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Metabolic syndrome and dairy products : results from a French prospective study, D.E.S.I.R. (Data from the Epidemiological Study on the Insulin Resistance Syndrome)

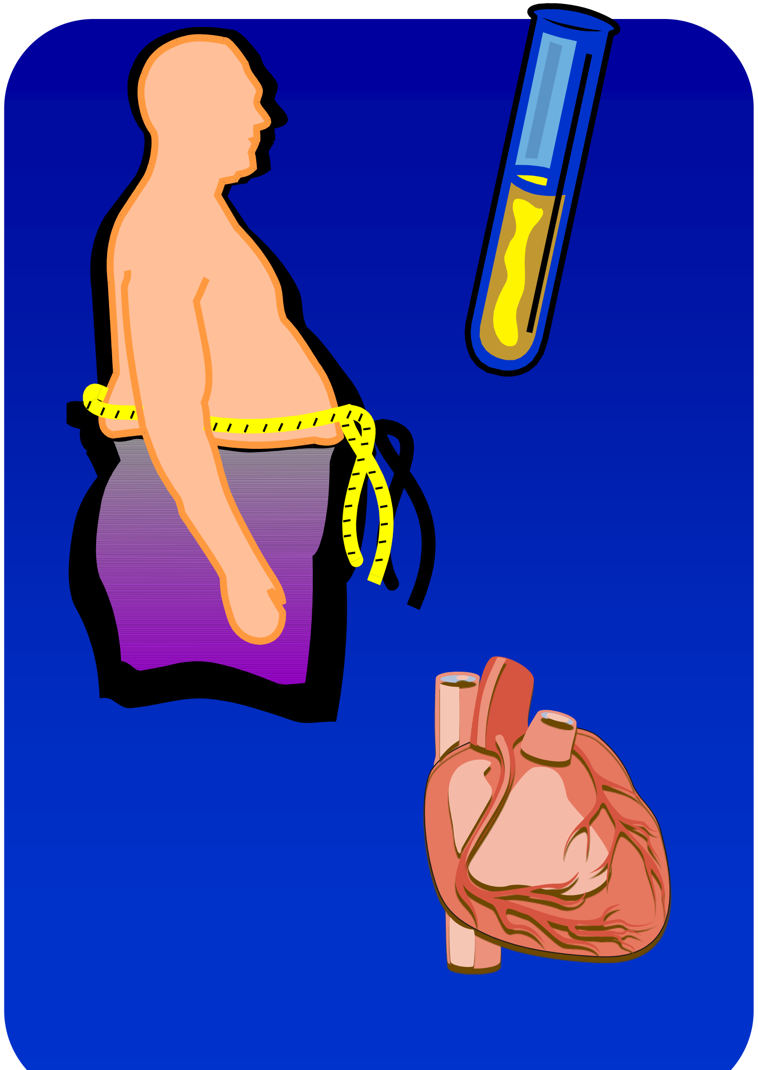
F. Fumeron, A. Lamri, C. Abi Khalil, R. Jaziri, I. Porchay-Baldérelli, O. Lantieri, S. Vol, B. Balkau, M. Marre.

Dairy consumption and the incidence of hyperglycaemia and metabolic syndrome:
results from a French prospective study, D.E.S.I.R. (Data from the Epidemiological Study on the
Insulin Resistance Syndrome). Diabetes Care 2011;34:813–817

Adipose tissue distribution

Gynoid vs. android pattern

Metabolic syndrome
= Insulin Resistance Syndrome



- Abdominal obesity
- Hyperinsulinemia
- High fasting plasma glucose
- Impaired glucose tolerance
- Hypertriglyceridemia
- Low HDL-cholesterol
- Hypertension

Cardiovascular risk

- LDL-C = risk factor +++
- Saturated fats and dietary cholesterol from animal products ↗ LDL-C
- However: no clear evidence ↗ cardiovascular risk with milk and dairy products

Dairy products and insulin resistance : epidemiological data

- CARDIA prospective study (USA)
  - High intake: ↓ 72% metabolic syndrome risk, compared to low intake *(Pereira et al. 2002)*

- D.E.S.I.R. cross sectional study (France)
  - At least one daily portion of milk products: ↓ 40% metabolic syndrome risk in men *(Mennen et al. 2000)*

  - Calcium intake: ↓ arterial blood pressure, ↑ HDL-cholesterol, ↓ insulin *(Drouillet et al. 2007)*

AIM

To study prospectively the associations in the D.E.S.I.R. cohort between the intake of dairy products at baseline and the incidence of Metabolic Syndrome and related parameters during a 9-year follow-up

METHODS

D.E.S.I.R. study

(Data from the Epidemiological Study on the Insulin Resistance Syndrome)

- Prospective study with a 9-year follow-up
- 5212 volunteer subjects from ten Health Examination Centres in the western central part of France
- Visits : 0, 3, 6 et 9 years → clinical, biological, anthropometric variables + questionnaires for lifestyle, etc.

D.E.S.I.R. study

(Data from the Epidemiological Study on the Insulin Resistance Syndrome)

	Baseline characteristics
N (Men/Women)	**5212 (2576 / 2636)**
Age (years) [30-64]	**46.7 ± 10.0**
Fasting plasma glucose (mmol/L)	**5.33 ± 0.89**
BMI (kg/m²)	**24.7 ± 3.8**

For this study, subjects on diet or with type 2 diabetes at inclusion, subjects without IFG/T2D or MetS but lost at-follow-up (T9) were excluded ➔ # 3400 subjects in the analyses

Metabolic syndrome criteria

- NCEP-ATP III (at least 3 of the following)
  - Waist circumference ≥ 102 cm (men), ≥ 88 cm (women)
  - HDL-Cholesterol < 1.03 mmol/l (men), <1.29 mmol/l (women)
  - Triglycerides ≥ 1.70 mmol/l
  - Systolic blood pressure ≥ 130mm Hg OR diastolic ≥ 85 mm Hg
  - Fasting plasma glucose ≥ 6.1 mmol/l (1.10g/l)

- IDF (International Diabetes Federation)
  - Waist circumference ≥ 94 cm (men), ≥ 80 cm (women)

  \+ 2 other criteria
  - HDL-Cholesterol < 1.03 mmol/l (men), <1.29 mmol/l (women)
  - Triglycerides ≥ 1.70 mmol/l
  - Systolic BP ≥ 130 mmHg OR diastolic ≥ 85 mmHg OR antihypertensive treatment
  - Fasting plasma glucose ≥ 5.6 mmol/l OR antidiabetic treatment

Food questionnaire

- Very simple food frequency questionnaire with 23 questions on usual diet, including for dairy products :
  - "How many times do you take milk or milk products per day, including breakfast?" (milk, yoghurt, cream cheese, etc.)
    - → never ; < 1 portion/day ; 1-2 portions/day ; > 2 /day
  - "How much cheese do you eat per day?"
    - → 0-1 portion/day ; 2-3 portions/day ; > 3/day
  - One portion = 125 mL milk or milk products = 30 g cheese (1/8 camembert!)
- The questionnaire has been validated, its results can be transformed into amounts of energy and nutrients.
- Sex specific quartiles of calcium density (calcium intake/1000kcal) were calculated

Dairy products consumption I (T0)

DAIRY PRODUCTS (no cheese)

	never %	< 1/day %	1-2/day %	2/day %	*N*
Men	13.0	25.3	50.7	11.0	*2 527*
Women	6.2	19.7	54.8	19.4	*2 582*
Total	**9.5**	**22.5**	**52.8**	**15.3**	
N	*487*	*1 147*	*2 695*	*780*	*5 109*

P<0.001

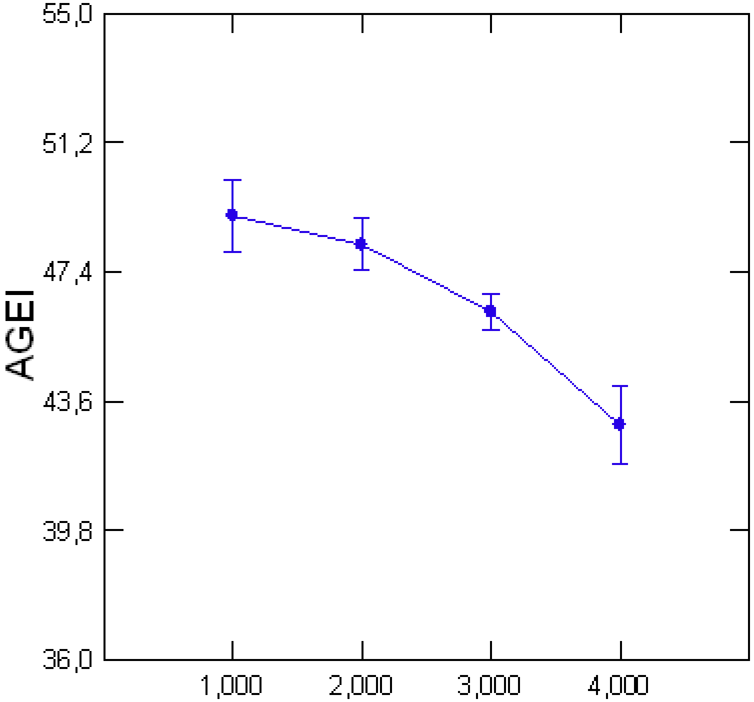
CHEESE

	0-1/day %	2-3/day %	> 3/day %	*N*
Men	36.2	56.6	7.2	*2 527*
Women	48.9	46.0	5.0	*2 579*
Total	**42.6**	**51.3**	**6.1**	
N	*2 177*	*2 618*	*311*	*5 106*

P<0.001

Dairy products consumption II (T0)

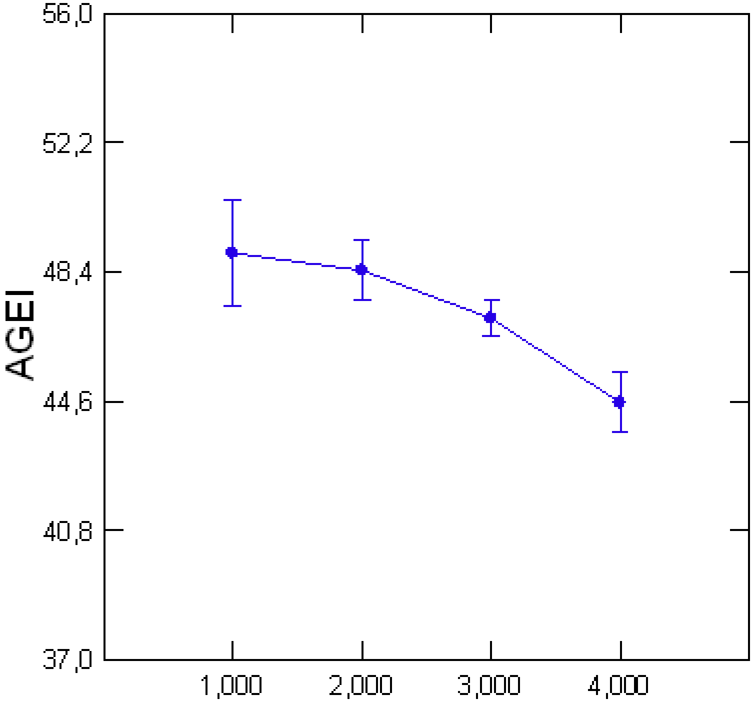
Least Squares Means



DAIRY (no cheese)

MEN : P<0.001

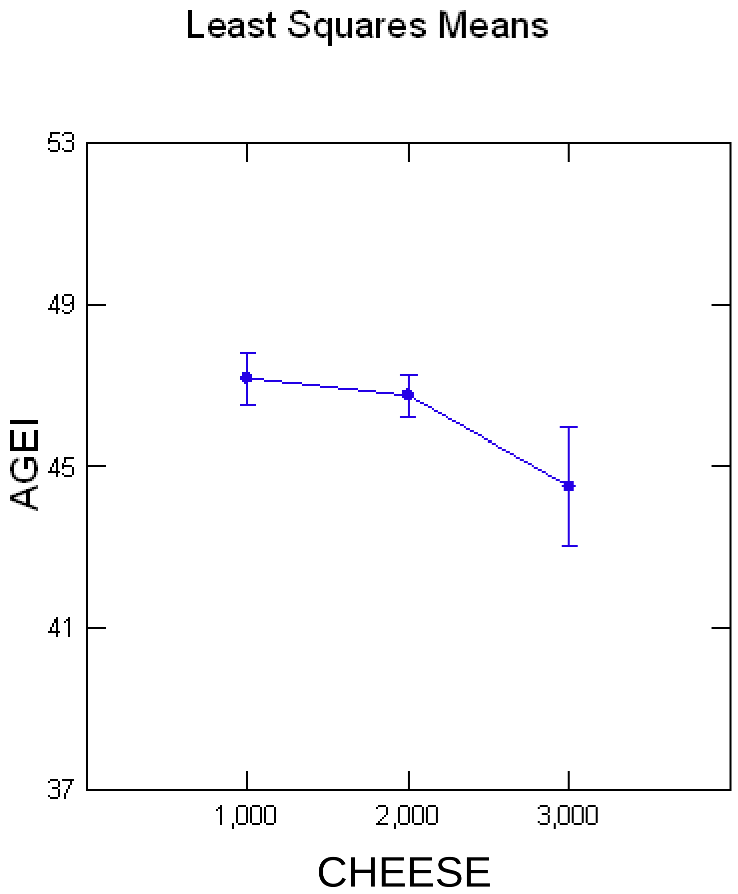
Least Squares Means



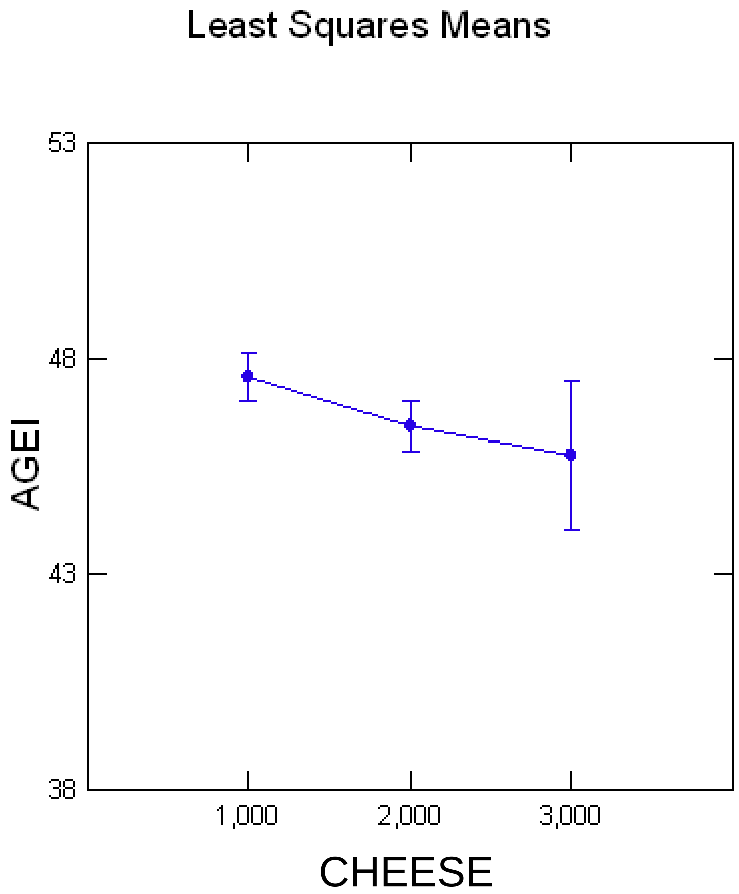
DAIRY (no cheese)

WOMEN : P<0.001

Dairy products consumption III (T0)

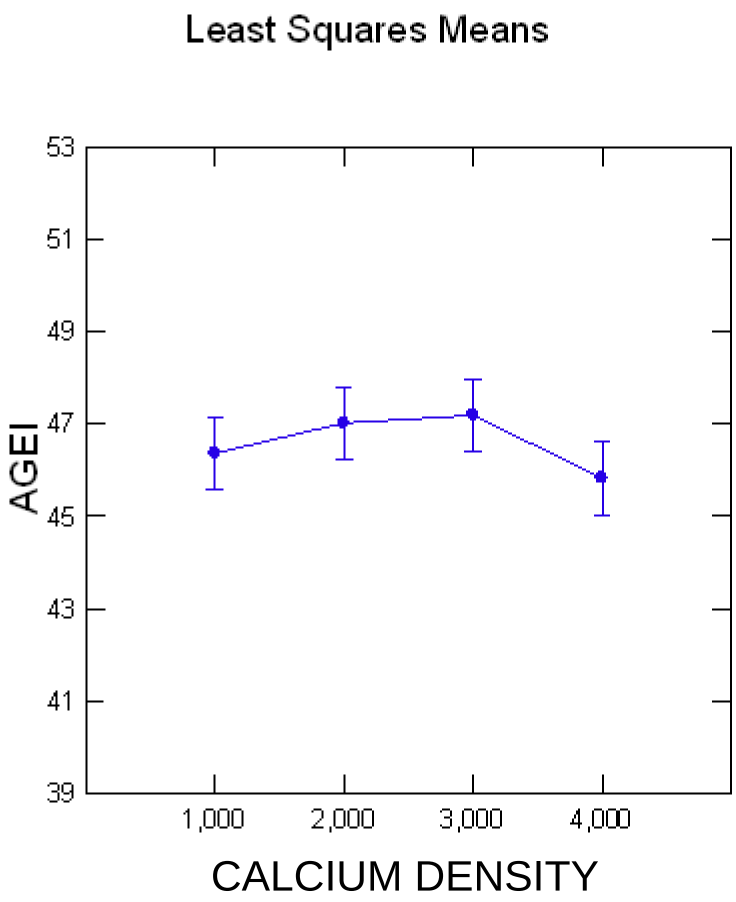


MEN : P=0.005
(2 groups : p = 0.10)

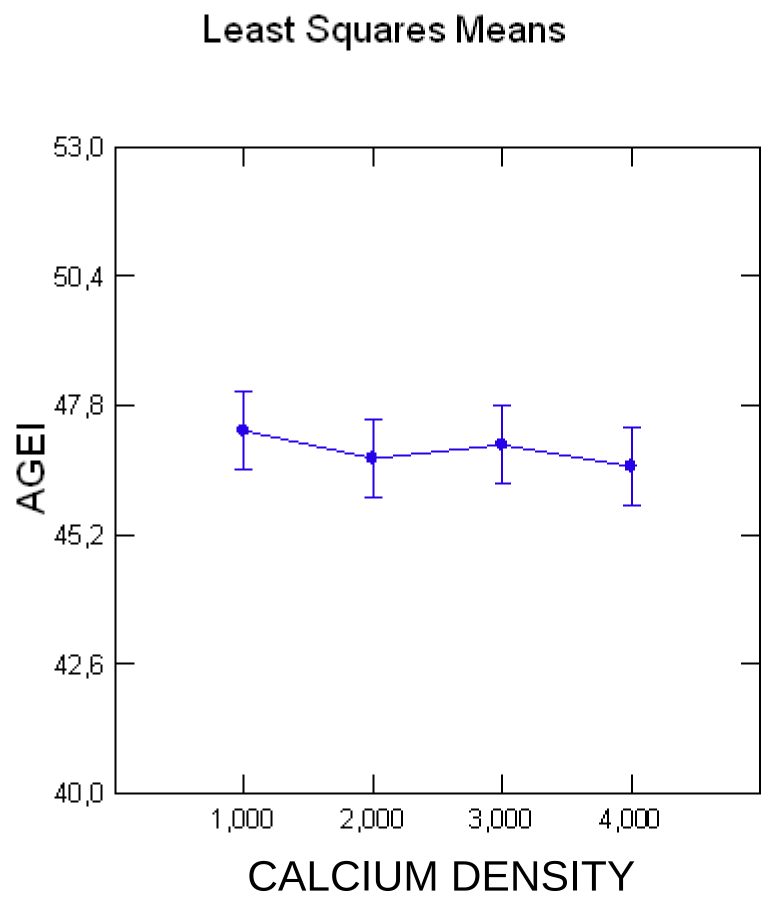


WOMEN : P=0.008
2 groups : p = 0.002

Dairy products consumption IV (T0)



MEN : P=0.07



WOMEN : P=0.60

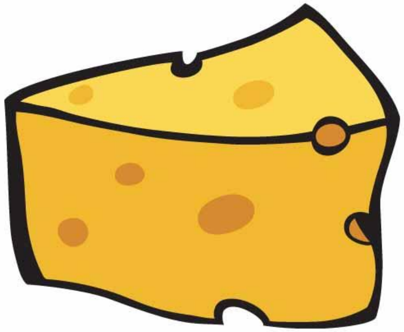
Statistics

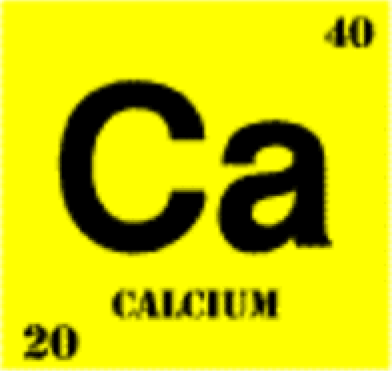
Tests for associations between dairy variables and

- incidence of diseases (metabolic syndrome, impaired fasting glycemia, type 2 diabetes) by: logistic regression
  - Model 1 : Covariates = age, sex, alcohol consumption, smoking status, physical activity, fat intake
  - Model 2 = model 1 + BMI (mean T0-T9) as covariate
  - Odds ratios indicate the risk for a change from one group to the next (e.g. from one quartile of calcium density to the next quartile)

- continuous variables (BMI, blood pressure, etc.) by: ANCOVA for repeated measures
  - to test for average effect of dairy products and effects on changes between baseline and the end of the follow-up (9 years), adjusted for age, sex, alcohol, smoking, physical activity, fat intake, BMI (meanT0-T9)

RESULTS



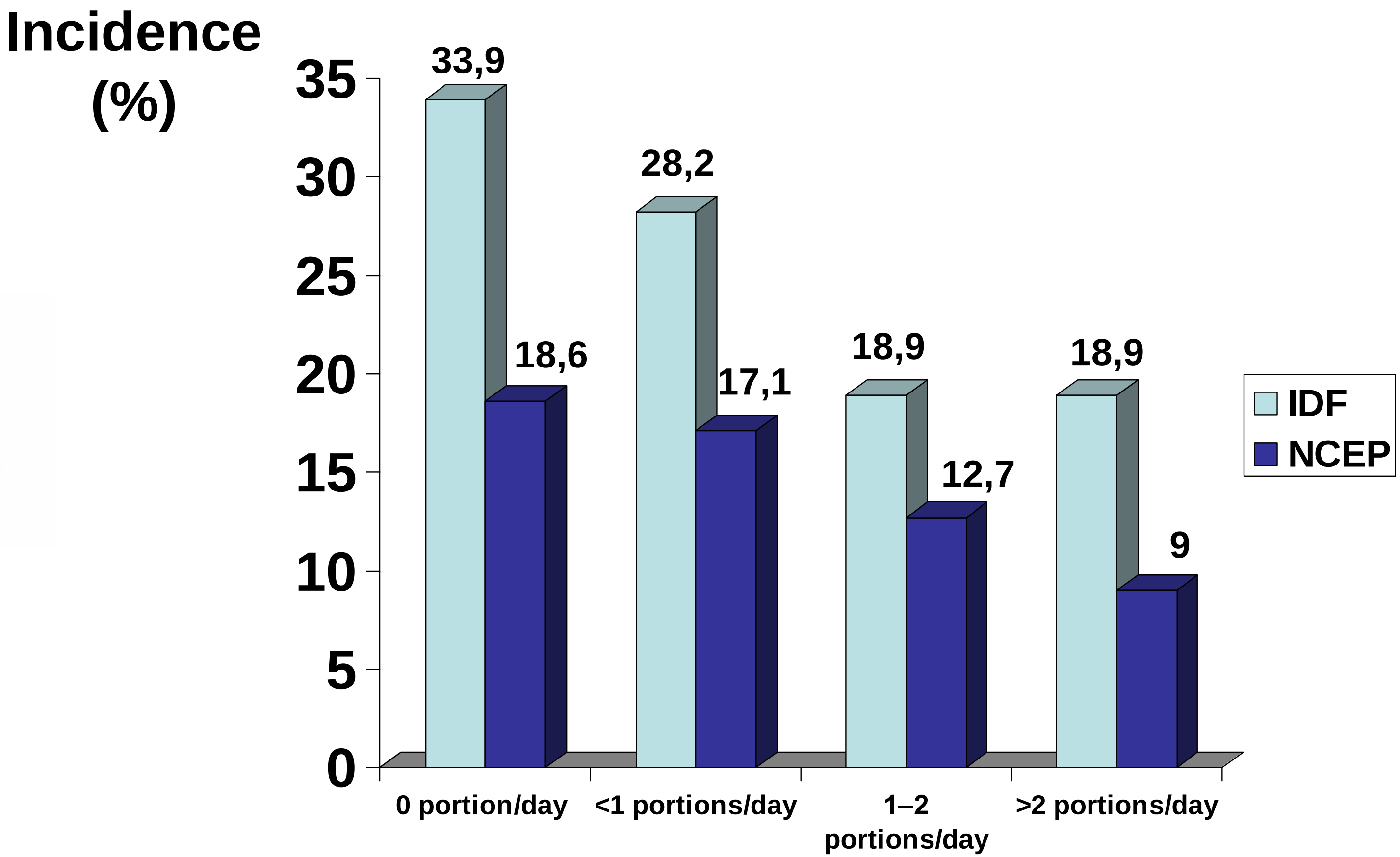


Results

- Milk products (cheese excluded)

Milk product consumption and metabolic syndrome

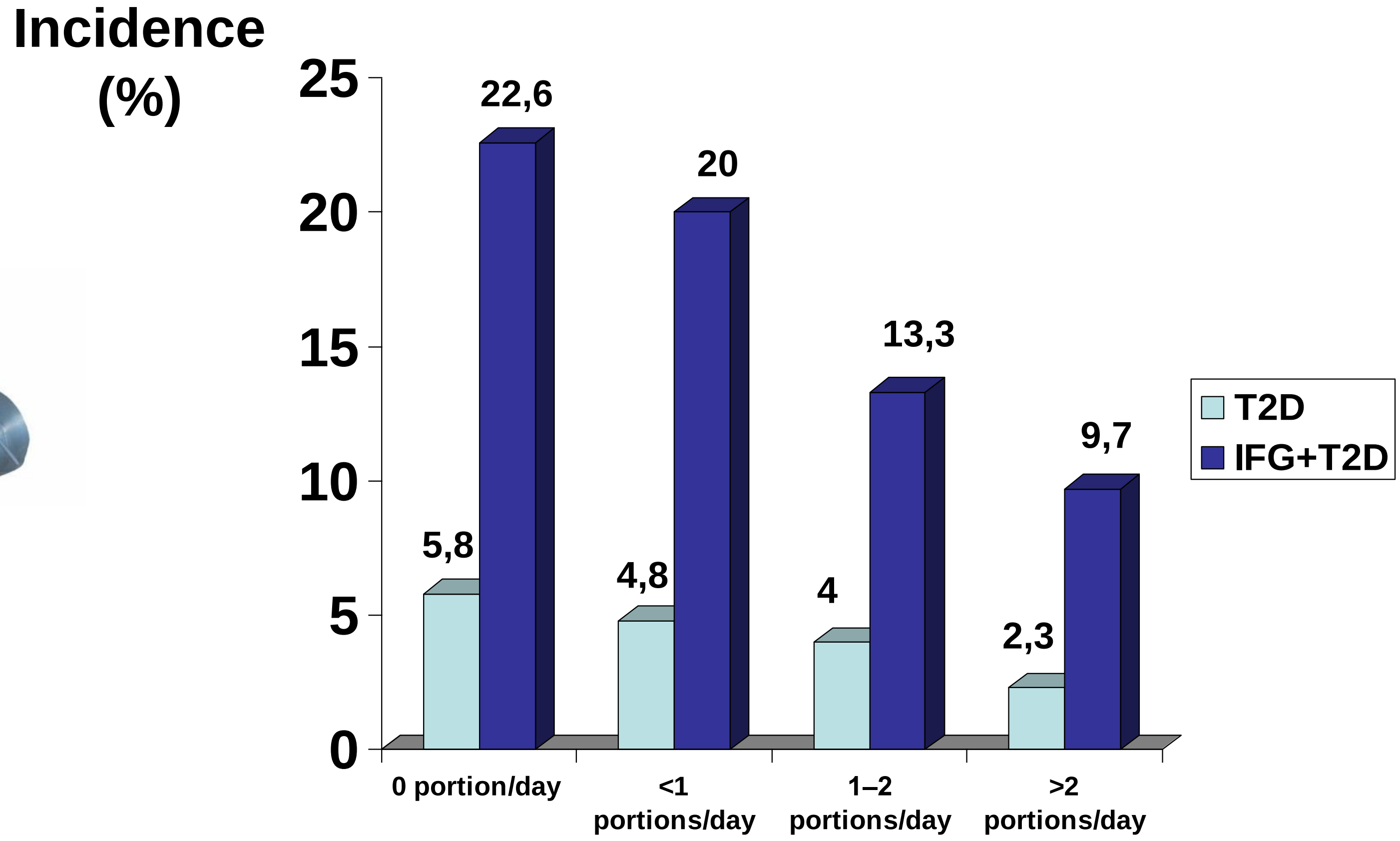
Whole population



IDF : Model 1 : OR = **0.83** (0.74-0.93) ; p=0.002
Model 2 : OR = **0.84** (0.74-0.93) ; p = 0.008

NCEP : Model 1 : OR = **0.81** (0.72-0.92) ; p= 0.001
Model 2 : OR = **0.89** (0.77-1.02) ; p = 0.09 (NS)

Milk product consumption and incidence of type 2 diabetes and/or impaired fasting glycemia



No effect on T2D alone

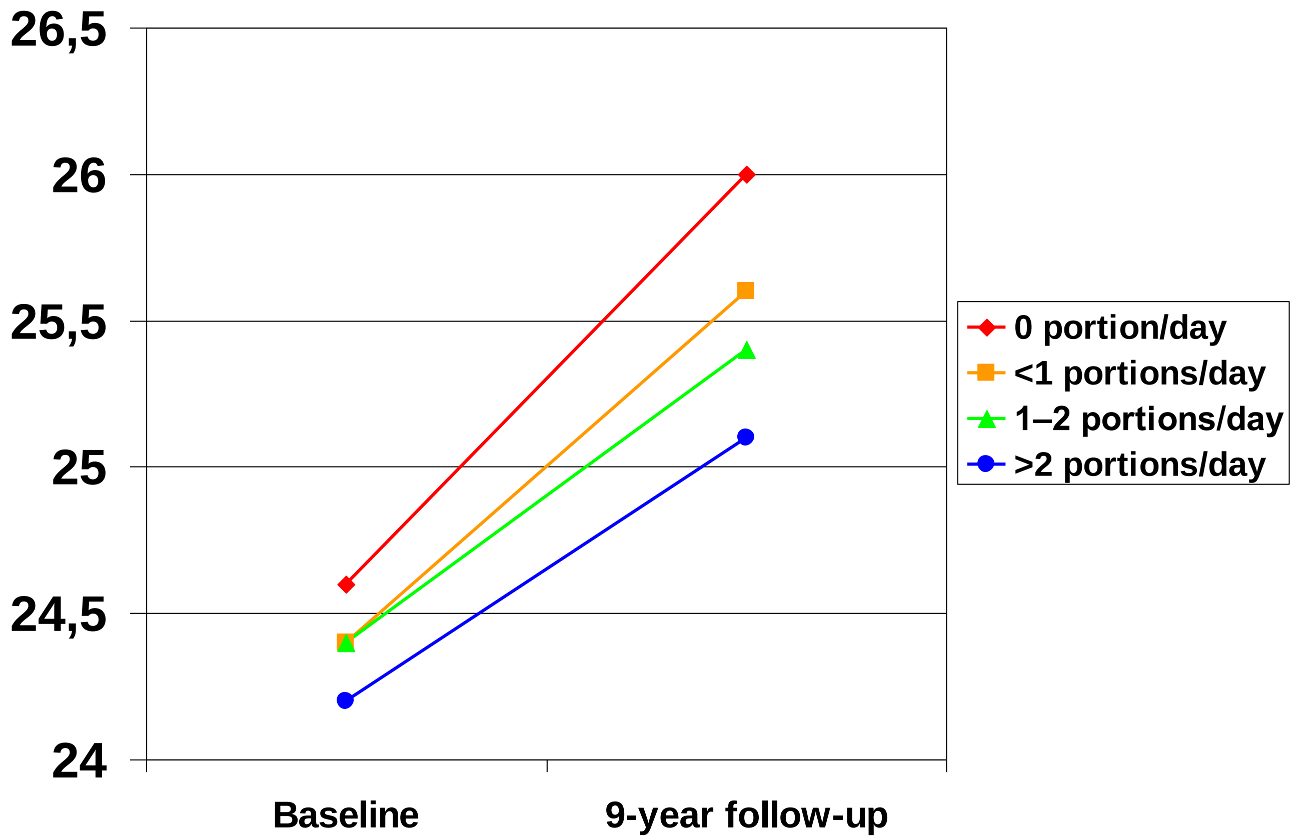
IFG+T2D model 1 : OR = **0.78** (0.69-0.88); p=0.0002

model 2 : OR = **0.80** (0.71-0.91); p= 0.001

Milk product consumption and BMI

Whole population

BMI at baseline and after a 9-year follow-up, by milk product consumption at baseline



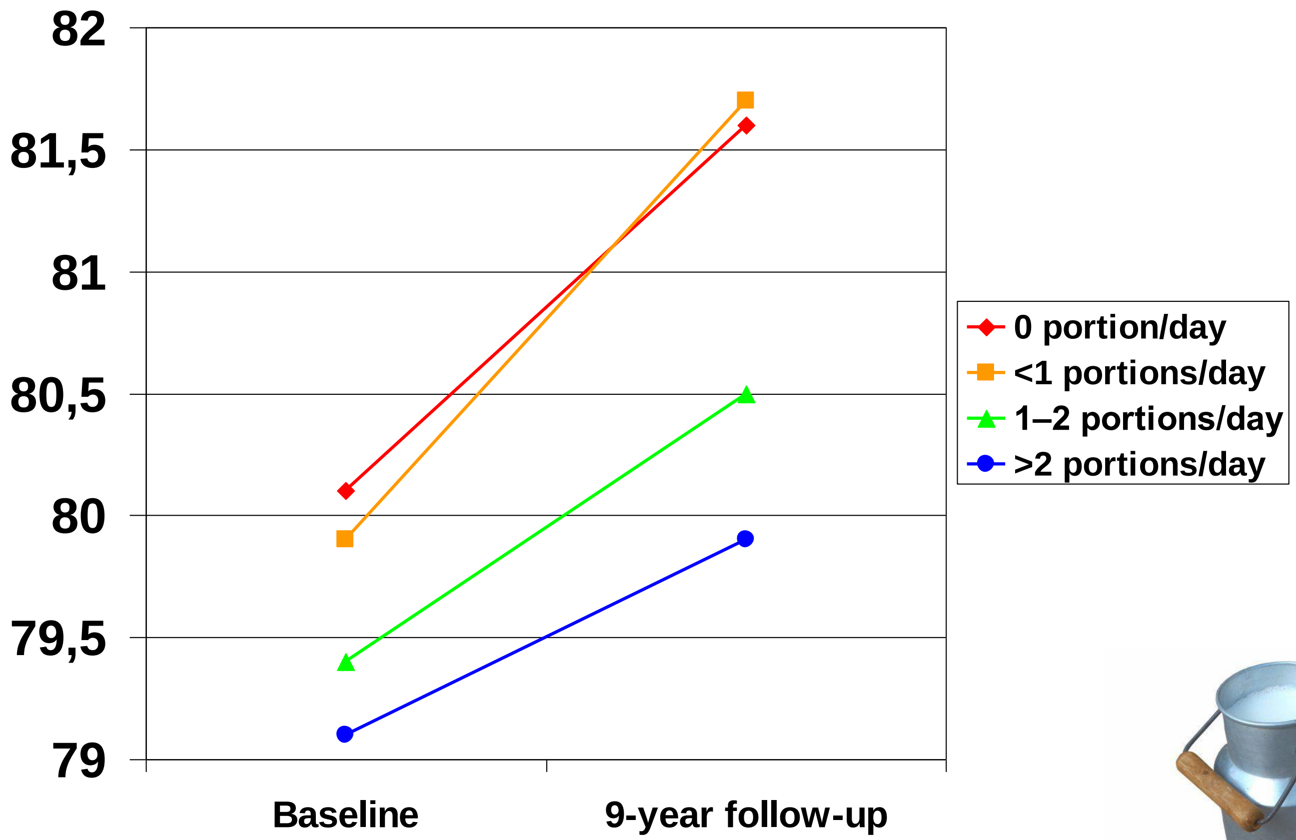
Average effect of milk product on BMI: p=0.10

Effect of milk products on changes in BMI : p=0.002

Milk product consumption and Diastolic Blood Pressure

Whole population

DBP (mmHg) at baseline and after a 9-year follow-up, by milk product consumption at baseline

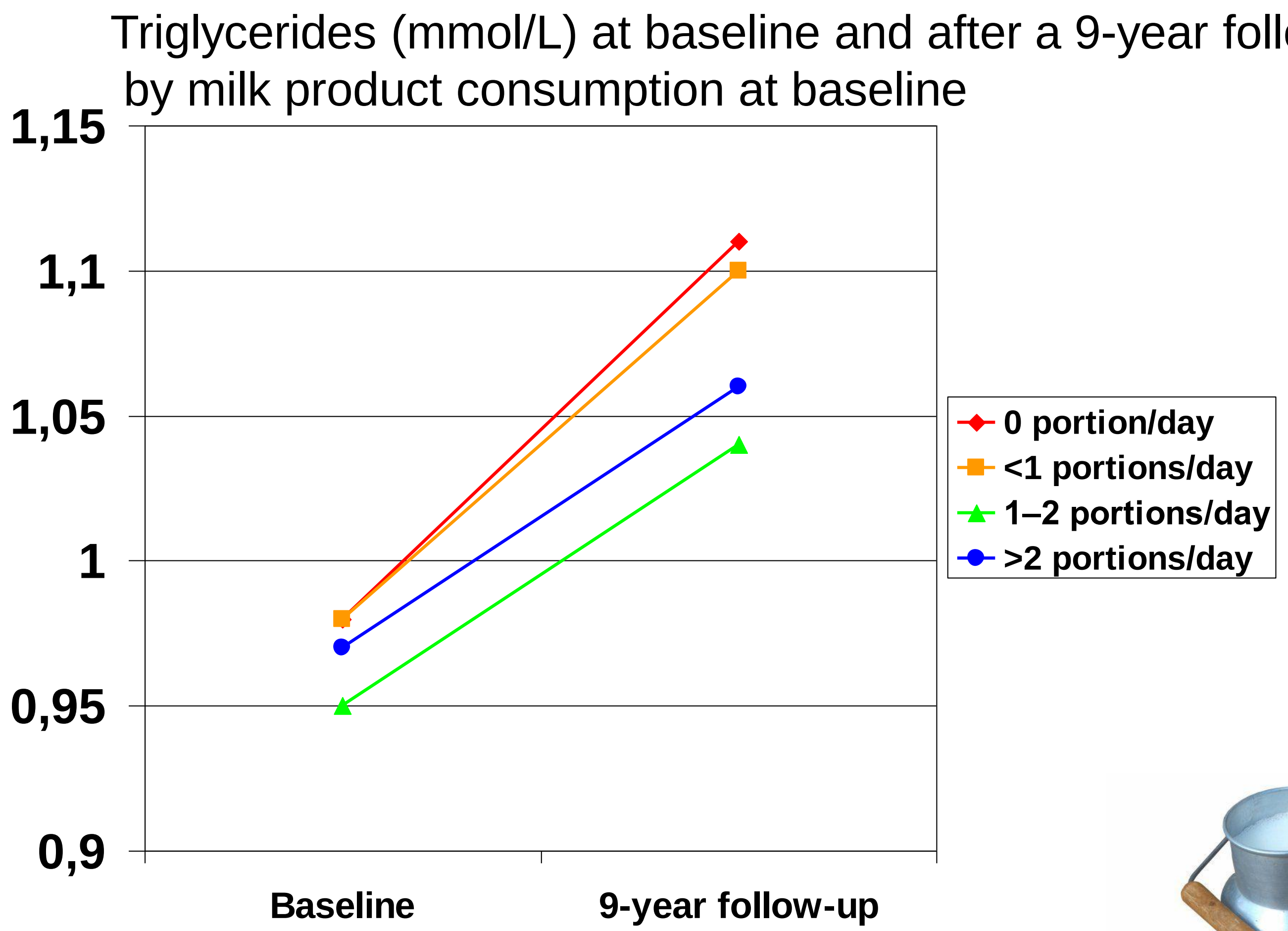


Average effect of milk product on DBP: p=0.009

Effect of milk products on changes in DBP : NS

Milk product consumption and plasma triglycerides

Whole population



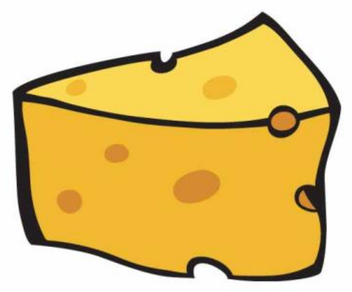
Average effect of milk product on TG: p=0.03

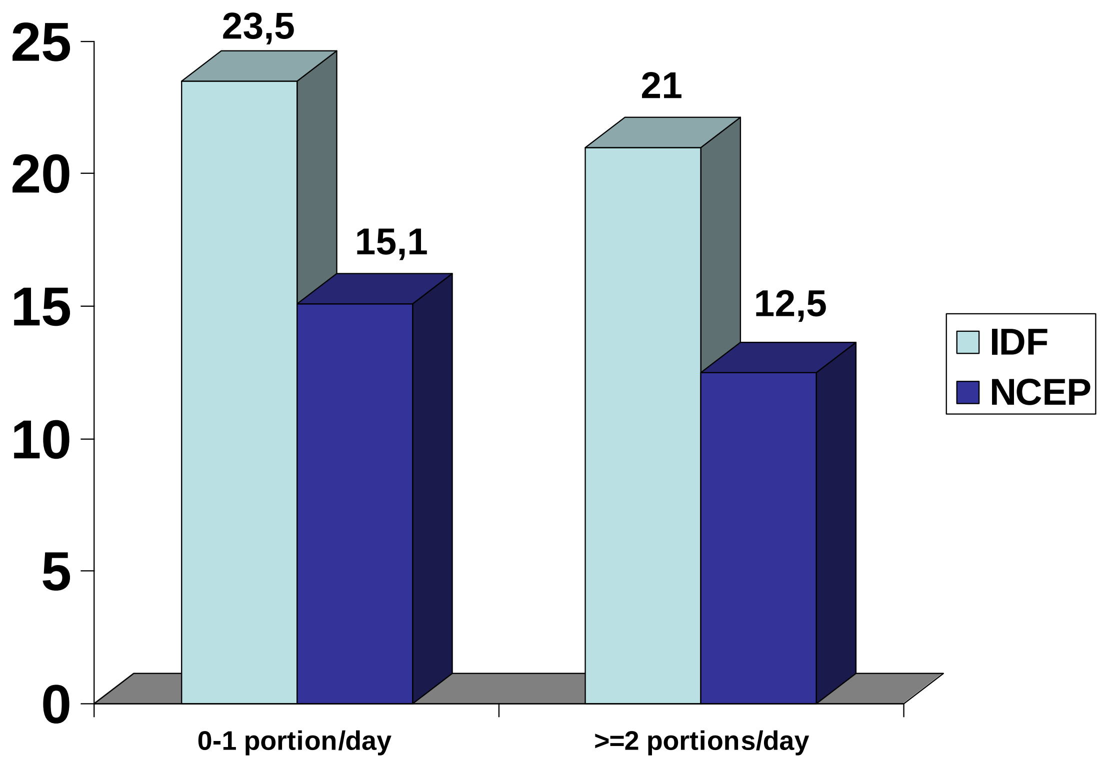
Results

- Milk products (cheese excluded)
- Cheese

Cheese consumption and metabolic syndrome

Whole population



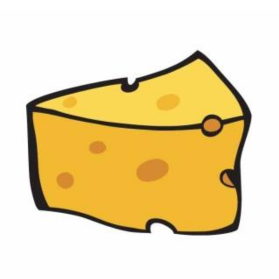


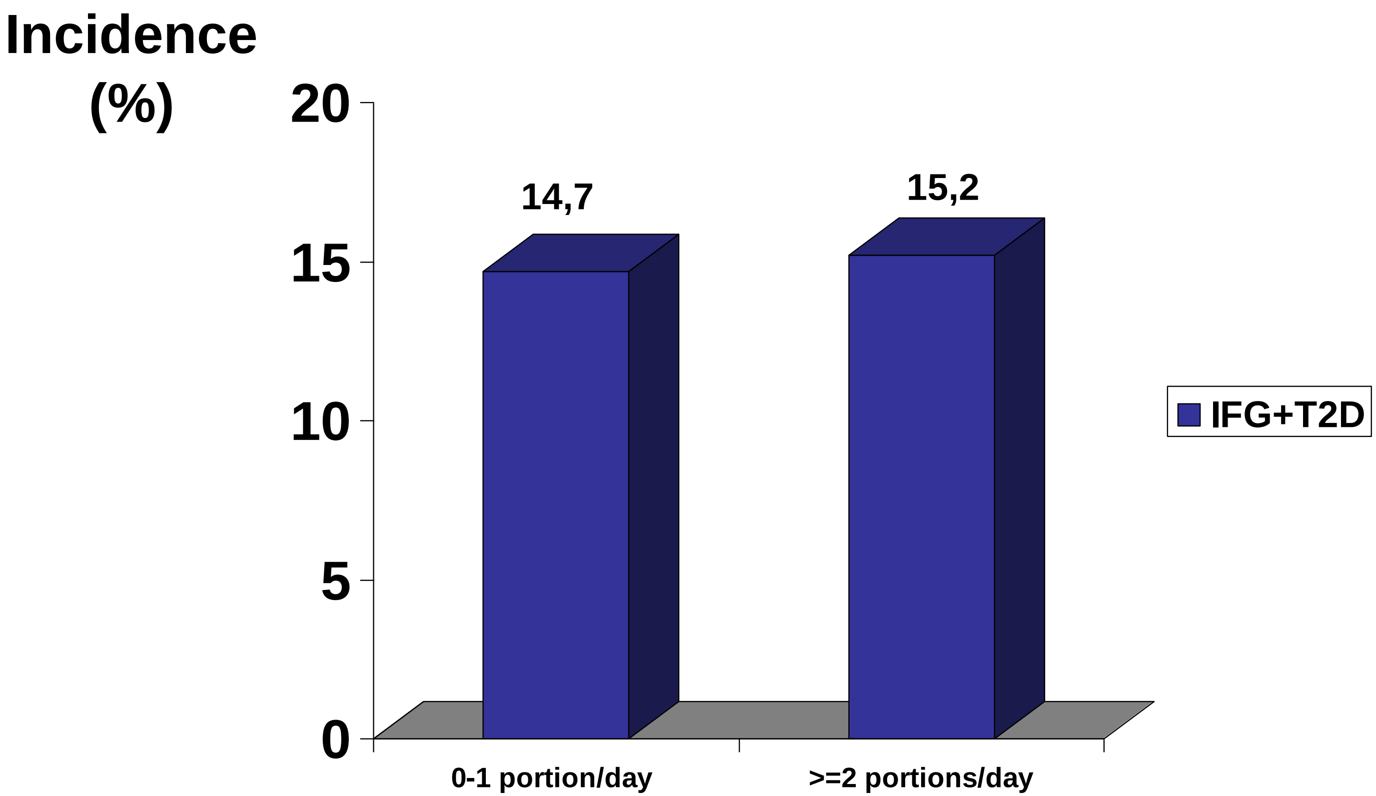
IDF : Model 1 : OR = 0.85 (0.70-1.04); p=0.12 (NS)
Model 2 : OR = 0.84 (0.67-1.06) ; p = 0.14

NCEP : Model 1 : OR = **0.72** (0.58 – 0.91) ; p= 0.006
Model 2 : OR = **0.71** (0.55 - 0.92); p = 0.01

Cheese consumption and incidence of type 2 diabetes and/or impaired fasting glycemia

Whole population



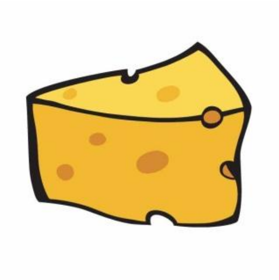


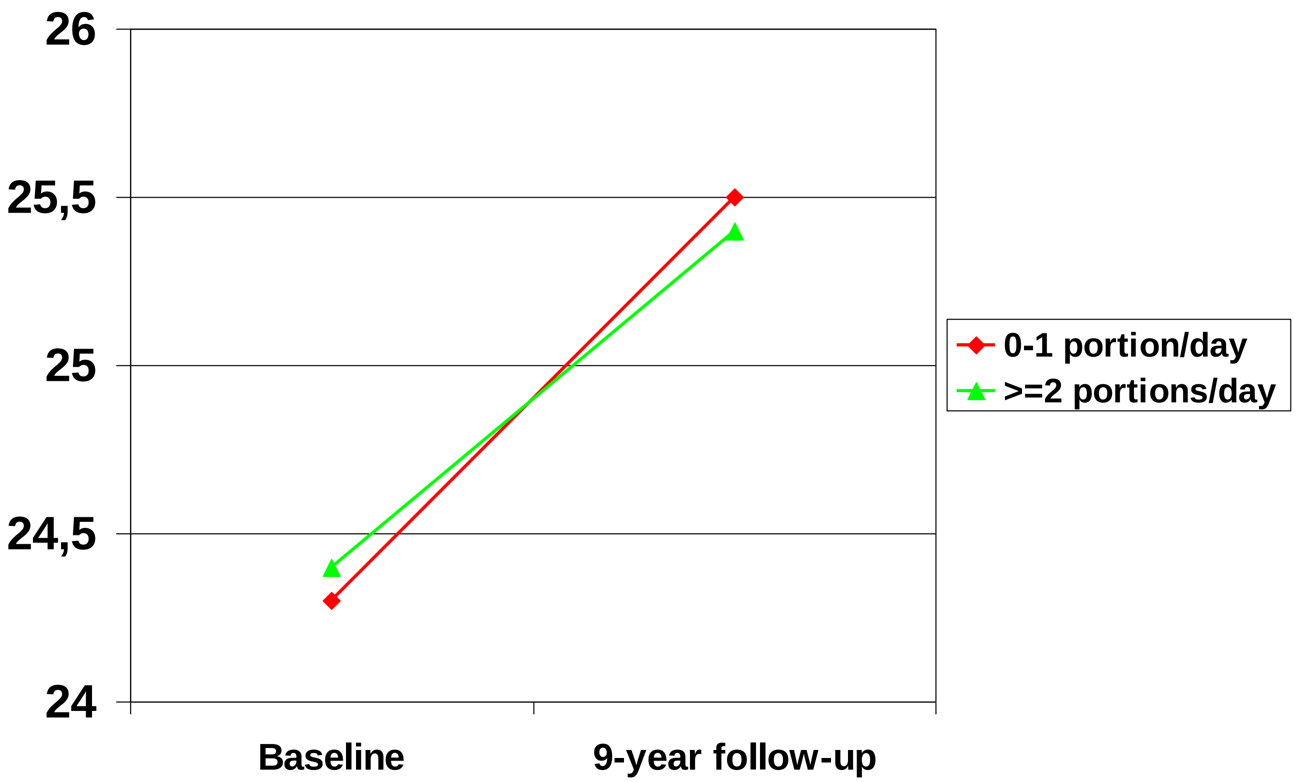
No significant effect on T2D alone, neither on IFG+T2D

Cheese consumption and BMI

Whole population

BMI at baseline and after a 9-year follow-up, by cheese consumption at baseline



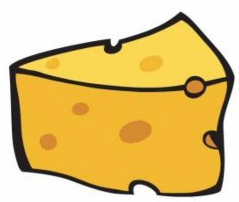


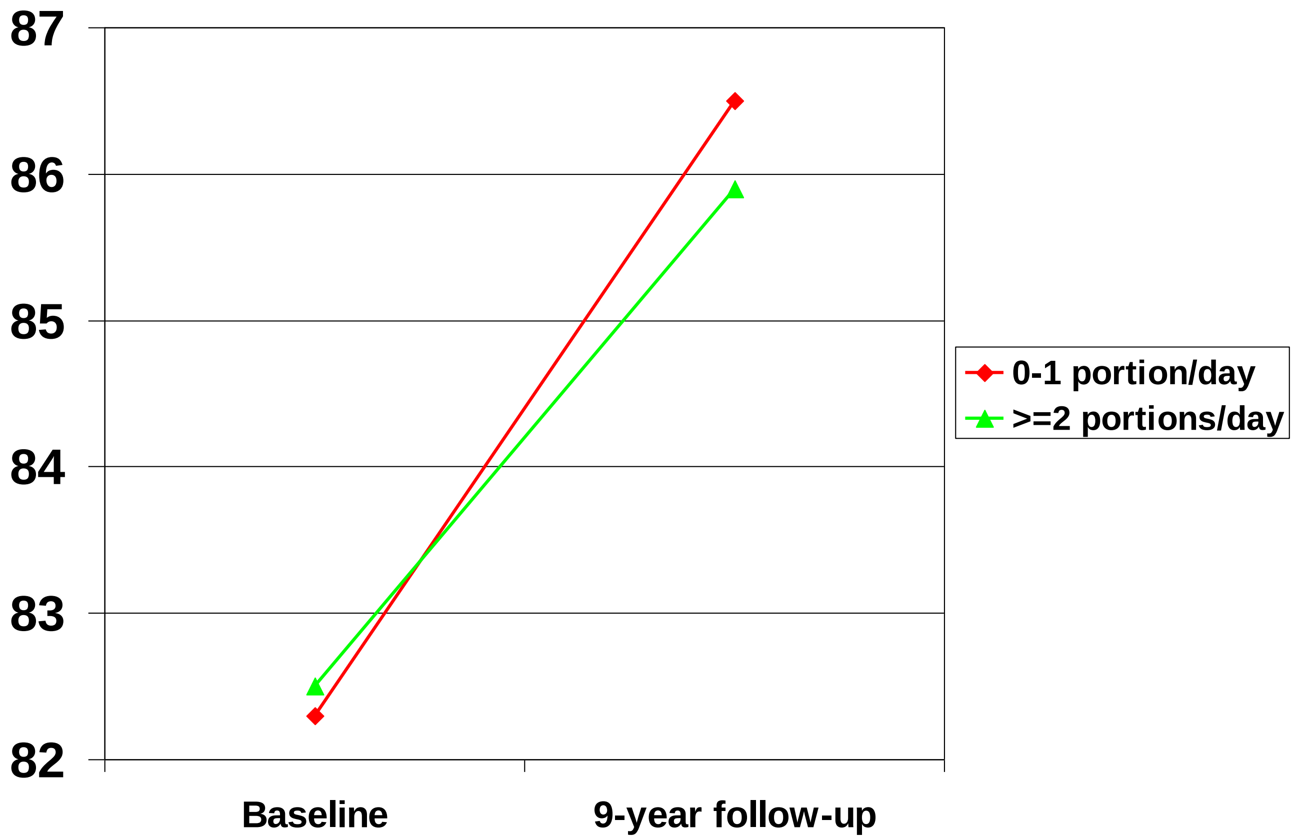
Average effect of cheese consumption on BMI: NS
Effect of cheese on changes in BMI : 0.007

Cheese consumption and waist circumference

Whole population

Waist (cm) at baseline and after a 9-year follow-up, by cheese consumption at baseline



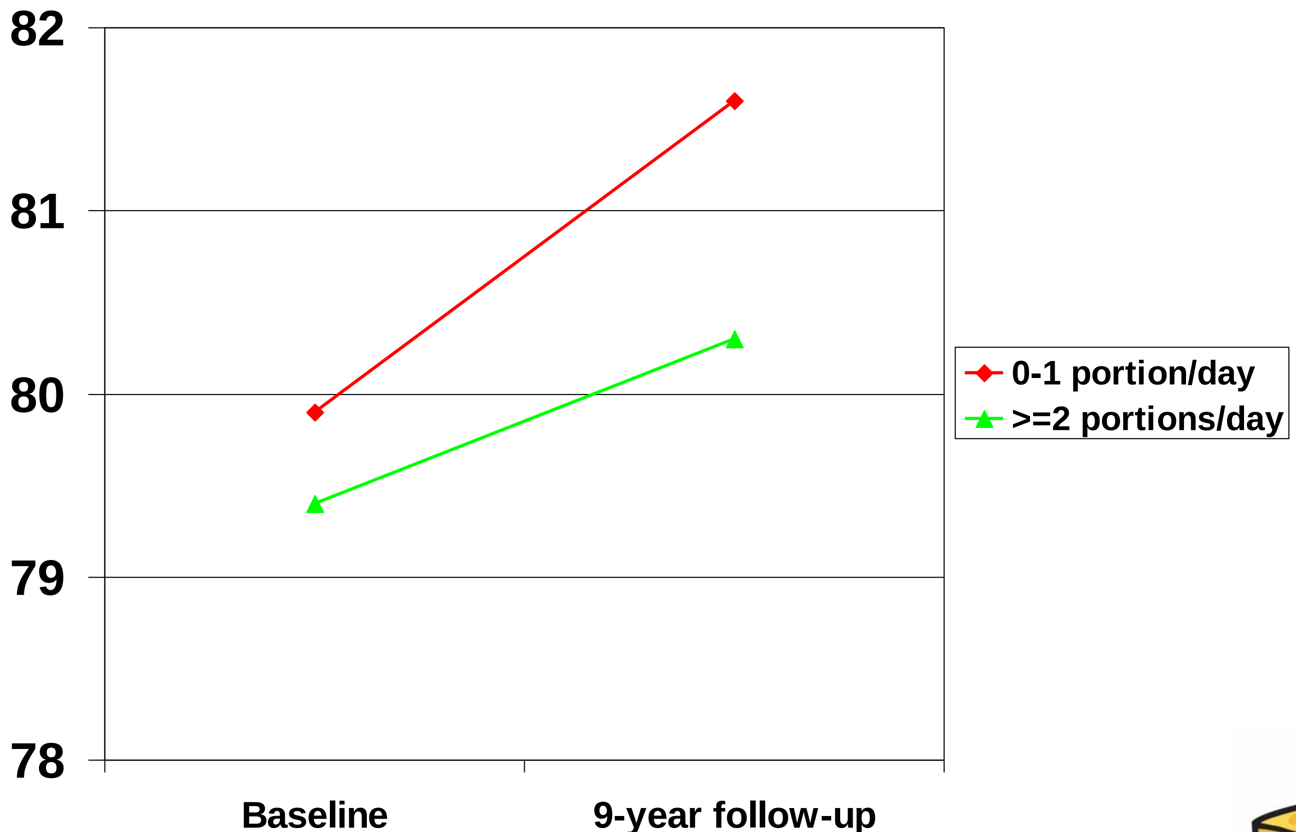


Average effect of cheese on waist circumference: p=0.20 (NS)
Effect of cheese on changes in waist circumference : 0.002

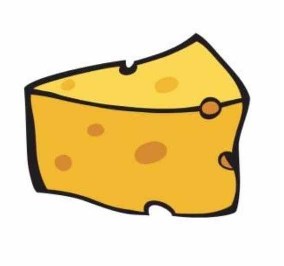
Cheese consumption and Diastolic Blood Pressure

Whole population

DBP (mmmHg) at baseline and after a 9-year follow-up,
by cheese consumption at baseline

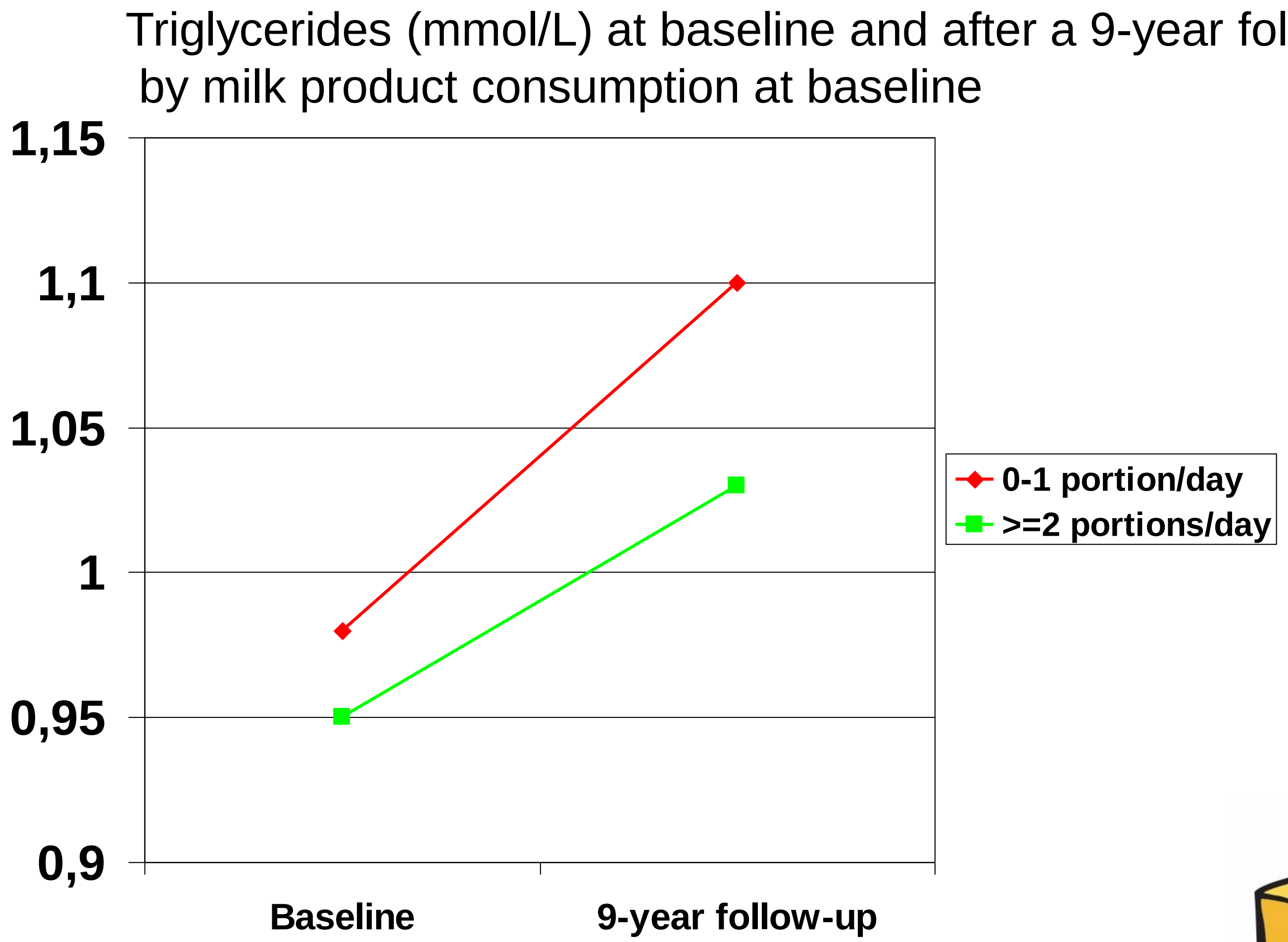


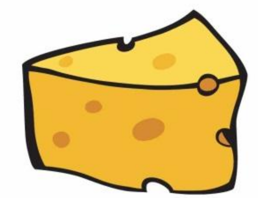
Average effect of cheese on DBP: p=0.001
Effect of cheese on changes in DBP : p=0.06



Cheese consumption and plasma triglycerides

Whole population





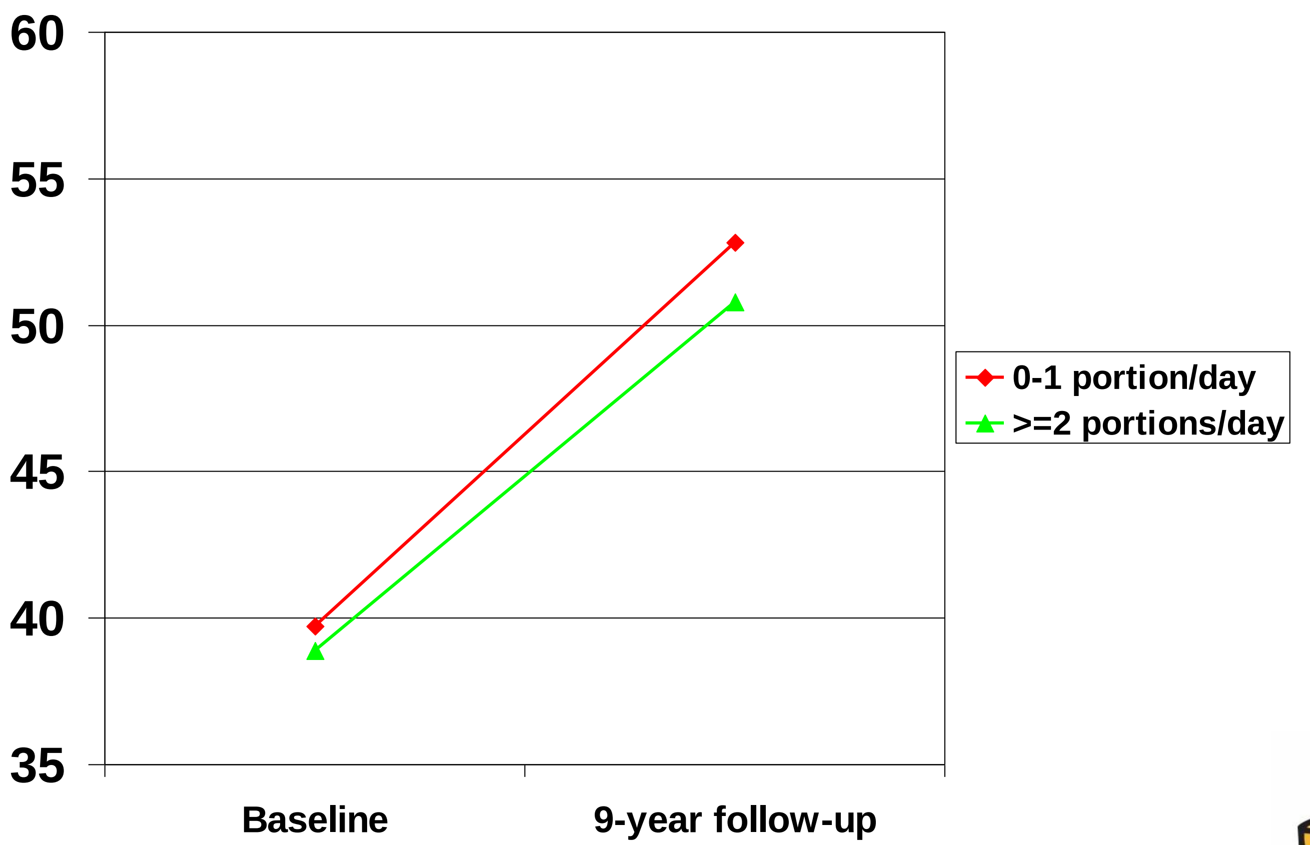
Average effect of cheese on TG: p=0.001

Effect of cheese on changes in TG : p=0.01

Cheese consumption and plasma insulin

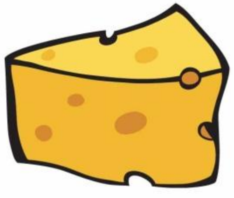
Whole population

Insulin (pmol/L) at baseline and after a 9-year follow-up, by cheese consumption at baseline



Average effect of cheese on insulin: p=0.05

Effect of cheese on changes in insulin : NS



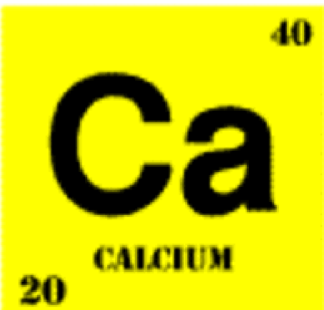
Results

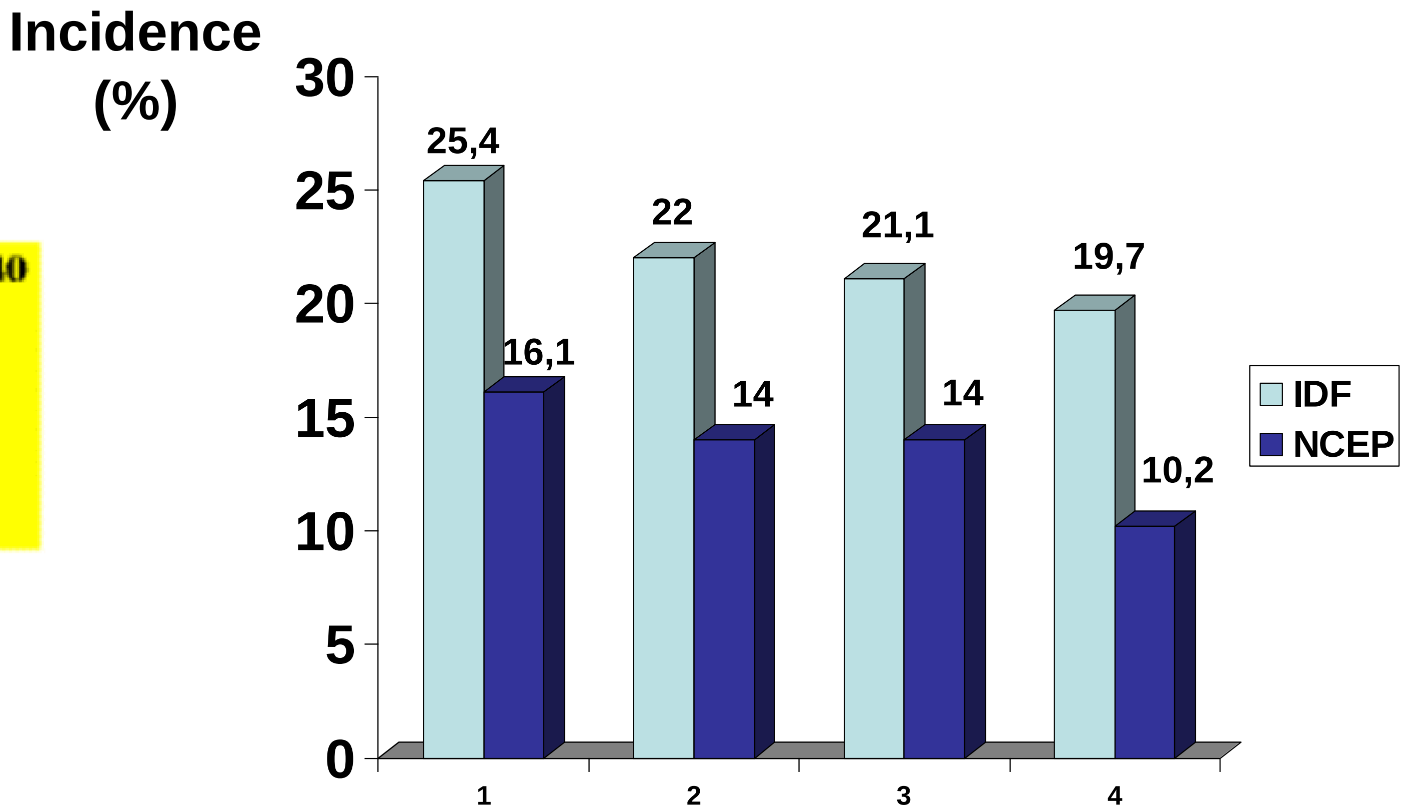
- Milk products (cheese excluded)
- Cheese

- Calcium density
(=calcium in mg / calories)

Dietary calcium density and metabolic syndrome

Whole population



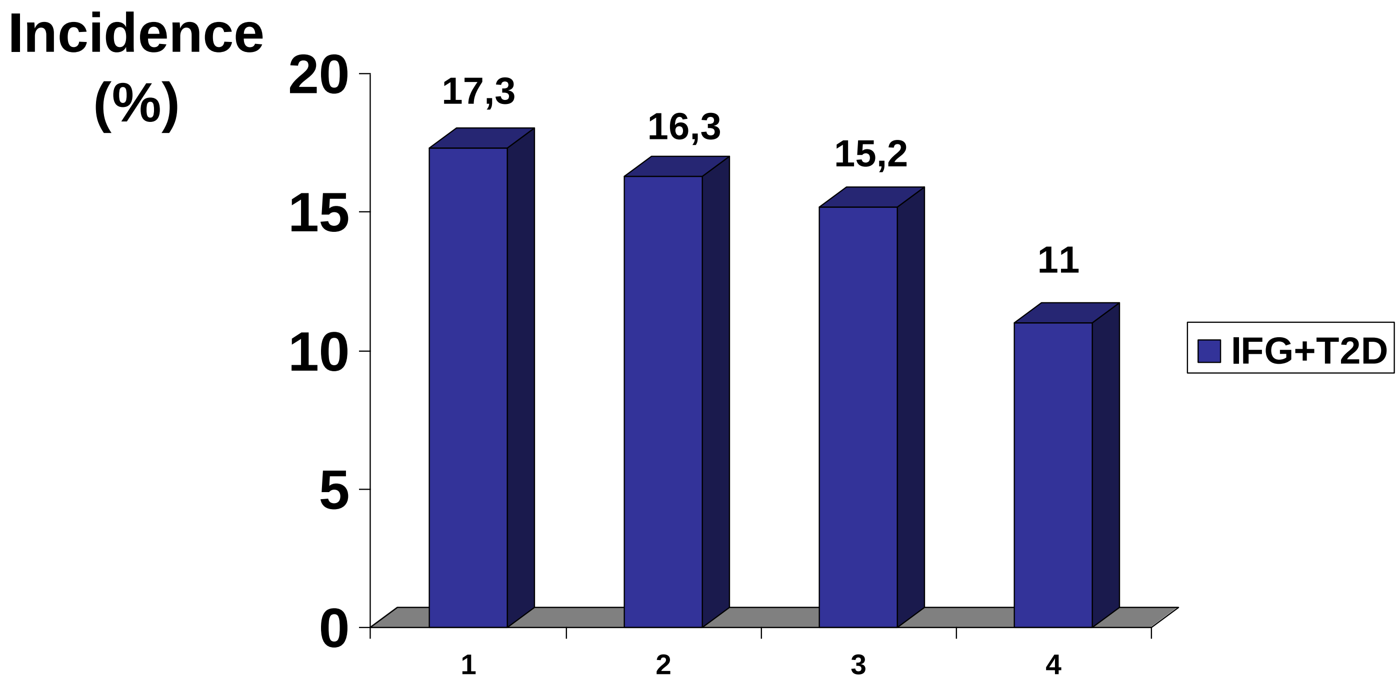


IDF : Model 1 : OR = **0.92** (0.85 -1.00) ; p=0.06 (NS)
Model 2 : OR = **0.88** (0.81 - 0.97); p =0.01

NCEP : Model 1 : OR = **0.87** (0.79-0.96) ; p= 0.004
Model 2 : OR = **0.85** (0.77-0.95) ; p = 0.003

Dietary calcium density and incidence of type 2 diabetes and/or impaired fasting glycemia

Whole population



No effect on T2D alone.

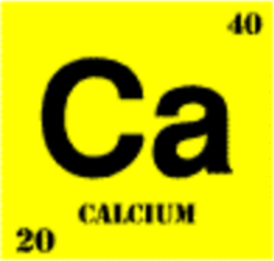
IFG+T2D, model 1 : OR = **0.89** (0.81 -0.97) ; p = 0.008

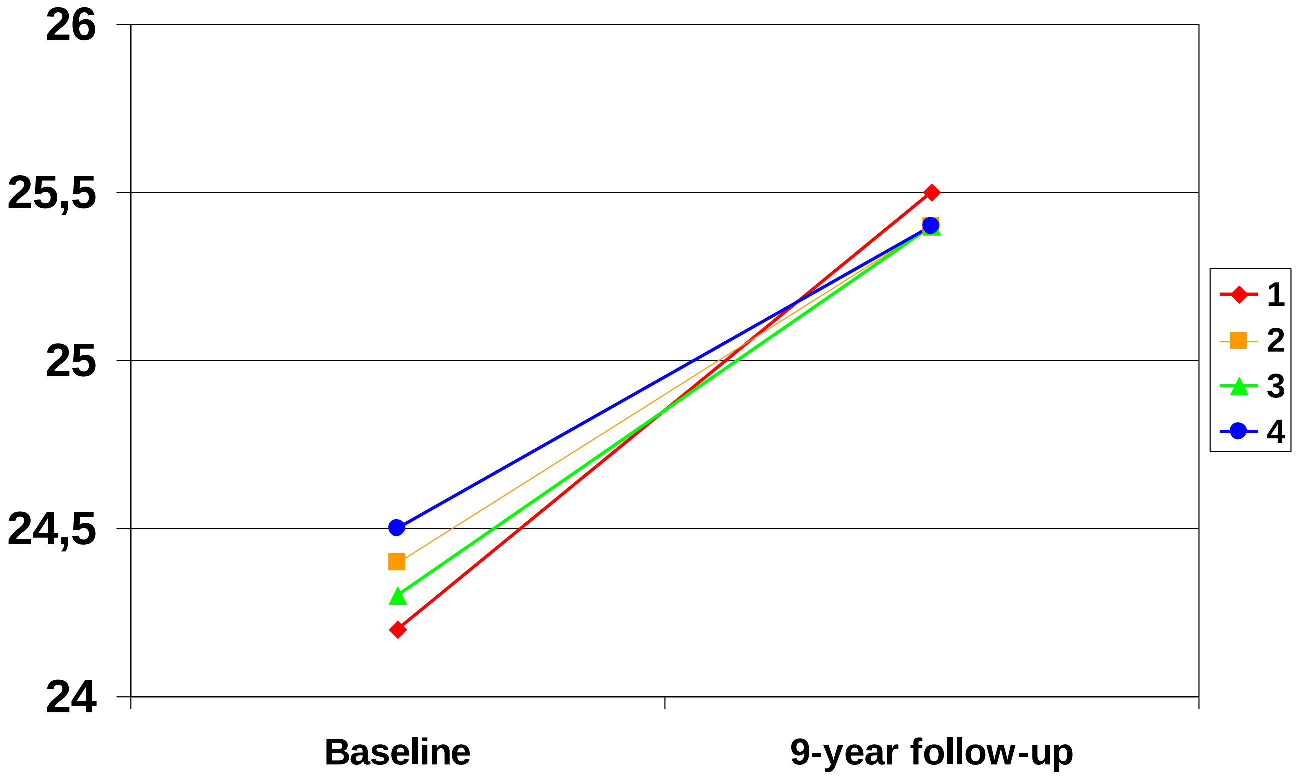
model 2 : OR = **0.88** (0.80-0.96) ; p = 0.006

Dietary calcium density and BMI

Whole population

BMI at baseline and after a 9-year follow-up, by dietary calcium density at baseline



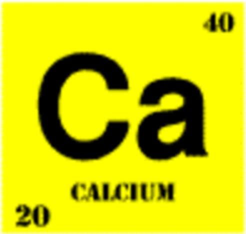


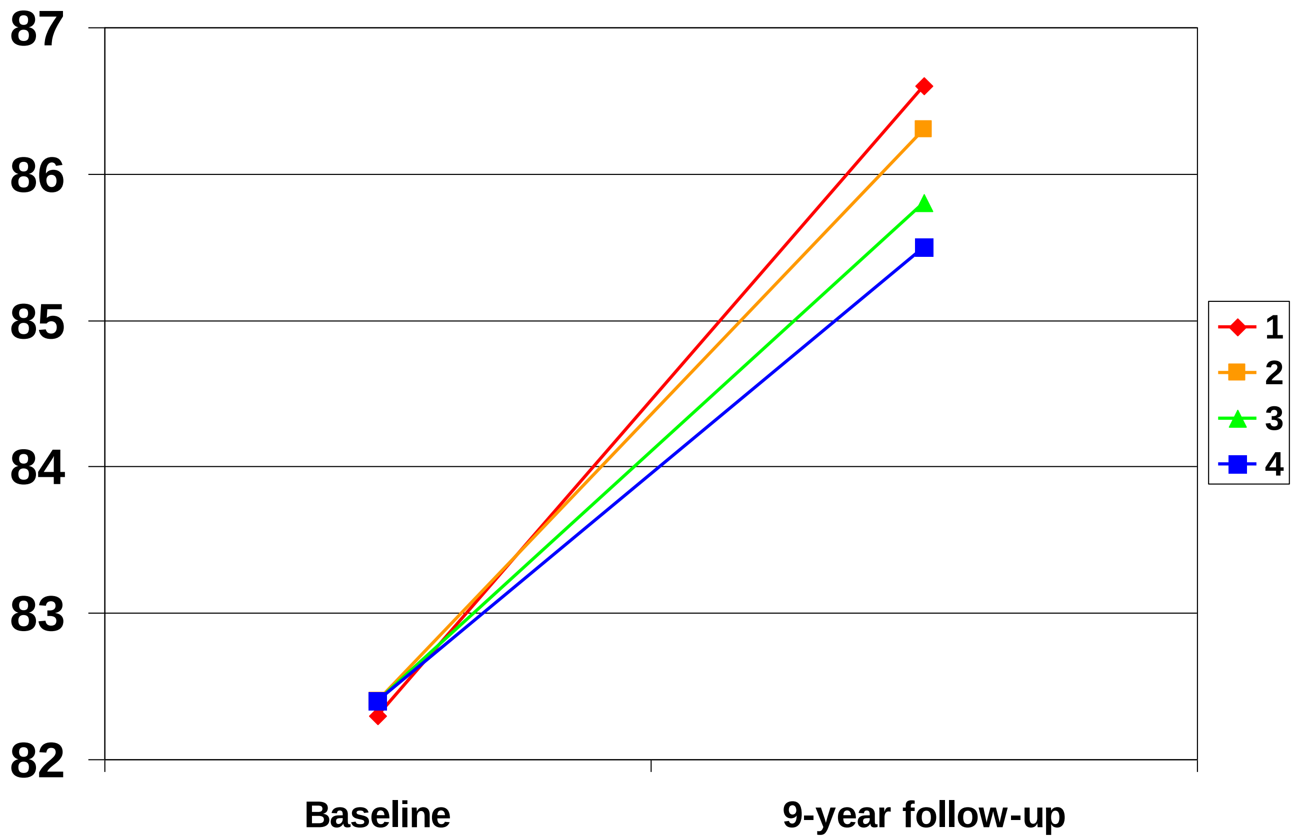
Average effect of dietary calcium density on BMI: NS
Effect of dietary calcium density on changes in BMI : p<0.001

Dietary calcium density and Waist circumference

Whole population

Waist (cm) at baseline and after a 9-year follow-up, by dietary calcium density at baseline





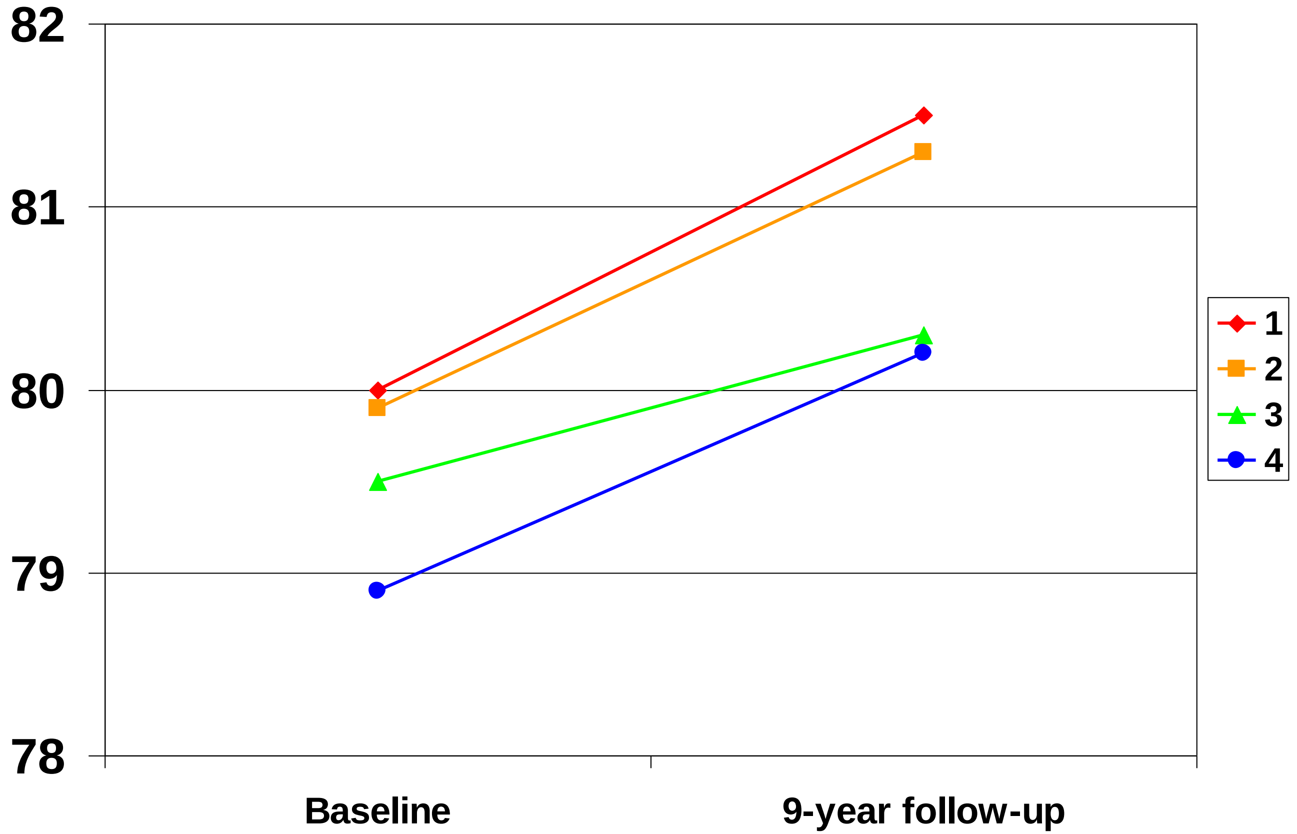
Average effect of dietary calcium density on waist circumference: 0.07

Effect of dietary calcium density on changes in waist circumference : 0.001

Dietary calcium density and Diastolic Blood Pressure

Whole population

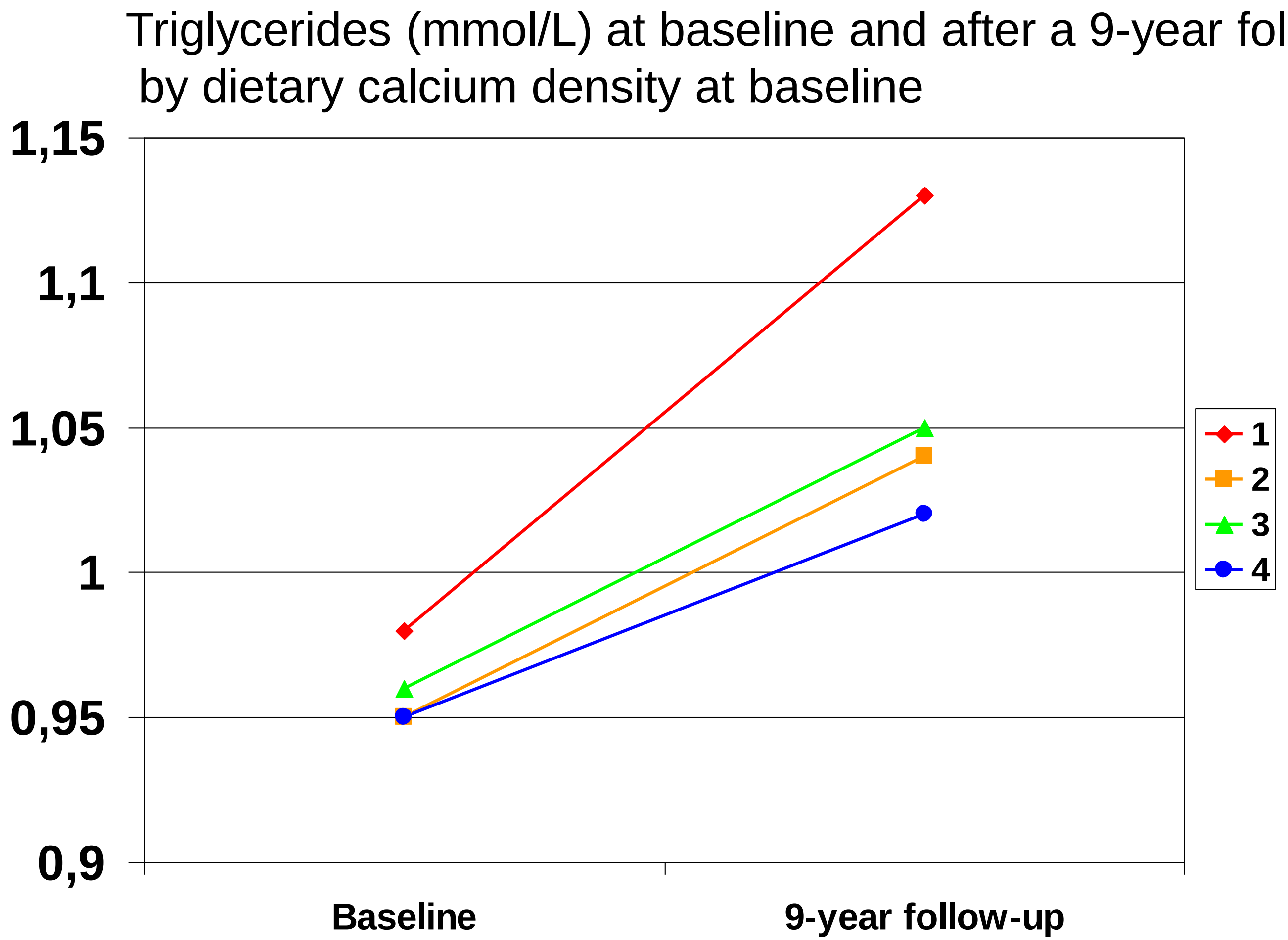
DBP (mmHg) at baseline and after a 9-year follow-up,
by dietary calcium density at baseline



Average effect of dietary calcium density on DBP: p=0.002
Effect of dietary calcium density on changes in DBP : NS

Dietary calcium density and plasma triglycerides

Whole population

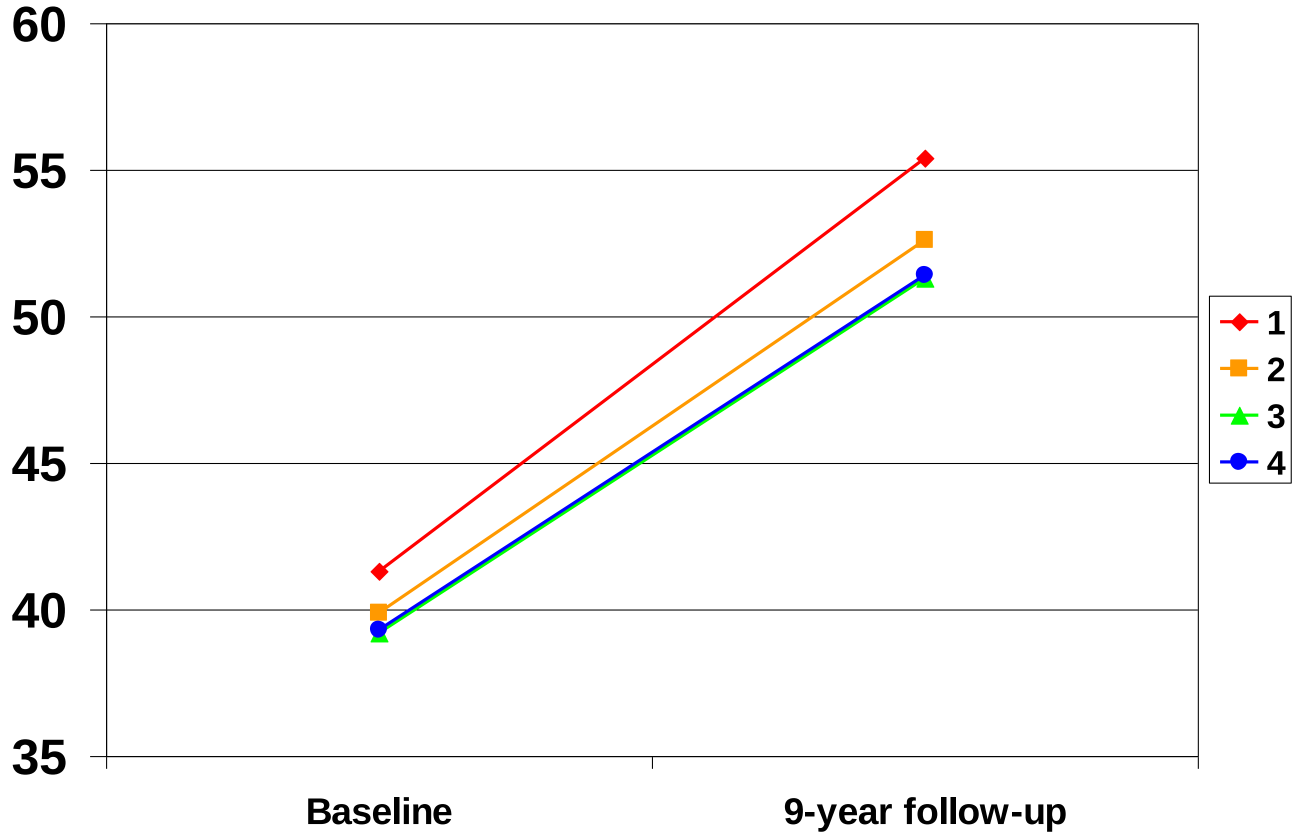


Average effect of dietary calcium density on TG: p=0.004
Effect of dietary calcium density on changes in TG : p=0.01

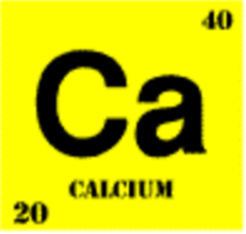
Dietary calcium density and plasma insulin

Whole population

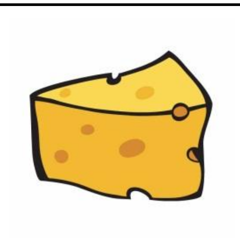
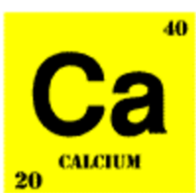
Insulin (pmol/L) at baseline and after a 9-year follow-up, by dietary calcium density at baseline



Average effect of dietary calcium density on insulin: p=0.002
Effect of dietary calcium density on changes in insulin : NS



Impact of dairy products and calcium consumption on the incidence of metabolic syndrome and on related variables in the D.E.S.I.R. cohort

	Metabolic syndrome	**IFG+T2D**	**BMI**	**WAIST**	**Blood pressure (diastolic)**	**TG**	**Insulin**
	↓	↓	↓ Δ		↓mean	↓ mean	♂↓ mean
	↓		↓ Δ	↓ Δ	↓mean ↓ Δ	↓mean ↓ Δ	↓mean
	↓	↓	↓ Δ	↓ Δ	↓ mean	↓mean ↓ Δ	↓mean

MECHANISMS ???

Milk and dairy components

Calcium, other minerals (magnesium, potassium, selenium, zinc)

Vitamin D

Fatty acids:
Cis-9, trans-11 conjugated linoleic acid (CLA)
Trans palmitoleic
Vaccenic

Proteins and peptides

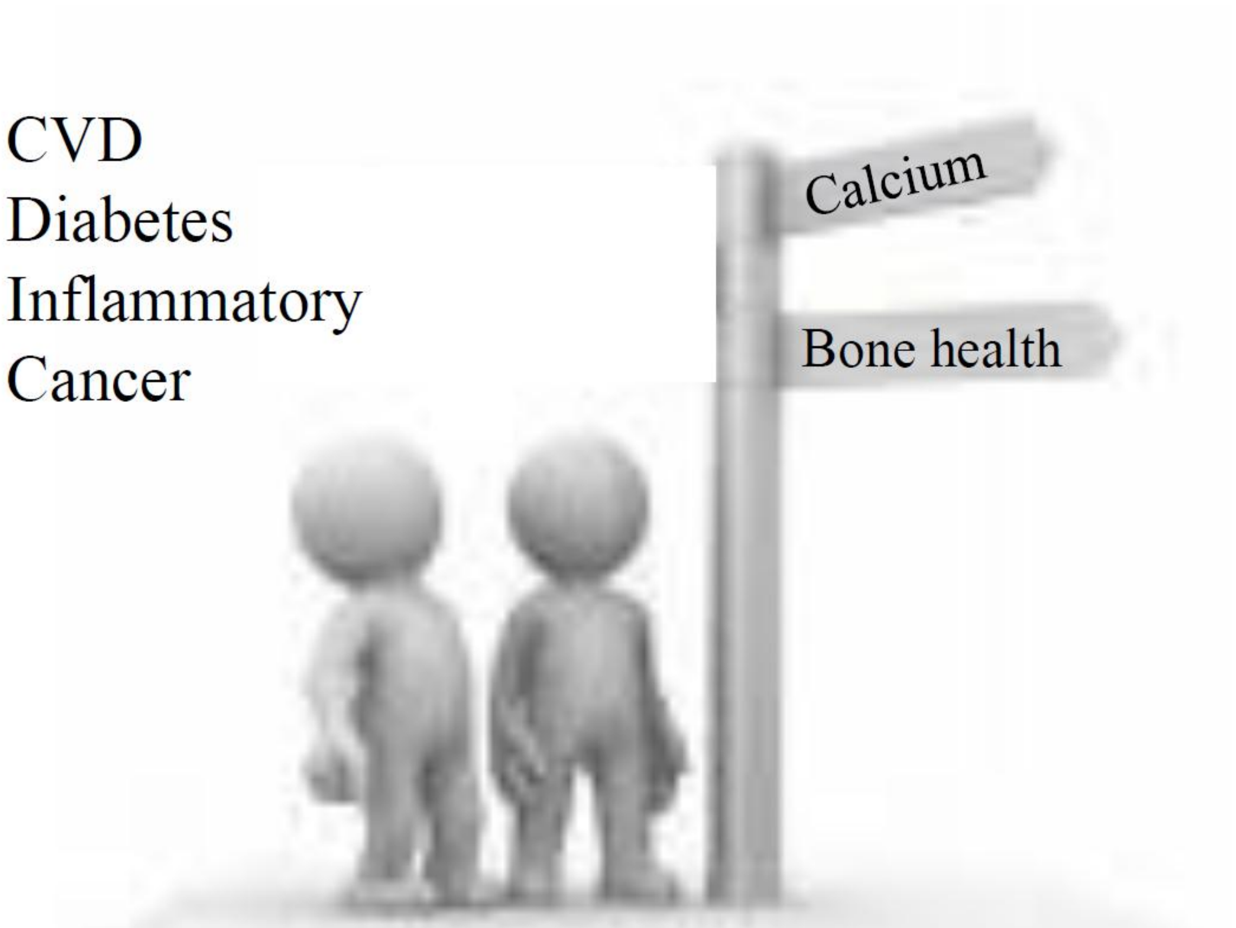
Calcium

- Inverse relationship between calcium consumption and intra-cellular calcium
- Involved in lipid metabolism regulation (lipolysis and lipogenesis), insulin and adiponectin signalling…
- Inflammation, oxidative stress

Other minerals

- Magnesium, potassium :
  - ➔blood pressure, type 2 diabetes
- Zinc, selenium :
  - ➔ inflammation, oxidative stress

Health effects of vitamin D…………



Remark: in Northern America (USA, Canada), milk and dairy are supplemented with vitamin D, but NOT IN FRANCE !!!

Dairy products and fatty acids

Cis-9, *trans*-11 conjugated linoleic acid (CLA)

- ↑ PPARγ expression ⇒ ↓ insulin resistance
- ↓ hyperinsulinism and hypertension, ↑ [adiponectin] in Zucker rat

Vaccenic acid (*trans*-11 18:1)

- Precursor of c9,t11 CLA
- PPAR-α agonist → hypolipidemiant, ↑ FA oxidation
- Inhibits effects of saturated-fat rich diet (↓ LDL, ↓ hepatic steatosis, fat mass distribution, ↑ energy expenditure)

Trans-palmitoleic acid (*trans*-7 16:1)

In the Four U.S. communities Cardiovascular Health Study, circulating levels ↓ T2D incidence, ↓ BMI, ↓ waist circumference, and independently ↑ HDL-C, ↓ TG , ↓ CRP, ↓ HOMA-IR.

Mozaffarian et al. *Ann Intern Med* 2010;153:790-9

Milk peptides: ACE inhibitor effect

IPP, VPP, ALPMHIR
= Peptides from caseins and whey proteins after chemical, physical, enzymatic treatments

→ digestive enzymes hydrolysis (*in vitro* or *in vivo*)
→ lactic fermentation

More active peptide from β-lactoglobulin

ACE inhibitor effect *in vitro* and *in vivo* (SHR rat)

Milk proteins : incretin effect

Effects of a Protein Preload on Gastric Emptying, Glycemia, and Gut Hormones After a Carbohydrate Meal in Diet-Controlled Type 2 Diabetes

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Karen L. Jones, PhD[1,2]
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Michael Horowitz, MBBS, PhD[1,2,3]
Christopher K. Rayner, MBBS, PhD[1,2]

sumed beef-flavored soup (3.8 g
loric beef flavoring dissolved in
water) 30 min before a mashed
meal containing 65 g powdered
(Deb Instant Mashed Potato, E

***Diabetes Care* 32:1600–1602, 2009**

➔ Whey preload before a CHO meal: secretion of incretins (GLP-1 and GIP), insulin, ↓ gastric emptying, ↓ glycemia.

Differential effects of protein quality on postprandial lipemia in response to a fat-rich meal in type 2 diabetes: comparison of whey, casein, gluten, and cod protein[1–3]

Lene S Mortensen, Merete L Hartvigsen, Lea J Brader, Arne Astrup, Jürgen Schrezenmeir, Jens J Holst, Claus Thomsen, and Kjeld Hermansen

Am J Clin Nutr 2009;90:41–8.

➔ Whey in meal ↓ iAUC TG, FFA, glucose

Conclusions

- A higher consumption of milk products and calcium reduces the incidence of the metabolic syndrome during a 9-year period in a large cohort drawn from the French general population.

- This inverse association is observed with most of the traits of the metabolic syndrome: hyperglycemia, high blood pressure, triglycerides, insulin levels

- These results indicate that dairy products consumption could improve the cardiovascular risk.

- Many components in milk and dairy products could explain these effects.

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