

# Bewegung und Gesundheit - Was Sport mit dem Immunsystem macht...

Univ.-Prof. Dr. Dr. Philipp Zimmer



**...hat gesagt:** “Bewegung ist gut für das Immunsystem!”

**...hat gemeint:** Bewegung schützt vor Krankheit.

**Wir wollen verstehen...**

...wie unser Immunsystem auf akute Belastungen und Training reagiert?

...ob diese Veränderungen dazu beitragen die Entstehung, die Schwere und den Verlauf von Krankheiten zu beeinflussen?



Johanna Quaas, 94

# Was sagt die WHO?

## EVERY MOVE COUNTS

Being active has significant health benefits for hearts, bodies and minds, whether you're walking, wheeling or cycling, dancing, doing sport or playing with your kids.



# Wie kommt die WHO auf diese Zahlen?

Every step counts: synthesising reviews associating objectively measured physical activity and sedentary behaviour with clinical outcomes in community-dwelling older adults

*Keenan A Ramsey, Carol G M Meskers, Andrea B Maier*

**1000 Schritte am Tag mehr erhöhen die Überlebenschancen um 11%**

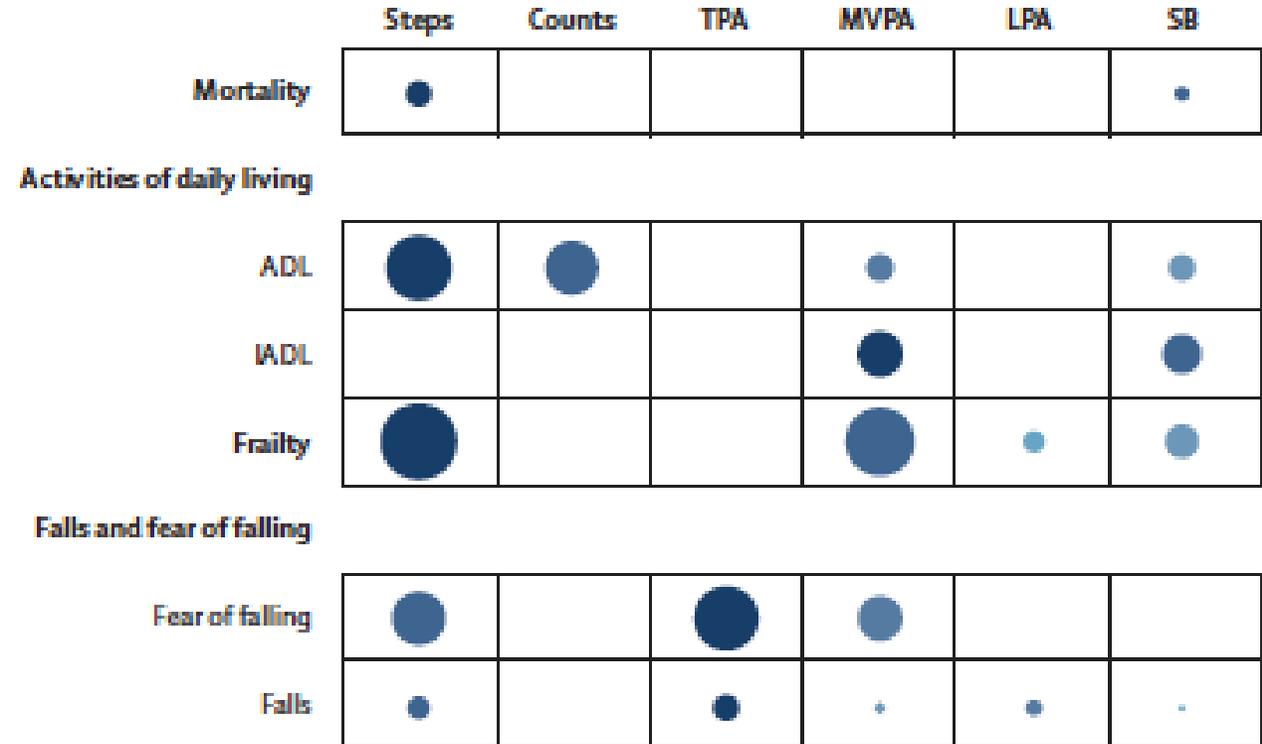


Figure 3: Relative ranking of physical activity and sedentary behaviour parameters per clinical outcome (hierarchy expressed by circle shade) and magnitude of median standardised regression coefficients ( $\beta$ s) across clinical outcomes (expressed by circle size)

ADL=activities of daily living. Counts=activity counts. IADL=instrumental activities of daily living. LPA=light physical activity. MVPA=moderate-to-vigorous physical activity. SB=sedentary behaviour. TPA=total physical activity.

# Geht es auch präziser? Was sagt die WHO?

## WHO GUIDELINES ON PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR



WHO guidelines on physical activity and sedentary behaviour

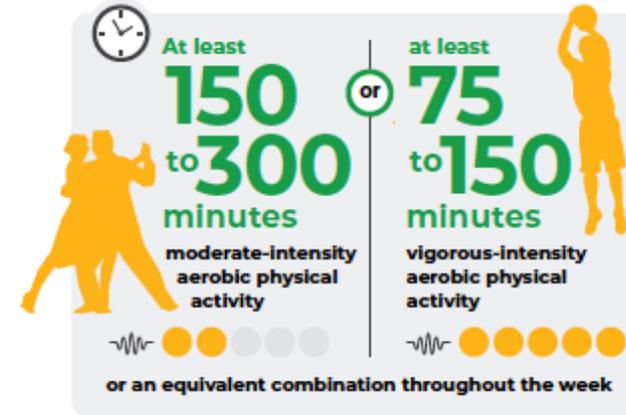
It is recommended that:

> All adults should undertake regular physical activity.

*Strong recommendation, moderate certainty evidence*

> Adults should do at least 150–300 minutes of moderate-intensity aerobic physical activity; or at least 75–150 minutes of vigorous-intensity aerobic physical activity; or an equivalent combination of moderate- and vigorous-intensity activity throughout the week, for substantial health benefits.

*Strong recommendation, moderate certainty evidence*



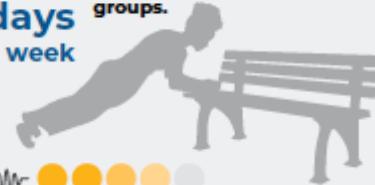
For additional health benefits:

On at least



**2**  
days  
a week

muscle-strengthening activities at moderate or greater intensity that involve all major muscle groups.



> Adults should also do muscle-strengthening activities at moderate or greater intensity that involve all major muscle groups on 2 or more days a week, as these provide additional health benefits.

*Strong recommendation, moderate certainty evidence*



# Wie kommt die WHO auf diese Zahlen?

N= 480 000

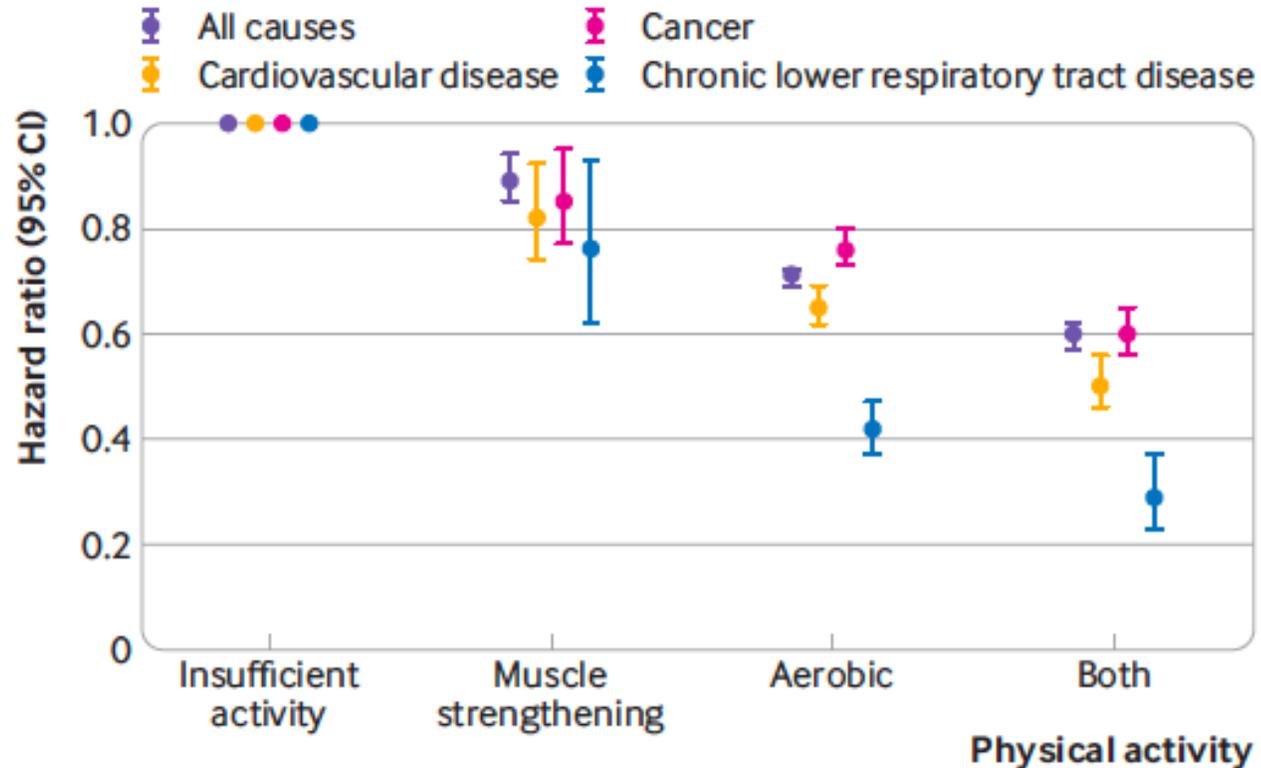
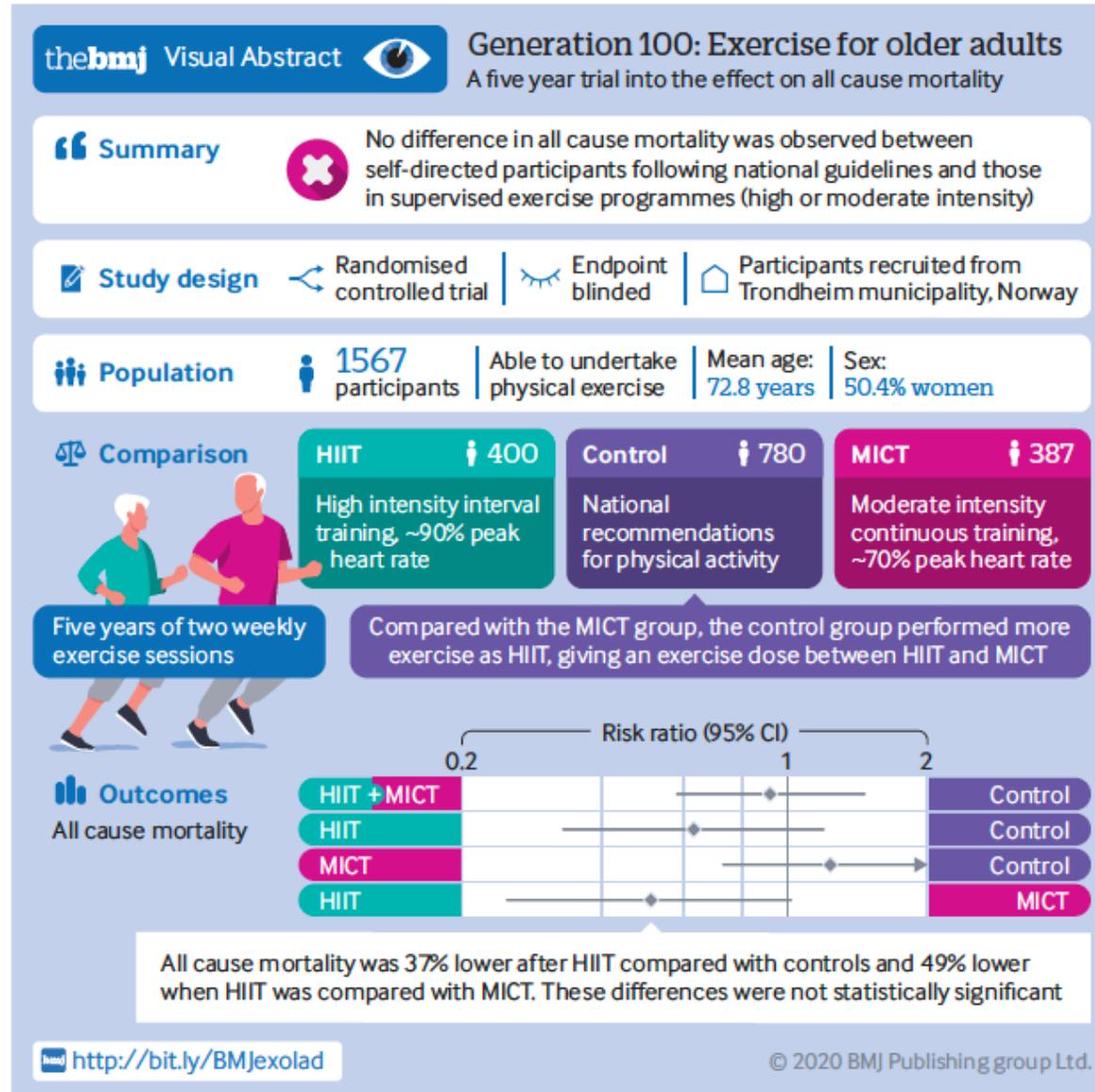


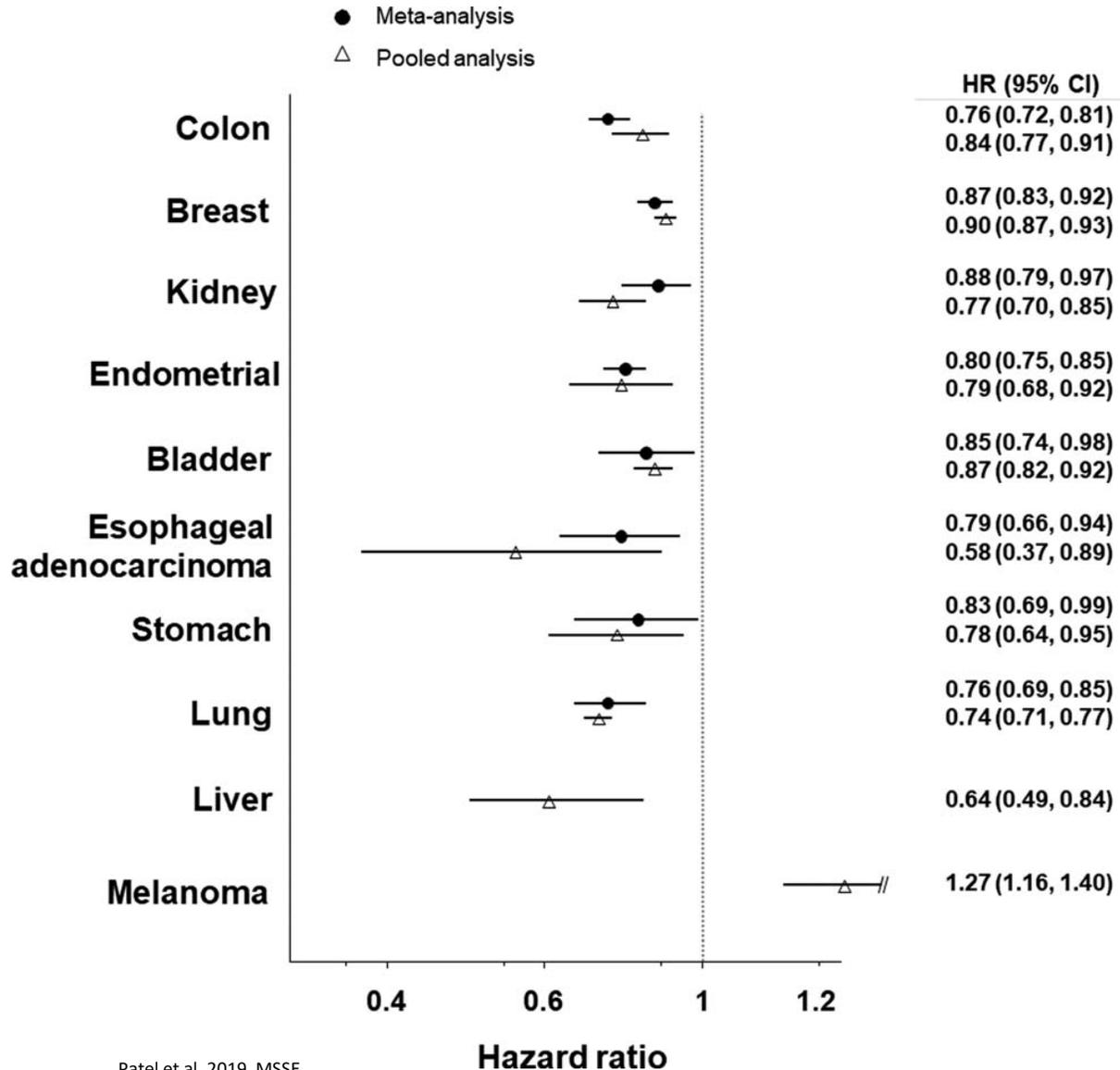
Fig 1 | Association between meeting the 2018 physical activity guidelines for Americans and all cause and cause specific mortality from three diseases. Estimates are from the fully adjusted model that includes the covariates of sex, age, race/ethnicity, education, marital status, body mass index, smoking, alcohol intake, and chronic conditions. Whiskers represent 95% confidence intervals Zhao et al. 2020

# Wie kommt die WHO auf diese Zahlen?



# Beispiel Krebs

Patel et al. 2019



Cancer Site	Prediagnosis Physical Activity			
	Cancer-Specific Mortality		All-Cause Mortality	
	<i>N</i> <sup>a</sup>	RR (95% CI)	<i>N</i>	RR (95% CI)
Breast	17	0.82 (0.73–0.92)	17	0.79 (0.72–0.86)
Colorectal	8	0.77 (0.68–0.87)	7	0.75 (0.68–0.83)
Prostate	6	0.99 (0.86–1.15)	2	0.87 (0.80–0.96)
Endometrium	2	1.04 (0.81–1.36)	2	0.92 (0.77–1.10)
Ovarian	2	1.01 (0.80–1.27)	3	0.90 (0.71–1.13)
Kidney	1	0.50 (0.27–0.93)	—	—

- Erhöhtes Aktivitätsniveau reduziert das Auftreten der häufigsten Krebserkrankungen um bis zu 36%
- Reduziert bei bestehenden Krebserkrankungen die Sterblichkeit um bis zu 50%



Cochrane Database of Systematic Reviews

## Exercise versus no exercise for the occurrence, severity, and duration of acute respiratory infections (Review)

Grande AJ, Keogh J, Silva V, Scott AM

- 14 Studien (n=1377; 16-419/Studie), Alter: 18-85
- Keine Unterschiede hinsichtlich der Anzahl der gemessenen Infektionen
- Sport scheint den Schweregrad von Symptomen und die Anzahl der Symptome im Nachgang zu reduzieren
- Evidenz der Gesamtstudienlage ist aufgrund der methodischen Qualität und der Heterogenität schwach

# Beispiel COVID19

Original research

Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study

Br J Sports Med: first published as 10.1136/bjsports-2020-103600 on 12 November 2020. Downloaded from https://www.bmj.com/ on 05 November 2020 by guest. Protected by copyright.

Original research

Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients

Robert Sallis,<sup>1</sup> Deborah Rohm Young,<sup>2</sup> Sara Y Tartof,<sup>2</sup> James F Sallis,<sup>3</sup> Jeevan Sall,<sup>1</sup> Qiaowu Li,<sup>2</sup> Gary N Smith,<sup>4</sup> Deborah A Cohen<sup>2</sup>

Lee et al. 2021

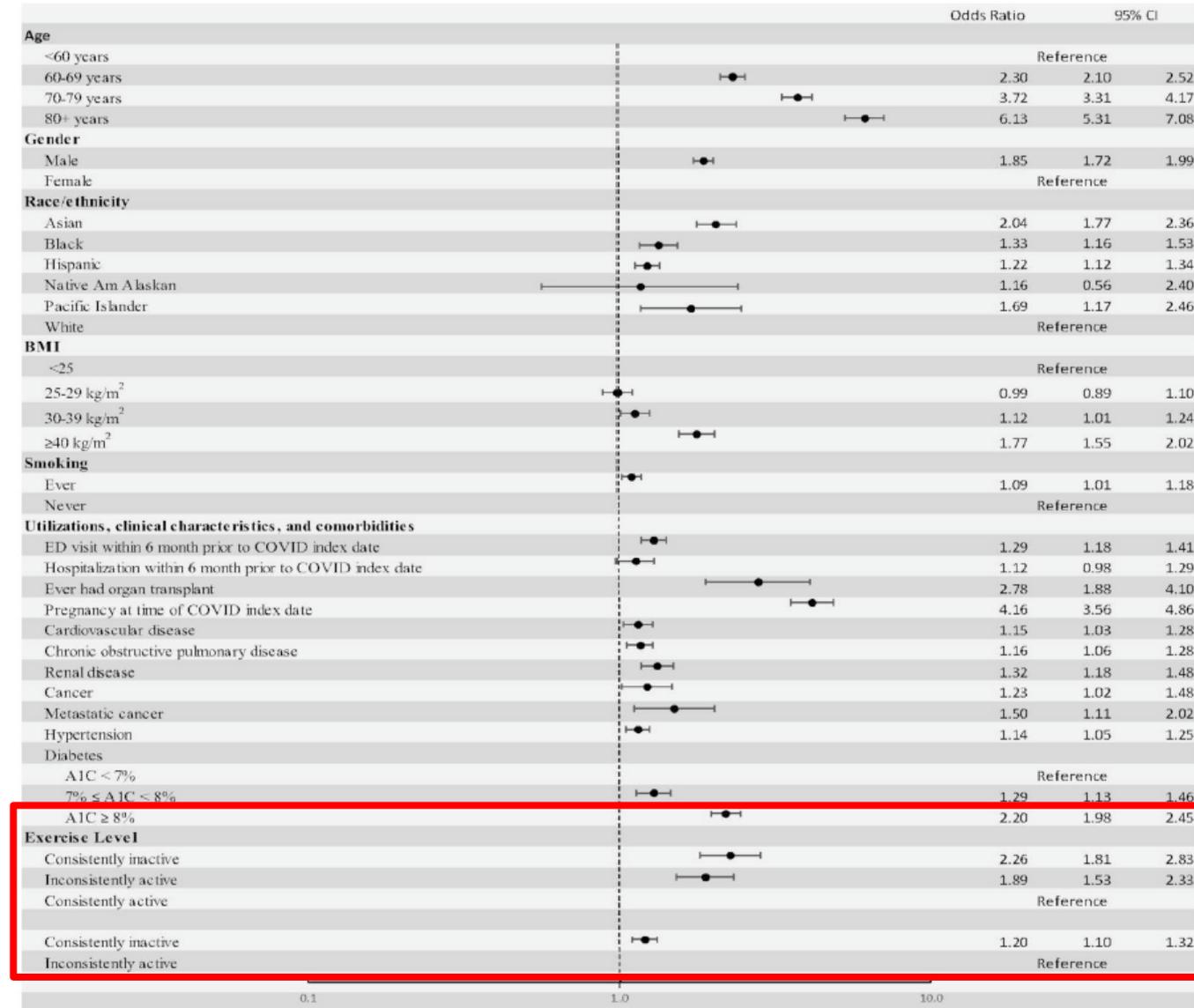
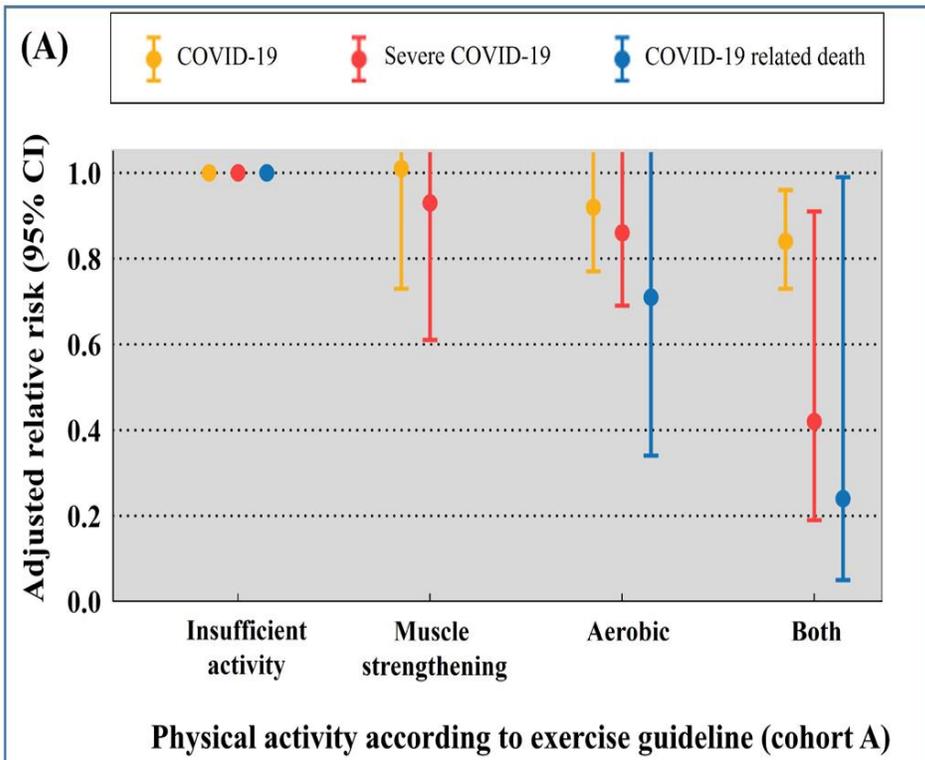


Figure 2 Adjusted risk factors for hospitalisation in patients with COVID-19. BMI, body mass index; ED, emergency department.

# Impfungen, Antikörpertiter und Sport

Vaccination	Study	SMD	Lower limit	Upper limit	p value
H1N1	Kohut et al [54]	0.817	0.031	1.603	0.042
H1N1	Hayney et al [55]	0.043	-0.353	0.44	0.83
H1N1	Kohut et al [56]	0.747	-0.034	1.527	0.061
H1N1	Woods et al [57]	0.192	-0.136	0.519	0.251
		<b>0.243</b>	<b>0.014</b>	<b>0.473</b>	<b>0.038</b>
H3N2	Kohut et al [54]	0	-0.755	0.755	1
H3N2	Haney et al [55]	0.079	-0.317	0.476	0.695
H3N2	Kohut et al [56]	-0.089	-0.845	0.666	0.816
H3N2	Woods et al [57]	0.223	-0.105	0.551	0.182
		<b>0.126</b>	<b>-0.102</b>	<b>0.355</b>	<b>0.278</b>
Pneumococcal	Long et al [58]	-0.14	-0.276	-0.556	0.508
Type B	Haney et al [55]	0.084	-0.312	0.481	0.677
Type B	Kohut et al [54]	-0.406	-1.169	0.357	0.296
Type B	Woods et al [57]	0.091	-0.236	0.418	0.583
		<b>0.04</b>	<b>-0.2</b>	<b>0.279</b>	<b>0.745</b>
VZV	Irwin et al [59]	0.389	0.014	0.763	0.0418
	<b>Overall</b>	<b>0.142</b>	<b>0.021</b>	<b>0.262</b>	<b>0.022</b>

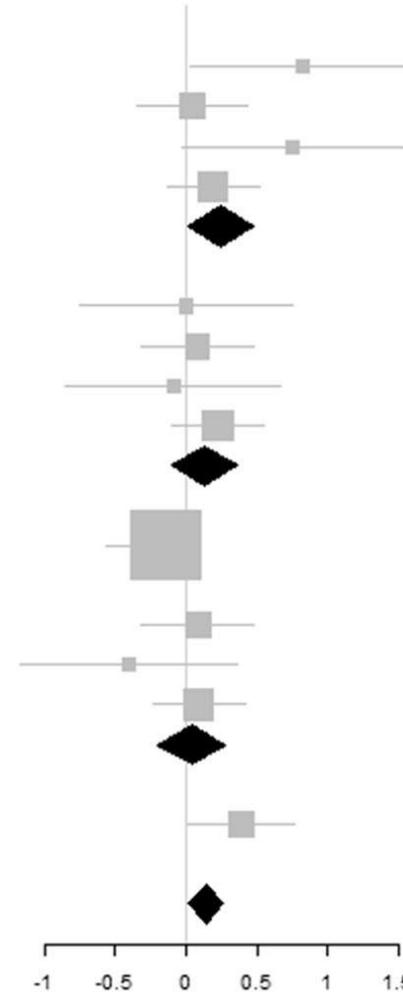


Fig. 5 Forest plot for antibodies titres after vaccination per vaccination type. Size of the square represents the weight of each study in the meta-analysis. SMD represented the standardised mean difference

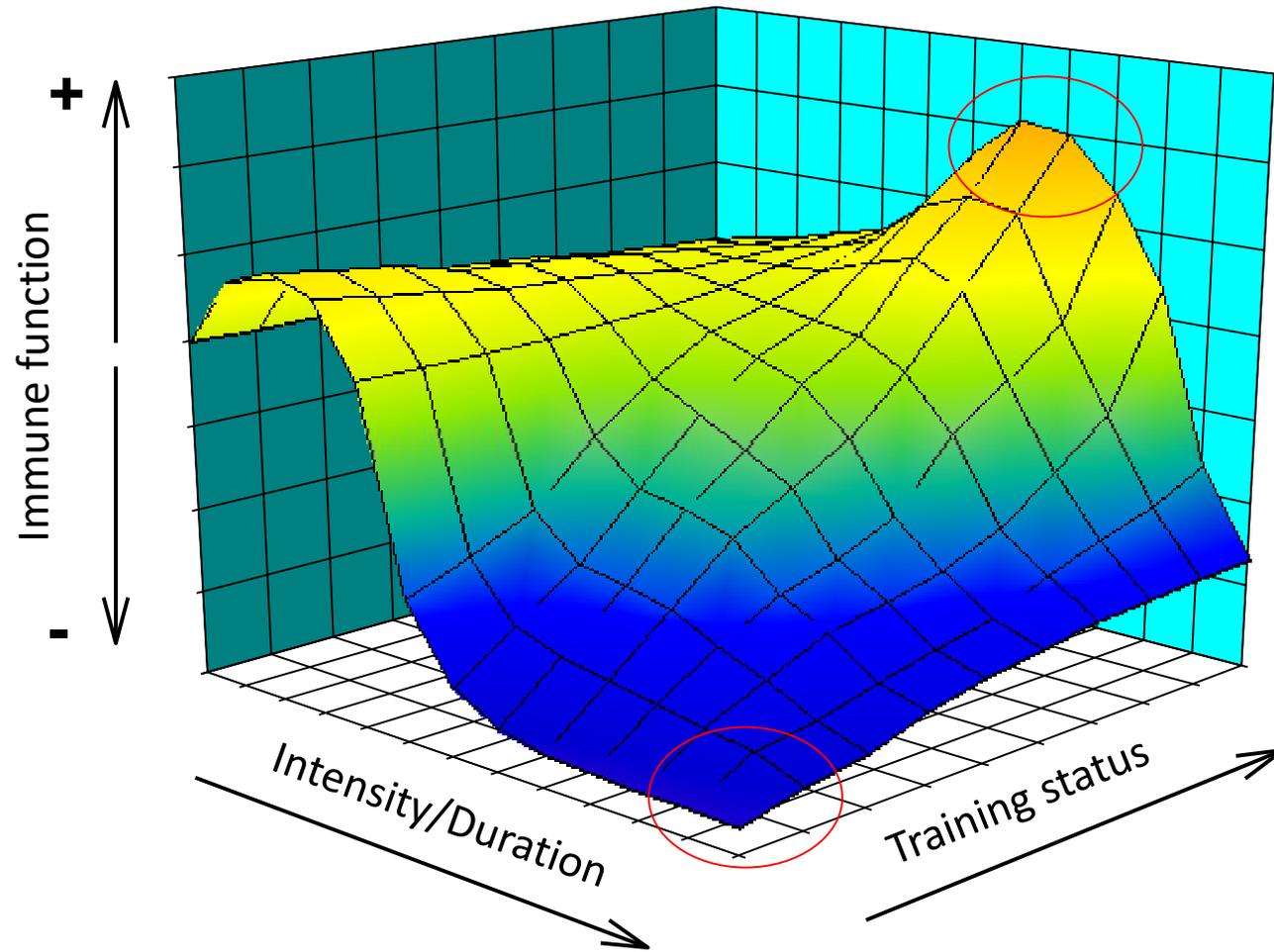
Körperliche Aktivität: Medikamente:

<b>Herzerkrankung (KHK)</b>	40 % Risikominderung 24 % Risikominderung (Statine)
<b>Stabile KHK</b>	88 % Überleben nach 1 Jahr 70 % Überleben nach 1 Jahr (PCI)
<b>Typ-2-Diabetes</b>	58 % weniger Auftreten 31 % weniger Auftreten (Metformin)
<b>Brustkrebs</b>	40 % Risikominderung 38 % Risikominderung (Tamoxifen)
<b>Brustkrebsrezidiv</b>	54 % Senkung der Mortalität 59 % Senkung der Mortalität (Tamoxifen)
<b>Schlaganfall</b>	Sig. Senkung der Mortalität gegenüber Kontrollbedingung (großer Effekt) Keine sig. Senkung der Mortalität gegenüber Kontrollbedingung (Antikoagulanzen, Plättchenhemmer)
<b>Schwere Depression</b>	KA gleich wirksam wie Sertralin, Rückfallrate 30 % Sertralin gleich wirksam wie KA, Rückfallrate 52 %
<b>Hüftfraktur</b>	55 % weniger Auftreten 38 % weniger Auftreten (Risedronat)

# Die traurige Realität

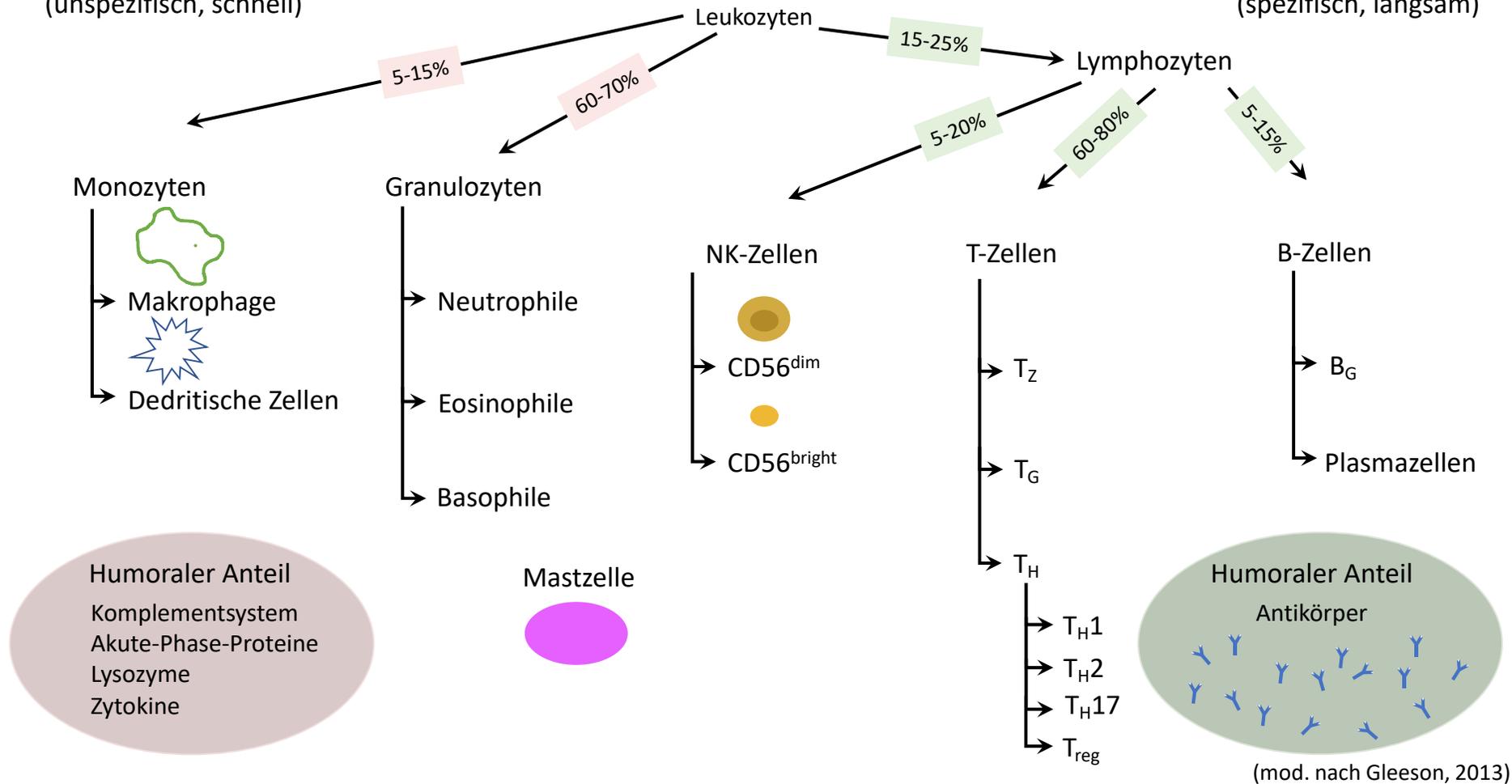
Frauen	Ausdaueraktivität mindestens 2,5 Stunden pro Woche		Muskelkräftigungsaktivität mindestens 2 mal pro Woche		Ausdauer- und Muskelkräftigungsaktivität entsprechend Empfehlung	
	%	(95 %-KI)	%	(95 %-KI)	%	(95 %-KI)
<b>Frauen (gesamt)</b>	<b>42,6</b>	<b>(41,3 – 43,9)</b>	<b>27,6</b>	<b>(26,7 – 28,6)</b>	<b>20,5</b>	<b>(19,6 – 21,4)</b>
<b>18–29 Jahre</b>	45,2	(42,3 – 48,2)	34,5	(32,1 – 37,0)	25,8	(23,6 – 28,2)
Untere Bildungsgruppe	40,1	(34,2 – 46,3)	29,5	(24,3 – 35,3)	21,9	(17,2 – 27,3)
Mittlere Bildungsgruppe	44,4	(40,6 – 48,2)	35,8	(32,6 – 39,1)	26,0	(23,1 – 29,1)
Obere Bildungsgruppe	55,0	(49,6 – 60,2)	35,6	(31,5 – 40,0)	29,3	(25,1 – 33,8)
<b>30–44 Jahre</b>	38,8	(36,7 – 41,0)	21,1	(19,5 – 22,9)	16,3	(14,8 – 17,9)
Untere Bildungsgruppe	34,2	(27,7 – 41,5)	12,7	(8,9 – 17,7)	11,1	(7,5 – 16,1)
Mittlere Bildungsgruppe	36,7	(34,0 – 39,5)	20,2	(18,1 – 22,5)	15,0	(13,1 – 17,1)
Obere Bildungsgruppe	46,4	(42,9 – 49,8)	28,1	(25,0 – 31,3)	22,3	(19,5 – 25,4)
<b>45–64 Jahre</b>	47,8	(46,0 – 49,6)	29,4	(27,9 – 30,9)	22,7	(21,3 – 24,2)
Untere Bildungsgruppe	44,3	(39,7 – 49,1)	26,1	(22,5 – 30,1)	20,0	(16,7 – 23,7)
Mittlere Bildungsgruppe	46,5	(44,3 – 48,8)	29,3	(27,4 – 31,2)	22,4	(20,6 – 24,2)
Obere Bildungsgruppe	55,0	(51,5 – 58,3)	32,7	(30,2 – 35,4)	26,2	(23,8 – 28,7)
<b>≥ 65 Jahre</b>	36,5	(34,0 – 39,1)	26,4	(24,4 – 28,4)	17,4	(15,6 – 19,3)
Untere Bildungsgruppe	29,0	(25,6 – 32,6)	20,7	(17,6 – 24,1)	12,1	(9,6 – 15,2)
Mittlere Bildungsgruppe	39,4	(35,7 – 43,2)	28,5	(25,7 – 31,5)	19,2	(16,6 – 22,1)
Obere Bildungsgruppe	51,1	(45,7 – 56,5)	38,8	(33,7 – 44,2)	29,0	(24,4 – 34,0)
<b>Gesamt (Frauen und Männer)</b>	<b>45,3</b>	<b>(44,2 – 46,4)</b>	<b>29,4</b>	<b>(28,6 – 30,2)</b>	<b>22,6</b>	<b>(21,8 – 23,4)</b>

# Zurück zu meiner Oma



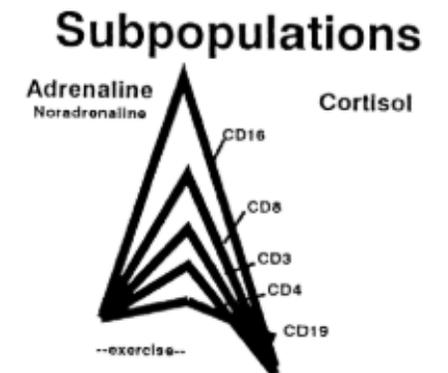
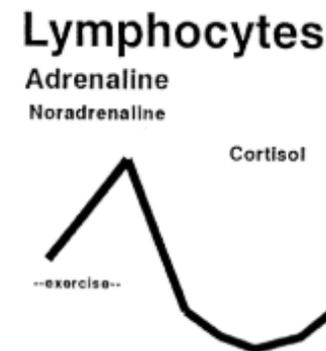
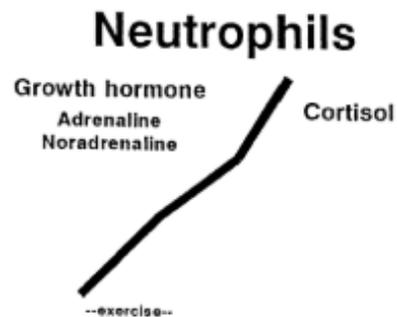
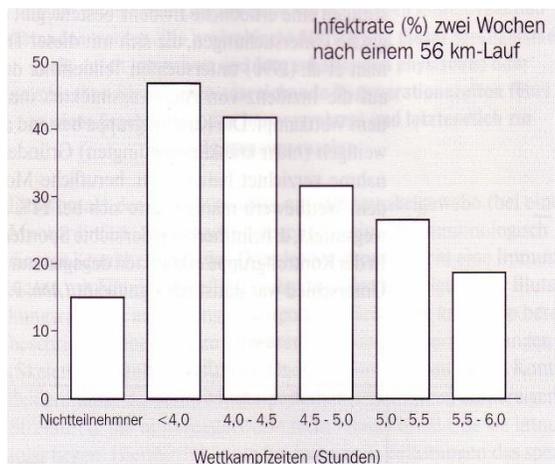
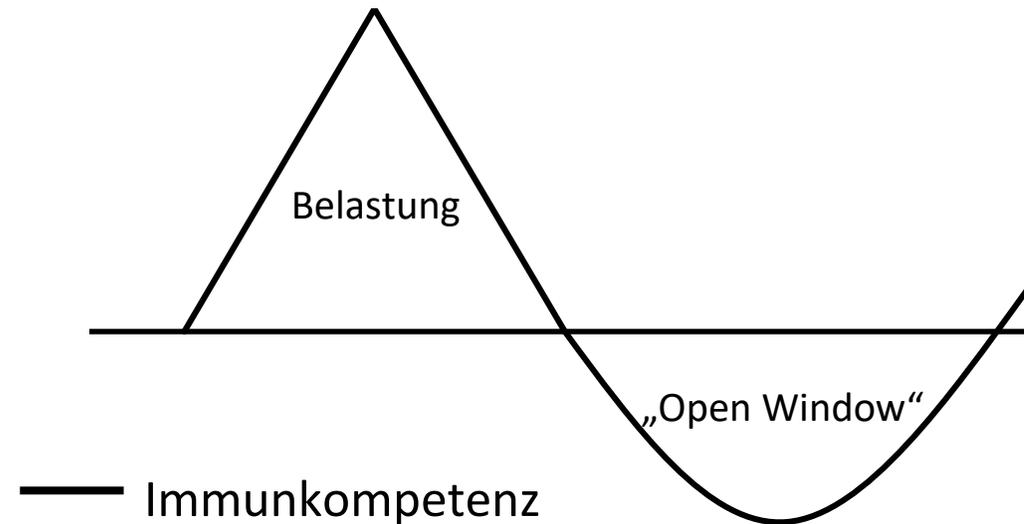
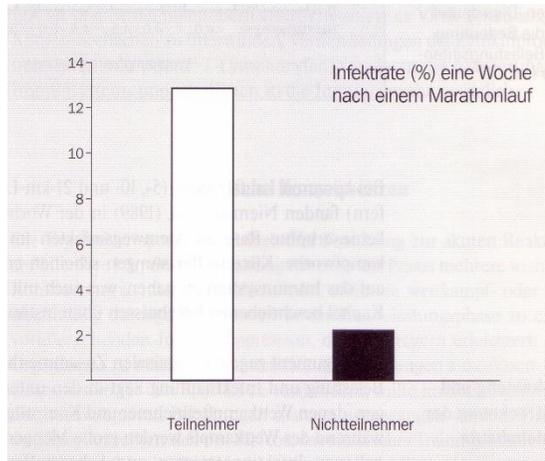
## Angeborenes Immunsystem (unspezifisch, schnell)

## Adaptives Immunsystem (spezifisch, langsam)



# Open Window

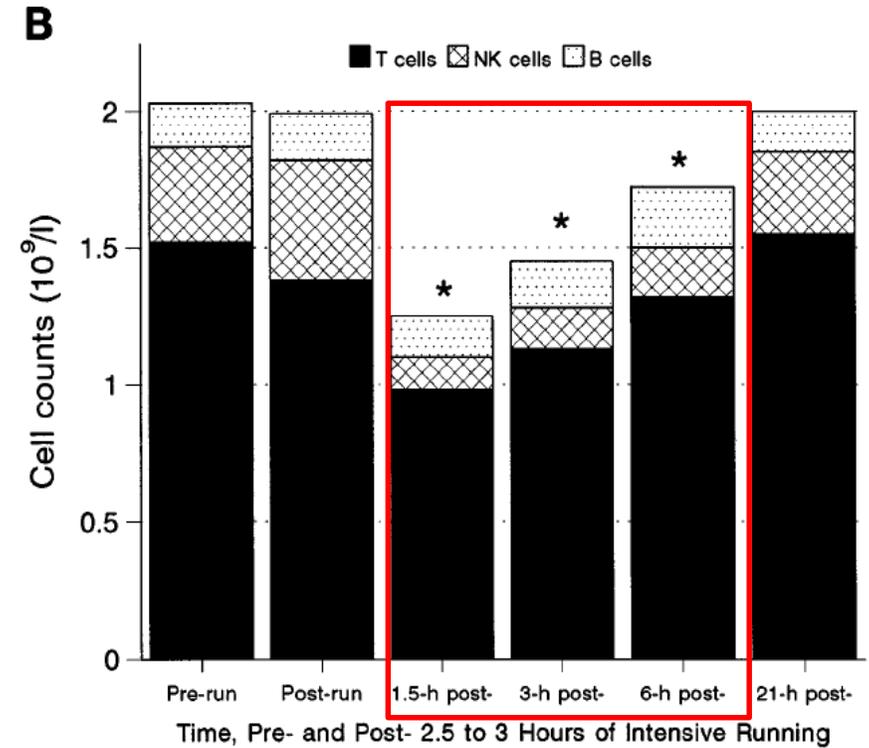
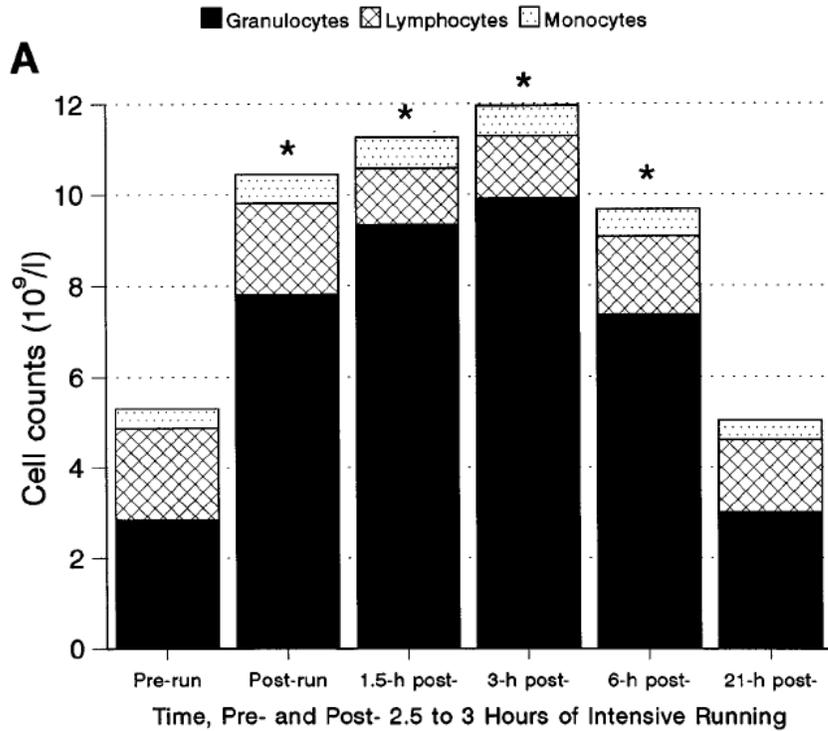
Erhöhte Anfälligkeit für Atemwegsinfekte nach einer akuten Belastung durch "Immunsuppression"



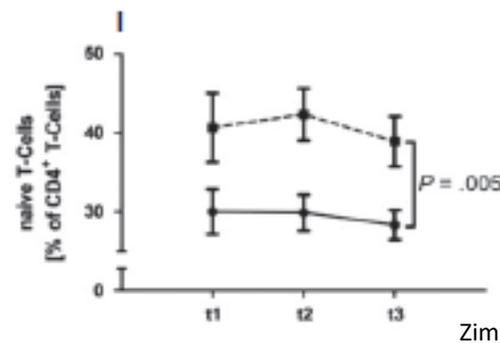
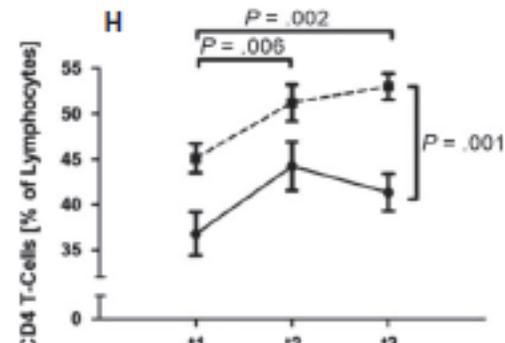
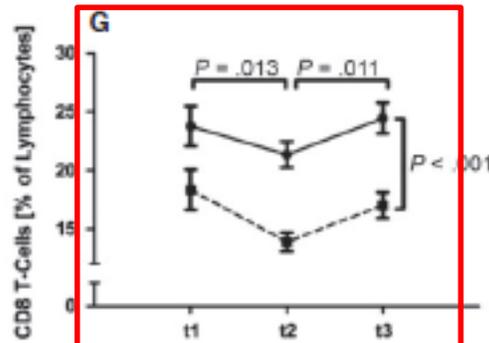
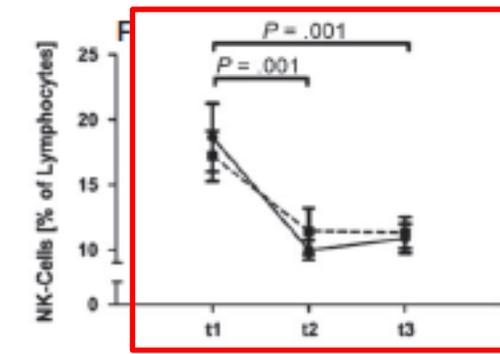
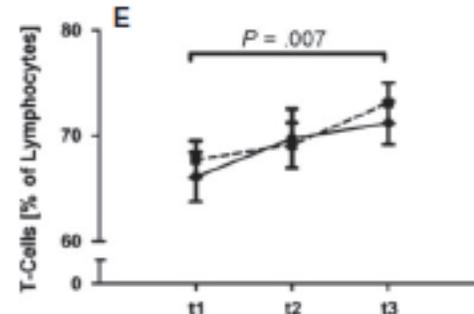
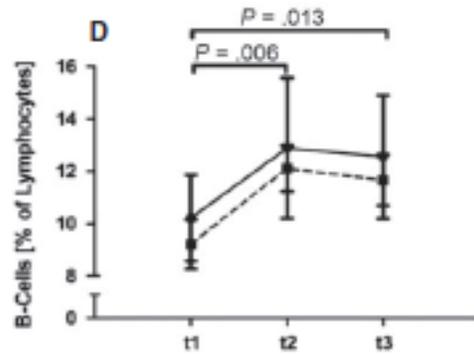
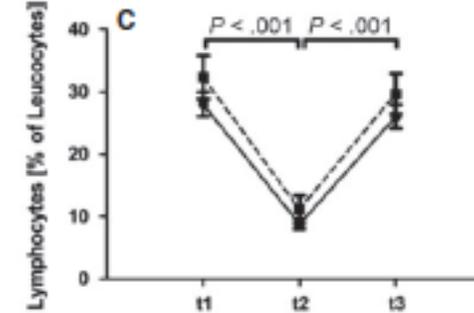
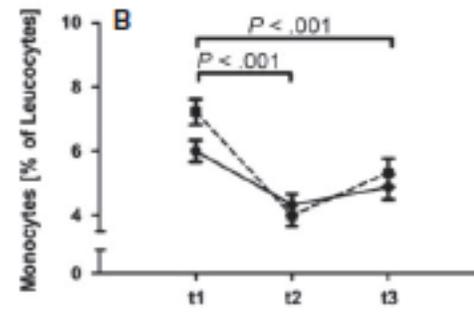
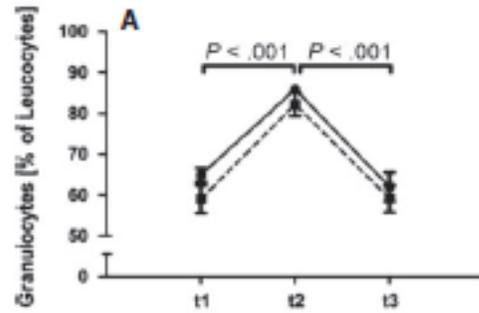
- **Per se haben Athleten kein erhöhtes Infektionsrisiko**
- **Auftreten von URS fast immer mittels Selbstauskunft**
- **Labordiagnostik bestätigt nur ca. 1/3 der Infektionen**
- **Athleten sind häufiger Risikofaktoren ausgesetzt**
  - **Flüge**
  - **Jetlag**
  - **Massenveranstaltungen**
  - **Akutes Nährstoffdefizit**
  - **Trockene Atemwege**

Campbell et al. 2019

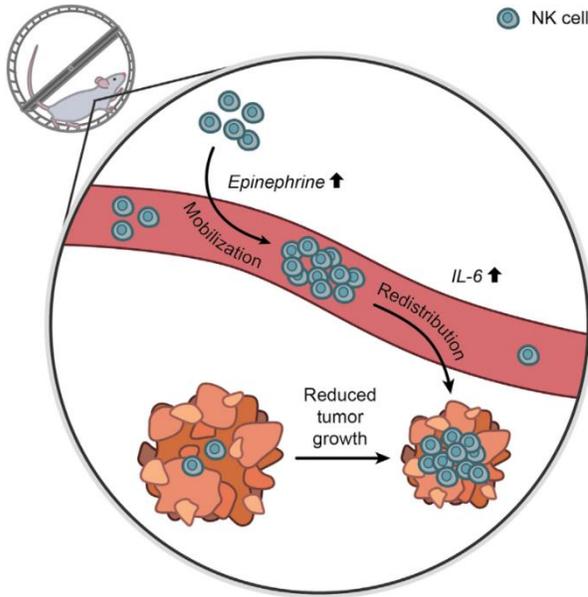




# Immunreaktion: Krebspatient\*innen vs. Gesunde



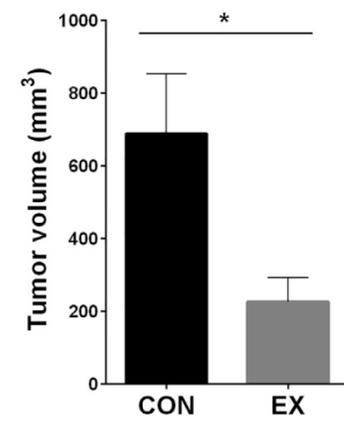
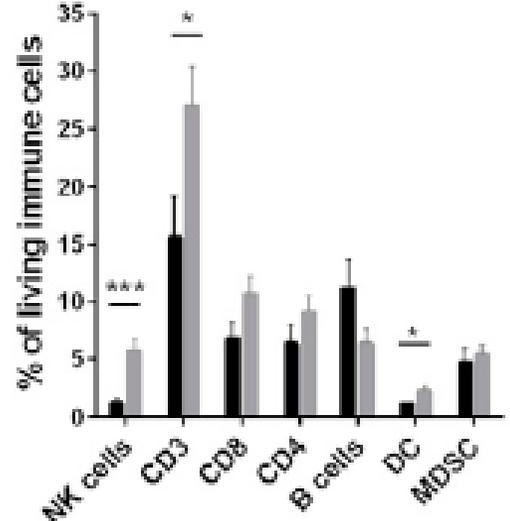
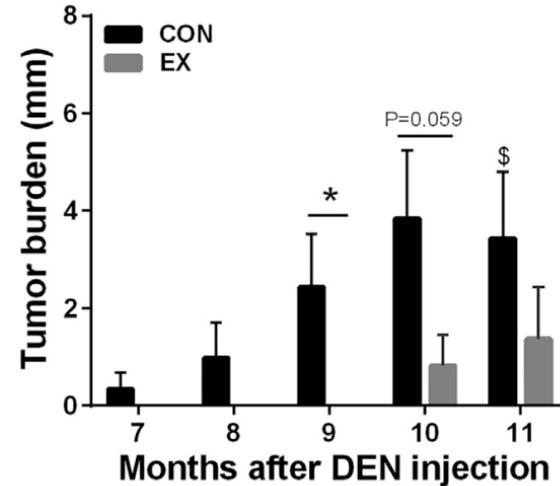
Pedersen et al. 2016



NK cell

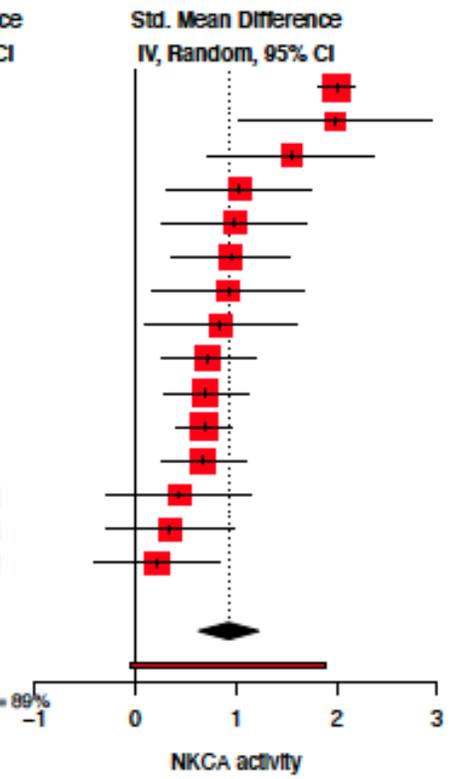
## NK-Zellzahl im Tumor ist mit Prognose assoziiert

Ishigami et al. 2000, Hsia et al. 2005, Villegas et al 2002



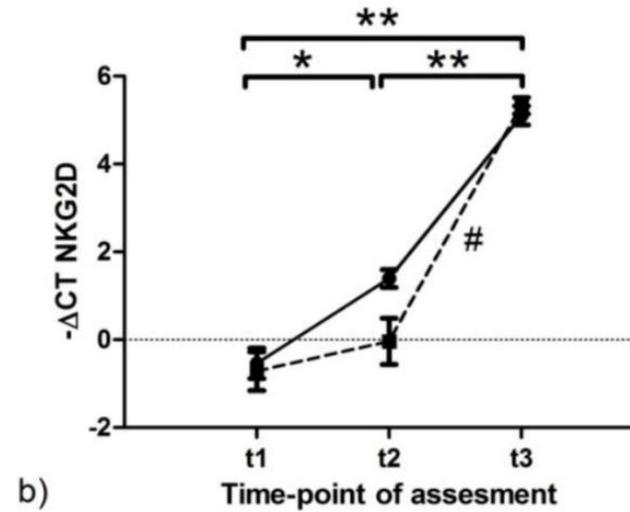
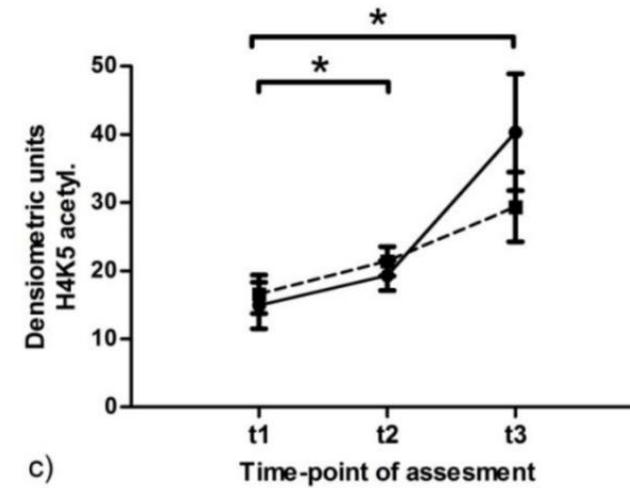
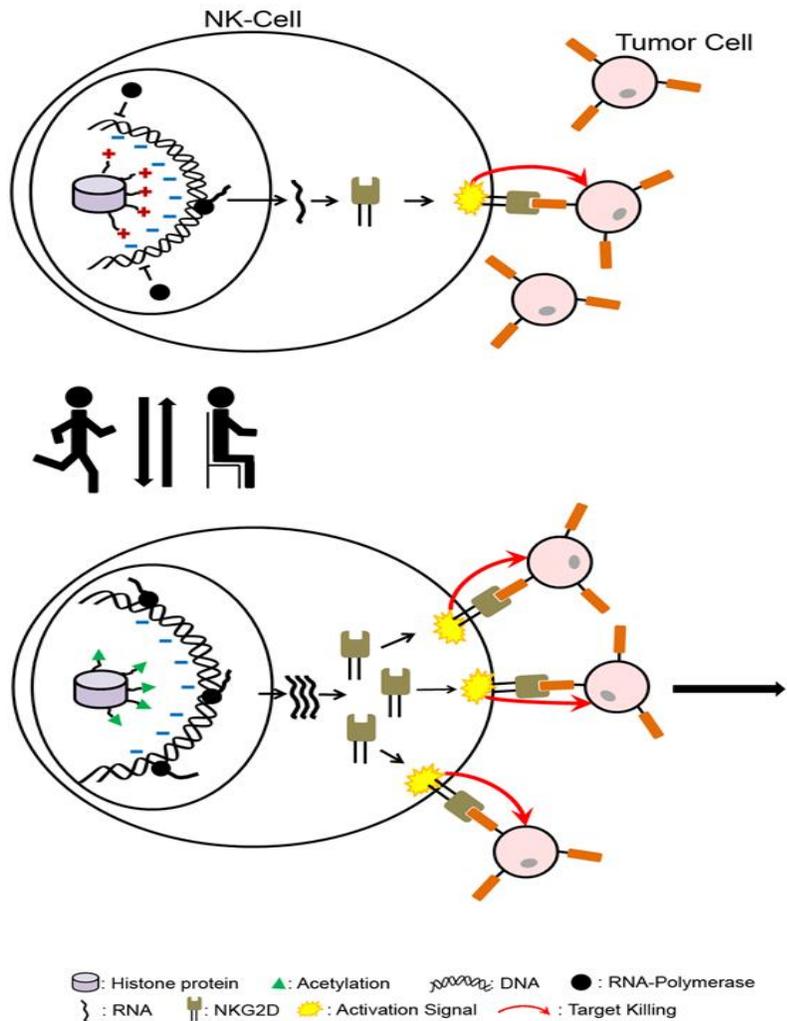
Study	TE	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Moyna(1996)	2.00	0.0920	9.6%	2.00 [ 1.82; 2.18]
Strasner(1997)	1.99	0.4940	4.4%	1.99 [ 1.04; 2.93]
Brenner(1996)	1.55	0.4200	5.1%	1.55 [ 0.73; 2.37]
Brenner(1996)	1.03	0.3640	5.8%	1.03 [ 0.32; 1.75]
Brenner(1999)	0.99	0.3660	5.8%	0.99 [ 0.27; 1.71]
Gannon(1998)	0.95	0.2960	6.8%	0.95 [ 0.37; 1.53]
Miles(2002)	0.92	0.3820	5.6%	0.92 [ 0.17; 1.67]
Bouillon(2006)	0.85	0.3880	5.5%	0.85 [ 0.09; 1.61]
Palmo(1995)	0.72	0.2400	7.6%	0.72 [ 0.25; 1.19]
Lee(2005)	0.70	0.2150	8.0%	0.70 [ 0.28; 1.12]
Flynn(1999)	0.69	0.1390	9.1%	0.69 [ 0.42; 0.96]
McFaddin(2005)	0.67	0.2140	8.0%	0.67 [ 0.25; 1.09]
Bouillon(2006)	0.43	0.3630	5.8%	0.43 [ -0.28; 1.15]
Brenner(1996)	0.34	0.3240	6.4%	0.34 [ -0.29; 0.98]
Strasner(1997)	0.21	0.3210	6.4%	0.21 [ -0.42; 0.84]
<b>Total (95% CI)</b>			<b>100.0%</b>	<b>0.93 [ 0.63; 1.22]</b>
<b>Prediction Interval</b>				<b>[ -0.04; 1.89]</b>

Heterogeneity: Tau<sup>2</sup> = 0.1808; Chi<sup>2</sup> = 131.99, df = 14 (P < 0.01); I<sup>2</sup> = 89%  
 Test for overall effect: I<sub>14</sub> = 6.70 (P < 0.01)



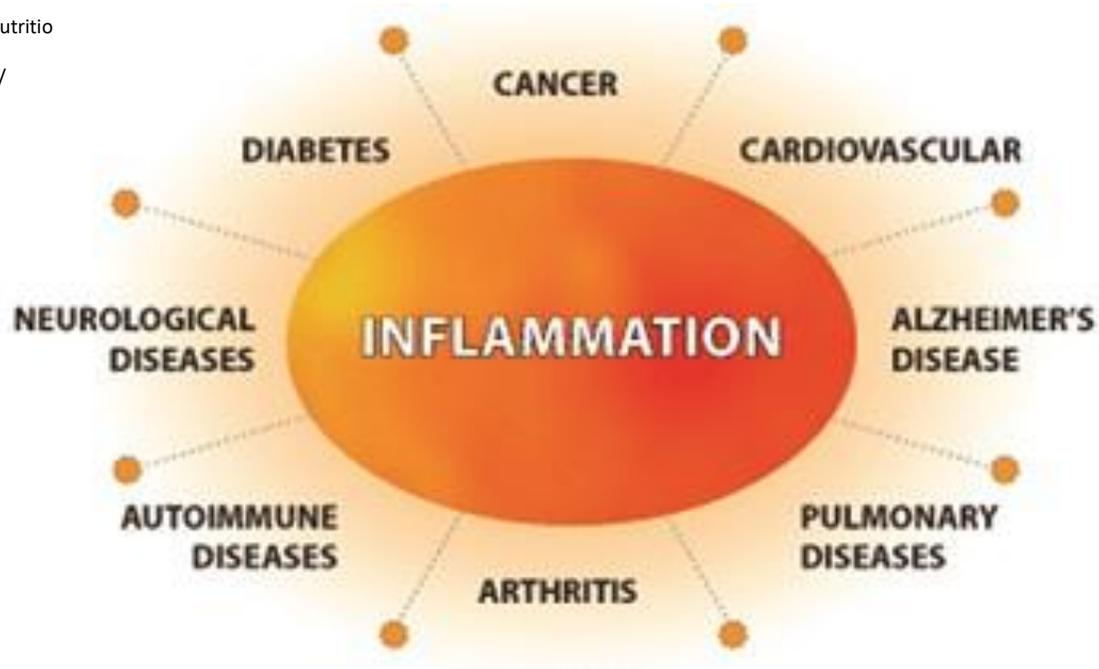
Rumpf et al. 2020

# Akute Belastung verändert das funktionelle Genom

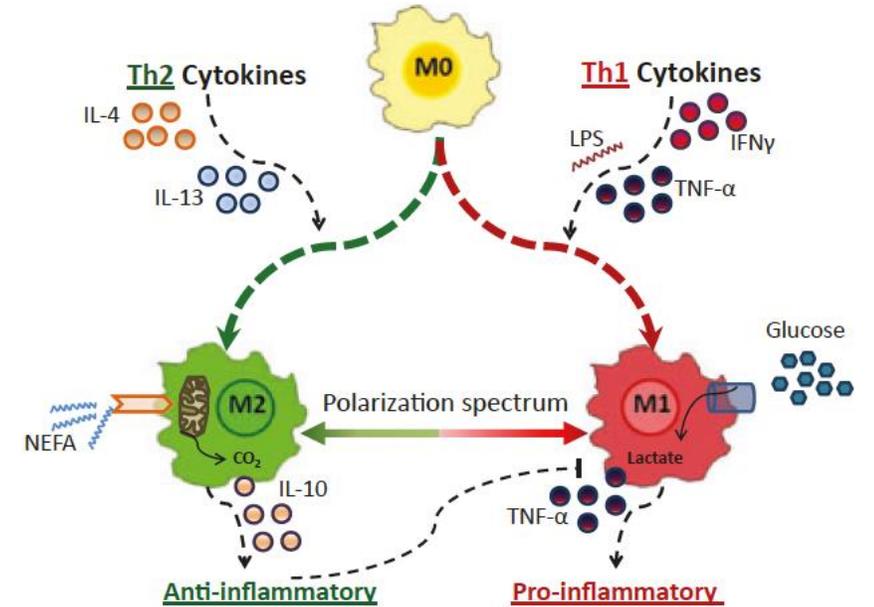


# Inflammation

<http://healthandnutrition.ie/low-grade-inflammation-test/>



Johnson et al. 2012

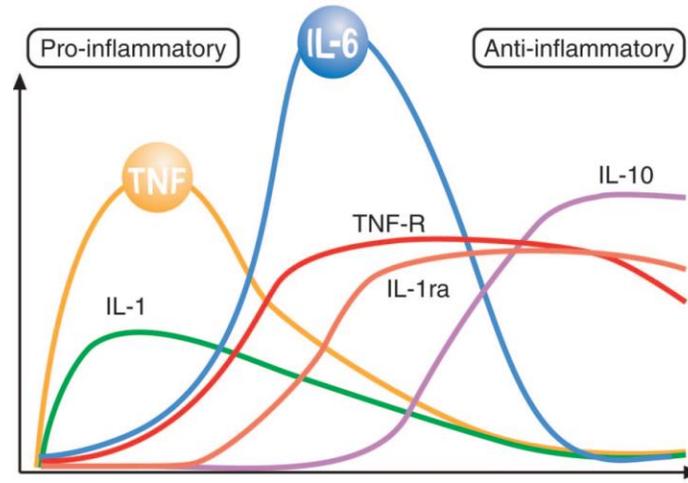
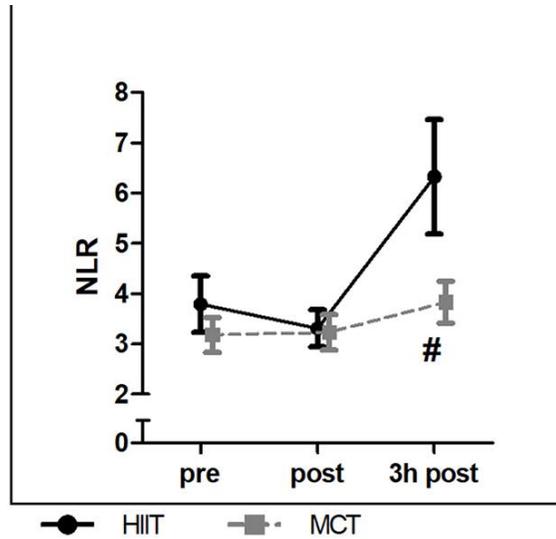


Akut - Physiologisch

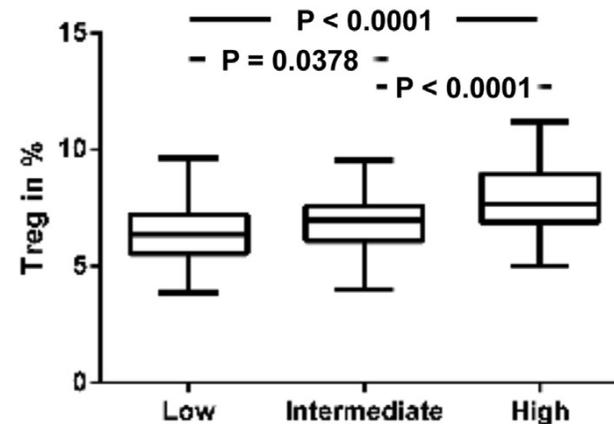
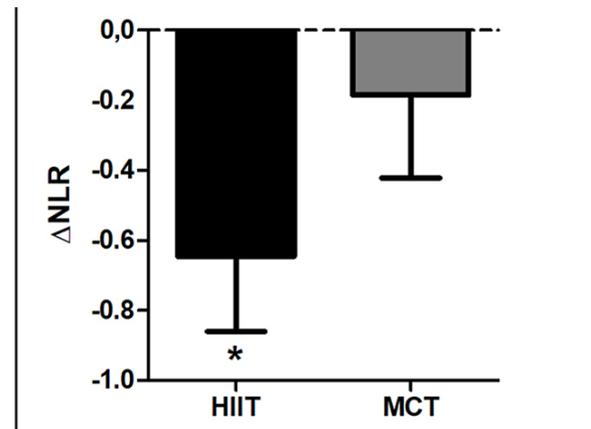


Chronisch - Pathophysiologisch

# Sport + Inflammation: Akut vs. Chronisch



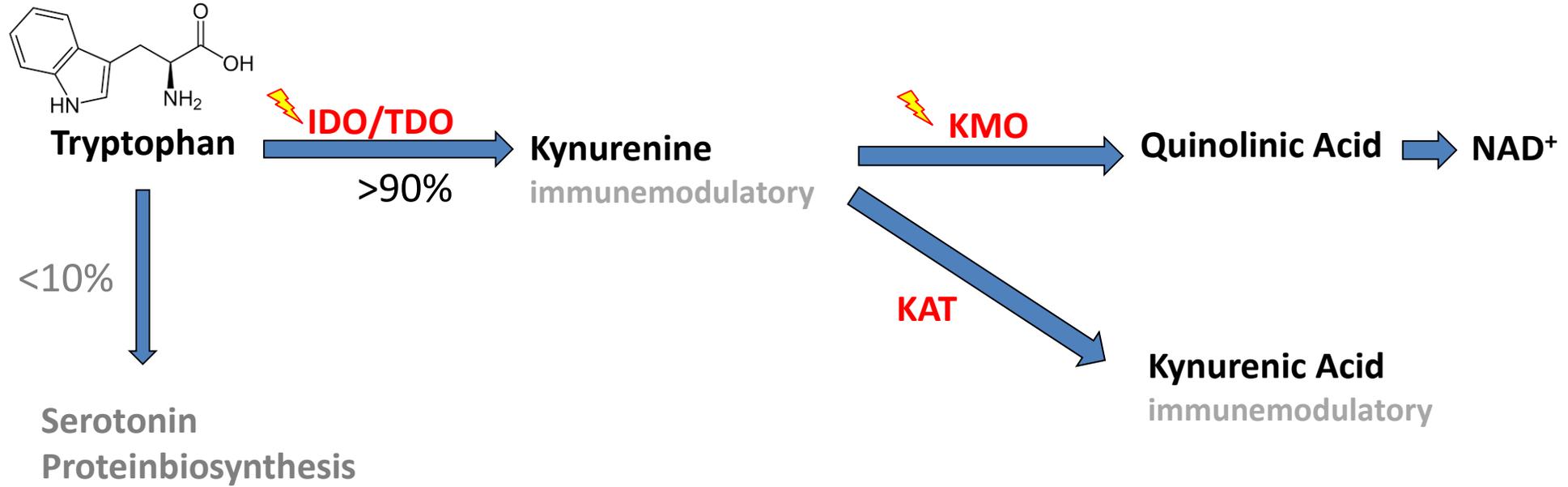
Petersen et Pedersen 2005



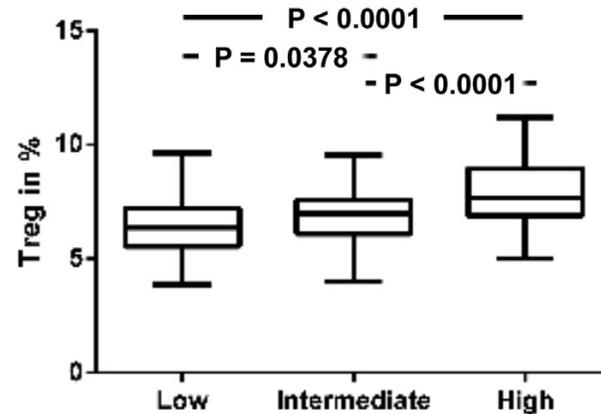
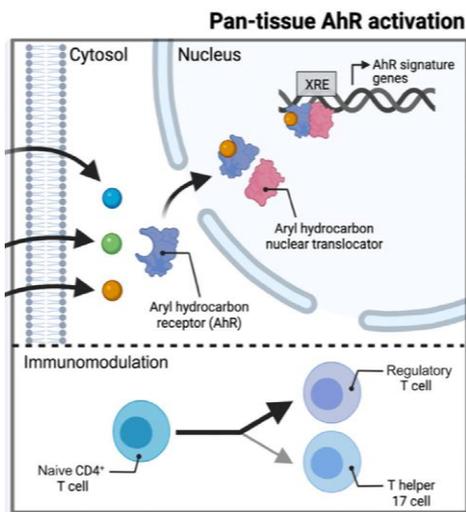
Weinhold et al. 2016

- **Akute Belastung provoziert kurzfristige, lokale und systemische Entzündungsreaktion**
- **Regelmäßige überschwellige, kurzfristige Entzündungsreize erhöhen das antientzündliche Potential ( $T_{regs}$ )**
- **NLR ist prognostischer Marker mit breiter klinischer Relevanz**

# Negativ Feedbackloop über Kynureninpfad vermittelt langfristige Antiinflammation



Joisten et al. 2021



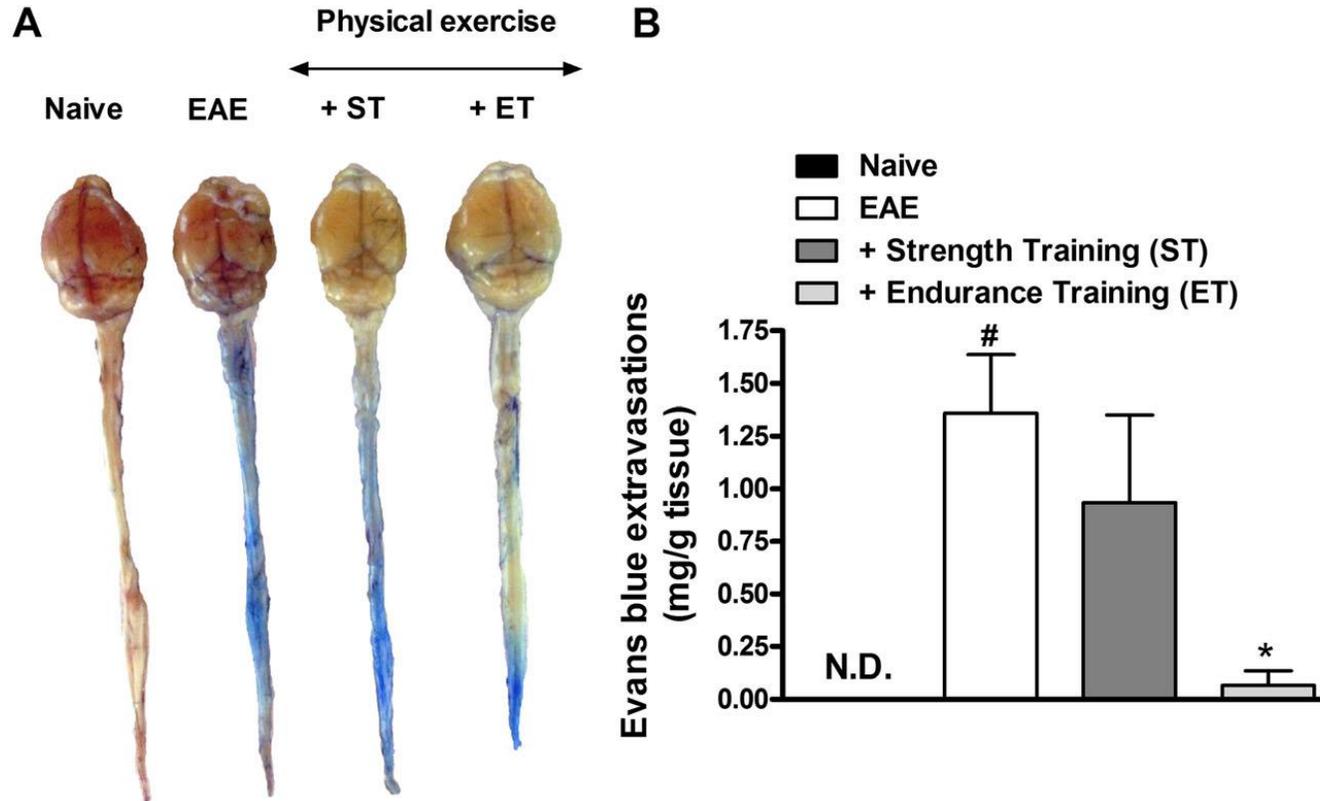
Weinhold et al. 20 16

Inflammation (IL-6, IFN- $\gamma$ )

**Table 1.** Pearson correlations between participants' blood markers (n = 19) at baseline.

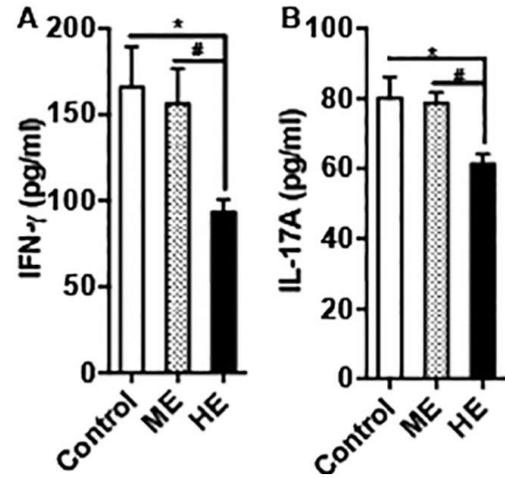
	BMI	TRP	KYN	KYN/TRP	Tcytotox	Treg
VO <sub>2</sub> max	-0.659**	-0.601**	-0.278	.454	.287	.689***

Koliamitra et al. 2019, J Sports Sc Med

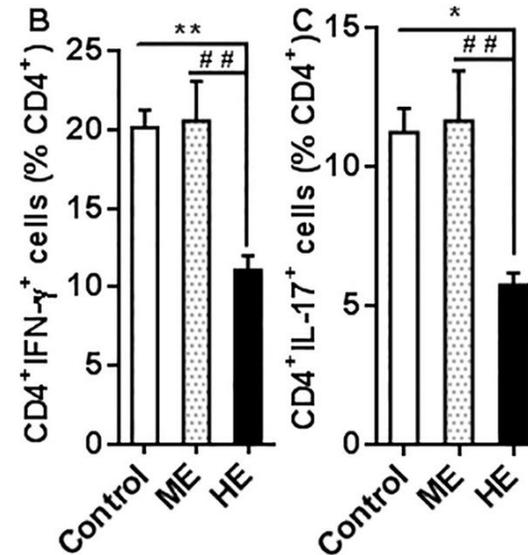


Inflammation

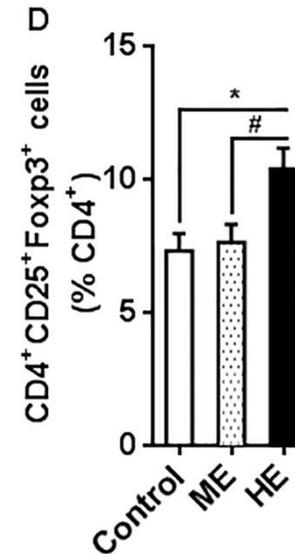
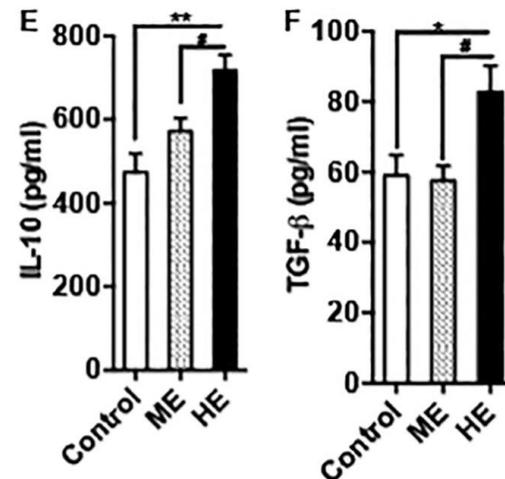
Humoral

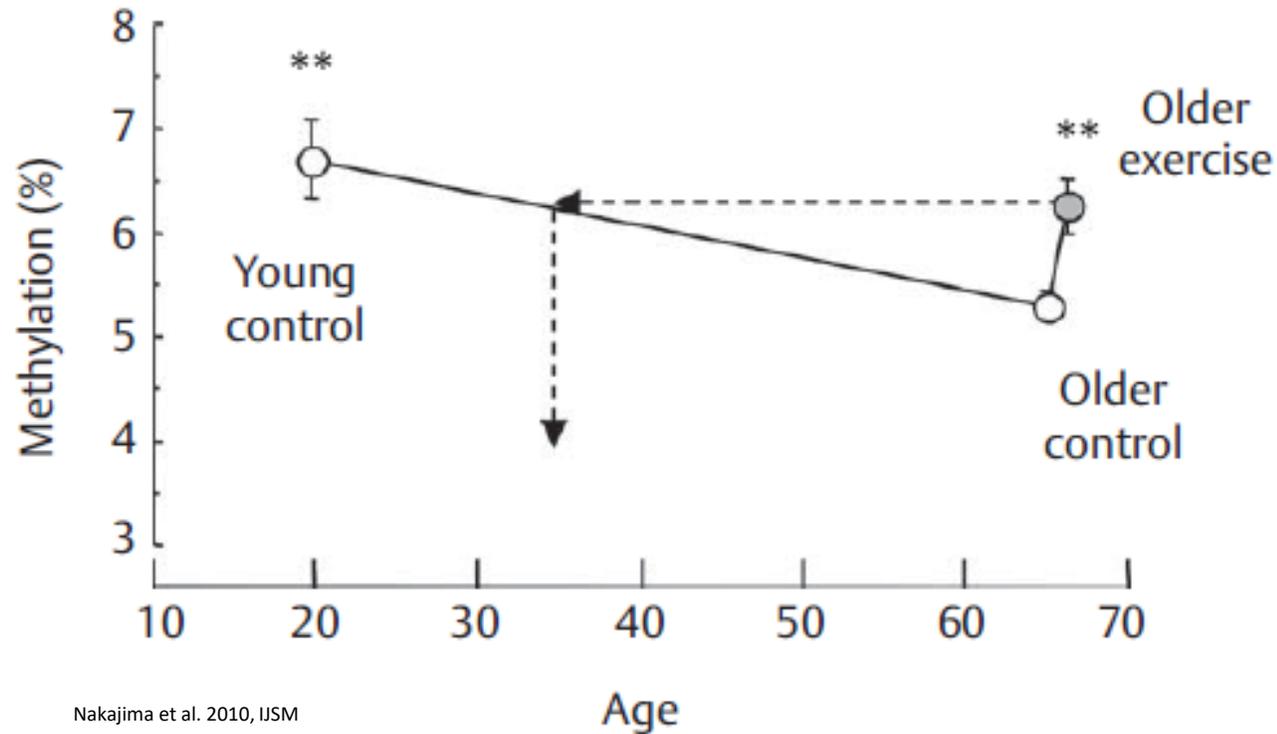


Zellulär



Anti-Inflammation





Nakajima et al. 2010, IJSM

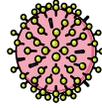
Junge Kontrollpersonen  
(m/w), n=34, 18-22 Jahre

Ältere Kontrollpersonen  
(m/w), n=153, 40-87 Jahre, MW: 65 Jahre

Ältere Personen mit Training  
(m/w), n=230, 41-86 Jahre, MW: 66 Jahre  
mind. 2\* Woche, Intervalltraining mind. 25 Minuten,  
40-70% max. Leistung

**Sport wirkt altersabhängiger  
Demethylierung des ASC Gens entgegen  
und reduziert inflammatorischen Stress**

# Last but not least



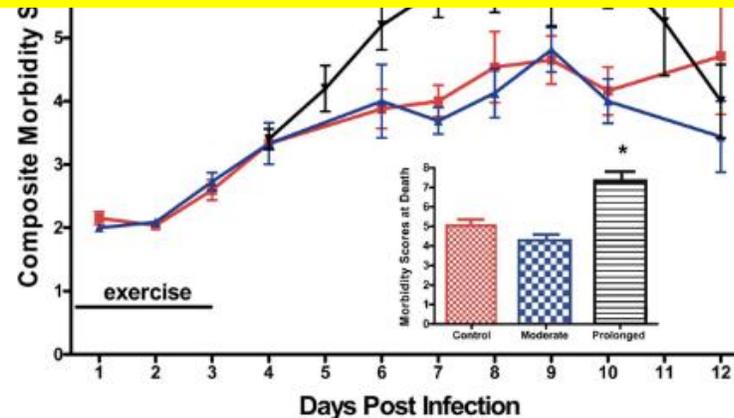
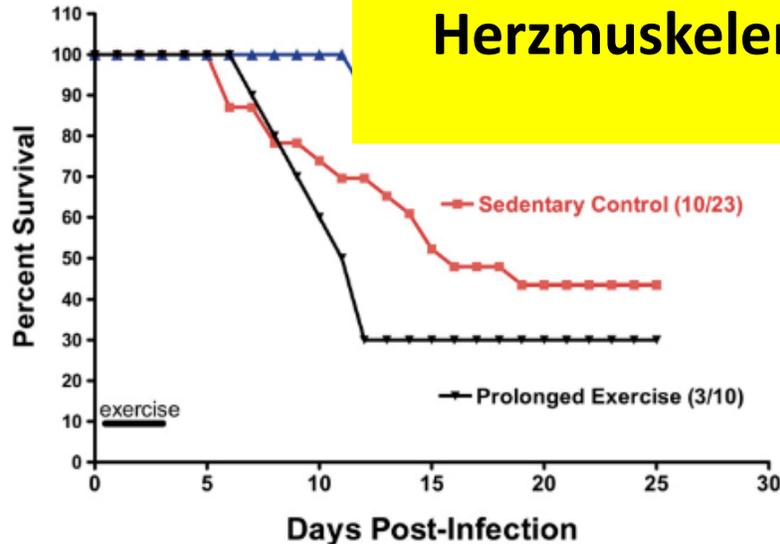
Influenza Virus Infektion

Moderates Training (Alltagsaktivität)  
hat positiven Effekt  
Intensives längeres Training hat

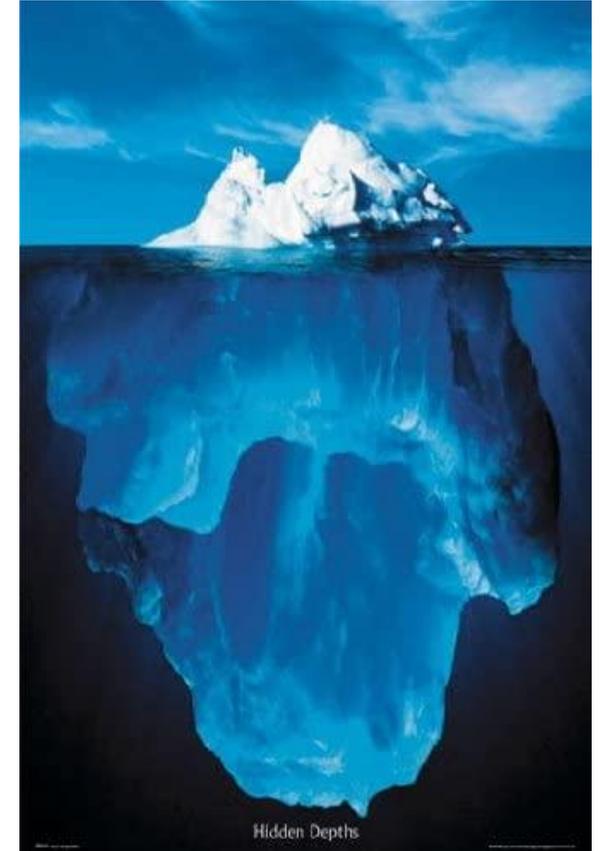
- Bei bestehenden Infektionen und Fieber ist von Sport in jedem Fall abzuraten!
- Eine deutlich erhöhte Herzaktivität kann eine potentiell tödliche Herzmuskelentzündung nach sich ziehen!



2,5h bei 65-70%  $\dot{V}O_{2m}$



- **Akute Belastung aktiviert das Immunsystem**
- **Extrembelastungen können kurzfristig Infektanfälligkeit erhöhen**
- **Regelmäßige Belastung (Training) reduziert chronische Entzündungsprozesse**
- **Training reduziert das Risiko für zahlreiche chronische Erkrankungen**



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 Dr. Niklas Joisten  
 Dr. Sina Trebing  
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