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Er der plads til smør i en sund kost?

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1. Title of the project

Er der plads til smør i en sund kost?

Is there room for butter in a healthy diet?

2. Project manager

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4. Sources of funding

DDRF: 2.406.000 DKK

1/3 PhD stipend from NEXS, KU-SCIENCE

5. Project period

Project period with DDRF funding: 1 January 2013 - 31 December 2015

Revised, if necessary: 1 January 2013 - 9 February 2018 (Hand-in date for PhD project)

6. Project summary

The project was based on three studies, of which two human intervention trials were conducted during the project period (A and B) and one was a secondary analysis of a 6-month human intervention trial finalized in 2010 (C). For all three studies the main aim was to contribute to fill in the missing pieces in the research area concerning the effect of dairy products given as whole foods on health.

Sub-project A: The aim was to examine the effect of a moderate butter intake (4.5 E%) on concentration of cholesterol (total-, LDL and HDL cholesterol), triglycerides and secondarily on insulin, glucose and the inflammation marker

CRP in the blood in healthy men and women. The effect of butter was compared with refined olive oil (without polyphenols) and the habitual diet of the participants. A diet with moderate butter content did increase total and LDL cholesterol significantly compared with olive oil and the habitual diet of the participants. In conclusion, the results of sub-project A suggest that people with high cholesterol should keep their intake of butter to a minimum, whereas there is room for a moderate butter intake in a healthy diet in the normocholesterolemic population.

Sub-project B: The aim was to examine the effect of a daily intake of 0.5 L whole milk compared with skimmed milk on concentration of total, LDL and HDL cholesterol, and triglycerides and secondarily on insulin and glucose in healthy men and women. The results showed no difference in effect on LDL cholesterol between whole milk and skimmed milk diets despite of the significantly higher content of saturated fat. However, HDL cholesterol concentration was significantly higher with whole milk compared with skimmed milk. Furthermore, correlations analysis with whole milk showed that glucose and HDL cholesterol were significantly, moderately negative correlated (the higher HDL, the lower the glucose concentration).

Sub-project C: The aim was to examine the effect of a high daily intake of semi-skimmed milk (1L/day) for a longer period (6 months) compared with sugar-sweetened soft drink (SSSD), non-caloric soft drink (NCSD) and water on insulin sensitivity evaluated by an oral glucose tolerance test (OGTT) in overweight and obese men and women. The results showed no difference between the beverages on risk of type 2 diabetes (T2D). Additionally, the milk intake did not change concentration of cholesterol or blood pressure compared with the other beverages, although SSSD significantly increased total cholesterol concentration compared with NCSD and triglycerides compared with NCSD and water.

For sub-project B and C, we conclude that despite of belonging to the category of high-fat dairy products, the results suggest that intake of whole milk and semi-skimmed milk were beneficial or neutral and results indicate that if the higher energy content is taken into consideration whole milk and semi-skimmed milk can be included in a healthy diet.

Projektresume (DK)

Projektet er baseret på tre studier, heraf to humane forsøg gennemført i projektperioden (A og B) samt en sekundær analyse af et humant forsøg afsluttet i 2010 (C). For alle tre studier har det overordnede formål været at bidrage til at udfylde det eksisterende hul i forskningsområdet omkring effekten af mælkeprodukter, som hele fødevarer, på vores sundhed.

Delprojekt A: Formålet var at undersøge effekten af et moderat smørindtag (4,5 E%) blandt raske mænd og kvinder på koncentrationen af kolesterolet i blodet (total, LDL og HDL kolesterol), triglycerider og sekundært på insulin, glukose og inflammationsmarkøren CRP. Effekten af smør blev sammenlignet med effekten af olivenolie (raffineret og uden polyfenoler) og forsøgspersonernes normale kost. En kost med et moderat smørindhold øgede signifikant total og LDL kolesterol sammenlignet med olivenolie og forsøgspersonernes normale kost. HDL kolesterolet steg også signifikant med smør sammenlignet med forsøgspersonernes normale kost. Det kan konkluderes for delprojekt A, at for personer med forhøjet kolesterol bør indtaget af smør holdes til et minimum, men at der er plads til et moderat smørindtag i en sund kost blandt befolkningen med et normalt kolesteroltal.

Delprojekt B: Formålet var at undersøge effekten af et dagligt indtag af 0,5 L sødmælk sammenlignet med skummetmælk på koncentrationen af kolesterol (total, LDL og HDL kolesterol) og triglycerider, og sekundært på insulin og glukose i blodet på raske mænd og kvinder. Udover mælken spiste forsøgspersonerne, som de plejede. Der var ingen forskel i effekten på LDL kolesterol mellem sødmælks- og skummetmælkskosten på trods af det signifikant højere indhold af mættet fedt i sødmælkskosten. Derimod var der signifikant højere koncentration af HDL kolesterol efter sødmælkskosten sammenlignet med skummetmælkskosten. Yderligere viste korrelationsanalyser for sødmælk, at HDL kolesterol var signifikant, moderat negativt korreleret med glukosekoncentrationen.

Delprojekt C: Formålet var at undersøge effekten af et højt dagligt indtag af letmælk (1L/dag) i en længere periode (6 mdr.) sammenlignet med sødet sodavand, kunstig-sødet sodavand og vand på insulinsensitiviteten evalueret med en oral-glukose tolerance test (OGTT). Resultaterne viste ingen forskel mellem drikkene på risikomarkører for T2D. Mælk ændrede heller ikke på koncentrationen af kolesterol i blodet eller blodtrykket sammenlignet med de andre drikke, dog øgede sukker-sødet sodavand signifikant koncentrationen af total kolesterol sammenlignet med kunstig-sødet sodavand og triglycerider sammenlignet med kunstig-sødet sodavand og vand.

Samlet for delprojekt B og C kan det konkluderes, at på trods af at tilhøre kategorien af fede mælkeprodukter indikerede resultaterne, at indtag af sødmælk og letmælk var henholdsvis gunstig eller neutral. Resultaterne tyder på, at tages der højde for det højere energiindhold, så kan sødmælk og letmælk inkluderes i en sund kost blandt raske mennesker.

7. Project aim

The aim of the project was:
a. to investigate the effects of a moderate butter intake on blood lipids (total, LDL and HDL cholesterol, triglycerides (TG)) and risk markers of T2D in humans.
b. to work out a healthy dietary regimen of which butter is a part.
c. to write an overview paper on the role of milk fat and risk parameters of life style diseases.

Projektet formål var (DK):
a. at undersøge virkningen af indtag af moderate mængder smør på blodets kolesterolindhold og risikoparametre for T2D hos voksne.
b. at udarbejde kostplaner for sund mad (ifølge de Nye Nordiske Næringsstofanbefalinger), hvori smør indgår.
c. at skrive en opdateret oversigtsartikel, som belyser mælkefedtets rolle i relation til risikoparametrene.

8. Background for the project

Worldwide, cardiovascular disease is the largest cause of death. Constriction of the arteries in the heart is the single disease most Danes die from, and LDL cholesterol increases the risk of constriction of the arteries and thrombosis. For decades dietary guidelines have recommended that consumption of saturated fat should be limited and therefore also to choose low-fat dairy products, as dairy products have a high content of SFA, known to increase LDL cholesterol in the

blood. However, meta-analyses of cohort studies show no relation between intake of dairy and increased risk of cardiovascular disease (CVD) or between high-fat dairy products and risk of T2D. Moreover, there is a gap in research, when it comes to controlled dietary studies investigating the true effect of specific dairy products on cholesterol in the blood as well as risk markers of T2D. As a consequence, dietary guidelines regarding dairy products are today primarily based on expected effect of macronutrients and on that basis leave very limited room for high-fat dairy products such as butter, whole milk and semi-skimmed milk.

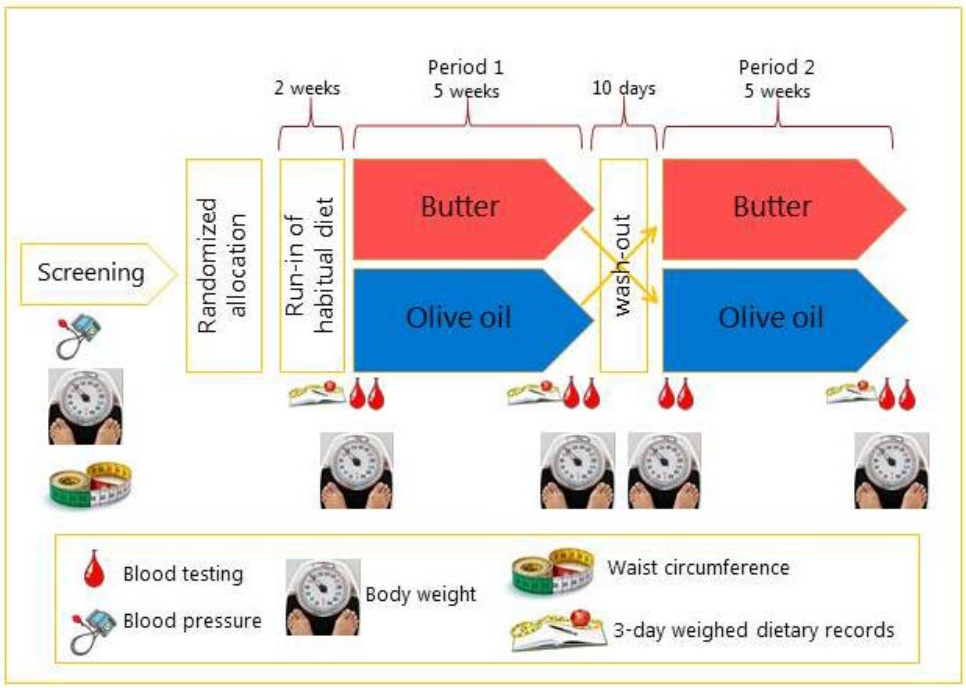
Butter in large amounts increases cholesterol in the blood, but the effect of a moderate butter intake in a normal diet had not been examined. Furthermore, a study comparing butter with cheese showed a modest increase in LDL cholesterol after a relative high butter intake of 13 E%. Dietary guidelines recommend low-fat milk, but is there a difference in the effect of whole milk and skimmed milk on cholesterol? Only very few studies have looked into the effect of milk on risk of T2D and it demands a longer study to see a possible effect on insulin sensitivity.

Therefore, the aim of this project is to study A) the effect of a moderate butter intake in a normal diet and B) the effect of whole milk compared with skimmed milk on cholesterol, triglycerides and risk markers of T2D and C) the effect of intake of whole milk compared with sugar-sweetened soft drinks, non-caloric soft drinks and water on risk markers of T2D and CVD in a longer study.

9. Sub-activities in the entire project period

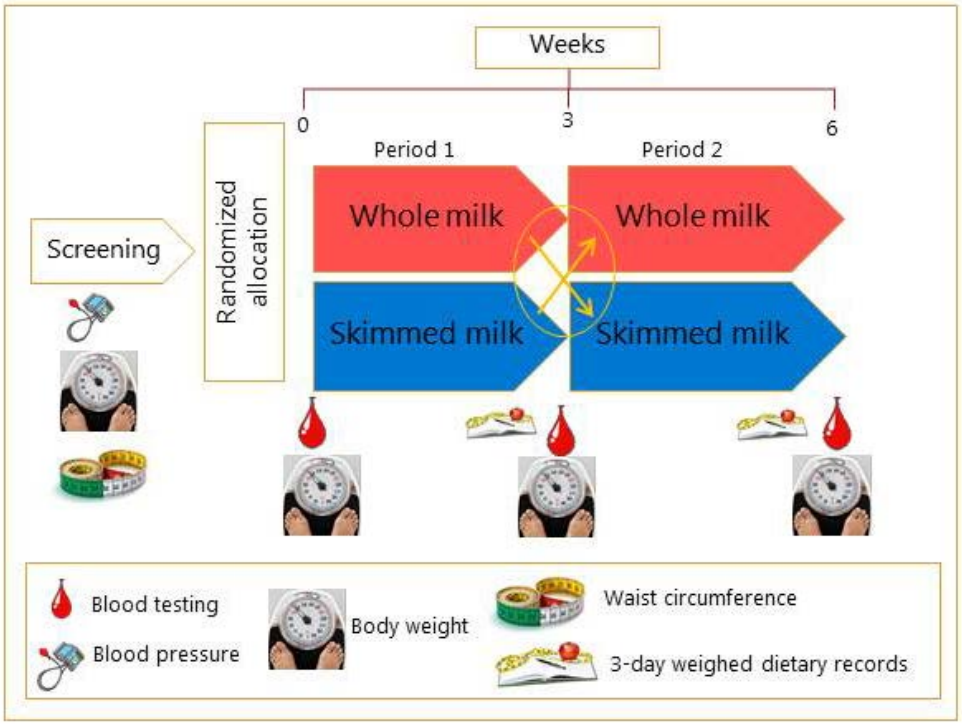
Sub-project A

Human intervention study of butter: In a double-blinded, randomized, controlled 2x5 weeks dietary intervention study with healthy subjects the effect of a moderate butter intake (4.5 E%) was compared with a diet of the same amount of olive oil (refined, without polyphenols) and the habitual diet of the study participants. Clinical measurements were blood cholesterol concentration (serum total-, LDL- and HDL-cholesterol) and serum triglycerides, risk markers of T2D (plasma glucose and serum insulin) as well as the inflammation marker high-sensitivity C-Reactive Protein (hs-CRP). The study was a crossover study with 10 days of wash-out and a run-in period of 2 weeks with the habitual diet of the participants. The study was blinded as butter and olive oil were baked into a bun for the participants to consume each day. The participants completed dietary records during run-in (habitual diet), butter and olive oil periods.
Status: Completed and published.



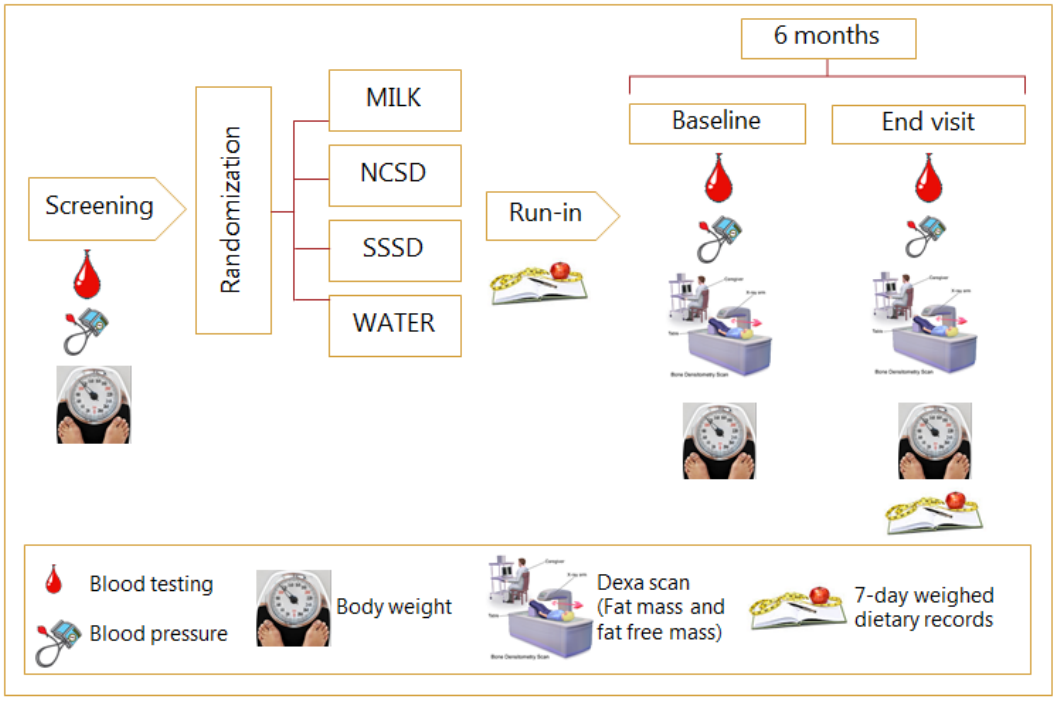
Sub-project B

Human intervention study of milk: In a randomized controlled 2x3 weeks dietary crossover intervention study a daily intake of ½L of whole milk (17.5g milk fat/d) was compared with skimmed milk (1.5 g milk fat/d). Clinical measurements were blood cholesterol (serum total-, LDL- and HDL cholesterol) and serum triglycerides, insulin and plasma glucose.
Status: Completed and article accepted for publication in European Journal of Clinical Nutrition.



Sub-project C

Secondary analysis of human intervention study with milk: The study was a 6-month randomized controlled intervention study investigating the effect of intake of 1L/d milk, sugar-sweetened soft drinks, non-caloric soft drinks and water on insulin sensitivity evaluated by an oral-glucose tolerance test (OGTT) and plasma FFA in a parallel design. Secondarily, fasting blood lipids and blood pressure were investigated.
Status: Completed and article accepted for publication in European Journal of Clinical Nutrition.



10. Project results

Sub-project A

The effect of a moderate butter intake was compared with iso-caloric amounts of refined olive oil **(Table 1)** and the habitual diet of the participants on changes in total-, LDL- and HDL cholesterol, triglycerides, insulin, glucose and hsCRP. 47 participants completed the intervention. A daily moderate intake of butter increased total and LDL cholesterol significantly compared to olive oil and the participants habitual diet **(Table 3+Figure 1)**. Additionally a significant increase in HDL cholesterol was shown with butter compared to the habitual diet. No difference was seen for any of the other measurements.

TABLE 1
Fatty acid composition of butter and refined olive oil[1]

Fatty acid	Butter, % of total fatty acids	Olive oil, % of total fatty acids
Sum of 6:0–12:0	8.20	0.00
14:0	11.17	0.02
14:1	0.95	0.0
15:0	1.09	0.0
16:0	31.95	12.65
16:1	1.57	0.85
17:0	0.55	0.10
18:0	10.43	3.33
cis 18:1n–9	20.55	71.18
18:1n–7	0.86	1.95
cis 18:2n–6	1.59	7.63
18:3n–6	0.04	0.00
18:3n–3	0.48	0.67
Other	8.53	1.63

[1]Analyzed by the National Food Institute, Technical University of Denmark.

TABLE 3
Results after the run-in, butter, and olive oil periods[1]

	Run-in	Butter	Olive oil
Total cholesterol, mmol/L	5.22 ± 0.90	5.50 ± 0.98††,*	5.27 ± 0.95
LDL cholesterol,[2] mmol/L	2.88 ± 0.81	3.04 ± 0.86†,*	2.87 ± 0.86
HDL cholesterol,[3] mmol/L	1.69 ± 0.39	1.75 ± 0.41†	1.73 ± 0.39
		A^{A}1.73 ± 0.37	B^{A} 1.65 ± 0.41
		A^{B}1.82 ± 0.52†	B^{B} 1.77 ± 0.38†
Total cholesterol:HDL cholesterol	3.24 ± 0.89	3.29 ± 0.92**	3.17 ± 0.88
Triacylglycerol,[4] mmol/L	1.0 ± 0.35	1.0 ± 0.35	0.93 ± 0.38
hsCRP,[5] mg/L	1.51 ± 2.81	1.40 ± 2.47	1.67 ± 3.19
Glucose, mmol/L	5.67 ± 0.46	5.58 ± 0.45	5.56 ± 0.43
Insulin, pmol/L	53.77 ± 30.04	57.56 ± 34.28	55.04 ± 29.0
HOMA-IR	1.92 ± 1.16	2.01 ± 1.29	1.91 ± 1.0

[1]All values are means ± SDs, n = 47. Statistical differences were based on linear mixed models with Bonferroni corrections. *,**Significantly different from the olive oil period: *$P < 0.05$, **$P < 0.01$; †,††significantly different from the run-in period: $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.005$.

[2]n = 46 because one subject was considered an outlier with high LDL-cholesterol concentrations and was removed from the analysis.

[3]Values are also shown for each treatment group (butter: A^{AB}; olive oil: B^{AB}) because of the time-by-treatment effect.

[4]n = 45 because 2 subjects were considered outliers with high triacylglycerol concentrations, and both subjects were removed from the analysis.

[5]hsCRP, high-sensitivity C-reactive protein. n = 37 because some samples were below the detection limit, and one subject was considered an outlier with high hsCRP concentrations.

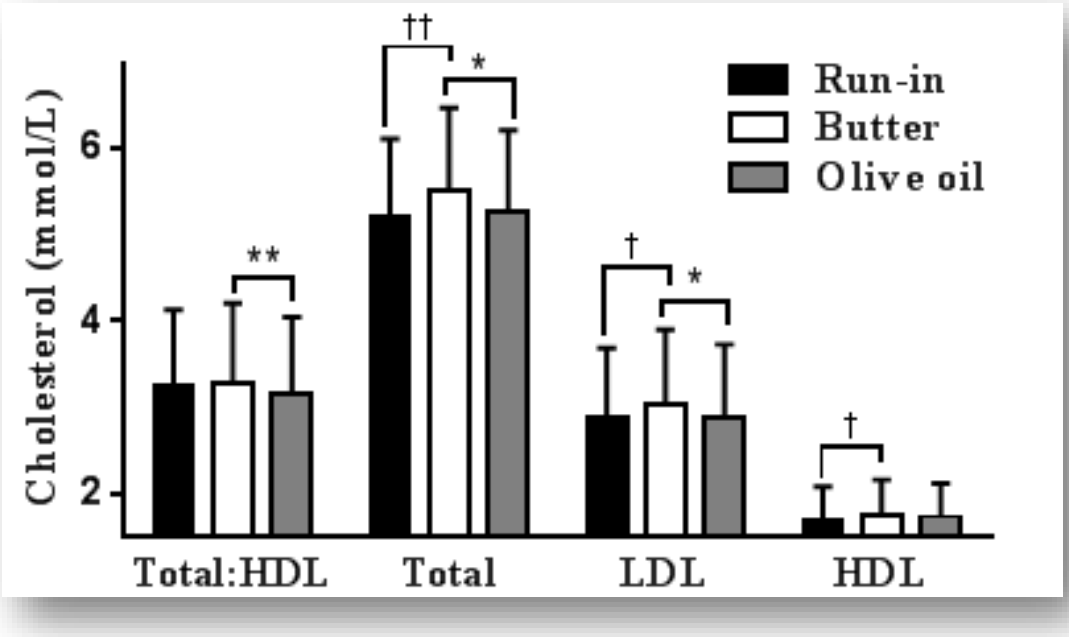


Figure 1 Mean ± SD serum concentrations of total:HDL, total, LDL and HDL cholesterol in subjects after the run in (black bars), butter (white bars), and olive oil (grey bars) periods. Statistical differences are based on linear mixed models with Bonferroni corrections. *, **Significantly different from olive oil period: *P < 0.05, ** P < 0.01. †Significantly different from run-in period: † P < 0.05, †† P < 0.005.

Publication: Sara Engel and Tine Tholstrup. Butter increased total and LDL cholesterol compared with olive oil but resulted in higher HDL cholesterol compared with a habitual diet. *Am J Clin Nutr* 2015;102:309-15.

Sub-project B

In this study, the effect of a daily intake of 0.5 L whole milk was compared with skimmed milk (difference in SFA of 10.5g/d (table 1)) on blood concentration of cholesterol (total, LDL and HDL cholesterol), triglycerides, and secondarily on insulin and glucose. Analysis showed no difference in effect on LDL cholesterol (**tabel 3+figur 1**) between the whole milk and skimmed milk diets in spite of the significantly higher content of SFA in the whole milk diet according to the diet records (**tabel 4**). Also with total cholesterol, triglycerides, insulin and glucose analysis showed no difference. However, with HDL cholesterol there was a significantly higher concentration after the whole milk period compared with the skimmed milk period.

Table 1.

Composition of 0.5 Liter of whole and skimmed milk and the calculated differences

	Whole	Skimmed	Difference
Energy/d (kJ)	1345	750	595
Fat (g)	17.5	1.5	16
SFA	11.5	1	10.5
MUFA	4	0.5	3.5
PUFA	0.5	0.0	0.5
Protein (g)	17	17.5	0.5
Carbohydrates (g)	24	23.5	0.5

Table 3

Results after skimmed and whole milk periods

	Skimmed	Change from baseline	Whole	Change from baseline	*P*
Total cholesterol (mmol/L)	4.31 ± 0.15[1]	-0.04 ± 0.12	4.45 ± 0.15	0.10 ± 0.11	0.06
LDL cholesterol (mmol/L)	2.27 ± 0.11	-0.07 ± 0.10	2.33 ± 0.11	-0.01 ± 0.09	0.54
HDL cholesterol (mmol/L)	1.63 ± 0.10	0.02 ± 0.04	1.69 ± 0.10	0.08 ± 0.04	0.04
Total:HDL cholesterol	2.74 ± 0.13	-0.05 ± 0.07	2.73 ± 0.12	-0.06 ± 0.06	0.82
Triacylglycerols (mmol/L)	0.98 ± 0.08	-0.02 ± 0.07	1.06 ± 0.08	0.05 ± 0.07	0.24
Insulin (pmol/L)[2]	41.99 ± 4.13	1.6 ± 3.76	45.66 ± 4.23	5.30 ± 4.39	0.22
Glucose (mmol/L)	5.24 ± 0.07	-0.05 ± 0.08	5.32 ± 0.09	0.03 ± 0.09	0.38
HOMA-IR[2]	1.37 ± 0.14	-0.06 ± 0.09	1.50 ± 0.14	0.10 ± 0.15	0.23

[1]All values are means ± SE. Statistical differences are based on linear mixed models with baseline values as covariates and adjustments for sex, age, BMI, and waist circumference. $n = 17$. [2]$n = 16$ because one sample was below the detection limit (14.4 pmol/L) and was removed from the analysis. HOMA-IR, homeostasis model assessment – insulin resistance.

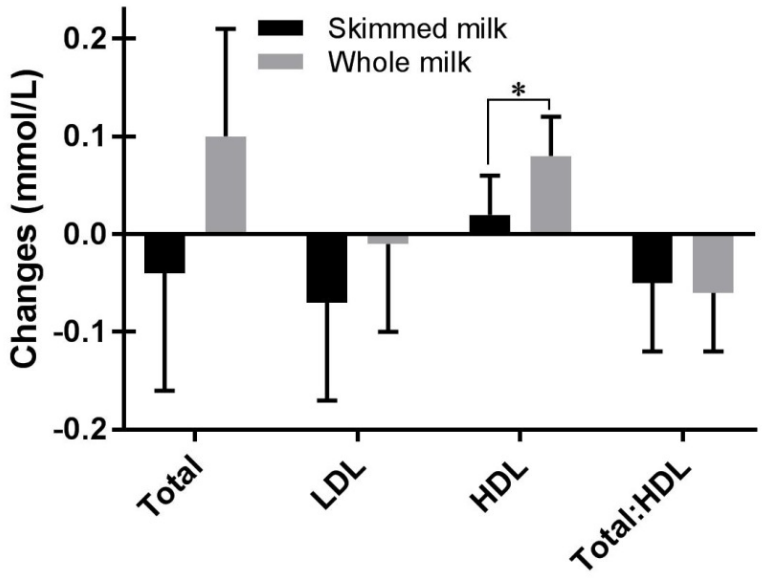


Figure 1. Mean ± SE concentrations of total, LDL, HDL and total:HDL cholesterol in healthy subjects after skimmed milk (black bars) and whole milk (grey bars) periods. Statistical differences were based on linear mixed models with baseline values as covariates and adjustments for sex, age, and waist circumference. *n*=17.*, Significantly different: $P < 0.05$.

Table 4

Average daily consumption of energy, macronutrients, and calcium during the skimmed- and whole milk periods[1]

	Skimmed	Whole	*P*
Total Energy (kJ)	8817 ± 359	10261 ± 672	0.02
Energy Density (kcal/g)	1.3 ± 0.0	1.4 ± 0.1	0.32
Fat (% of Energy)	32.7 ± 1.3	37.6 ± 0.8	< 0.001
Fat (g)	77.9 ± 4.1	103.6 ± 6.4	< 0.001
Saturated fat	27.0 ± 2.0	39.8 ± 2.5	< 0.001
Monounsaturated fat	28.5 ± 1.7	35.0 ± 2.3	0.02
Polyunsaturated fat	13.1 ± 1.0	16.7 ± 1.2	0.02
Carbohydrate (% of Energy)	48.9 ± 1.4	44.8 ± 1.1	0.002
Protein (% of Energy)	17.4 ± 0.5	16.6 ± 0.6	0.43
Calcium (mg)	1147 ± 48	1185 ± 57	0.47
Alcohol (g)	2.9 ± 0.9	4.0 ± 1.3	0.50
Dietary fiber (g)	28.7 ± 2.5	29.8 ± 2.7	0.49

[1]All values are means ± SEs. Statistical differences are based on paired t-test or Wilcoxon Signed Rank test for non-parametric variables (saturated fat and protein). $n = 17$. Data was assessed with a 3-d weighed dietary record. Estimated by using Dankost Pro dietary assessment software (Dankost).

Publication: Sara Engel, Mie Elhauge and Tine Tholstrup. Effect of whole milk compared with skimmed milk on fasting blood lipids in healthy adults: a 3-week randomized crossover study.

Accepted for publication in the EJCN.

Sub-project C

In this study, the effect of a high daily intake of semi-skimmed milk (1L/d) for 6-months was compared with sugar-sweetened soft drinks, non-caloric soft drinks and water on insulin sensitivity evaluated by an oral-glucose tolerance test (OGTT) (**Table 1**). The results showed no difference on insulin sensitivity between the beverages (**Figure 1 A-B**) or on any other risk markers of T2D. Furthermore, milk had no effect on concentration of cholesterol or the blood pressure compared with the other beverages, although sugar-sweetened soft drink consumption significantly increased total cholesterol compared with non-caloric soft drinks and triglycerides compared with non-caloric soft drinks and water (**Figure 2**). This implies that milk is neutral compared with sugar-sweetened soft drinks. Furthermore, analysis showed that there were no differences in change in weight during the intervention between the beverages (**Table 2**).

Table 1

Composition of the test beverages[1]

	Milk	NCSD	SSSD	WATER
Carbohydrate (g/100 mL)	4.7	0	10.6	0
Protein (g/100 mL)	3.4	<0.1	0	0
Fat (g/100 mL)	1.5	0	0	0
SFA	1.0	0	0	0
MUFA	0.4	0	0	0
PUFA	0.1	0	0	0
Energy (kJ/d)	1900	15	1800	0
Volume (mL)	1000	1000	1000	1000

[1]Subjects were randomized to consume 1 L of milk, NCSD, SSSD, or WATER daily for 6 months.

MUFA, mono-unsaturated fatty acid; NCSD, non-calorie soft drink; PUFA; poly-unsaturated fatty acid; SSSD, sugar-sweetened soft drink; SFA, saturated fatty acid

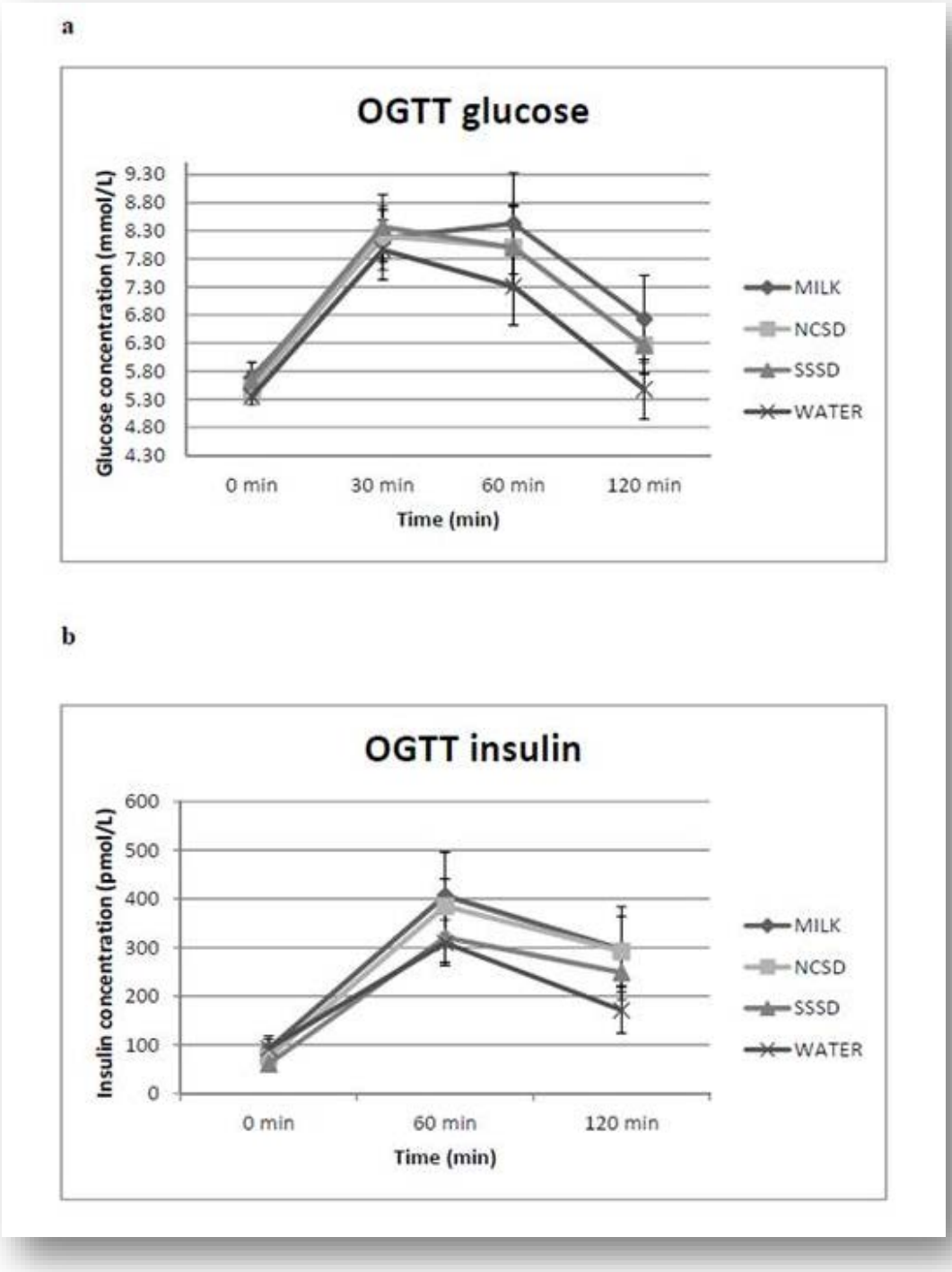


Figure 1. Oral glucose tolerance test (OGTT) measurements performed after 6 months of intervention. All values are means ± SE. *n* = 58 (glucose) and 57 (insulin). Subjects were randomly assigned to the 4 groups of 1 daily L of test beverage. Glucose-tolerance was measured using a standard 75 g oral glucose-tolerance test. There was no significant difference in the time course of glucose and insulin concentration after the 4 different beverage groups according to the repeated measures analysis of variance.

Table 2

Sex, age and anthropometric measurements and body composition at baseline, after 6 months intervention and differences between the beverage groups[1]

	MILK	NCSD	SSSD	WATER	*P*
Sex [n (%)]	15 (25)	15 (25)	14 (23.3)	16 (26.7)	
Women	11 (18.3)	12 (20)	6 (10)	11 (18.3)	
Men	4 (6.7)	3 (5)	8 (13.3)	5 (8.3)	
[2]Age, y	37.7 ± 9.1	39 ± 7.6	37.8 ± 8.0	39 ± 7.3	0.94
Body weight, kg					
Pre-intervention	94.0 ± 17.1	94.5 ± 12.6	94.9 ± 11.6	98.4 ± 21.8	0.87
Post-intervention	95.5 ± 4.3	95.0 ± 3.3	96.4 ± 3.0	99.1 ± 5.8	0.43
BMI, kg/m^2					
Pre-intervention	31.4 ± 3.0	33.4 ± 4.1	30.8 ± 2.8	31.5 ± 4.5	0.25
Post-intervention	32.0 ± 0.8	33.6 ± 1.1	31.3 ± 0.7	31.7 ± 1.1	0.30
Fat mass, kg					
Pre-intervention	34.6 ± 6.9	38.3 ± 11.3	33.5 ± 7.5	35.7 ± 10.9	0.56
Post-intervention	35.9 ± 2.4	38.5 ± 2.8	35.6 ± 2.3	35.9 ± 3.3	0.27
Fat free mass, kg					
Pre-intervention	56.7 ± 14.1	53.6 ± 10.6	59.7 ± 11.3	56.3 ± 12.3	0.64
Post-intervention	57.3 ± 3.8	54.1 ± 2.8	58.4 ± 3.1	56.4 ± 3.3	0.34

The subjects were randomly assigned to the 4 groups of 1 daily L of test beverage. [1]All values are means ± SEs. Statistical differences were analysed in an ANCOVA model with gender and values from baseline included as covariates. $n = 60$ ($n = 58$ for fat mass and fat free mass due to 2 subjects had missing values). [2]For age values are means ± SDs and difference analyzed by ANOVA. NCSD: non-caloric soft drink, SSSD: sugar-sweetened soft drink

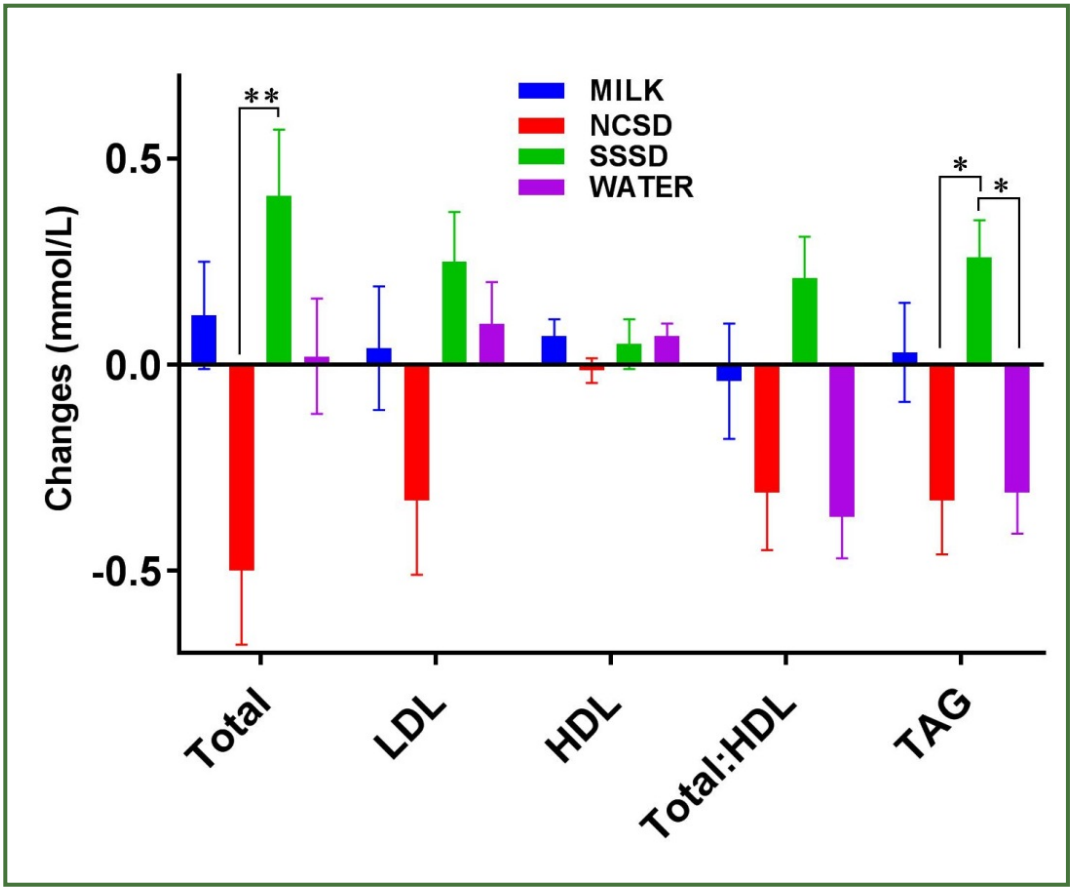


Figure 2. Means ± SEM changes in total, LDL, HDL, Total:HDL cholesterol and triacylglycerol (TAG) concentrations after 6 months intake of the beverages, *n* = 58 because 2 subjects had missing values for change in FM. Statistical differences were analyzed in an ANCOVA model with Tukey pairwise comparisons adjusted for baseline and the covariates; age, gender, baseline BMI and change in FM (kg). Significant difference: **P*<0.05, ***P*<0.01.

Publication: Sara Engel, Tine Tholstrup, Jens M Bruun, Arne Astrup, Bjørn Richelsen, and Anne Raben. Effect of high milk and sugar-sweetened and non-caloric soft drink intake on insulin sensitivity after 6 months in overweight and obese adults: a randomized controlled trial.
Accepted for publication in the EJCN

Short overall conclusion

In conclusion, as even a moderate intake of butter increased total and LDL cholesterol compared to olive oil and the habitual diet, people with raised cholesterol levels should keep their consumption of butter to a minimum, however as the HDL cholesterol also was raised significantly compared with the habitual diet the results suggests that there is room for at moderate butter intake in a healthy diet among people with a healthy cholesterol level. Furthermore, we conclude that in spite of belonging to the category of high fat dairy products whole milk (3.5%) and semi-skimmed milk (1.5%) were shown to be beneficial or neutral, respectively, and results suggests that if the higher energy content is taken in to

consideration compared to skimmed milk (0.5%) whole milk can be included in a healthy diet among healthy people.

11. Deviations

11.1 Scientific

The following changes were made: The project **aim** initially included development of diet plans for healthy diets including butter and an overview article on the role of dairy fat in relation to risk markers of CVD. We believe that many similar overview articles have been published in recent years and by leaving out these two activities we got room for two additional human intervention trials examining dairy products and risk of CVD and T2D.

11.2 Financial

No deviations

11.3 Timetable

The project was prolonged almost 2 years due to 2 periods of maternity leave (April 2014-April 2015 and January 2016-December 2016).

12. The relevance of the results, including relevance for the dairy industry

In this project the effect of intake of so-called high fat dairy products such as butter, whole milk and semi-skimmed milk on risk markers of CVD and T2D was investigated. As whole foods are consumed every day by many people the result of these studies have a high level of practical relevance and applicability to the consumers. For decades dietary guidelines have recommended that intake of saturated fat should be limited and therefore that one should choose low fat dairy products. The literature behind these recommendations is in large part based on expected effects of macronutrients, as very few studies have been conducted examining the effect of whole foods.

The role of butter in a healthy diet has been further elucidated and the results can help nuance the consumers' understanding of butter. The study results showed that butter even in moderate amounts increase LDL cholesterol compared with a neutral oil such as refined olive oil and the habitual diet of the participants. However, butter also showed to increase HDL cholesterol compared to the habitual diet. Hereby, the role of butter in a healthy diet has been further examined and showed that for healthy people there is room for a moderate butter intake, but among people with elevated cholesterol level butter intake should be kept to a minimum.

Despite of belonging to the category of high fat dairy products, whole milk and semi-skimmed milk were shown to be respectively beneficial or neutral and the results implies that if the higher energy content is taken into consideration there are room for whole milk and semi-skimmed milk in a healthy diet.

Today, dietary guidelines recommends that intake of dairy should be limited to low-fat dairy products. We showed that ½L/d of whole milk increased HDL cholesterol without adversely affecting LDL cholesterol, which implies taking the higher energy content into account that whole milk can be consumed just as well

as skimmed milk in a healthy diet. In addition, Raziani et al found no difference in effect on LDL cholesterol and risk markers of the metabolic syndrome after comparing a diet with regular fat cheese and reduced fat cheese(1). Further studies could address other high-fat and low-fat dairy products and in light of the interesting results from a very recent observational study from Laursen et al at Aarhus University(2), where substitution of whole fat yoghurt with low fat yoghurt (semi-skimmed) resulted in lower risk of ischemic stroke with whole fat yoghurt, a comparison between whole fat yoghurt and low-fat yoghurt would be very interesting to undertake in a controlled crossover intervention study in relation to risk of CVD and T2D.

1. Raziani F, Tholstrup T, Kristensen MD, Svanegaard ML, Ritz C, Astrup A, Raben A. High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome: a randomized controlled trial. Am J Clin Nutr. 2016;104:973–81.
2. Laursen ASD, Dahm CC, Johnsen SP, Tjønneland A, Overvad K, Jakobsen MU. Substitutions of dairy product intake and risk of stroke: a Danish cohort study. Eur J Epidemiol. 2017;

13. Communication and knowledge sharing about the project

Papers in international journals:
Sara Engel and Tine Tholstrup. *Butter increased total and LDL cholesterol compared with olive oil but resulted in higher HDL cholesterol compared with a habitual diet*. *Am J Clin Nutr* 2015;102:309-15.

Sara Engel, Mie Elhauge and Tine Tholstrup. *Whole milk increased HDL cholesterol compared with skimmed milk without adversely affecting LDL cholesterol: a 3-week randomized crossover study.*
Accepted for publication in EJCN

Sara Engel, Tine Tholstrup, Jens M Bruun, Arne Astrup, Bjørn Richelsen, and Anne Raben. *Effect of high milk and sugar-sweetened and non-caloric soft drink intake on insulin sensitivity after 6 months in overweight and obese adults: a randomized controlled trial.*
Accepted for publication in EJCN

Easily read papers:
Engel, S. *Er der plads til smør?* Mælkeritidende nr. 20, 2013

Student theses:
Mie Elhauge Kristensen. *Effect of Whole- and Skimmed Milk Consumption on Risk Markers of Cardiovascular Disease and Type Two Diabetes Mellitus – A Randomized Crossover Trial*. (Master thesis project)

Drejer *et al* 2014. *Cheese may not increase LDL-cholesterol, which is a risk marker of cardiovascular disease.* (Report based on group work in the MSc course: Thematic course in Human Nutrition)

Oral presentations at scientific conferences, symposiums etc.:
Engel, S. *Dairy products and risk of CVD and type 2 diabetes*. Summer Section Seminar, NEXS, KU-SCIENCE 12. June 2015

Engel, S. *Er der plads til smør?* Fedtstoffer i Mejeriindustrien ved Danmarks Mejeritekniske Selskab, Hotel Legoland, Billund 3. December 2015.

Engel, S. *Dairy and risk of cardiovascular disease and type 2 diabetes*. NEXS Annual Research Day, 19. April 2017 (Blitz talk competition).

Engel, S. *Is butter back?* Nordic Dairy Congress, Copenhagen 8-9. June 2017. (Flash talk presentation)

Engel, S, Tholstrup, T, Bruun, JM, Astrup, A, Richelsen, B and Raben A. *High intake of milk does not affect insulin sensitivity after 6 months in overweight adults: a randomized controlled trial.* 35th International Symposium on Diabetes & Nutrition at DNSG 19-22 June 2017. (Short oral presentation)

Poster presentations at scientific conferences:
Engel, S, Tholstrup, T, Bruun, JM, Astrup, A, Richelsen, B and Raben A. *High intake of milk does not affect insulin sensitivity after 6 months in overweight adults: a randomized controlled trial.* 35th International Symposium on Diabetes & Nutrition at DNSG 19-22 June 2017.

Engel S and Tholstrup T. *Whole milk increased HDL cholesterol compared to skimmed milk without adversely affecting other lipids, glucose and insulin in a 2x3 week crossover study.* IUNS 21st International Congress of Nutrition, Buenos Aires, Argentina 15-20 October 2017.

Oral presentations at meetings:
Engel, S. *Is there room for butter in a healthy diet?* Section meeting, Preventive and Clinical Nutrition, NEXS, KU-SCIENCE, 19. March 2015.

Engel, S. *Dairy and risk of cardiovascular disease and type 2 diabetes*. Ph.D. status seminar 18. May 2017 for the section and supervisors, Preventive and Clinical Nutrition, NEXS, KU-SCIENCE.

14. Contribution to master and Ph.D. education

Sara Engel was at a 3-month research stay at Research Center for Prevention and Health in the Section of Health Promotion and Health, Capital Region, Denmark (August - October 2017).

15. New contacts/projects

None

16. Signature and date

The project is formally finalised when the project manager and DDRF-representative (e.g. steering committee leader) have signed this final report.

Date: _____Signature, Project manager:_____

Date:1. Nov 2017 Signature, DDRF-representative: