# Gesundheitsförderung und Prävention durch Bewegung

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### Evidenz

### Epidemiologische Studien

# Mechanismen körperlicher Aktivität

### Individuelle Dosis-Wirkungsbeziehung





### Körperliche Aktivität und Krankheitsrisiko – Die historische Entwicklung

#### A DRIVERS (MACTIVE) CONDUCTORS(Active) TELEPHONISTS (WACT/VE) DOSTMEN (ACTIVE) INCIDENCE INCIDENCE TOTAL AS ANGINA AS CORONARY INCIDENCE PECTORIS HEART DISEASE 1949-50 1949-50 DYING IN 3 MOS. Fig. 2 .--- First clinical episodes of coronary heart-disease in 1989-62: A. drivers and male conductors, aged 35-64, of Central London Buns: B, G.P.O. male telephonists and postmen, aged 35-59.

Inzidenz der KHK

Morris et al. (1953) Lancet 265: 1111-20

Gemindertes Sterberisiko

#### SPIEGEL ONLINE

15 Minuten Bewegung am Tag verlängern Leben um drei Jahre 22.11.2011



Jogger im Londoner Hyde Park: Tod hinausgezögert

Schon eine Viertelstunde körperliche Aktivität pro Tag senkt das Risiko, vorzeitig zu sterben um 14 Prozent - im Durchschnitt leben Menschen dadurch drei Jahre länger. Das zeigen medizinische Daten von 400.000 Taiwanern.

#### Wen et al. Lancet (2011) 378: 1244-1253





#### Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study

Chi Pang Wen\*, Jackson Pui Man Wai\*, Min Kuang Tsai, Yi Chen Yang, Ting Yuan David Cheng, Meng-Chih Lee, Hui Ting Chan, Chwen Keng Tsao, Shan Pou Tsai, Xifeng Wu

Lancet (2011) 378: 1244-1253

N = 416.175 Personen 199.265 Männer, 216.910 Frauen

Gruppen körperliche	er Aktvität (MET-Std. / Woche):
inaktiv:	< 3.75
gering:	3.75 – 7.49
mittlere:	7.49 – 16.49 (z.b. 2.5 Std. Walking)
hohe:	16.49-25.49
Sehr hohe:	> 25.49 (e.g. >3.5 hrs. Jogging)

### **Epidemiologische Evidenz - Subgruppenanalyse**



Wen et al. (2011) Lancet 378: 1244-1253

### **Epidemiologische Evidenz - Gesamtaktivität**



Kyu et al. (2016) BMC 354: j3857

MET (minutes/week 000s)

### - Koronare Herzerkrankung -

#### Dose Response Between Physical Activity and Risk of Coronary Heart Disease

A Meta-Analysis

Jacob Sattelmair, MSc, ScD; Jeremy Pertman, MS; Eric L. Ding, ScD; Harold W. Kohl III, PhD; William Haskell, PhD; I-Min Lee, MBBS, ScD

Circulation (2011) 124: 789-795



### Table.Pooled Relative Risks of Coronary Heart Disease ComparingHighest and Lowest Physical Activity Categories

ype of Activity	Sex	Studies	Relative Risk (95% Cl)	l <sup>2</sup> , %	Studies, n*
.TPA	Combined	All studies	0.74 (0.69-0.78)	28.3	26
		Quant	0.71 (0.63–0.80)	39.8	9
	Men	All studies	0.78 (0.73–0.82)	0	15
		Quant	0.79 (0.72–0.86)	0	5
	Women	All studies	0.67 (0.61–0.74)	12.5	11
		Quant	0.64 (0.52–0.79)	40.6	5
Total PA	Combined	All studies	0.74 (0.62–0.90)	0	3
	Men	All studies	0.79 (0.59–1.07)	18.9	2
	Women	All studies	0.66 (0.44–0.99)	0	2



### Epidemiologische Evidenz - Typ 2 – Diabetes -

#### Risikoreduktion pro 10 MET-Stunden pro Woche

Physical activity and incident type 2 diabetes mellitus: a systematic review and dose–response meta-analysis of prospective cohort studies

Andrea D. Smith<sup>1,2</sup> · Alessio Crippa<sup>3</sup> · James Woodcock<sup>4</sup> · Søren Brage<sup>5</sup>

Diabetologia (2016) 59: 2527-2545

Authors (date) [ref.] ES (95% CI)	
LTPA Helmrich et al (1991) [14] Lynch et al (1996) [13] Haapanen et al (1) (1997) [36] Haapanen et al (1) (1997) [36] Haapanen et al (1) (1997) [36] James et al (1998) [63] Folsom et al (2000) [62] Okada et al (2000) [66] Hu et al (2000) [66] Hu et al (2004) [70] Weinstein et al (2005) [37] Weinstein et al (2005) [37] Weisinger et al (1) (2005) [37] Weisinger et al (1) (2005) [37] Willegas et al (2006) [47] Carlsson et al (2009) [68] Fretts et al (2009) [68] Chien et al (2009) [64] Chien et al (2009) [66] Chien et al (2009) [64] Craftscon et al (2009) [66] Chien et al (2012) [67] Crontved et al (11) (2012) [38] Crontved et al (11) (2014) [35] Crontved et al (11) (2014) [35] Cro	
Total PA         Burchfiel et al (1995) [58]         Nakanishi et al (2004) [57]         Ekelund et al (1) (2012) [39]         Ekelund et al (1) (2012) [39]         Ekelund et al (11) (2012) [39]         Subtotal (1 <sup>2</sup> =85.6%, p<0.001)	
.2 .4 1 2 4	3

Dosis an körperlicher Aktivität	Risikoreduktion
Pro 10 MET-Stunden/Woche	13% (95% Cl 11 – 16%)
150 min moderat 11.25 MET-Stunden/Woche	26% (95% Cl 20 – 31%)
300 min moderat	36% (95% CI 27 – 46%)
60 MFT-Stunden/Woche	53%



### - Neoplastische Erkrankungen -

n = 1.44 Mio. Teilnehmer

In 13 von 26 Tumorentitäten geringeres Risiko unter körperlicher Aktivität

Bei 7 Tumorentitäten Risikoreduktion > 20%

Cancer	# of Studies	Cases		HR (95% CI)	P	P <sub>heterogeneity</sub> ‡
Esophageal adenocarcino	ma 5	899 —		0.58 (0.37-0.89)	0.01	0.01
Gallbladder	6	382		0.72 (0.51-1.01)	0.06	0.29
Liver	10	1,384	<b>e</b>	0.73 (0.55-0.98)	0.04	0.02
Lung	12	19,133	-	0.74 (0.71-0.77)	< 0.001	0.47
Kidney	11	4,548		0.77 (0.70-0.85)	< 0.001	0.40
Small intestine	7	503		0.78 (0.60-1.00)	0.05	0.85
Gastric cardia	6	790	<b>_</b>	0.78 (0.64-0.95)	0.02	0.99
Endometrial	9	5,346	<b>——</b>	0.79 (0.68-0.92)	0.003	<0.01
Esophageal squamous	6	442		0.80 (0.61-1.06)	0.12	0.78
Myeloid leukemia	10	1,692	<b>——</b>	0.80 (0.70-0.92)	0.002	0.78
Myeloma	9	2,161	<b>—•</b>	0.83 (0.72-0.95)	800.0	0.36
Colon	12	14,160	-8-	0.84 (0.77-0.91)	<0.001	0.01
Head and neck	11	3,985		0.85 (0.78-0.93)	<0.001	0.45
Rectum	12	5,531		0.87 (0.80-0.95)	0.001	0.38
Bladder	12	9,073	-	0.87 (0.82-0.92)	< 0.001	0.84
Breast	10	35,178		0.90 (0.87-0.93)	< 0.001	0.30
Non-Hodgkin lymphoma	11	6,953		0.91 (0.83-1.00)	0.05	0.18
Thyroid	11	1,829		0.92 (0.81-1.06)	0.26	0.48
Gastric non-cardia	7	1,428		0.93 (0.73-1.19)	0.56	0.09
Soft tissue	10	851		0.94 (0.67-1.31)	0.70	0.03
Pancreas	10	4,186		0.95 (0.83-1.08)	0.40	0.14
Lymphocytic leukemia	10	2,160		0.98 (0.87-1.11)	0.73	0.99
Ovary	9	2,880	-+	1.01 (0.91-1.13)	0.81	0.98
Brain	10	2,110	<b>-</b>	1.06 (0.93-1.20)	0.41	0.43
Prostate	7	46,890		1.05 (1.03-1.08)	<0.001	0.90
Malignant melanoma	12	12,438		1.27 (1.16-1.40)	<0.001	0.02
		0.3	06 1 1	5		
		0.0	0.0			

Hazard Ratio (90th vs 10th percentile of physical activity)

- Sitzen und Sterblichkeitsrisiko -

А for the Lancet Physical Activity Series 2 Executive Committe\* and the Lancet Sedentary Behaviour Working Group\* 2.0 1.7-Hazard ratio (95% CI) 1.4-MALIN XA. 225 CARP. 1.2 -GERMANWIN Watern der Coole rots Depression 1.1 BILLIONENSPIE Verapoken die Euro-Re 1.0 0.9 0.8 LANDAY LEG NIDAY NIDAY NIDAY 4 hiday LA hiday Ahlday hiday hiday hiday A hilder hider hider 26 hlbay hlbay hlbay ten Sitzen erhöht das Risiko für schwere Krankheite STERN Nr. 16 20-04-2015 >35.5 MET-h/week 30 MET-h/week 16 MET-h/week <2.5 MET-h/week Quartiles of physical activity

Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women

Ulf Ekelund, Jostein Steene-Johannessen, Wendy J Brown, Morten Wang Fagerland, Neville Owen, Kenneth E Powell, Adrian Bauman, I-Min Lee,

Lancet (2016) 388: 1302-1310

### - Inaktivität und Seelische Gesundheit



Depressive symptoms and objectively measured physical activity and sedentary behaviour throughout adolescence: a prospective cohort study

Aaron Kandola, Gemma Lewis, David PJ Osborn, Brendon Stubbs, Joseph F Hayes

Lancet Psychiatry (2020) 7: 262-271

	Unadjusted model		Fully adjusted model*		
	IRR (95% CI)	p value	IRR (95% CI)	p value	
Exposure at 12 years (n=2486)					
Count per minute (per 100)	0.910 (0.882-0.939)	<0.0001	0.941 (0.910-0.972)	<0.0001	
Sedentary behaviour (per 60 min)	1.108 (1.054-1.165)	<0.0001	1.111 (1.051–1.176)	<0.0001	
Light activity (per 60 min)	0.883 (0.834-0.933)	<0.0001	0.904 (0.850-0.961)	0.0012	
Moderate-to-vigorous activity (per 15 mins)	0.848 (0.863-0.965)	<0.0001	0.910 (0.857-0.966)	0.0018	
Exposure at 14 years (n=1938)					
Count per minute (per 100)	0.933 (0.902-0.965)	<0.0001	0·965 (0·932-0·999)	0.0443	
Sedentary behaviour (per 60 min)	1.114 (1.057–1.175)	<0.0001	1.080 (1.012-1.152)	0.0200	
Light activity (per 60 min)	0.908 (0.851-0.970)	0.0044	0.922 (0.857-0.992)	0.0299	
Moderate-to-vigorous activity (per 15 mins)	0.913 (0.863-0.965)	0.0409	0.960 (0.905–1.018)	0.1691	
Exposure at 16 years (n=1220)					
Count per minute (per 100)	0.939 (0.896-0.983)	0.0072	0.984 (0.937-1.033)	0.5092	
Sedentary behaviour (per 60 min)	1.101 (1.026-1.180)	0.0068	1.107 (1.015-1.208)	0.0210	
Light activity (per 60 min)	0.882 (0.810-0.961)	0.0040	0.889 (0.809-0.974)	0.0133	
Moderate-to-vigorous activity (per 15 mins)	0.938 (0.883-0.997)	0.0413	1.001 (0.936–1.071)	0.9662	

Depression at 18 years of age was assessed with the Clinical Interview Schedule-Revised. IRR=incidence rate ratio. \*Adjusted for sex, maternal social class, parental psychiatric history, parental education, ethnicity, baseline depression, and total accelerometer wear time at each timepoint.

Table 3: Longitudinal associations between depression scores at 18 years and different levels of physical activity and sedentary behaviour at 12 years, 14 years, and 16 years of age

### "Polypill" Körperliche Aktivität



http://www.healthexpress.eu/de





### Wirkmechanismen körperlicher Aktivität

### - Insulinresistenz -

#### Glucose Transporter Number, Function, and Subcellular Distribution in Rat Skeletal Muscle After Exercise Training

LAURIE J. GOODYEAR, MICHAEL F. HIRSHMAN, PATRICIA M. VALYOU, AND EDWARD S. HORTON

Diabetes (1992) 41: 1091-1099



### Wirkmechanismen körperlicher Aktivität - Kardiovaskuläre Erkrankungen –



Schuler et al. (2018) Eur Heart J 34: 1790–1799

TGF-B

### Wirkmechanismen körperlicher Aktivität - Krebserkrankungen -



### **Cell Metabolism**

#### Voluntary Running Suppresses Tumor Growth through Epinephrine- and IL-6-Dependent NK Cell Mobilization and Redistribution

#### **Graphical Abstract**



#### Authors

Line Pedersen, Manja Idorn, Gitte H. Olofsson, ..., Bente K. Pedersen, Per thor Straten, Pernille Hojman

#### Correspondence

phojman@inflammation-metabolism.dk

(2016) 23, 554–562

#### In Brief

The beneficial effects of exercise are countless. Pedersen et al. now link exercise, cancer, and immunity and reveal that exercise decreases tumor incidence and growth by over 60% across several mouse tumor models through a direct regulation of NK cell mobilization and trafficking in an epinephrine- and IL-6-dependent manner.

### Wirksamkeit körperlicher Aktivität

- Qualitative Aspekte

### Kraft vs. Ausdauertraining

Nieß & Thiel (2017) Diabetologie 12: 112-126

Adapted from Pollok et al., 2001; Mandic et al., 2012 Fagard et al. 2006

Variable	Aerobes Ausdauertraining	Kraft- training	
Maximale Sauerstoffaufnahme	† †	↔/↑	
Leistung an der individuellen anaeroben (Laktat-)Schwelle	↑ ↑ ↑	↔/↑	
Körperfettanteil (%)	11	Ļ	
Fettfreie Körpermasse	↔/↑	î î	
Muskelkraft	↔/↑	111	
Ektope Fettspeicher (Leber, viszeral)	111	↔/↓	
Insulinsensitivität	11	† †	
HDL-Cholesterin	t	↔/ ↑	
LDL-Cholesterin	↔/↓	↔/↓	
Ruheumsatz	t	Ť	
Herz-Kreislauf-System:			
<ul> <li>Ruheherzfrequenz</li> </ul>	↓↓	↔/↓	
<ul> <li>Schlagvolumen</li> </ul>	11	↔	
<ul> <li>Ruheblutdruck (systolisch)</li> </ul>	Ļ	Ļ	
<ul> <li>Ruheblutdruck (diastolisch)</li> </ul>	Ţ	Ļ	

### Wirksamkeit körperlicher

#### Cardio-metabolic risk factors adaptations in HIIE and MICT: A meta-analysis

### **Aktivität - Qualitative Aspekte**

#### Metabolic Adaptations to Short-term High-Intensity Interval Training: A Little Pain for a Lot of Gain?

Martin J. Gibala,<sup>1</sup> and Sean L. McGee<sup>2</sup>

<sup>1</sup>Exercise Metabolism Research Group, Department of Kinesiology, McMaster University, Hamilton, Ontario, Canada; and <sup>2</sup>Department of Physiology, University of Melbourne, Melbourne, Victoria, Australia





Meta-Analysis	Number of Studies	Favours MICT	Favours HIIE	d	95% CI	p-value	Effect Size	Egger p-value
$VO_{2max}$ Heterogeneity: I <sup>2</sup> = 77%, $\tau^2$ = 0.5788, p < 0.01	46		+	0.73	[ 0.47; 0.98]	<0.001	medium	> 0.05
Flow-mediated Dilation Heterogeneity: $l^2 = 95\%$ , $\tau^2 = 2.8667$ , p < 0.01	8		<del></del>	1.72	[ 0.48; 2.96]	0.006	large	> 0.05
<b>BMI</b> Heterogeneity: $I^2 = 85\%$ , $\tau^2 = 0.9450$ , p < 0.01	28	-	-	0.01	[-0.39; 0.40]	0.974	trivial	< 0.001
Body Mass Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , p = 1.00	41			-0.10	[-0.22; 0.02]	0.111	trivial	< 0.001
Body Fat Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , p = 0.75	28		त्म्ब सन्द	0.13	[-0.02; 0.29]	0.096	trivial	> 0.05
Systolic Blood Pressure Heterogeneity: $I^2 = 90\%$ , $\tau^2 = 1.3828$ , p < 0.01	23		-	-0.19	[-0.70; 0.32]	0.475	trivial	< 0.05
Diastolic Blood Pressure Heterogeneity: $I^2 = 94\%$ , $\tau^2 = 2.6750$ , p < 0.01	23		-	0.02	[-0.67; 0.71]	0.954	trivial	> 0.05
HDL Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 8.2475$ , p < 0.01	26			-1.75	[-2.94; -0.56]	0.004	large	> 0.05
<b>LDL</b> Heterogeneity: $i^2 = 97\%$ , $\tau^2 = 7.7425$ , p < 0.01	21	_	-	0.52	[-0.71; <b>1</b> .76]	0.407	medium	> 0.05
Triglycerides Heterogeneity: $I^2 = 94\%$ , $\tau^2 = 3.4677$ , p < 0.01	25		<u> </u>	0.06	[-0.73; 0.84]	0.888	trivial	> 0.05
Total Cholesterol Heterogeneity: $I^2 = 94\%$ , $\tau^2 = 3.5453$ , p < 0.01	24			0.80	[ 0.00; 1.60]	0.049	large	< 0.01
<b>C-reactive Protein</b> Heterogeneity: Ι* = 92%, τ* = 2.1578, p < 0.01	6			-1.80	[-3.05; -0.55]	0.005	large	> 0.05
Fasting Insulin Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , p = 0.56	18			0.10	[-0.09; 0.29]	0.317	trivial	> 0.05
Fasting Glucose Heterogeneity: $I^2 = 95\%$ , $\tau^2 = 3.5120$ , p < 0.01	25	-	*	0.54	[-0.24; 1.33]	0.176	medium	> 0.05
$\label{eq:holest} \begin{array}{l} \textbf{Hb}_{\textbf{A1c}} \\ \text{Heterogeneity: I}^2 = 76\%, \ \tau^2 = 0.5981, \ p < 0.01 \end{array}$	9			-0.88	[- <b>1</b> .46; -0.29]	0.003	large	> 0.05
$\label{eq:homoson} \begin{array}{l} \textbf{HOMA-IR} \\ \text{Heterogeneity: } \mathbf{I}^2 = 94\%, \ \tau^2 = 4.2601, \ p < 0.01 \end{array}$	16	_ <del></del>		-1.09	[-2.14; -0.03]	0.043	large	< 0.01
		-3 -2 -1	0 1 2 3					

Mattioni et al. (under review)

Cohen's d Effect Sizes

### Individuelle Trainierbarkeit

Maximale Sauerstoffaufnahme



Bouchard & Rankinen (2001) Med Sci Sports Exerc 33: S446



Bouchard et al. (2012) PLoS ONE 7: e37887



### **Individuelle Trainierbarkeit**

50

OPEN a ACCESS Freely available online

#### Adverse Metabolic Response to Regular Exercise: Is It a **Rare or Common Occurrence?**

Claude Bouchard<sup>1</sup>\*, Steven N. Blair<sup>2</sup>, Timothy S. Church<sup>3</sup>, Conrad P. Earnest<sup>3</sup>, James M. Hagberg<sup>4</sup>, Keijo Häkkinen<sup>5</sup>, Nathan T. Jenkins<sup>42</sup>, Laura Karavirta<sup>5</sup>, William E. Kraus<sup>6</sup>, Arthur S. Leon<sup>7</sup>, D. C. Rao<sup>8</sup>, Mark A. Sarzynski<sup>1</sup>, James S. Skinner<sup>9</sup>, Cris A. Slentz<sup>6</sup>, Tuomo Rankinen<sup>1</sup>

PLoS ONE (2012) 7: e37887

PLos one

Anteil Non – Responder für	1 RF: 31% 2 RF: 6%
	3-4 RF: 0,8%

50-40-40 se respo 8,3% 30-3 30 rage of adver 5 20 쳝 19 10-10 Perce 12 17 HERITAGE HERITAGE HERITAGE HERITAGE INFLAME STRRIDE MARYLAND JYVASKYLA Total DREW **Plasma Fasting Insulin** 50 50



Anteil Non-Responder (%)



87

21

13,3%

32

Plasma HDL-C

8

INFLAME STRRIDE MARYLAND JYVASKYLA Total

27

222

Resting Systolic BP

### Individuelle Trainierbarkeit

Metabolic Effects of Exercise Training Among Fitness-Nonresponsive Patients With Type 2 Diabetes: The HART-D Study Diabetes Care 2015;38:1494-1501 | DOI: 10.2337/dc14-2378 Ambarish Pandey,<sup>1</sup> Damon L. Swift,<sup>2</sup> Darren K. McGuire,<sup>1,3</sup> Colby R. Ayers,<sup>3</sup> Ian J. Neeland,<sup>1</sup> Steven N. Blair,<sup>4</sup> Neil Johannsen,<sup>5</sup> Conrad P. Earnest,<sup>6</sup> Jarett D. Berry,<sup>1,3</sup> and Timothy S. Church<sup>2</sup>



n = 202 Personen mit Typ-2-Diabetes

9-monatiges Trainingsintervention 3-5 x Ausdauer-/Kraft-/Kombitraining/Woche bei 50-80% VO<sub>2peak</sub>



#### Refuting the myth of non-response to exercise training: 'non-responders' do respond to higher dose of training

David Montero<sup>1,2</sup> D and Carsten Lundby<sup>1</sup>

J Physiol (2017) 595: 3377-3387

### Individuelle Trainierbarkeit Alles nur eine Frage der Dosis ?





### Vom vom Trainingsreiz zur Trainingsanpassung



modifiziert nach: M. Flück (2006) J Exp Biol 209: 2239 • Hood et al. (2006) J Exp Biol 209: 2265 • Yan et al. (2011) J Appl Physiol 110: 264

### Zusammenfassung

Große Evidenz zur Wirksamkeit körperlicher Aktivität aus epidemiologische Studien mit Hinweisen zu Dosis-Wirkungsbeziehung (Gruppeneffekte) als robuste Basis für Empfehlungen zur aktivitätsbasierten Prävention

Wachsende Erkenntnisse zu den zugrundeliegenden Mechanismen körperlicher Aktivität bei der Risikoreduktion mit präzisierenden Hinweisen zur Dosis-Wirkungsbeziehung und Reizqualität sowie unter entitätsspezifischen Gesichtspunkten

Individuelle Dosis-Wirkungsbeziehung körperlicher Aktivität als "offene Flanke" in der aktivitätsbezogenen Prävention mit der Notwendigkeit des Verfolgens interdisziplinärer Forschungsansätze



## Vielen Dank für Ihre Aufmerksamkeit



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