Oslo University Hospital

HELSE SØR-ØST

The Norwegian Radium Hospital

Obesity and **cancer** risk:

does decrease of serum

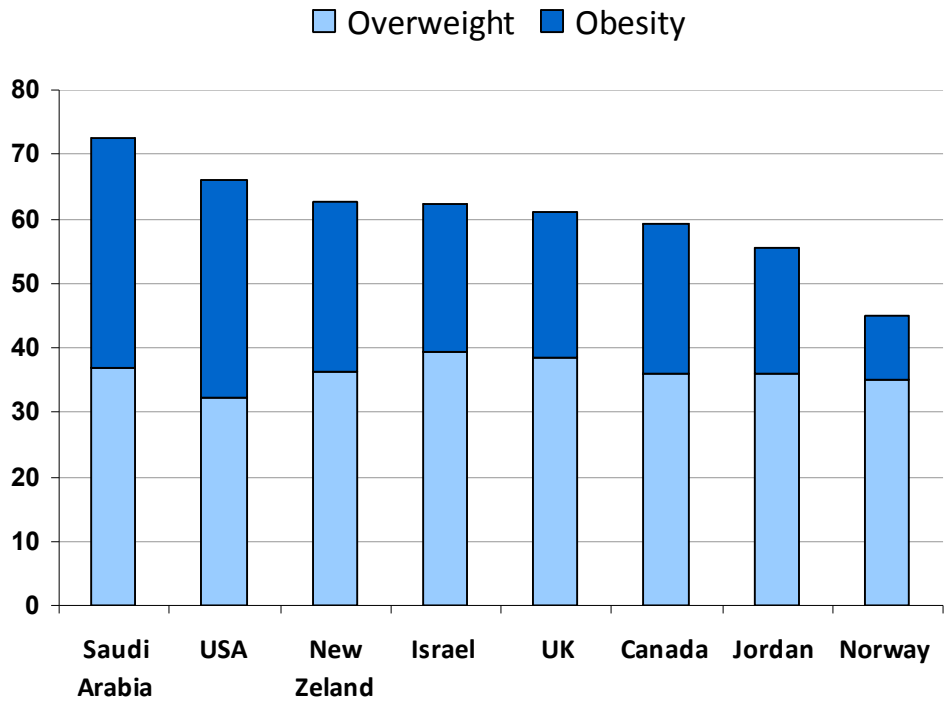
vitamin D level with increasing **BMI** explain

some of the association?

Presentation overview

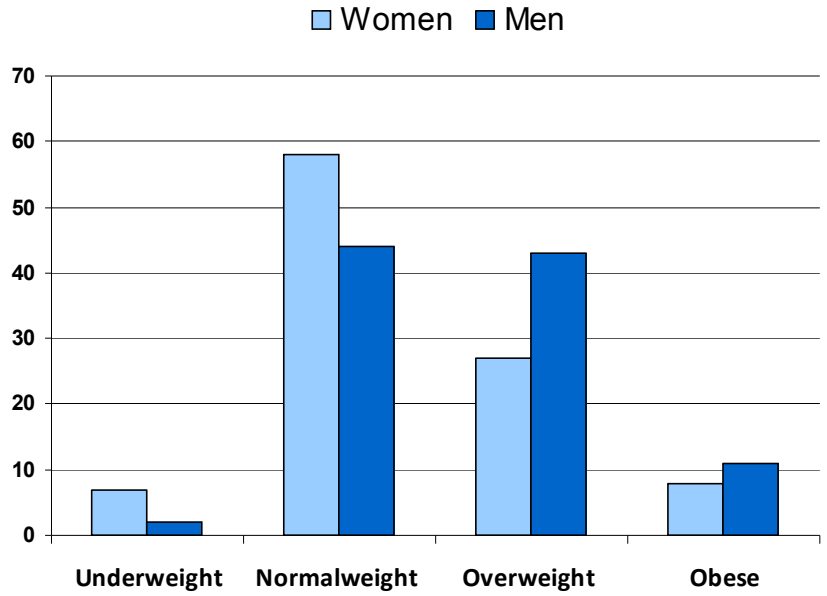
- Obesity and vitamin D status, prevalence of vitamin D deficiency
- Obesity and cancer risk
- Vitamin D status and cancer
- An association between obesity, vitamin D status and cancer risk

World Health Organization predicts there will be **2.3 billion overweight** adults in the world **by 2015** and more than **700 million** of them will be **obese**

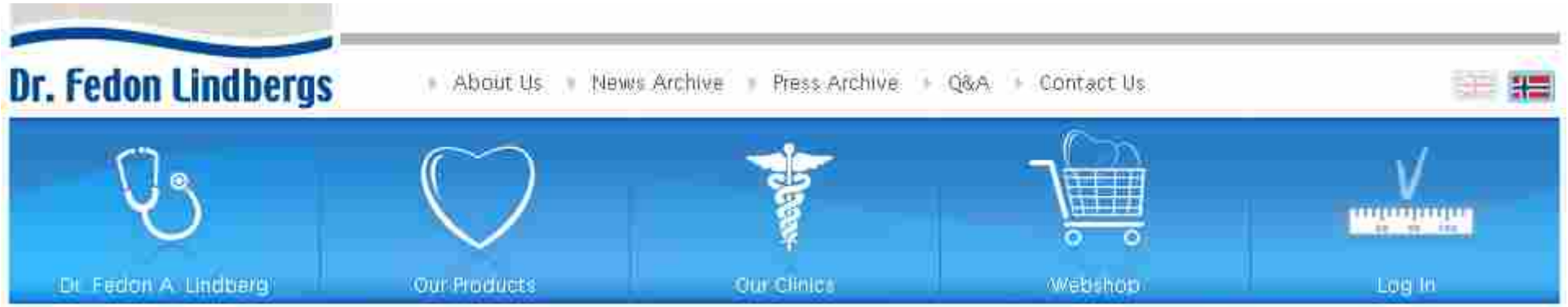


http://www.who.int/mediacentre/factsheets/fs311/en/

Overweight and obesity in Norway - fact sheet



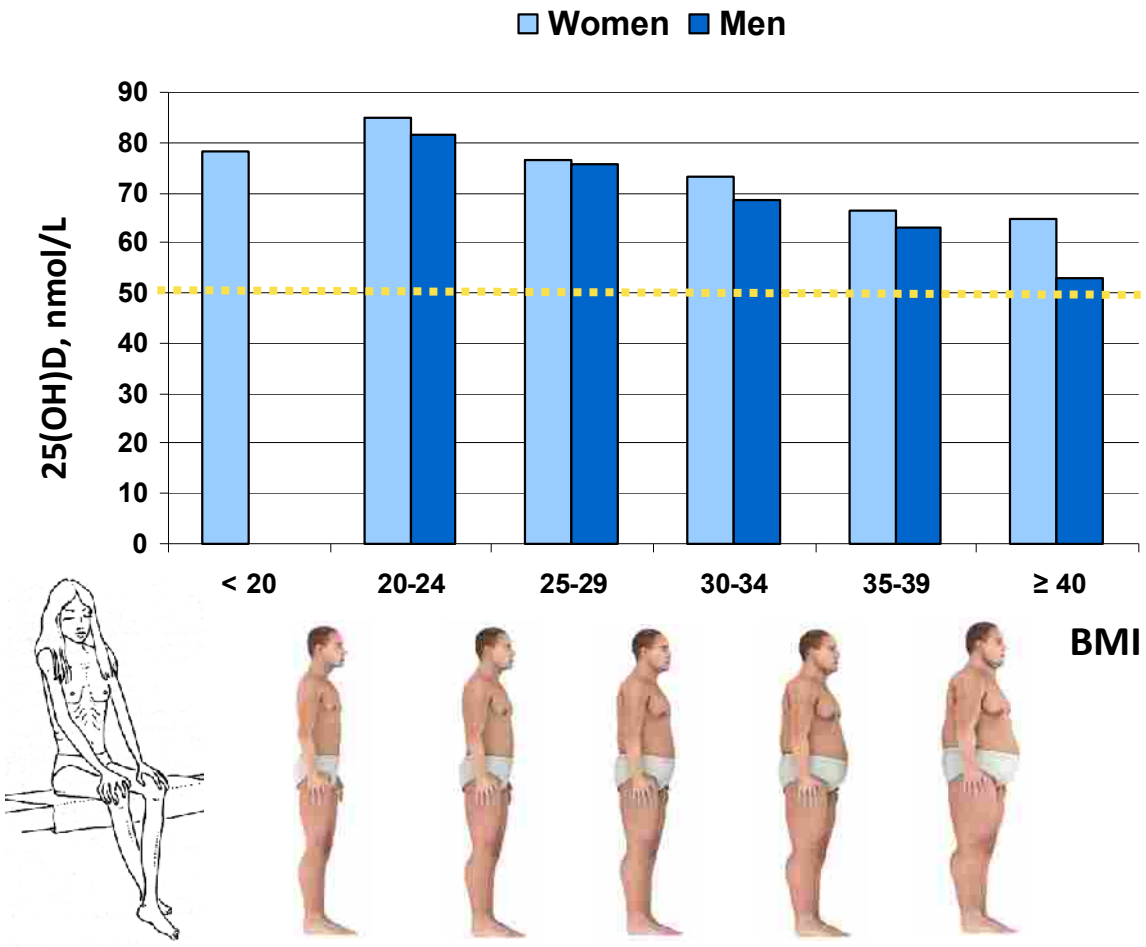
- 15-20 % of 8-12-year old children are overweight or obese
- 8-14 % of 15-16-year olds are overweight or obese
- Adults became 5-6 kg heavier and a mean BMI increased by 2 kg/m^2 during the last 20-30 years



1,800 individuals were included in the study

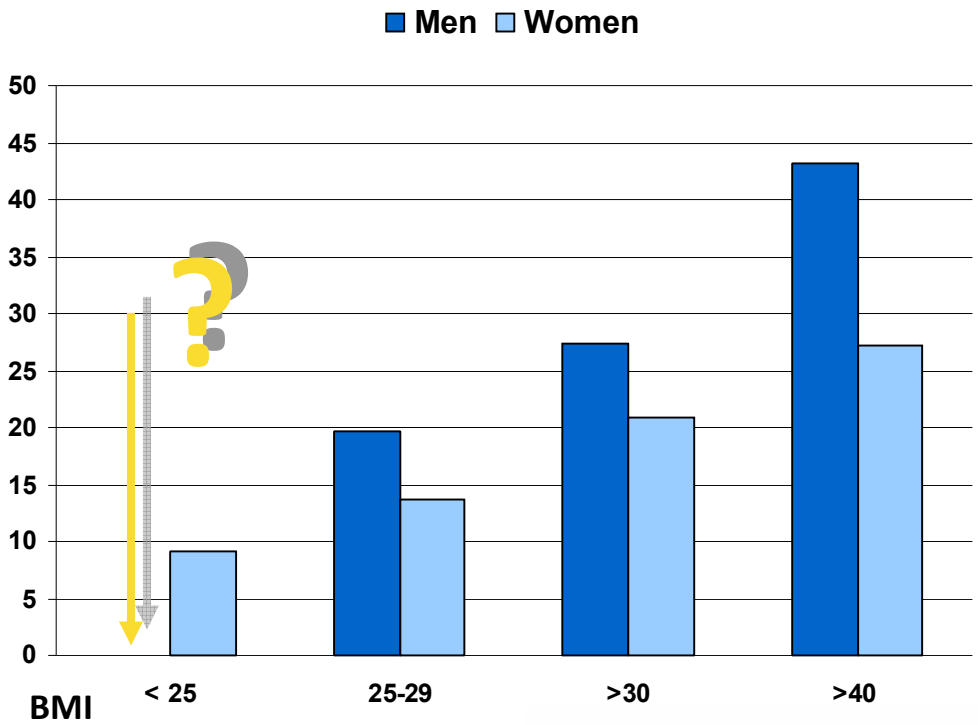
Parameter	Median (range) or %
Age (years)	49 (20-79)
Females (%)	82.3
Males (%)	17.4
Body weight (kg)	90.6 (46.4-188.3)
BMI (kg/m^2)	**31.6 (18.6-57.8)**
Fat mass (kg)	36.9 (8.1-95.1)
Adiposity (%)	41.5 (11.3-63.4)
25(OH)D (nmol/l)	**71 (12-160)**
$1,25(OH)_2D$ (pmol/l)	101 (10-256)

Serum 25(OH)D concentrations versus BMI



- 62% obese
- 27% overweight
- 25(OH)D levels increased with age
- Women had better vitamin D status than men
- Underweight is possibly a risk factor for low vitamin D status

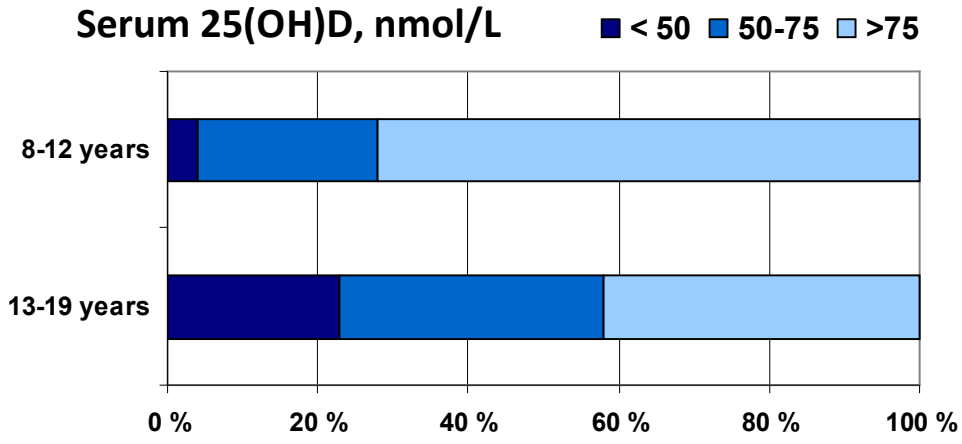
Prevalence of vitamin D deficiency



- **71 % of men and 62 % of women** with obesity had vitamin D levels < 75 nmol/L
- **19 % of men and 27 % of women** with BMI < 25 kg/m^2 had vitamin D levels **> 100 nmol/L !!!**
- **75 % of men and 40 % of women** with BMI > 40 kg/m^2 had vitamin D deiciency **during the winter** and 25 % of them still stayed **deficient** during the summer!

Vitamin D status in children and adolescents

- 50% of the children and adolescents had serum 25(OH)D < 75 nmol/L
- 19% had vitamin D deficiency



What is the difference between obese and normalweight man?

BMI 45 kg/m² **25(OH)D 50 nmol/L**

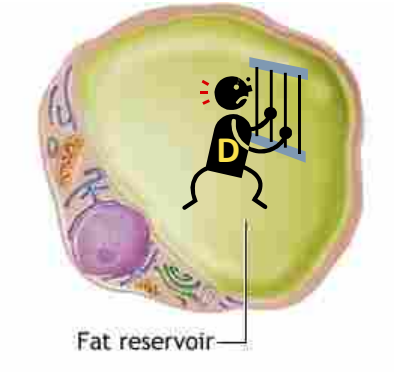
43 % < 50 nmol/L 93 % < 75 nmol/L

BMI 23 kg/m² **25(OH)D 75 nmol/L**

0 % < 50 nmol/L 39 % < 75 nmol/L

Physiological risk factors

Wortsman J. et al. Am J Clin Nutr 2000;72(3):690-3.
Heaney RPet al. J Am Coll Nutr 2009;28(3):252-6.



- **Sequestration in fat tissue**

A fat-soluble vitamin D accumulates in the excess body fat and has reduced bioavailability

- **Volume of distribution effect**

Vitamin D content in tissues of normal weight woman

35 % in fat
30 % in serum
20 % in muscles
15 % in all other tissues

Lagunova et al. J Nutr. 2011;141(1):112-7.

Other risk factors

- **Inadequate vitamin D consumption**

Obese persons benefit less from the same dose of oral vitamin D supplementation than non-obese persons

- **Sun exposure habits**

Reduced outdoor activity during the summer

Cover large surfaces of the body

Sun exposure is 60 % less effective to induce an increase in serum 25(OH)D

Obesity and cancer risk

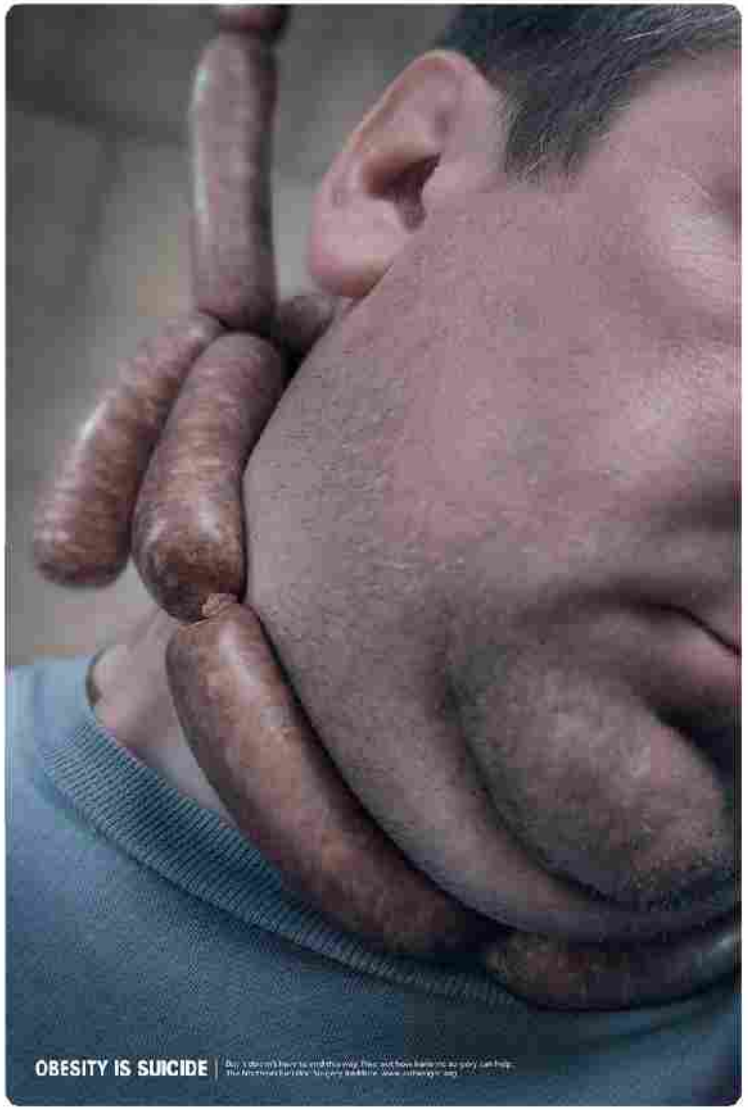
Renehan AG et al. Lancet 2008; 371: 569–78

Men

Cancer site and type	Number of studies	RR (95% CI)	p
Oesophageal adenocarcinoma	5	1·52 (1·33 1·74)	<0·0001
Thyroid	4	1·33 (1·04–1·70)	0·02
Colon	22	1·24 (1·20–1·28)	<0·0001
Renal	11	1·24 (1·15–1·34)	<0·0001
Liver	4	1·24 (0·95–1·62)	0·12
Malignant melanoma	6	1·17 (1·05–1·30)	0·004
Multiple myeloma	7	1·11 (1·05–1·18)	<0·0001
Rectum	18	1·09 (1·06–1·12)	<0·0001
Gallbladder	4	1·09 (0·99–1·21)	0·12
Leukaemia	7	1·08 (1·02–1·14)	0·009
Pancreas	12	1·07 (0·93–1·23)	0·33
Non-Hodgkin lymphoma	6	1·06 (1·03–1·09)	<0·0001

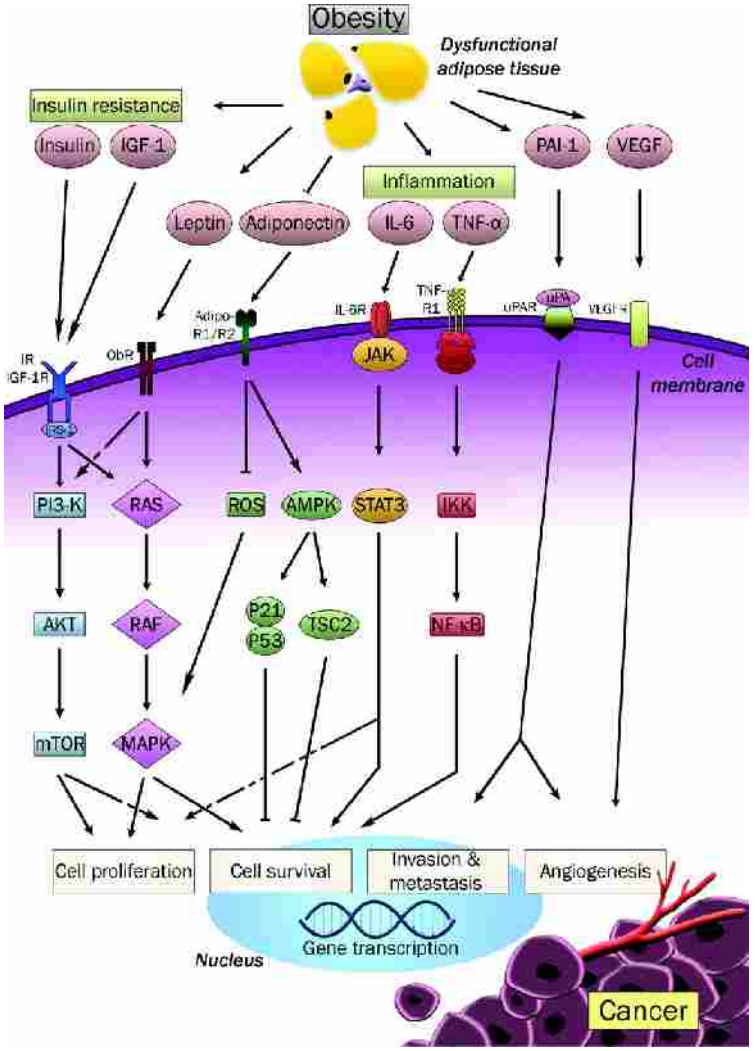
Women

Endometrium	19	1·59 (1·50–1·68)	<0·0001
Gallbladder	2	1·59 (1·02–2·47)	0·04
Oesophageal adenocarcinoma	3	1·51 (1·31–1·74)	<0·0001
Renal	12	1·34 (1·25–1·43)	<0·0001
Leukaemia	7	1·17 (1·04–1·32)	0·01
Thyroid	3	1·14 (1·06–1·23)	0·001
Postmenopausal breast	31	1·12 (1·08–1·16)	<0·0001
Pancreas	11	1·12 (1·02–1·22)	0·01
Multiple myeloma	6	1·11 (1·07–1·15)	<0·0001
Colon	19	1·09 (1·05–1·13)	<0·0001

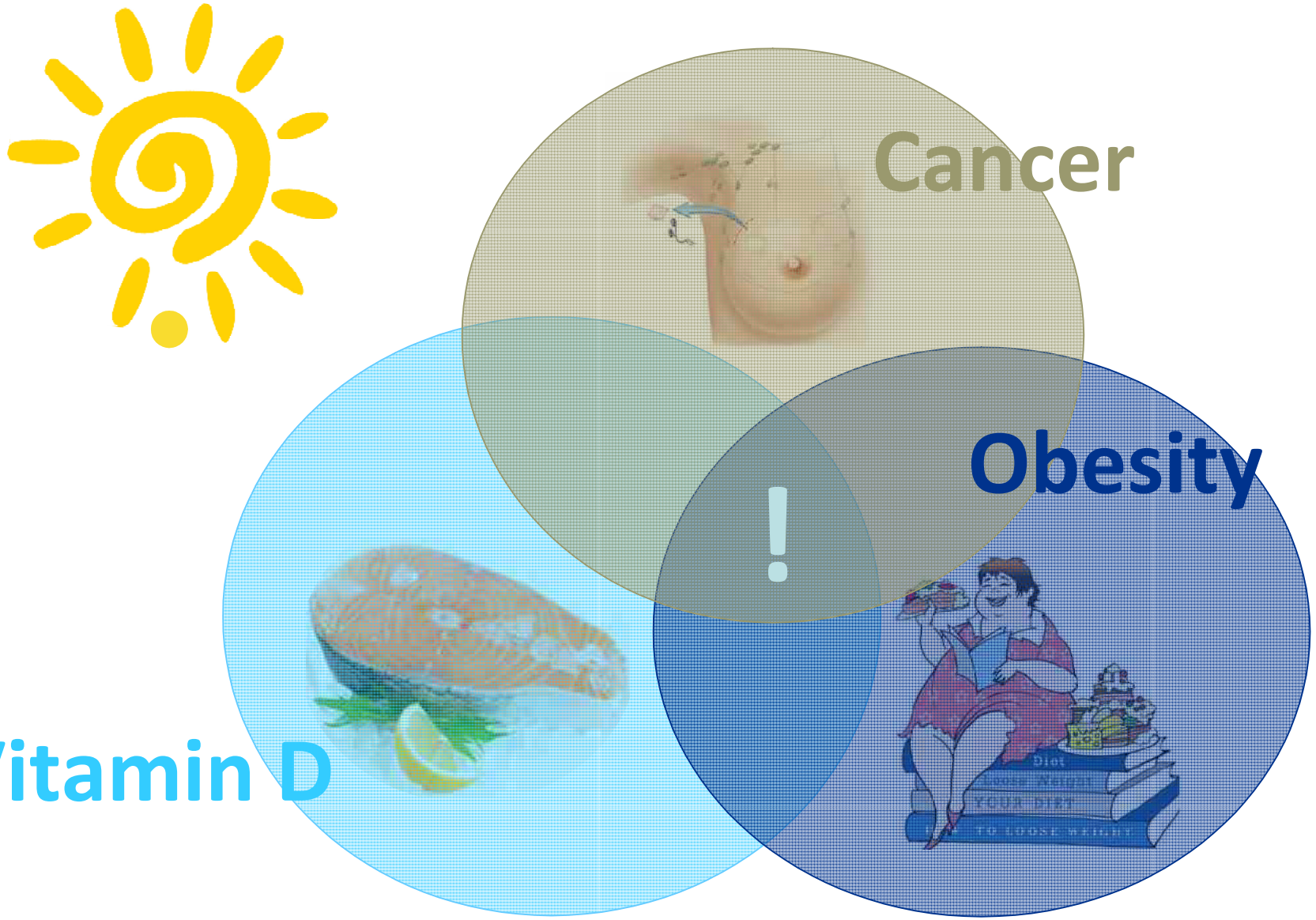


Obesity and Cancer: Pathophysiological Mechanisms

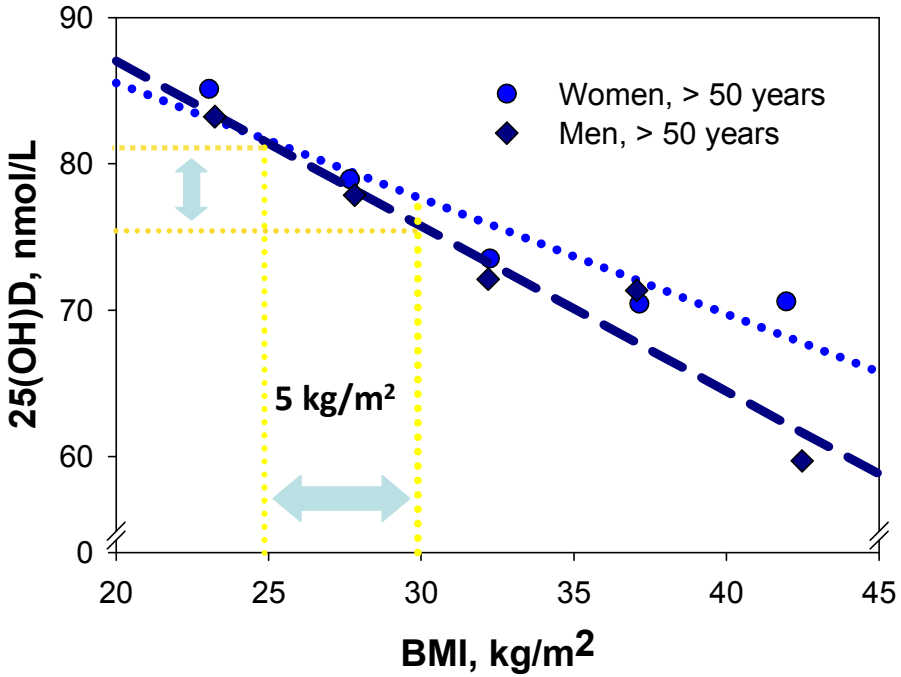
- **Insulin resistance**
- Altered serum levels of **adipokines**: adiponectin, leptin, PAI-1
- Obesity-induced **inflammation**: increased CRP, increased systemic levels of proinflammatory cytokines, such as TNF-α and IL-6
- **Sex steroids**: increased plasma concentrations of bioavailable estradiol and testosterone and decreased plasma concentration of SHBG
- **…**



Lagunova et al. Mol. Nutr. Food Res. 2010; 54: 1127–1133.



Decay in serum 25(OH)D levels with increasing BMI



25 (OH)D decrease per each 5 kg/m² BMI increase

- Women: 4,5 nmol/L
- Men: 5,5 nmol/L
- All: 5 nmol/L

Study	25(OH)D (±SD) (nmol/L)	Age (±SD) (years)	BMI range (kg/m^2)	Gender	25(OH)D decrease[a)]	*p*-Value
McGill *et al.*	62.2 (22.7)	47.6 (±11.6)	28–50	Women, men	0.7 nmol/L	0.002
Rodrigues–Rodrigues	56.5	27.8 (±4.6)	24–35	Women	1.2 nmol/L	<0.05
Stein *et al.*	44.9 (22)	39 (12)	35–65	Women, men	1.3 nmol/L	<0.01

Lagunova et al. J Nutr. 2011;141(1):112-7.

Serum 25(OH)D is a predictor of serum 1,25(OH)$_2$D in overweight and obese patients

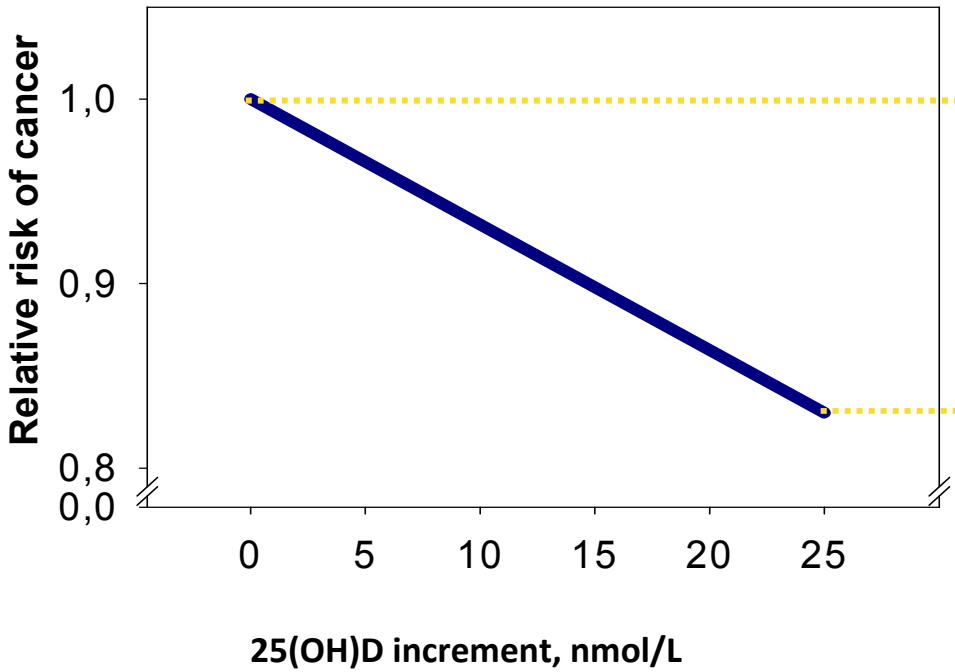
Variable	25(OH)D quartiles				
	Q1 (lowest): ≤55 nmol/L	Q2: 56–71 nmol/L	Q3: 72–88 nmol/L	Q4 (highest): ≥89 nmol/L	*P*-value[2]
n	462	452	430	435	
Serum 25(OH)D, *nmol/L*	42.7^{d} ± 0.46	63.8^{c} ± 0.21	79.3^{b} ± 0.24	105.6^{a} ± 0.71	<0.001
Serum 1,25(OH)$_2$D, *pmol/L*	93.2^{c} ± 1.44	105^{b} ± 1.69	108^{b} ± 1.66	119^{a} ± 1.92	<0.001
BMI, *kg/m^2*	34.6^{a} ± 0.32	32.7^{b} ± 0.29	31.0^{c} ± 0.28	30.4^{c} ± 0.27	<0.001
Fat mass, *kg*	42.7^{a} ± 0.68	38.7^{b} ± 0.62	35.3^{c} ± 0.59	34.7^{c} ± 0.61	<0.001
Adiposity, *% body mass*	41.9^{a} ± 0.36	40.3^{b} ± 0.38	38.9^{c} ± 0.38	38.8^{c} ± 0.39	<0.001

[1] Data are means ± SEM. Means in a row with superscripts without a common letter differ, $P < 0.05$.
[2] ANOVA.

- The 1,25(OH)$_2$D concentrations were **25.4 pmol/L** lower in the lowest 25(OH)D quartile to compared with highest quartile
- A **decrease** in 25(OH)D concentrations **by 1 nmol/L** was associated with a mean decrease in 1,25(OH)$_2$Dconcentrations of **0,4 pmol/L**

Lagunova et al. Mol. Nutr. Food Res. 2010; 54: 1127–1133.

Vitamin D status and cancer risk



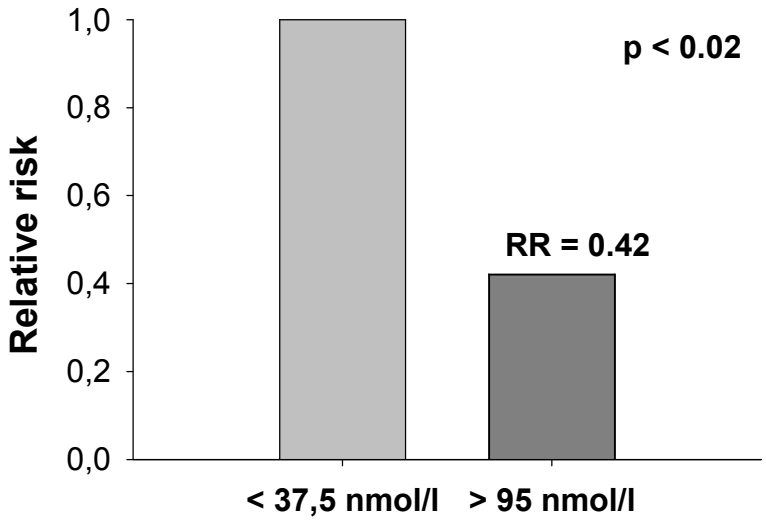
17% decrease in cancer risk with 25 nmol/L increase

Or 20,5% increase in cancer risk with 25 nmol/L decrease

Giovannucci E. et al. J. Natl. Cancer Inst. 2006, 98, 451–459.

Vitamin D status and cancer risk

Breast cancer risk

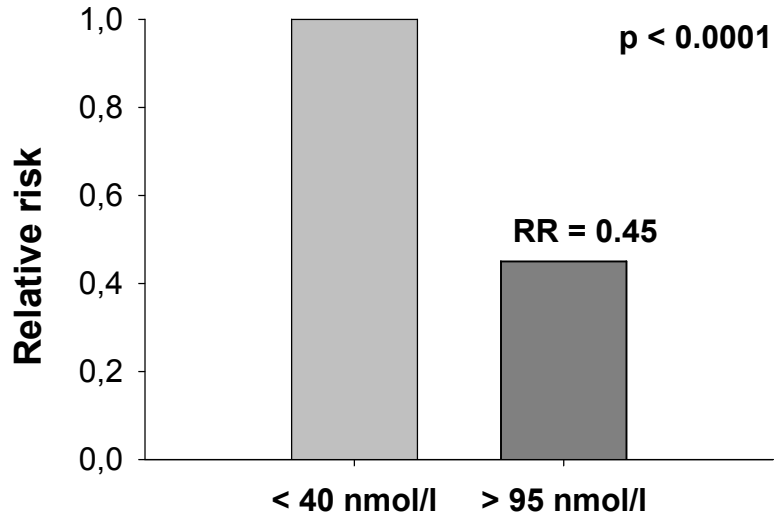


20% risk reduction

with 25 nmol/L increase

Garland CF et al. J. Steroid. Biochem. Mol. Biol. 2007, 103, 708-711.

Colorectal cancer risk



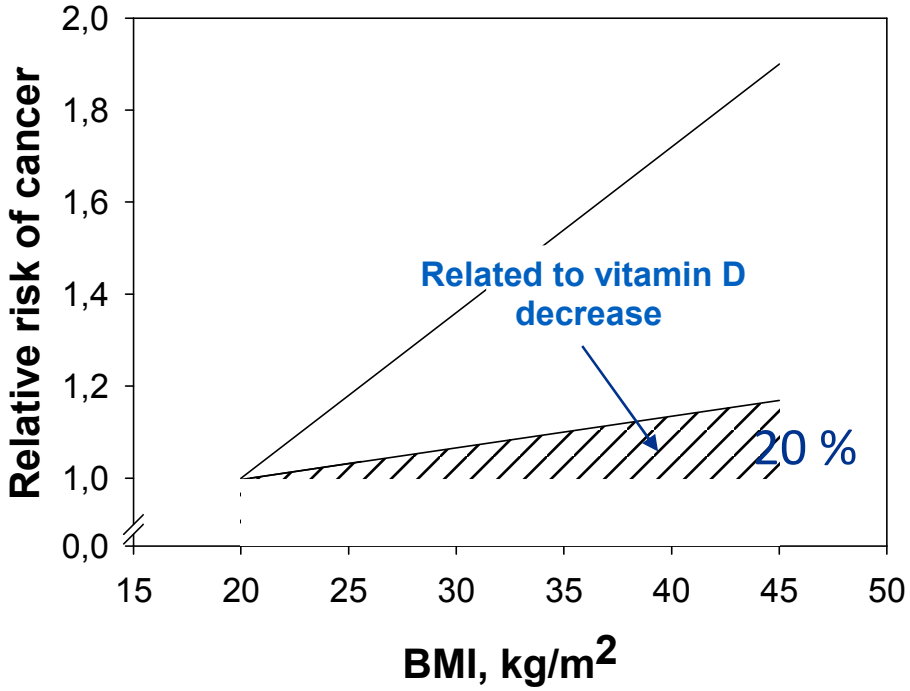
18% risk reduction

with 25 nmol/L increase

Gorham ED et al. Am. J. Prev. Med. 2007; 32: 210-216.

Lagunova et al. Mol. Nutr. Food Res. 2010; 54: 1127–1133.

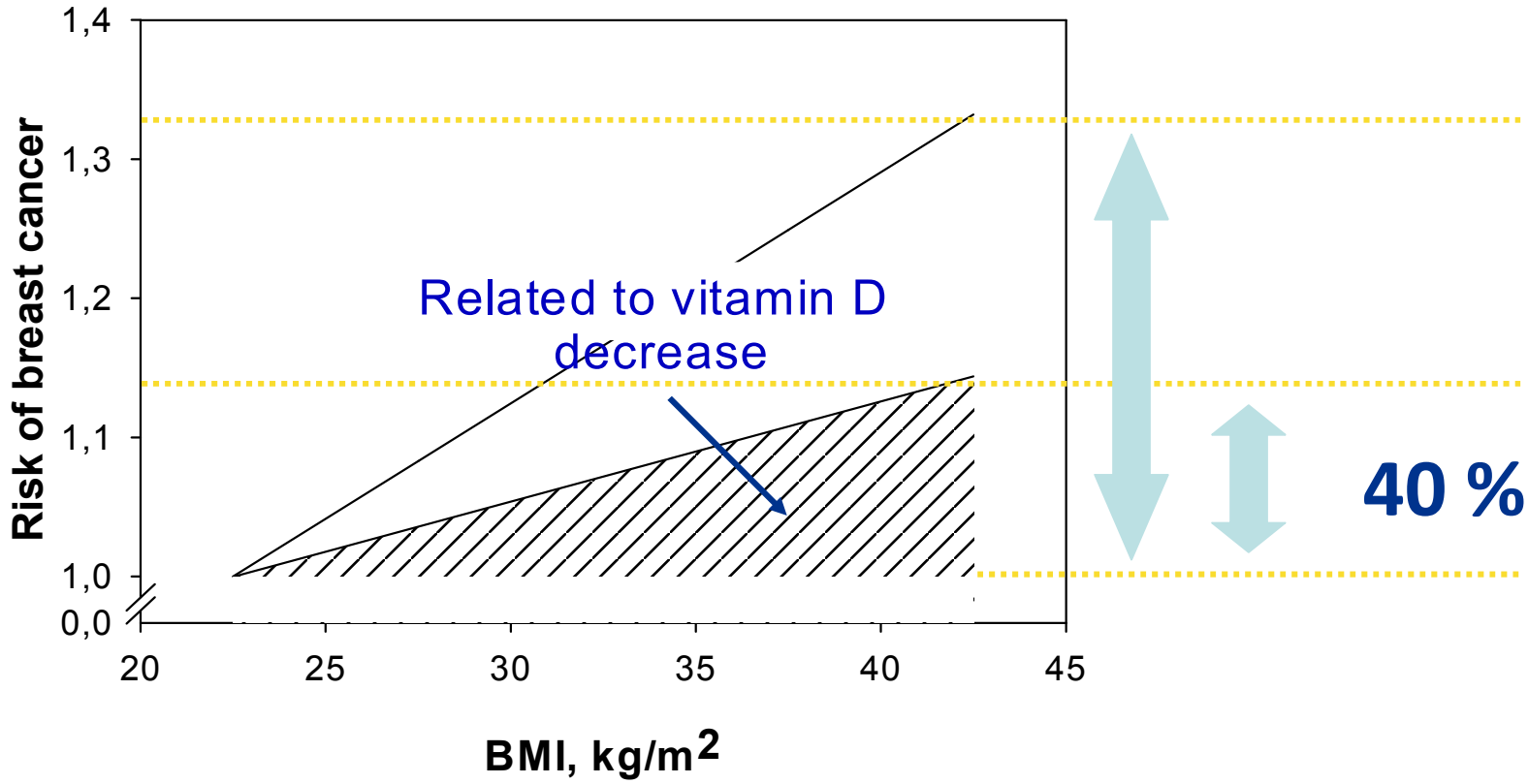
RR of cancer according to BMI and vitamin D contribution



- Almost two times higher risk for cancer in individuals with BMI close to 45 kg/m^2 compared to those with BMI around 20 kg/m^2
- About 20% of the effect of obesity on cancer risk may be explained by changes in vitamin D status

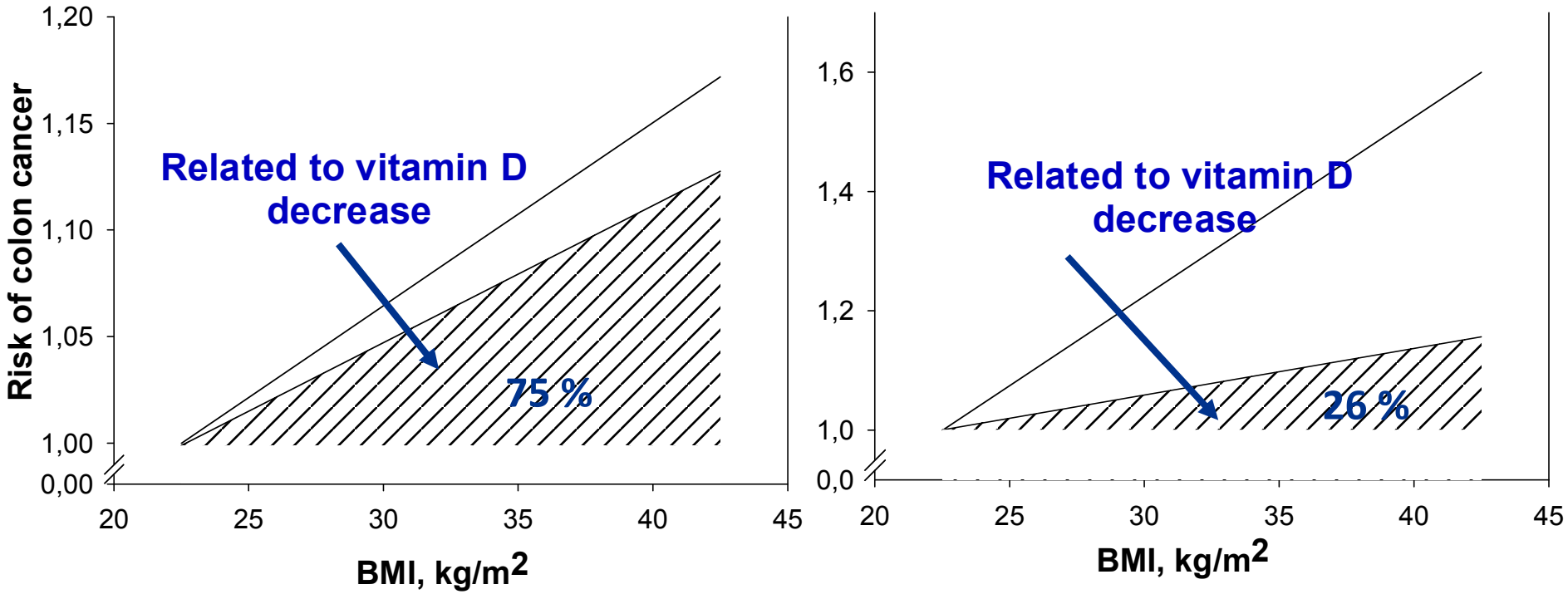
Lagunova et al. Mol. Nutr. Food Res. 2010; 54: 1127–1133.

RR of breast cancer according to BMI and vitamin D contribution



Lagunova et al. Mol. Nutr. Food Res. 2010; 54: 1127–1133.

RR of colorectal cancer according to BMI and vitamin D contribution



What is the difference between obese and normalweight man?

BMI 45 kg/m² **25(OH)D 50 nmol/L** **BMI 23 kg/m²** **25(OH)D 75 nmol/L**

$RR_{obesity + low\ vitamin\ D} = 1.65$ $RR_{obesity} = 1.49$ **26 %**

What is the difference between obese and normalweight woman?

BMI 45 kg/m² **25(OH)D 55 nmol/L** **BMI 23 kg/m²** **25(OH)D 75 nmol/L**

$RR_{obesity\ +\ low\ vitamin\ D} = 1.4$ $RR_{obesity} = 1.24$ **40 %**

Thank you for your attention!

My serum 25(OH)D is > 100 nmol/L !

Ok, ok... you won!