA (C22:6, n-3) (g/100g)	11.1	11.2	0
DPA (C22:5, n-3) (g/100g)	1.1	1.1	0
ALA (C18:3, n-3) (g/100g)	0.8	0.8	0.3
Oxidation level:			
PV (mekv/kg)	4	18	4
AV	3	9	3

1 Cod liver oil (*Gadidae sp.)* was provided from TINE SA (Norway)

PV and AV were measured using methods according to AOCS Official Method Cd 8-53 and Cd 18-90, respectively.

Markers measured in this study

Markers	Compartment	Methods
8-iso-$PGF_{2\alpha}$	Urine spot	LC/MS/MS (Vitas)
4-HHE	Plasma	GC/MS (Nofima)
4-HNE	Plasma	GC/MS (Nofima)
α-tocoferol	Plasma	HPLC (Nofima)
Fatty acids	Plasma	GC (Nofima)
Glutathione (tGSH)	RBC	Bio Rad kit (Vitas)
Glutathione peroxidase (GPx)	RBC	Spectrophotom. Assay (Denmark)
Glutathione transferase (GR)	RBC	Spectrophotom. Assay (Denmark)
Catalase	RBC	Spectrophotom. Assay (Denmark)
hsCRP	Serum	Routine lab (Furst)
Lipids (t-chol, LDL, HDL, TG) Liver markers: AST, ALT, G-GT,ALP	Serum	Routine lab (Furst)

Results

Baseline characteristics

	CLO	Ox CLO	HOSO	*P*
Male/Female (*n*)	5 /12	5 /13	5 /14	
Age (y)	25 (23-32)	22 (21-28)	25 (22-31)	0.32
BMI (kg/m^2)	22.1 ± 2.5	22.2 ± 1.7	23.5 ± 3.1	0.20
TC (mmo/L)	4.6 ± 0.8	4.7 ± 0.9	4.9 ± 0.8	0.57
LDL-C (mmol/L)	2.5 ± 0.8	2.7 ± 0.8	2.7 ± 0.6	0.63
HDL-C (mmol/L)	1.5 ± 0.3	1.4 ± 0.4	1.5 ± 0.4	0.88
TG (mmol/L)	0.8 (0.7-0.9)	0.9 (0.5-1.5)	1.0 (0.4-5.0)	0.77
Glucose (mmol/L)	4.6 ± 0.3	4.8 ± 0.4	4.8 ± 0.5	0.27
AST (U/L)	22 ± 5	21 ± 5	21 ± 4	0.61
ALT (U/L)	20 ± 7	20 ± 13	21 ± 7	0.61
G-GT (U/L)	21 ± 14	16 ± 7	17 ± 8	0.30
ALP (U/L)	69 ± 20	62 ± 23	59 ± 14	0.30

At baseline, no significant difference between the randomization groups was observed

Plasma fatty acids

Variables	CLO		Ox CLO		HOSO		*P*
Fatty acids (%wt)	Basline	End of study	Basline	End of study	Basline	End of study	
18:2n-6 (LA)	32.7 ± 3.4	29.3 ± 4.4	28.2 ± 4.5	28.0 ± 2.6	28.9 ± 5.0	29.1 ± 3.8	0.01
20:4n-6 (AA)	6.3 ± 1.1	5.7 ± 0.8	6.3 ± 1.0	5.7 ± 0.8	6.2 ± 1.7	6.4 ± 1.4	0.02
18:3n-3 (ALA)	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.98
20:5n-3 (EPA)	0.7 ± 0.2	2.5 ± 0.8	0.6 ± 0.3	2.6 ± 1.0	0.6 ± 0.2	0.7 ± 0.3	<0.001
22:5n-3 (DPA)	0.5 ± 0.1	0.7 ± 0.2	0.5 ± 0.1	0.7 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	<0.001
22:6n-3 (DHA)	2.2 ± 0.5	3.8 ± 0.9	2.0 ± 0.6	3.9 ± 0.8	2.2 ± 0.5	2.2 ± 0.5	<0.001

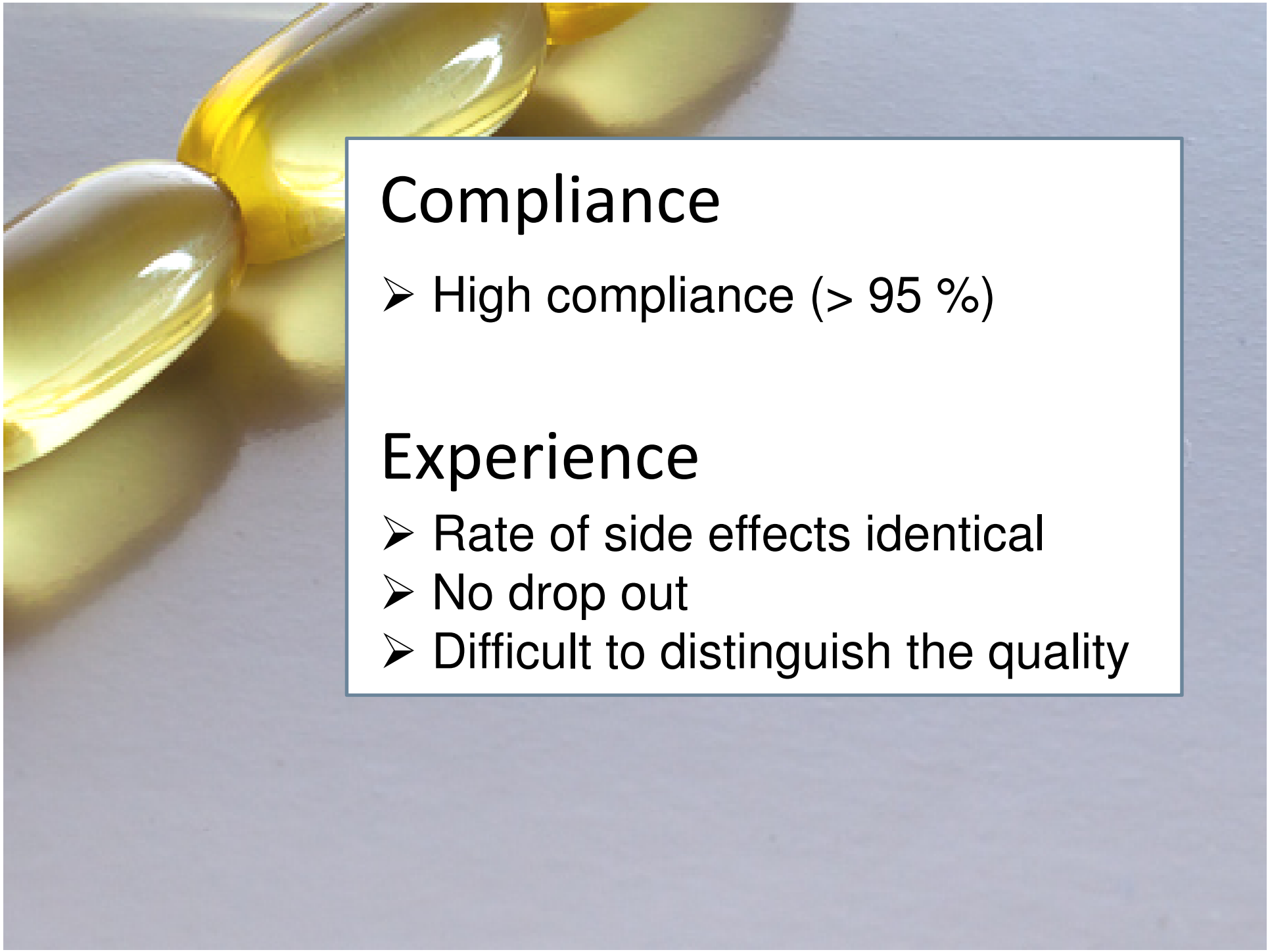
No difference between the CLO groups at baseline or after 3 and 7 wk.

Markers of lipid peroxidation, oxidative stress and inflammation

Variables	CLO		Ox CLO		HOSO		*P*
Plasma:	Basline	End of study	Basline	End of study	Basline	End of study	
4-HHE(ng/ml)	3.0 (1.6-3.8)	2.2 (1.6-3.6)	3.7 (1.9-5.0)	3.1 (1.9-5.1)	4.3 (1.6-5.5)	3.5 (2.1-4.8)	0.54
4-HNE(ng/ml)	3.4 (2.4-2.2)	3.3 (2.7-4.5)	4.4 (3.7-4.2)	4.3 (1.3-4.9)	3.9 (2.6-6.3)	3.3 (2.3-4.3)	0.47
α-tocopherol/total lipids	4.0 (3.6-4.6)	4.0 (3.6-4.5)	4.0 (3.5-4.3)	4.0 (3.5-4.3)	3.9 (3.7-4.2)	4.1 (3.7-4.3)	0.67
Serum:							
Serum-hsCRP (mg/L)	0.5 (0.2-1.2)	0.8 (0.2-1.3)	0.6 (0.3-1.4)	0.7 (0.3-1.7)	1.0 (0.5-2.7)	1.2 (0.6-3.1)	0.68
Urine:							
8-iso-PGF-2α pg/mg creatinine	288 (225-339)	239 (156-320)	280 (194-381)	248 (171-307)	237 (149-360)	280 (103-414)	0.15
Erytrocytes:							
Glutathione (mM)	1.3 (1.0-1.7)	1.4 (1.1-1.6)	1.5 (1.3-1.7)	1.7 (1.4-2.0)	1.6 (1.2-1.7)	1.3 (1.2-1.9)	0.44
GR U/g (Hb)	7.3 (6.8-8.6)	7.5 (6.8-8.5)	8.2 (7.4-9.0)	8.2 (7.1-8.5)	7.8 (7.2-9.2)	8.1 (7.5-8.8)	0.58
GPx U/g (Hb)	120 (115-124)	118 (114-126)	110 (105-124)	109 (96-121)	113 (101-122)	111 (103-120)	0.54
CAT U/g (Hb)	10.3 (9.2-10.6)	9.6 (9.1-10.1)	9.3 (8.5-10.7)	9.6 (8.7-10.0)	10.1 (9.2-10.4)	9.4 (9.2-10.3)	0.70

Data are presented as mean (±SD) or median (25,75 percentiles) when not normally distributed
After 3 and 7 wk of intervention, no significant differences between the randomization groups were observed


Discussion

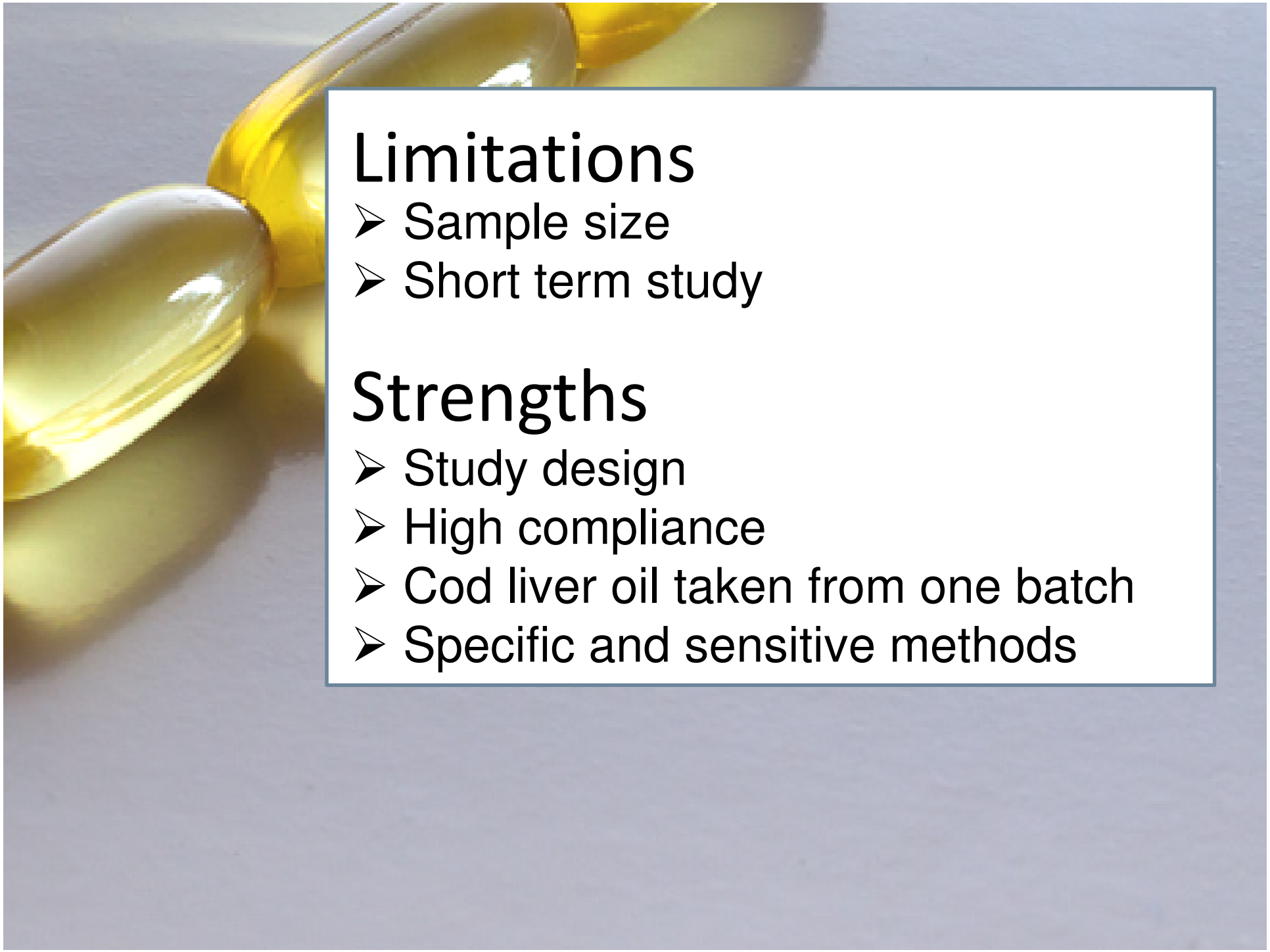


Compliance

- High compliance (> 95 %)

Experience

- Rate of side effects identical
- No drop out
- Difficult to distinguish the quality



Limitations

- Sample size
- Short term study

Strengths

- Study design
- High compliance
- Cod liver oil taken from one batch
- Specific and sensitive methods


Conclusion

Konklusjon

I friske personer,

inntak av oksidert tran oil for 3 and 7 uker

påvirket ikke markører for:

- oksidativt stress
- lipid peroksidering
- inflammasjon

EPA and DHA øker like mye i gruppene som fikk tran av ulik kvalitet.

Konklusjon

- I lys av de markørene vi har benyttet, så finner ingen negative effekter av oksidert tran
- Oksidert tran påvirker ikke opptak av n-3
- Med tanke på studiens varighet, størrelse og at den er gjort på friske personer, så bør en slik studie gjentas før man kan trekke endelige konklusjoner

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Oxidised fish oil does not influence established markers of oxidative stress in healthy human subjects: a randomised controlled trial

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Takk for meg!