

Endokrinologie und «Gender Medicine»

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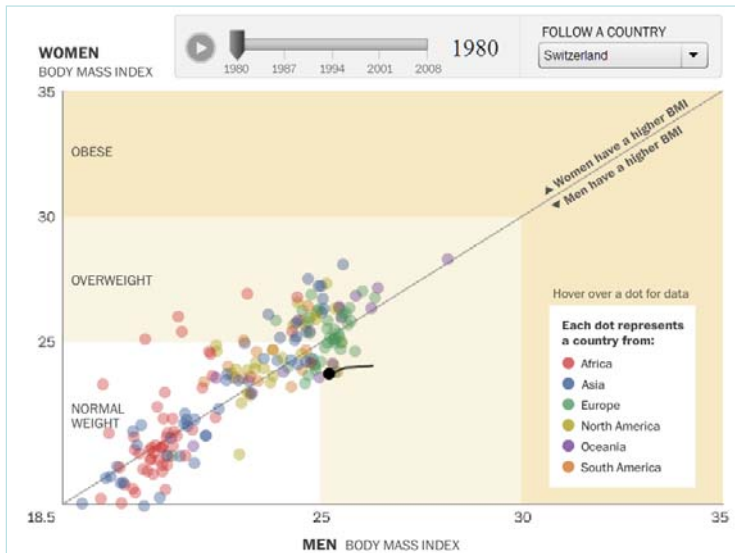
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Endokrine Erkrankungen und Gender Medicine

- ▶ Übergewicht
- ▶ Schilddrüse
- ▶ Primärer Hyperparathyroidismus
- ▶ Sexualhormone: Menopause vs Andropause
- ▶ Knochen
- ▶
- ▶

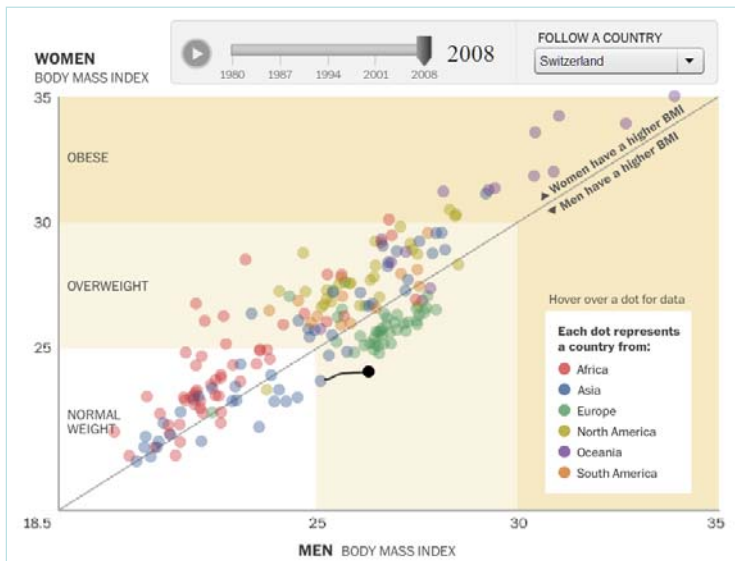
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Weight of the World 1980

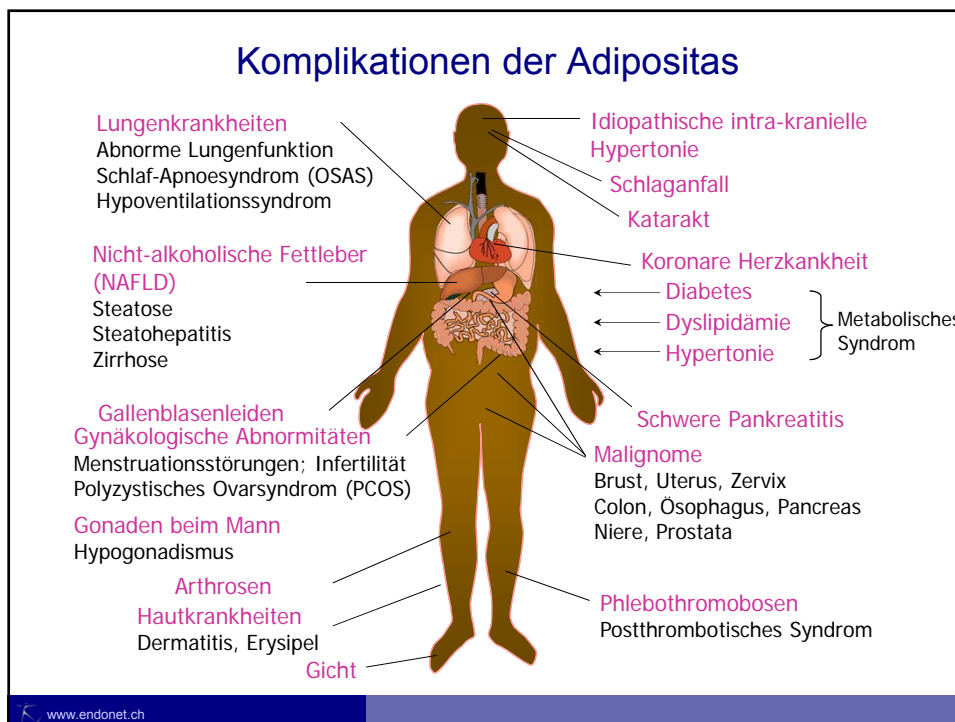
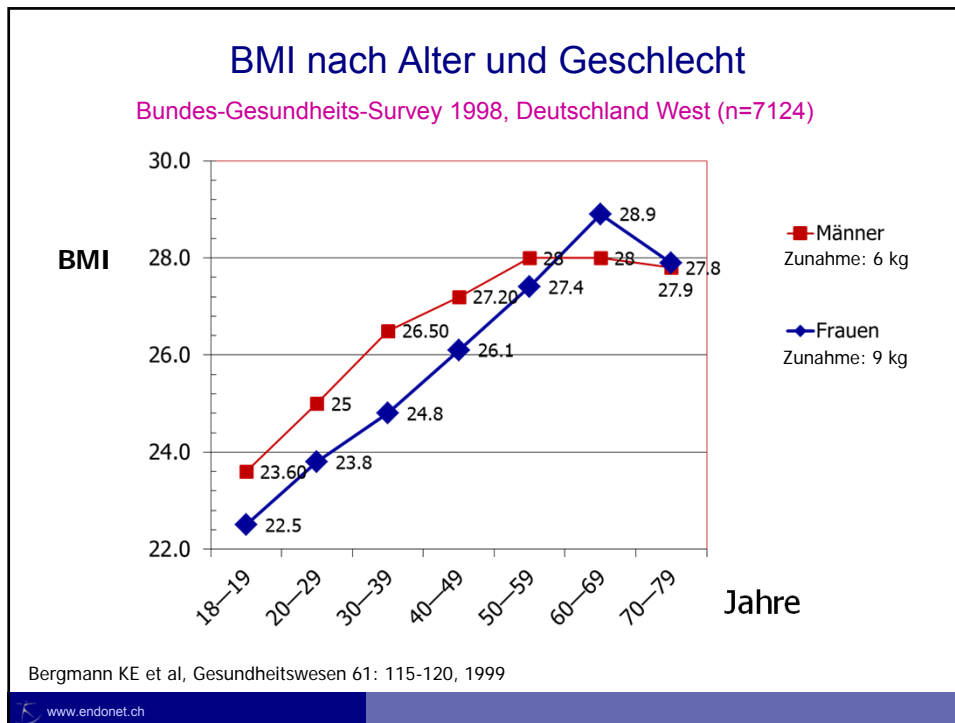


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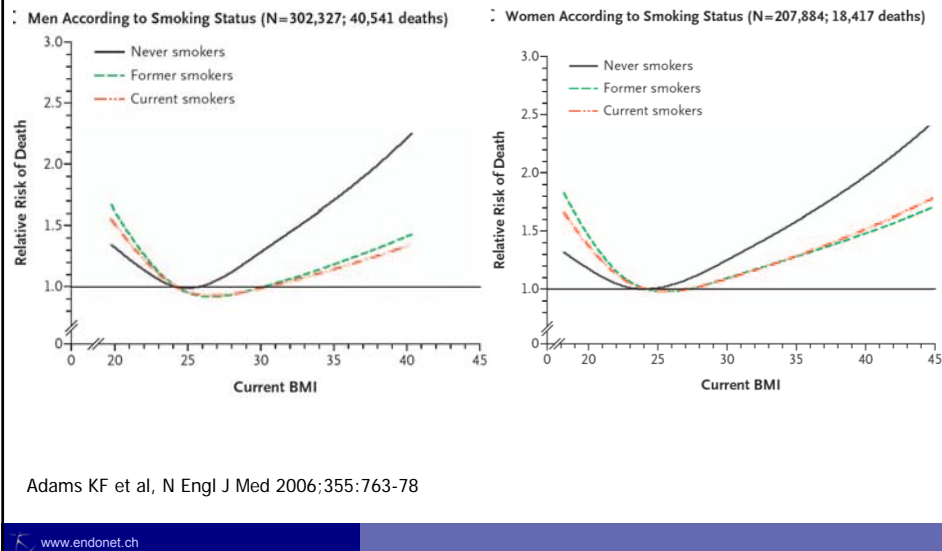
Weight of the World 2008



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Overweight, Obesity, and Mortality in a Large Prospective Cohort of Persons 50 to 71 Years Old



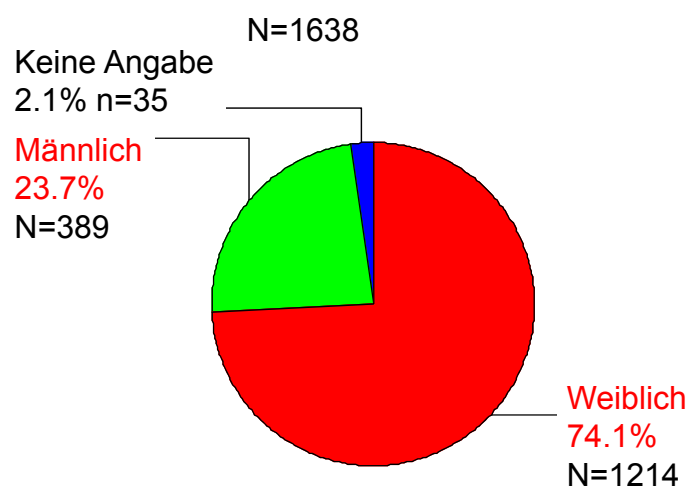
Soziale Komplikationen der Adipositas v.a. bei Frauen !

- ▶ Job- Diskriminierung
- ▶ Isolation, Vereinsamung
- ▶ verminderte Auswahl von Kleidern
- ▶ Beeinträchtigung des Sitz- und des Bewegungsvermögens (Sport, Schwimmen etc)
- ▶ verminderte Körperhygiene
- ▶ Einschränkungen im Sexualleben

Adipositas und Diabetes

- ▶ Body composition:
 - Männer mehr viszerales und hepatisches Fett und mehr «lean mass»
 - Frauen mehr subkutanes Fett
- ▶ Prävalenz Diabetes Typ II etwas höher bei Frauen als bei Männern: meisten Studien meist ohne oder nur mit wenig Frauen
- ▶ Adipositas stärkerer Risikofaktor für DM Typ II bei Frauen
Bessere Insulinsensitivität bei Männern
- ▶ Zielwert HbA1c weniger häufig erreicht bei Frauen
(Therapeutika anderes Wirkungsprofil bei Frauen ?)
- ▶ Primär- und Sekundärmaßnahmen für CHK kommen seltener zum Einsatz bei Frauen
Hyperlipidämie weniger konsequent therapiert bei Frauen

Bariatrische Chirurgie in der Schweiz im 2000. SMOB Register. Anzahl operierte Männer und Frauen



Predictive factors of mortality in bariatric surgery: (Nationwide US Inpatient Sample, 2006-2008)

- ▶ Insgesamt 304'515 Patienten wurden einer bariatrischen Operation unterzogen.
- ▶ **80%** der Patienten waren Frauen, 20% Männer.
- ▶ Die Mortalität war bei Männern **70% höher** als bei Frauen (Multivariate Regression).

NT Nguyen et al, Surgery 2011;150:347-51

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Schilddrüsenerkrankungen

- ▶ Struma
- ▶ Funktionsstörungen: Hypo- und Hyperthyreose
- ▶ Schilddrüsen-Knoten: benigne vs.- Schilddrüsen-Ca
- ▶ Thyreoditis

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Prevalence of Thyroid Disease by Age

The incidence of thyroid disease increases with age

	Elevated TSH, % (Age in Years)						
	18	25	35	45	55	65	75
Male	3	4.5	3.5	5	6	10.5	16
Female	4	5	6.5	9	13.5	15	21

Canaris GJ, et al. Arch Intern Med. 2000;160:523-534.

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Prevalence of Subclinical Thyroid Disease

	Subclinical Hypothyroidism			Subclinical Hyperthyroidism		
Women	USA	All ages	5.8%	USA	>60 yrs	1.5%
	GB	18-44 yrs	4-5%	Germany	50-80 yrs	5.9%
		45-74 yrs	8-10%			
		>75 yrs	17.4%			
Men	USA	All ages	3.4%	USA	>60 yrs	1%
	GB	18-65 yrs	1-3%	Germany	50-80 yrs	6.3%
		>65 yrs	6.2%			

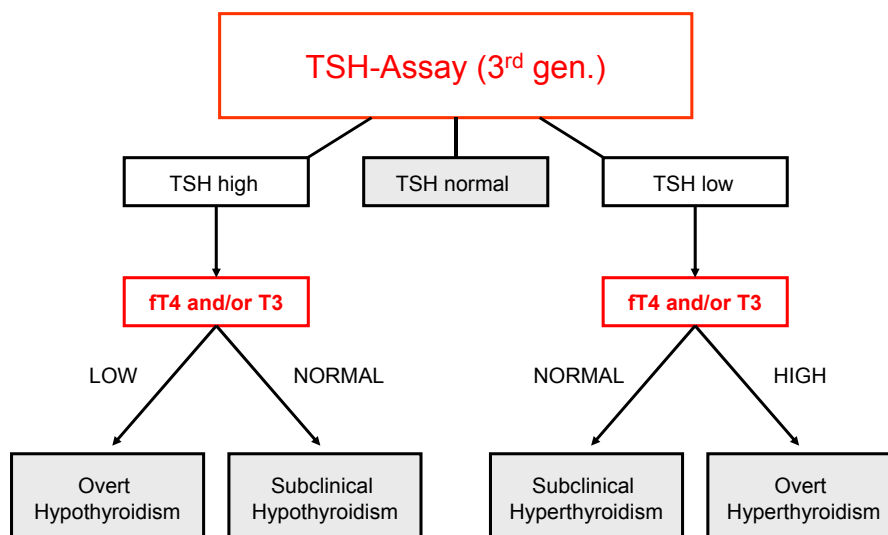
Hollowell et al, J Clin Endocrinol Metab 2002, 87: 489
 Tunbridge et al, Clin Endocrinol 1977, 7: 481
 Helfand et al, Ann Intern Med 1998, 129: 144
 Seck et al, Med Klin 1997, 15: 642

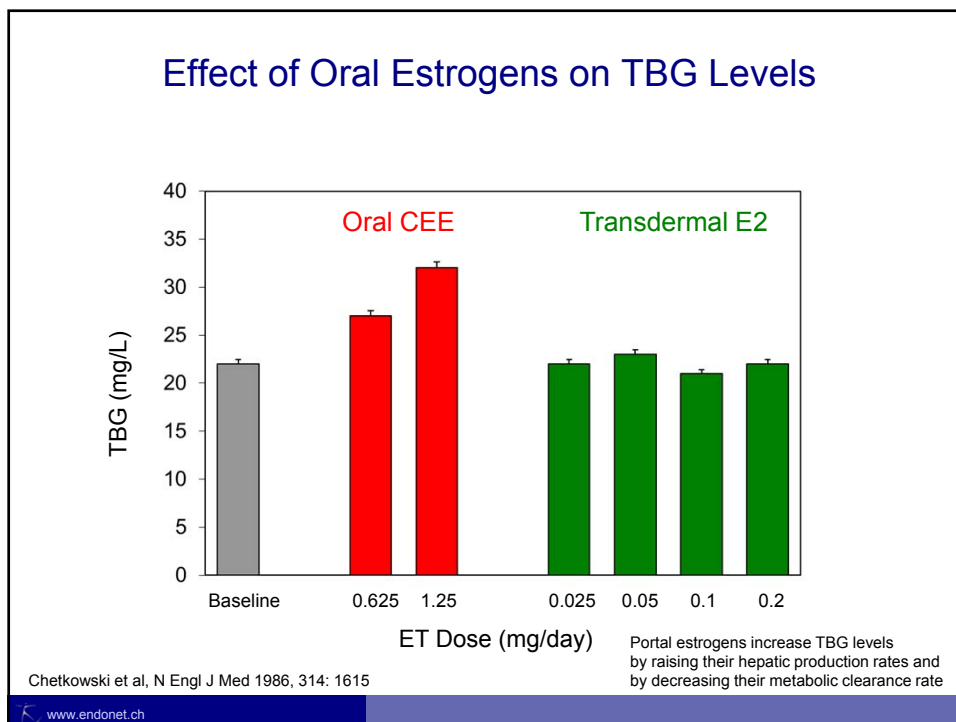
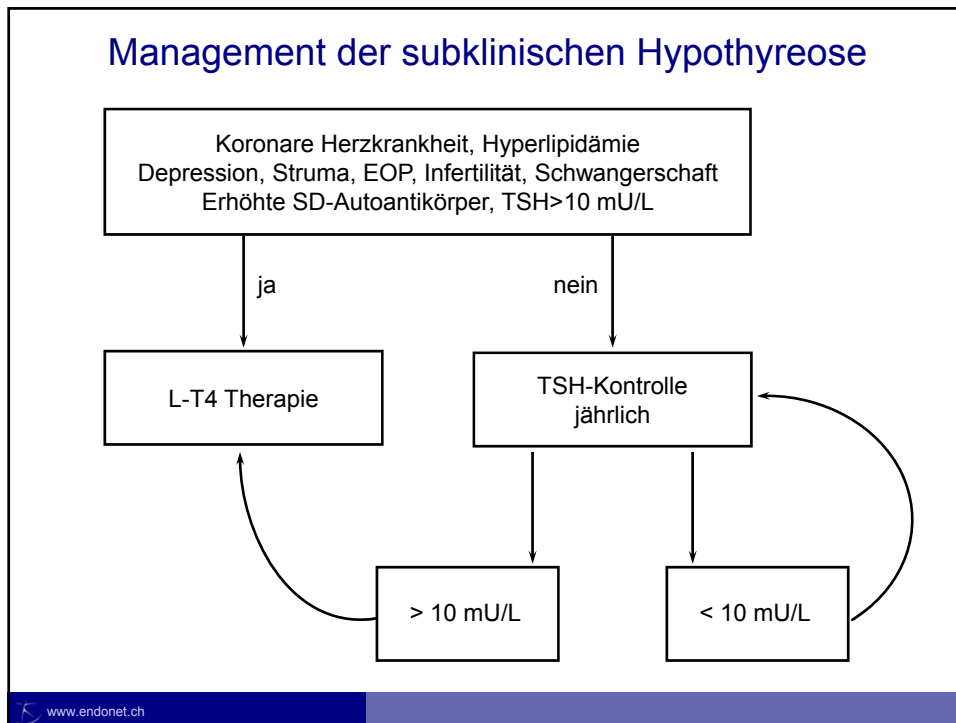
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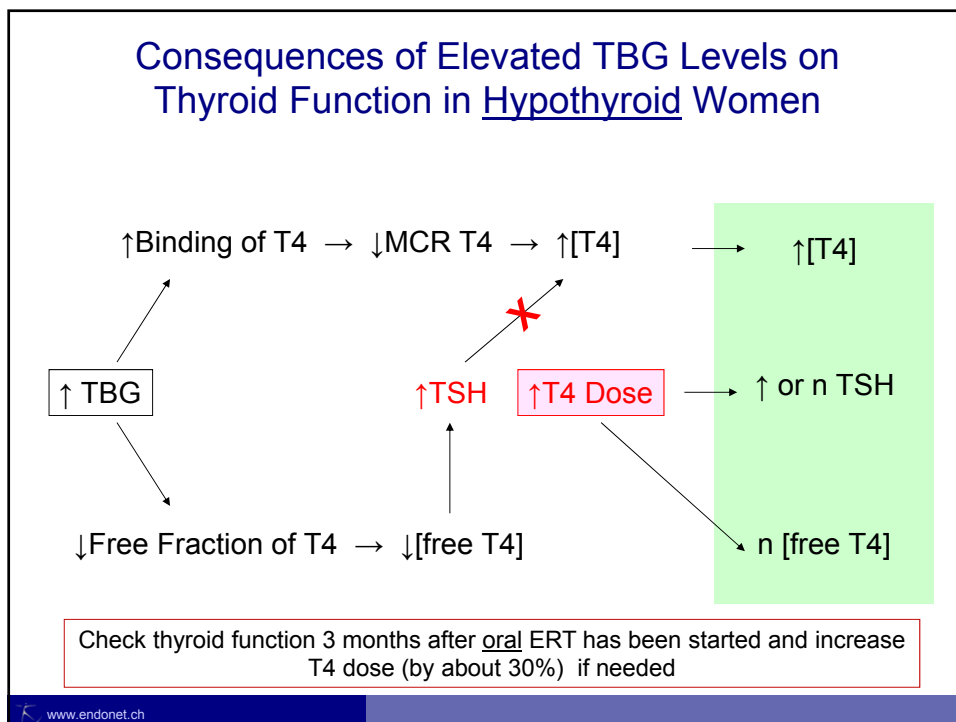
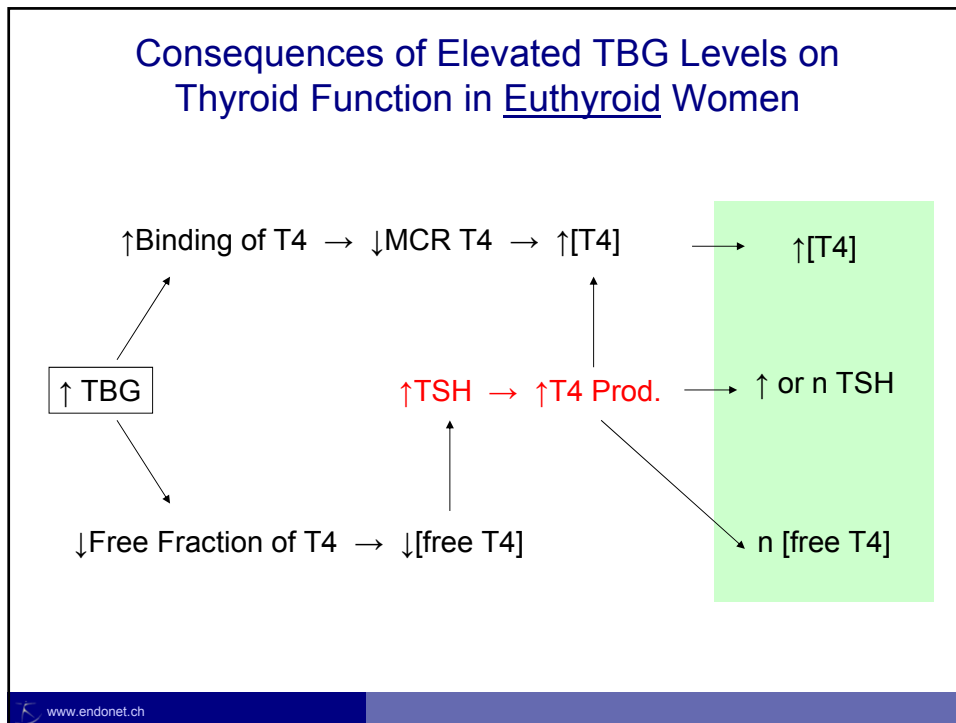
Hypothyreose: Ursachen

- ▶ **Thyreoiditis**
 - Autoimmun-Thyreoiditis (Hashimoto)
 - postpartale lymphozytäre Thyreoiditis, "silent thyroiditis"
 - subakute granulomatöse Thyreoiditis (De Quervain)
- ▶ **Medikamente**
 - Amiodaron, Lithium
- ▶ **Iatrogen**
 - Thyroidektomie, Radiojod-Therapie (Rx SD-Ca, Hyperthyreose)
 - Radiotherapie
- ▶ Kongenital (SD-Hypoplasie, Hormon-Synthesestörung)
- ▶ Iodmangel
- ▶ **Zentral:** Hypophyse / Hypothalamus

Thyroid Function Tests







Thyroid Carcinoma

- ▶ Incidence
 - Thyroid carcinoma occurs relatively infrequently compared to the common occurrence of benign thyroid disease
 - Thyroid cancers account for only 0.74% of cancers among men, and 2.3% of cancers in women in the US
 - The annual rate has increased nearly 50% since 1973 to approximately 18 000 cases
- ▶ Thyroid carcinomas (percentage of all US cases)
 - Papillary (80%)
 - Follicular (about 10%)
 - Medullary thyroid (5%-10%)
 - Anaplastic carcinoma (1%-2%)
 - Primary thyroid lymphomas (rare)
 - Metastatic from other primary sites (rare)

Thyroid Carcinoma

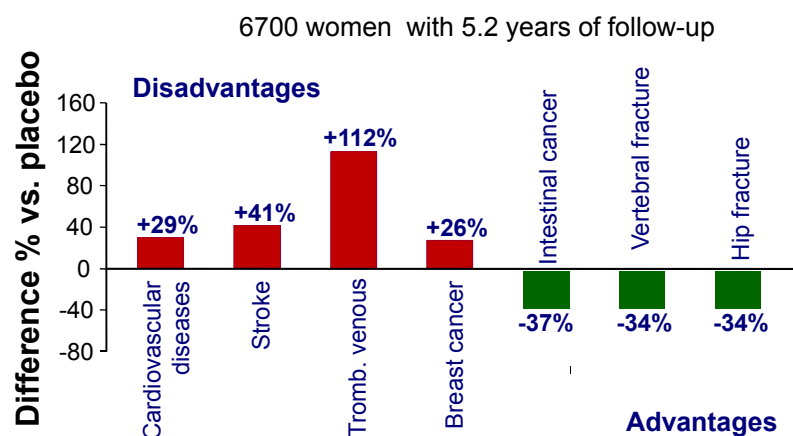
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Among patients with thyroid nodules, the rate of cancer is twice as high in men than women (8 versus 4 percent), and it is higher in adults over age 60 and under age 30 years than in those aged 30 to 60 years

Consequences of oestrogen loss

Symptoms (early)	Hot flushes Insomnia Irritability Mood disturbances
Physical changes (intermediate)	Vaginal atrophy Stress (urinary) incontinence Skin atrophy
Diseases (late)	Osteoporosis Cardiovascular disease Dementia of the Alzheimer's type Cancers

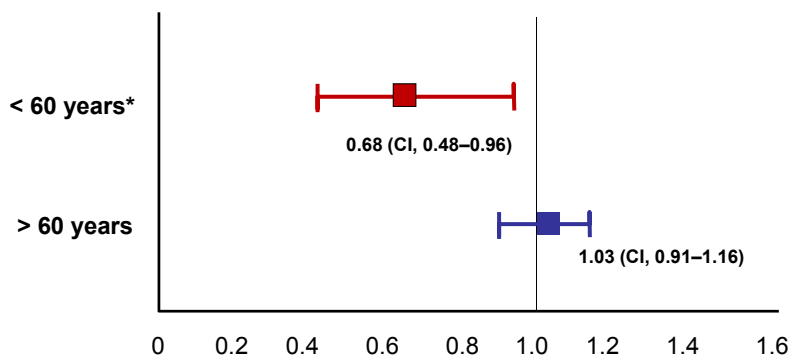
Women's Health Initiative - first randomized, controlled trial in women (50-79 yr) treated with HRT



Manson JE et al, N Engl J Med, 2002;347:523-534

Coronary heart disease events associated with hormone therapy in younger and older women: a meta-analysis

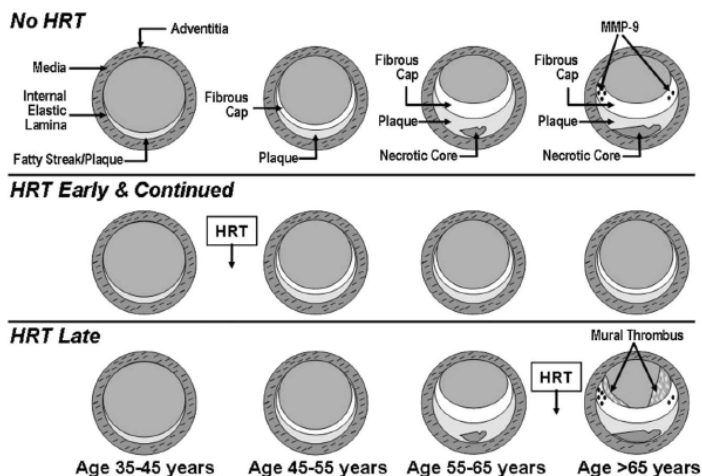
23 trials, with 39,049 participants followed for 191,340 patient-years Odds ratio for total mortality



Salpeter SR, et al. J Gen Intern Med 2006;21:363-6

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HRT and Atherosclerosis



D.Archer Climacteric 2009;12 (Suppl.1):26

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WHI: Hysterectomized Women

- 10'739 women; 50-79 years of age
- CEE 0.625 mg/d or placebo

CHD	0.91 (0.75 - 1.12)
Breast Cancer	0.77 (0.59 - 1.01)
Stroke	1.39 (1.10 - 1.77)
Hip Fracture	0.61 (0.41 - 0.91)
Global Index	1.01 (0.91 - 1.12)

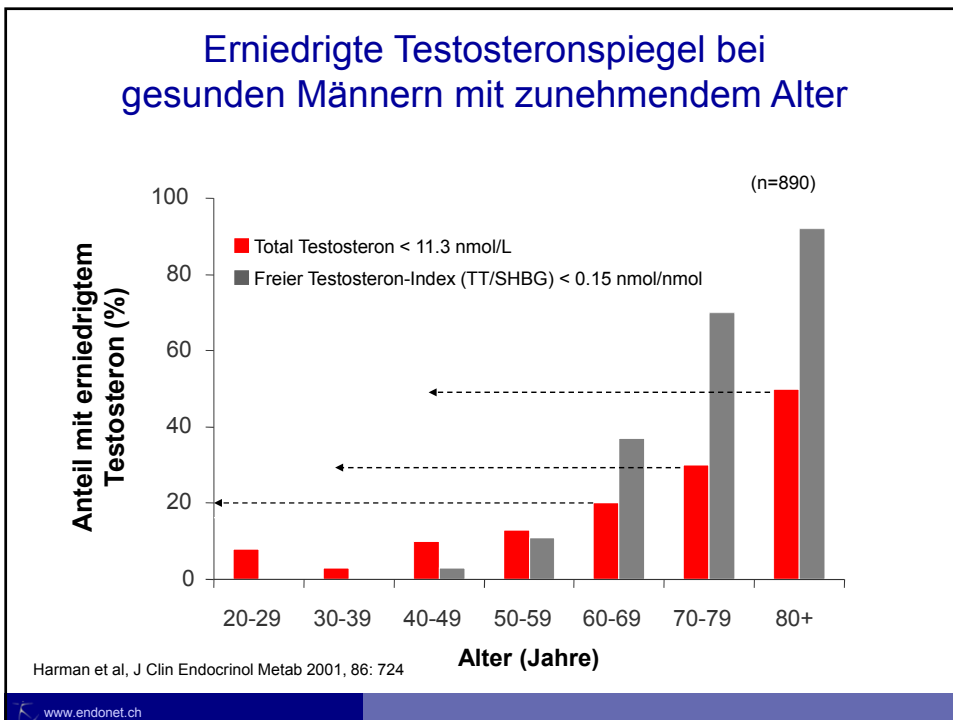
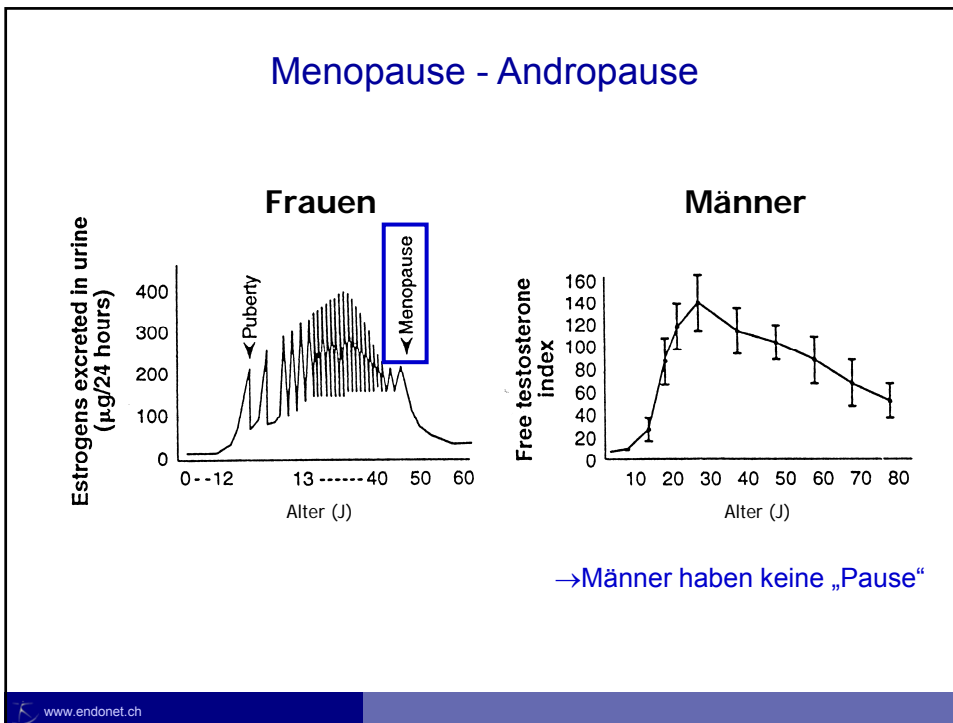
JAMA 2004; 291:1701

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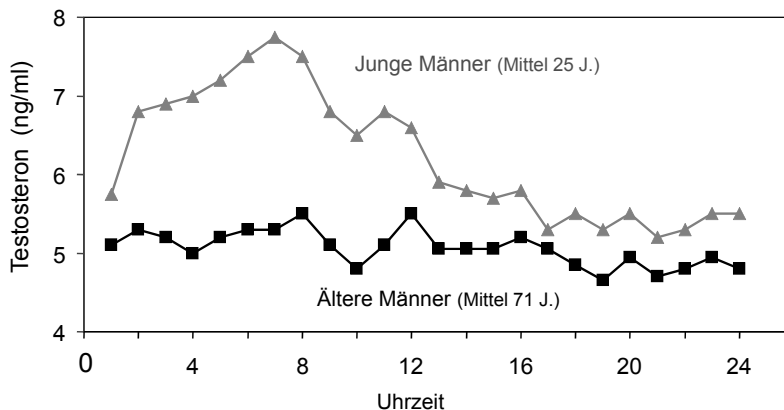
Recommendations for Use of HRT

- ▶ Menopausal symptoms / fracture prevention
- ▶ Cardiovascular disease prevention: not sustainable
- ▶ Avoid in presence of cardiovascular risk factors
- ▶ Breast cancer / venous thromboembolism advice unchanged
- ▶ Hysterectomized women uncertain

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Tagesrhythmus der Testosteronspiegel

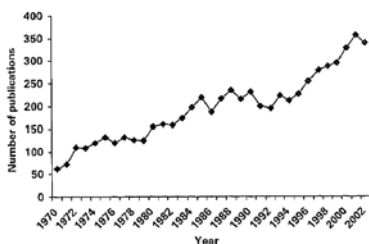


Bremner et al, J Clin Endocrinol Metab 1983; 56: 1278

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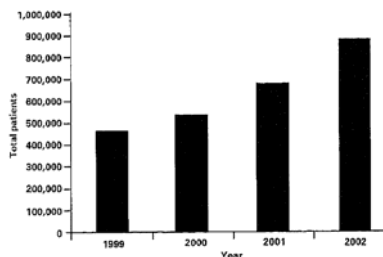
Exponential Growth of Testosterone Market

Publication activity 1970-2002



Number of publications identified from PubMed using the search terms 'testosterone therapy', 'human', and 'male'

ART 1999-2002



Number of patients treated with testosterone replacement therapy in the USA from 1999 to 2002

Nieschlag et al, Hum Reprod Update 2004, 10: 409

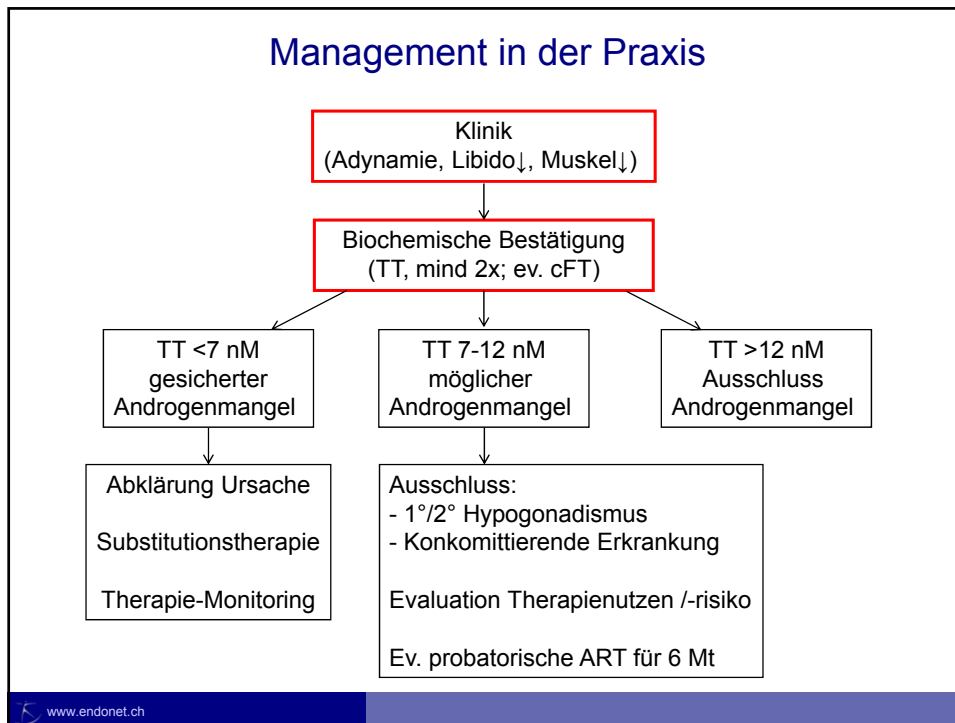
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Symptome des Climacterium Virile

- ▶ Antriebslosigkeit ↓, allg. Wohlbefinden ↓
- ▶ Depression, Schlafstörungen
- ▶ Nervosität, Hitzewallungen
- ▶ Kognitive Funktionen ↓
- ▶ Libido ↓
- ▶ Erektile Dysfunktion
- ▶ Muskelkraft ↓, Muskelmasse ↓
- ▶ Fettmasse (v.a. visceral)
- ▶ Knochendichte ↓

CLIMACTERIUM VIRILE

- ▶ Das Climacterium virile entwickelt sich graduell über Jahre, Beginn ab ca. 40 J., mit einer Abnahme von testikulären und adrenalen Androgenen, und von Wachstumshormon
- ▶ Der Grad der Hormonveränderungen ist individuell variabel, ebenso die davon stammenden Beschwerden
- ▶ Am ehesten wird der Hypogonadismus (Testosteronmangel) therapiebedürftig; allerdings gibt es über die Auswirkung einer Testosteron-Substitution wenig Langzeitdaten (>3 J.)



Potentielle Vorteile einer Testosteron-substitution beim alternden Mann

- ▶ Knochenmasse , Frakturrisiko ↓
- ▶ Muskelmasse
- ▶ Muskelkraft , allg. körperl. Funktion
- ▶ Libido , Sexualfunktion
- ▶ Wohlbefinden , Stimmungslage
- ▶ Verbesserung des Lipidprofils
(LDL-Cholesterol, Total cholesterol, Lp(a), TG)
- ▶ Fettmasse (visceral) ↓, Insulinsensitivität

Potentielle Risiken einer Testosteronsubstitution beim alternden Mann

- ▶ Prostatakarzinom, -hyperplasie
- ▶ Polyglobulie
- ▶ Flüssigkeitsretention
- ▶ Schlaf-Apnoe-Syndrom
- ▶ Gynäkomastie
- ▶ Hepatotoxizität
- ▶ HDL-Cholesterin ↓
- ▶ Risiko Herz-Kreislauf-erkrankungen (?)

Frakturrisiko zu Lebzeiten bei Frauen und Männern >50 Jahre

	Frauen (%)	Männer (%)
USA	39.7	13.1
Schweden	46.4	22.4
Australien	56.0	29.0
Schweiz	51.3	20.2

Jede 2. Frau Jeder 5. Mann

Melton et al, J Bone Miner Res 1992, 7: 1005
 Jones et al, Osteoporos Int 1994, 4: 277
 J.Kanis et al, Osteoporos Int 2000, 11: 669
K.Lippuner et al. Osteoporos Int. 2008: epub
 R.Rizzoli et al. Swiss Med. Forum 2008;8(Suppl.45): 1-12

Fracture mortality

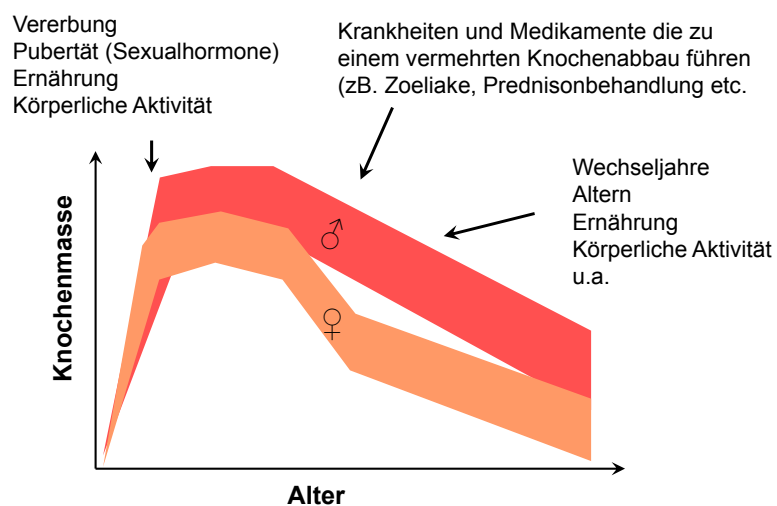
Standardised mortality ratio by gender and fracture type

Fracture type	Standardised mortality ratio (95% CI)
Women	
Proximal femur	2.18 (2.03–2.32)
Vertebral	1.66 (1.51–1.80)
Other major	1.92 (1.70–2.14)
Minor	0.75 (0.66–0.84)
Men	
Proximal femur	3.17 (2.90–3.44)
Vertebral	2.38 (2.17–2.59)
Other major	2.22 (1.91–2.52)
Minor	1.45 (1.25–1.65)

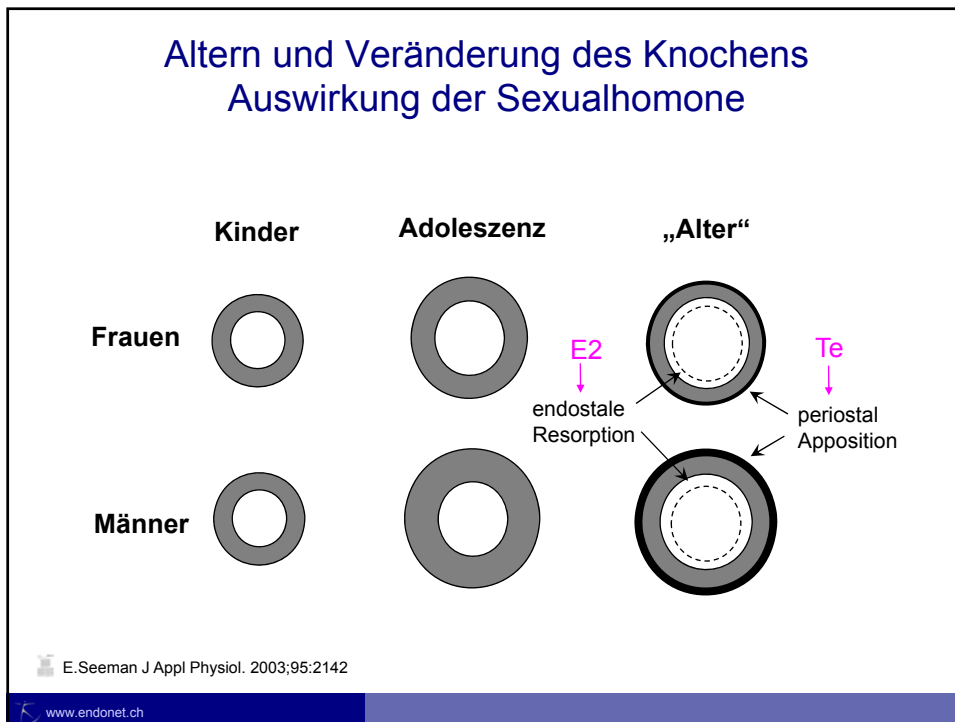
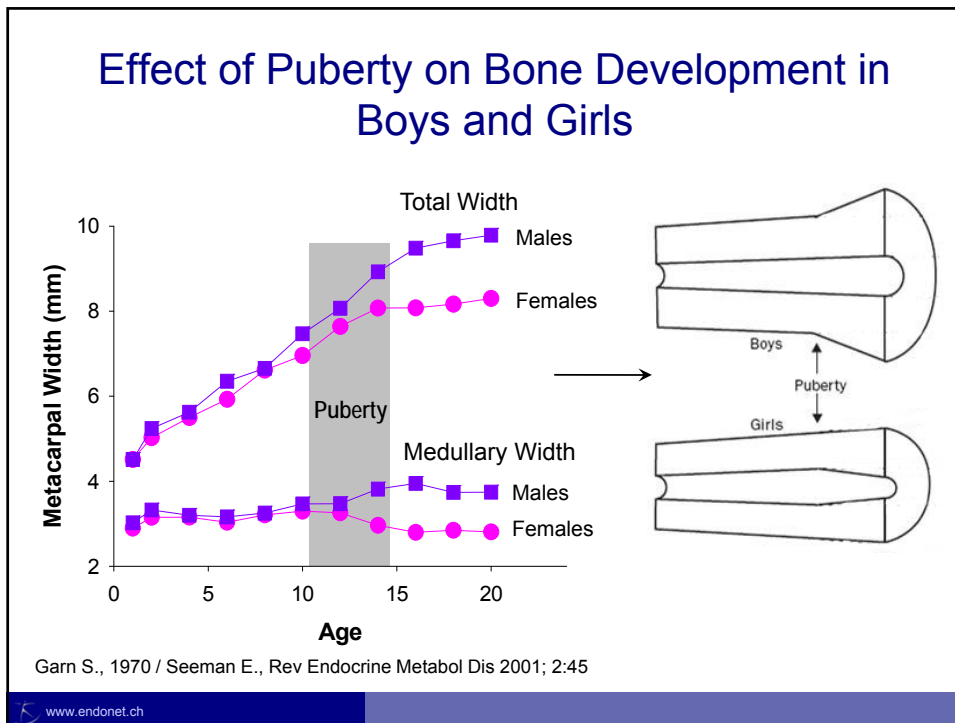
Center J et al. Lancet 1999; 353 (9156):878-882

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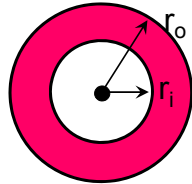
Determinanten der Knochenmasse



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Strength of Bone – Section Modulus (SM)



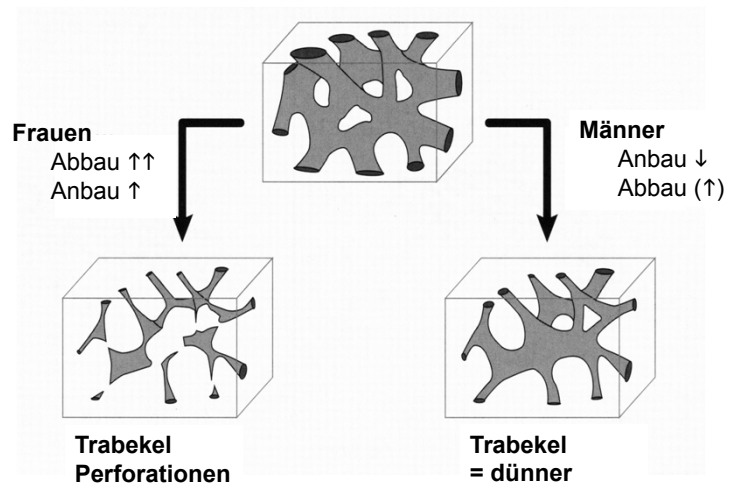
$$SM = \pi/4 r_o^3 [1 - (r_i/r_o)^4]$$

$$r_o = 1.6\text{cm} \quad r_i = 1.2\text{cm} \quad \rightarrow SM = 2.2$$

$$r_o = 1.7\text{cm} \quad r_i = 1.2\text{cm} \quad \rightarrow SM = 2.9 \text{ (+32\%)}$$

$$r_o = 1.6\text{cm} \quad r_i = 1.3 \quad \rightarrow SM = 1.8 \text{ (-18\%)}$$

Trabekulärer Knochen – Alters-bedingter Verlust



Case-Finding Strategie Indikation zur Diagnostik - Densitometrie

Frauen	<50 Jahre	50-60 Jahre	>60 Jahre
Männer	<60 Jahre	60-70 Jahre	>70 Jahre
<i>Wirbelfraktur(en)</i>	+ (D)	+ (A)	+ (A)
Orale Glukokortikoide ≥ 5.0 mg Prednisolonäquivalent ≥ 3 Mt	+ (A)	+ (A)	+ (A)
Cushing-Syndrom	+ (B)	+ (B)	+ (A)
Primärer Hyperparathyreoidismus (pHPT)	+ (B)	+ (B)	+ (B)
Hypogonadismus (auch vorzeitige Menopause <42 Jahre)	+ (B)	+ (B)	+ (B)
Therapie mit Glitazonen bei Frauen		+ (D)	+ (A)
<i>Nichtvertebrale Fraktur(en) nach dem 50. Lebensjahr</i>		**	+ (A)
Therapie mit Aromatasehemmern		**	+ (A)
Antiandrogene Therapie		**	+ (A)
Rheumatoide Arthritis		**	+ (A)
Proximale Femurfraktur eines Elternteils			+ (B)
Untergewicht (BMI <20)			+ (A)
Nikotinkonsum*			+ (A)
Multiple Stürze (mehr als 1x in letzten 12 Monaten)			+ (A)
Immobilität (kann ohne fremde Hilfe nicht ins Freie)			+ (A-B)
Diabetes mellitus Typ 1			+ (A)
TSH-Werte <0,3 mU/l			+ (B)

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Prevalence of secondary osteoporosis in men

UK	41%	(A.Scane et al. Osteopor Int 199;9:91)
UK	54%	(S.Baillie et al. Age Ageing 1992;21:39)
UK	57%	(R.Francis et al. Bone Miner 1989;5:347)
USA	33%	(E.Seeman et al. Am J Med 1983;75:977)
Germany	62%	(J.Ringe et al. Deutsch Med Wschr 1994;119:943)
Spain	78%	(P.Perin et al. Br J Rheumatol 1995;34:936)
Switzerland	43%	(M. Kraenzlin 2001)

(Prevalence of 2° Op in women $\pm 20\%$)

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Bisphosphonate – Indikationen

Perorale Präparate

	Alendronat Fosamax® 70 mg, wöchentlich	Ibandronat Bonviva® 150 mg, monatlich	Risedronat Actonel® 35 mg, wöchentlich
Postmenopausale Osteoporose	+	+	+
Osteoporose des Mannes	+	-	+
Steroidinduzierte Osteoporose	+	-	+

Parenterale Präparate

	Ibandronat Bonviva IV® 3 mg, 3-monatlich	Zoledronat Aclasta® 5 mg, jährlich	Pamidronat Aredia®
Postmenopausale Osteoporose	+	+	-
Osteoporose des Mannes	-	+	-
Steroidinduzierte Osteoporose	-	+	-

Behandlung der Osteoporose beim Mann nach einer Hüftfraktur

