



Lärm, Schlaf und kardiometabolische Krankheiten

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Schlafstörungen - Präventive Ansätze

Schmid et al. Lancet Diabetes Endocrinol 2015

Komplette Prävention von zu wenig Schlaf oder von Schlaf-
rhythmusstörungen ist in einer globalisierten 24h Gesellschaft
unmöglich

-

Verbesserung von Umgebungsbedingungen als ein Ansatz

-

? Verminderung der Lärmbelastung ?

Lärmquellen

Beruflicher Lärm



Sozialer Lärm

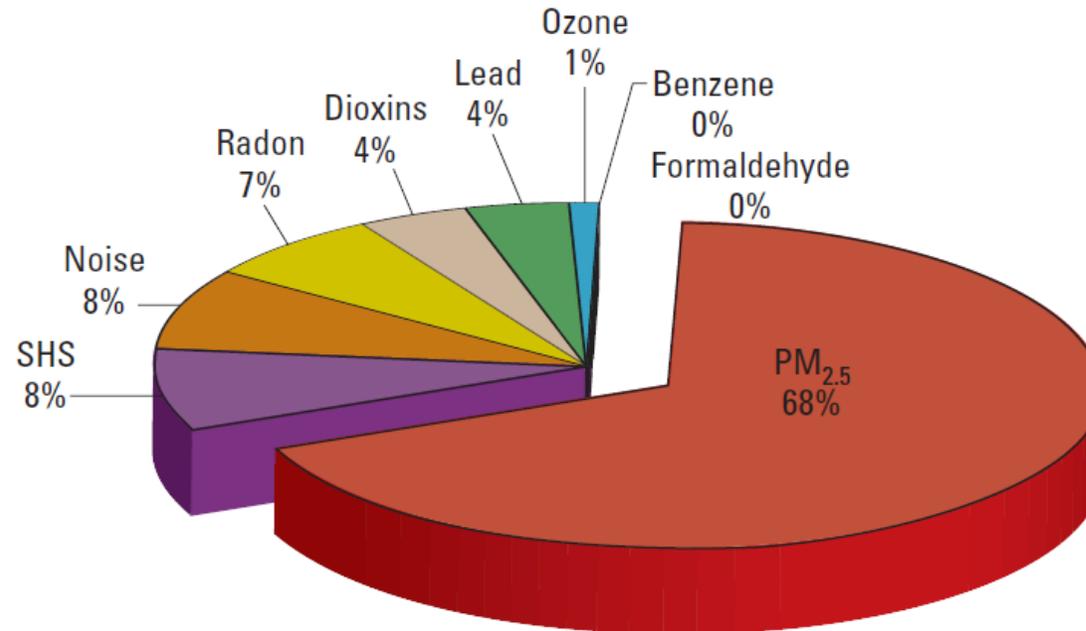


Umweltlärm (Verkehr; Industrie)



Krankheitslast durch Verkehrslärm in Europa

Hänninen 2014



Verkehrslärm an zweiter Stelle – nach Feinstaub – unter den neun Umweltrisikofaktoren mit den grössten Auswirkungen auf die Gesundheit in Europa

Verlust von 400–1500 gesunden Lebensjahren /1 Mio. Personen

ischemic heart disease & severe sleep disturbance; road/rail/air craft

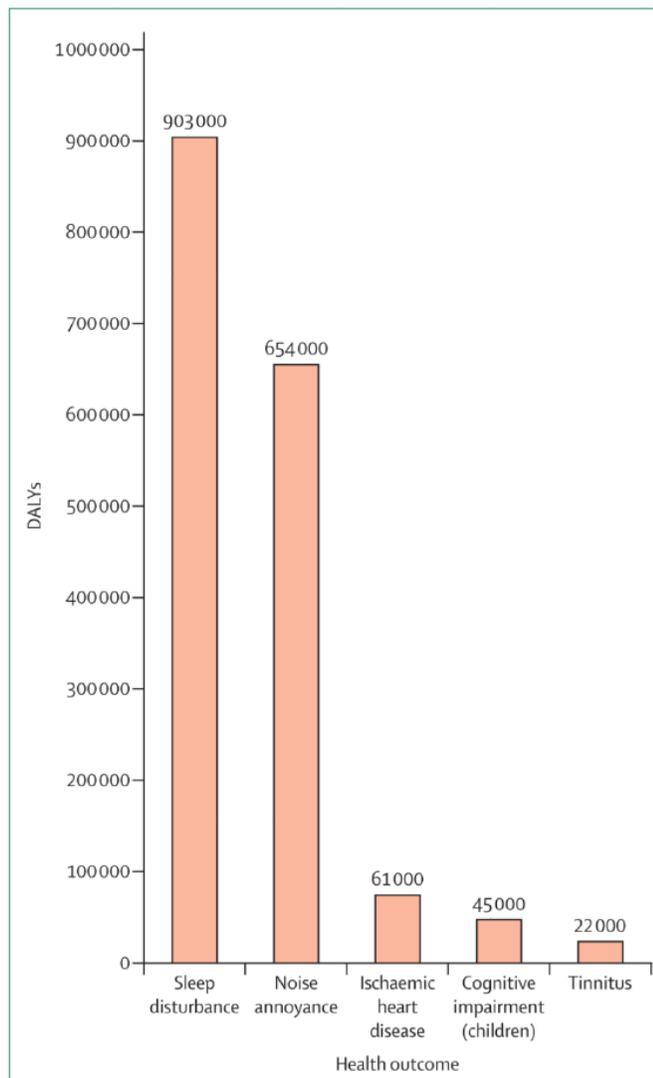


Figure 2. DALYs attributed to environmental noise exposure in Europe

According to WHO,¹⁴ more than 1 million healthy life years (DALYs) are lost annually because of environmental noise exposure in European A-member states alone. Most of these DALYs can be attributed to noise-induced sleep disturbance and annoyance.

DALYs=Disability-adjusted life years.

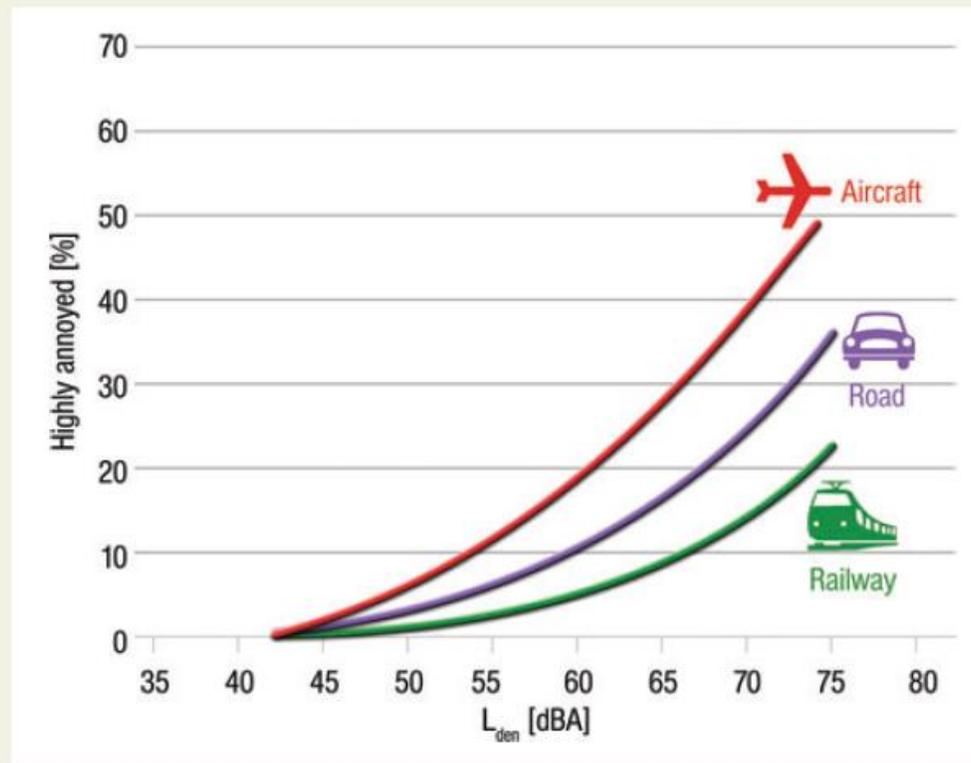


Figure 1 Percentage of persons highly annoyed by aircraft, road, and rail traffic noises. The curves were derived for adults on the basis of surveys (26 for aircraft noise, 19 for road noise, and 8 for railways noise) distributed over 11 countries. Adapted from Miedema and Oudcshoorn.¹

Münzel et al. Eur Heart J 2014



Auditive Lärmeffekte - Gehörverlust und Tinnitus

einmalige sehr laute Exposition (z.B. Gehörschuss)

chronische Lärmexposition $L_A > 75-80$ dB (>10% Weltbevölkerung)

Verlust von nicht-regenerierbaren sensorischen Zellen im Innenohr

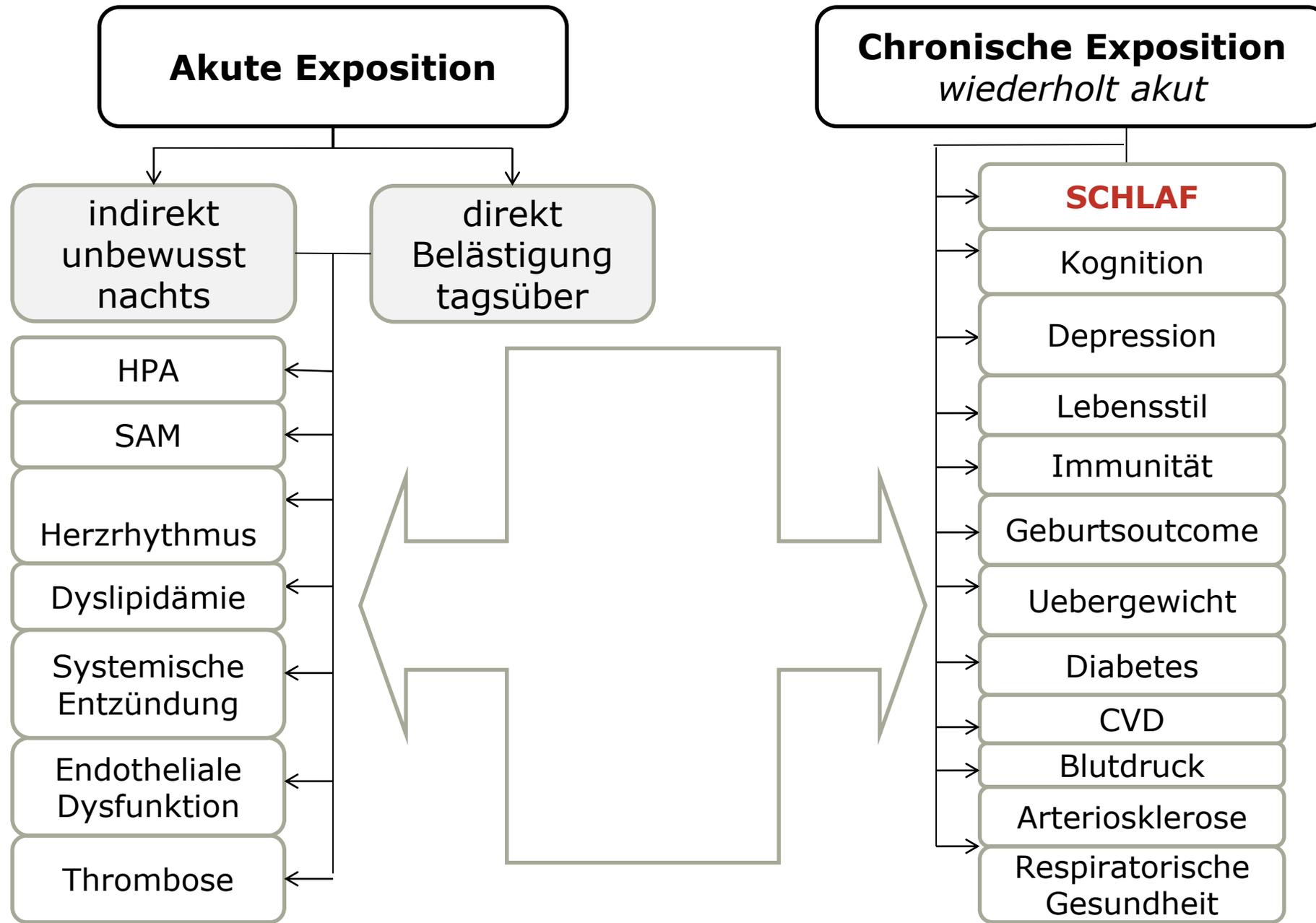
Tabak, Alkohol, Hyperglykämie können zu altersbedingter Schwerhörigkeit beitragen - Teufelskreis

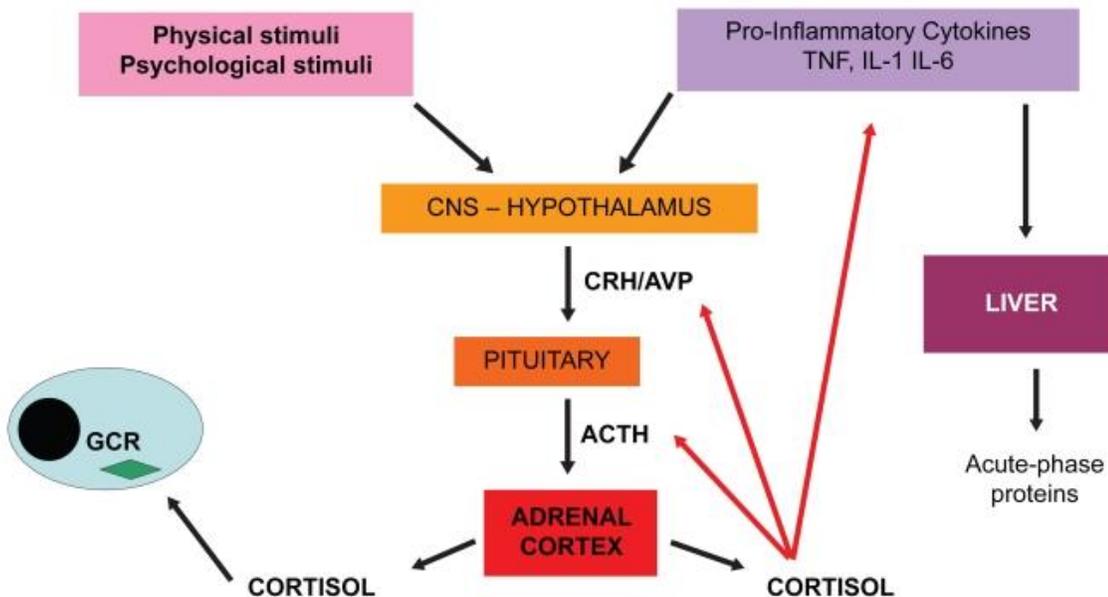
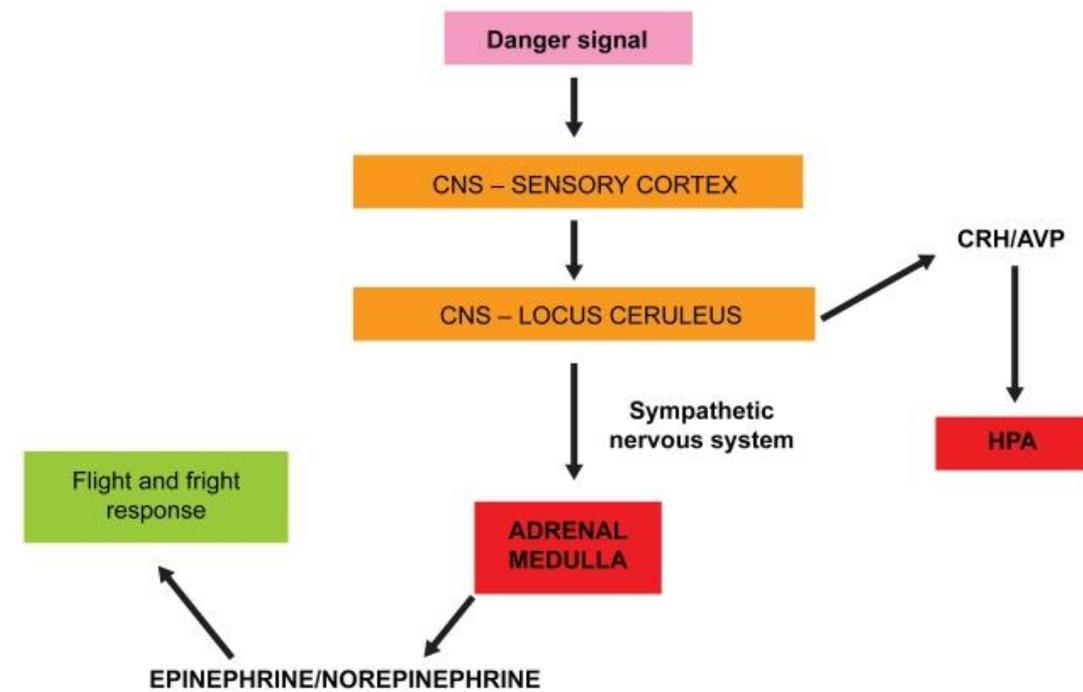
Sekundäreffekte – soziale Isolation, kognitive Funktion, Unfälle

Gehörverlust ≠ Gesunder Schlaf *Sekundäreffekte; unbewusste Effekte*

Nicht-auditive Lärmefeffekte

adapted from Müntzel Eur Heart J 2016; Recio et al. 2016





Objektiver und subjektiv wahrgenommener Lärm

eine Stressquelle

Sympathetisch-adrenale-
medulläre Achse der
Stressantwort

**“active fight or flight
response”**

**Neutralisierung Stressor
Katecholamin
Ausschüttung**

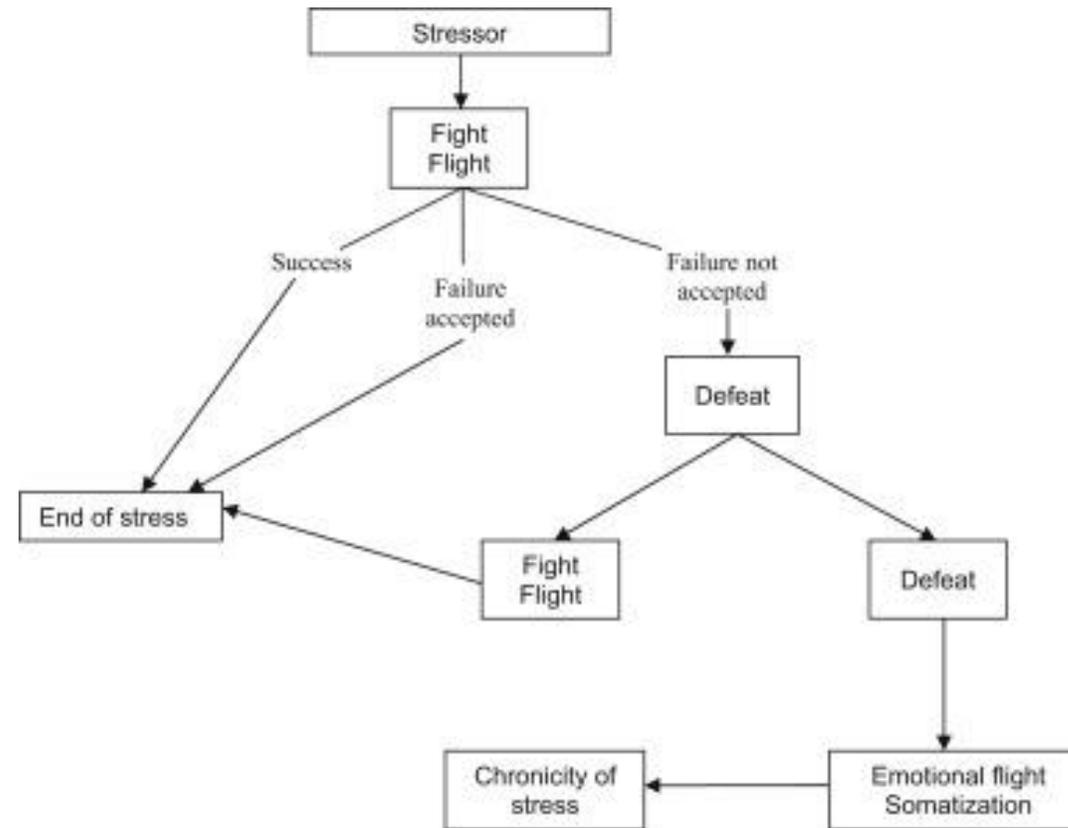
Hypothalamus-Hypophysen-
Nebennierenrinden Achse
der Stressantwort

**“repression/defeat
response”**

**Keine Kontrolle über
Stressor
Kortisol Ausschüttung**

«Learned helplessness» als Antwort auf wiederholten akuten Stress
Emotionale Flucht: bedeutsam für Metabolismus und Immunität

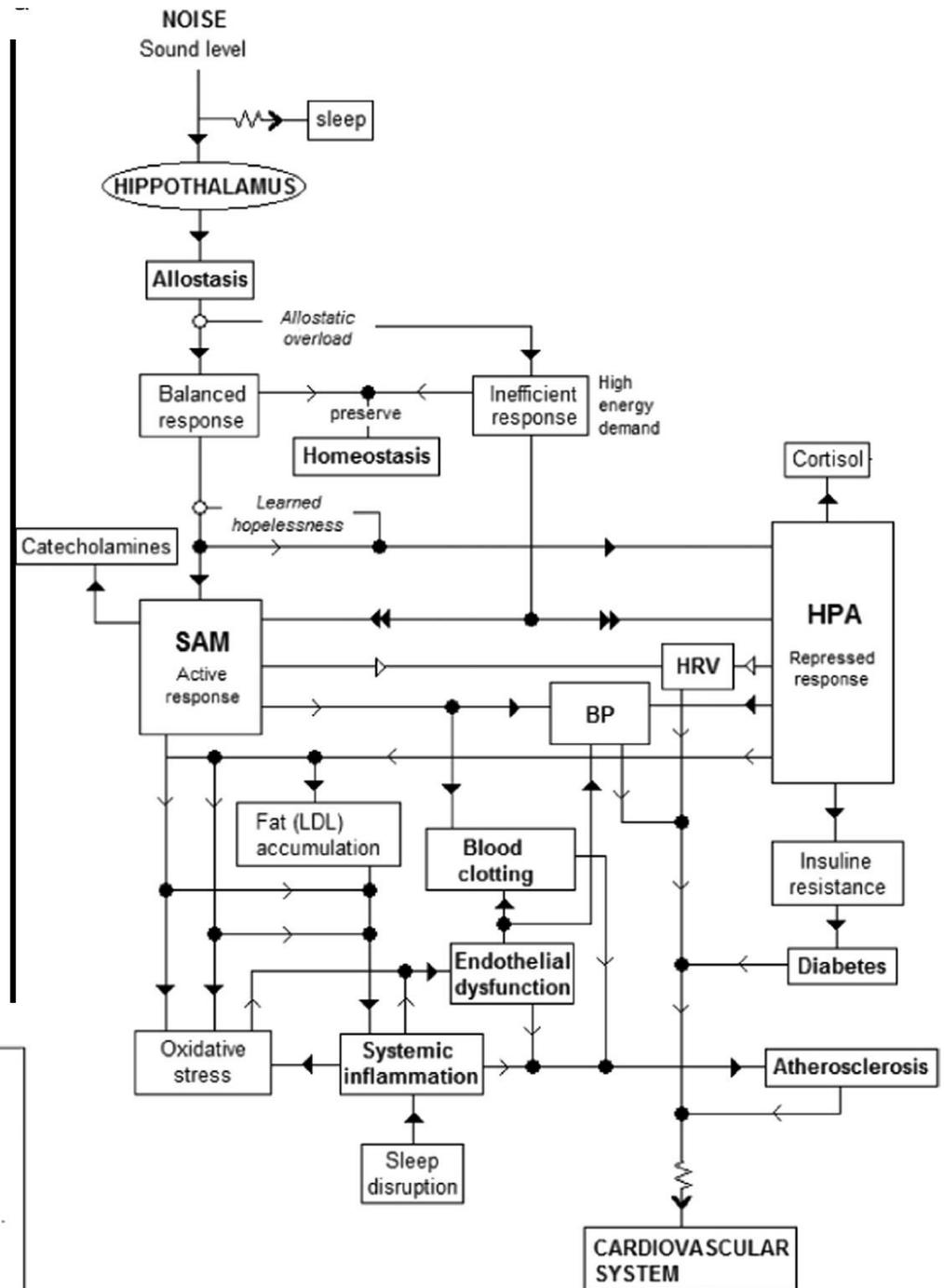
Priyadarshini S & Aich P PLoS One 2012



Integratives Stressmodell und schädliche Gesundheitseffekte

Umweltlärm

Recio 2016





Lärm und Insomnia

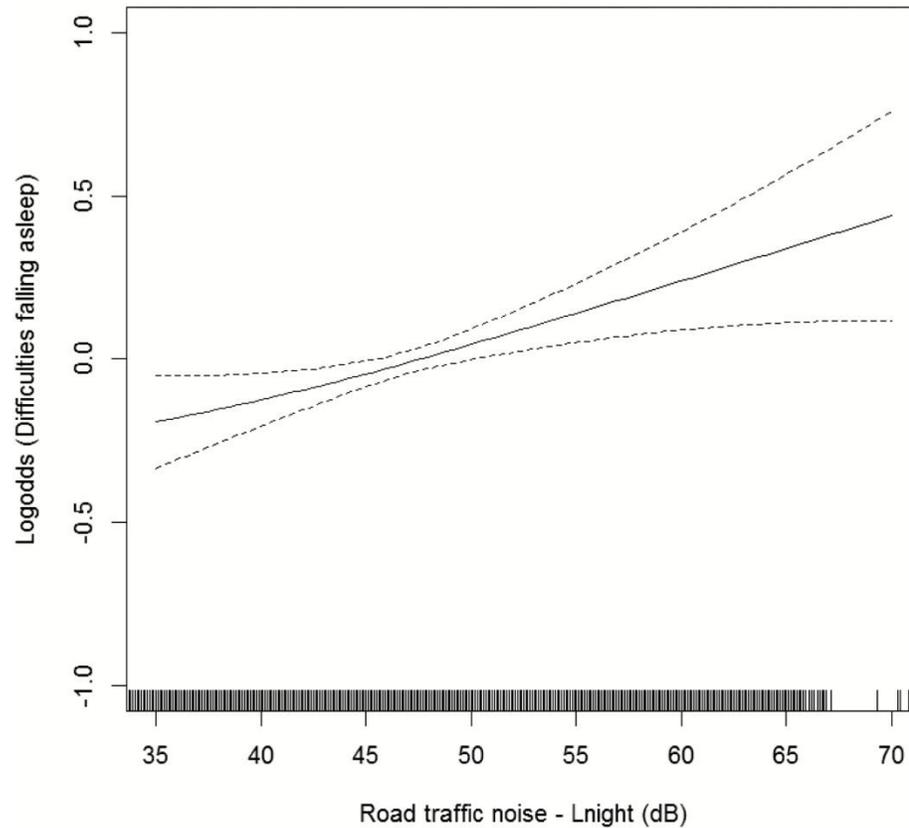
Evandth et al. Sleep 2017

Total Study Population	<i>n</i>	Model 1 ^a , OR (95% CI)	Model 2 ^b , OR (95% CI)
Difficulties falling asleep	11286	1.11 (1.06–1.15)	1.05 (1.01–1.09)
Awakenings during the night	11182	1.07 (1.03–1.11)	1.04 (1.00–1.08)
Waking up too early	11137	1.10 (1.06–1.14)	1.06 (1.02–1.11)
Use of sleep medication	11255	1.04 (1.00–1.09)	0.99 (0.95–1.03)
Bedroom facing road			
Difficulties falling asleep	3514	1.13 (1.05–1.21)	1.08 (1.00–1.16)
Awakenings during the night	3485	1.05 (0.99–1.13)	1.03 (0.96–1.10)
Waking up too early	3472	1.03 (0.96–1.10)	1.00 (0.93–1.08)
Use of sleep medication	3499	0.99 (0.92–1.06)	0.93 (0.87–1.01)

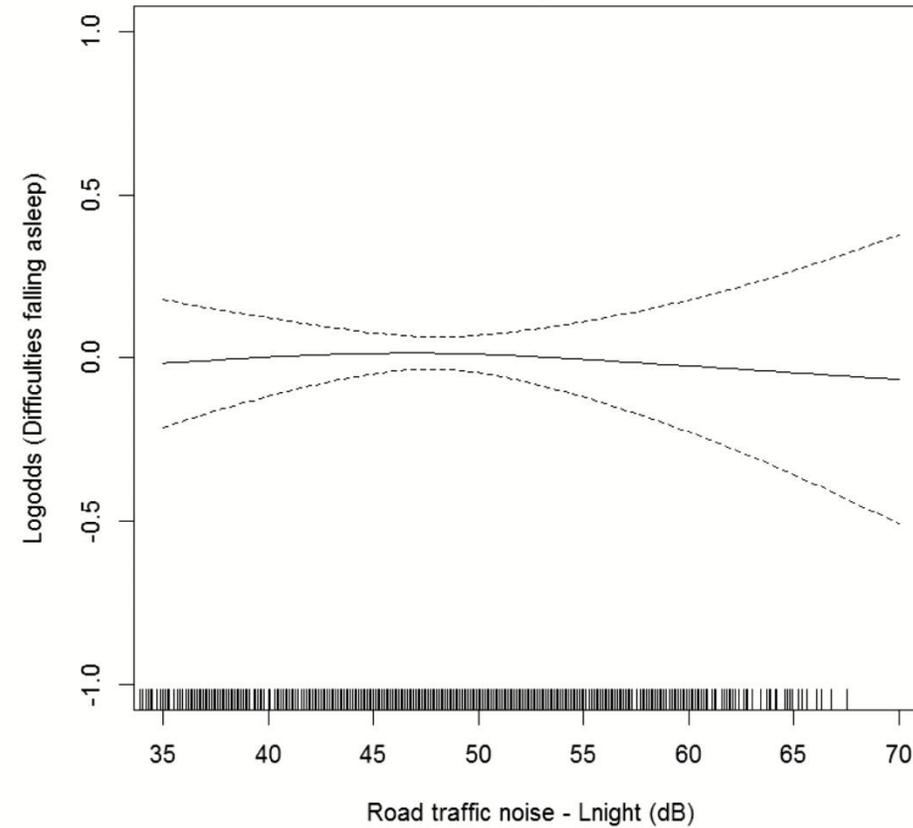


Lärm und Insomnia in Abhängigkeit von Schlafmittelgebrauch

Difficulties falling asleep
Nonusers of sleep medications



Difficulties falling asleep
Users of sleep medications



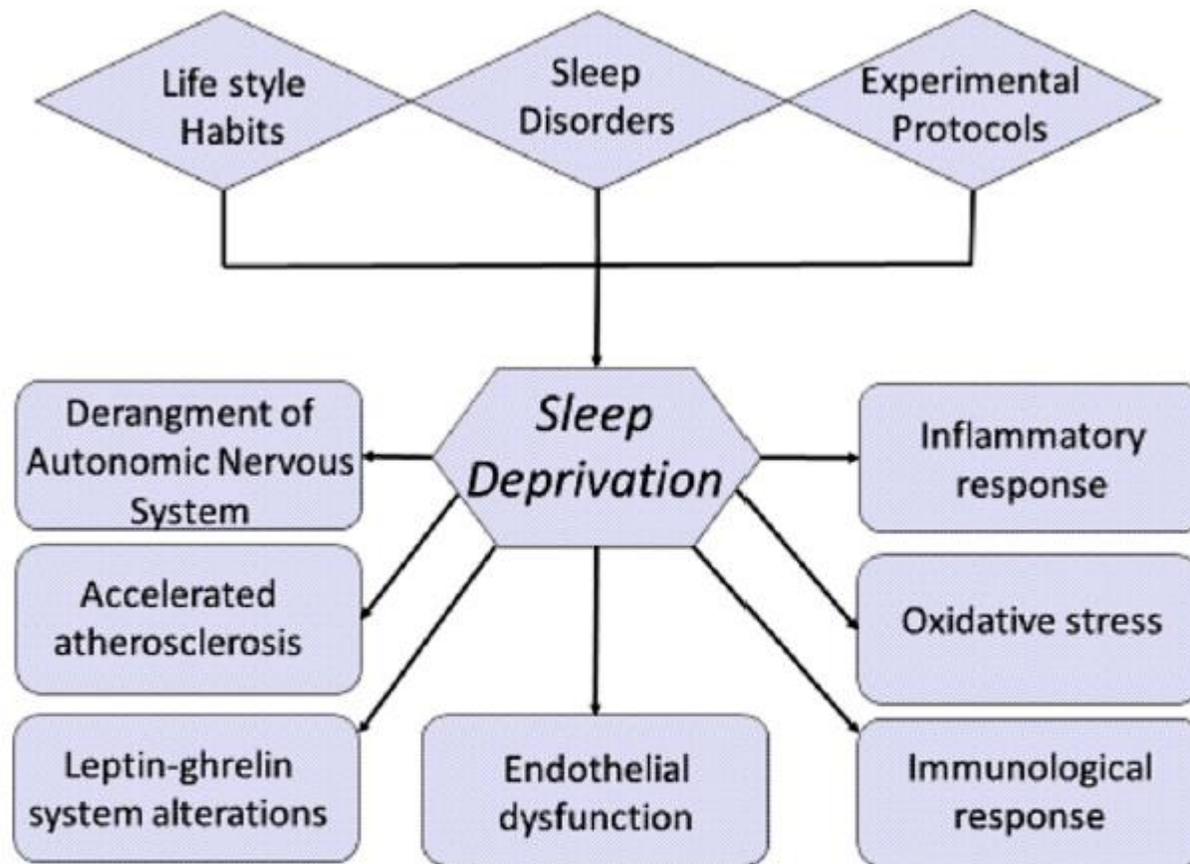
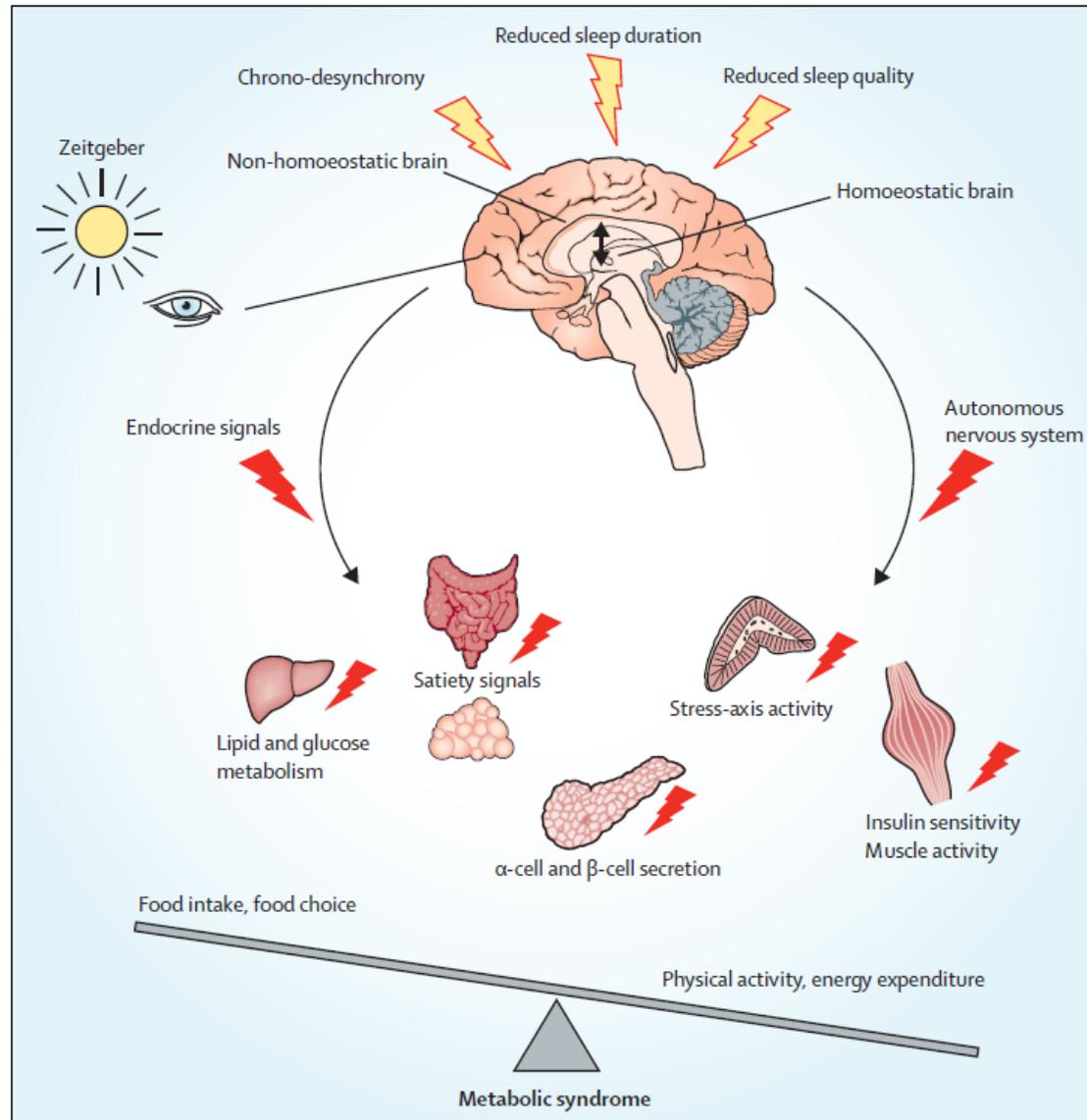


Fig. 1. Sleep deprivation (SD) can be due to lifestyle habits, sleep disorders and experimental sleep protocols. Despite the origine, SD activates several physiopathological pathways, such as autonomic nervous system dysfunction, endothelial dysfunction, increased inflammation, coagulation and oxidative stress responses, deregulation of hormones secretion. All these alterations are thought to be responsible for the link between SD and cardiovascular disorders.

Schlaf, Schlafentzug und kardiovaskuläre Erkrankungen

*Tobaldini Neuroscience
and Biobehavioral
Reviews 2017*



Schlafstörungen und metabolisches Syndrom

*Schmid et al. Lancet
Diabetes Endocrinol 2015*

epidemiologische und
experimentelle Daten
unterstützen einen
kausalen Zusammenhang
zwischen Schlafstörungen
und metabolischer
Gesundheit

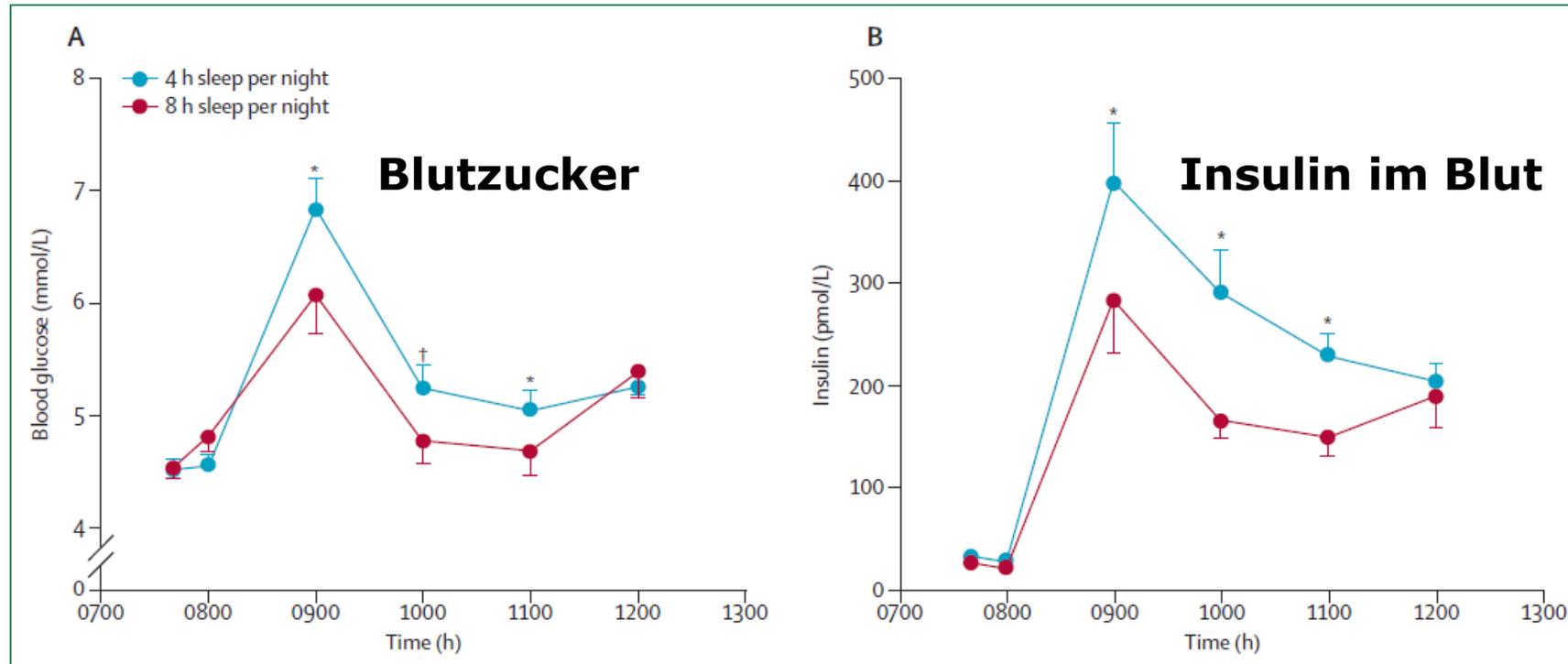


Figure 1: Effect of sleep restriction on glucose and insulin responses to a breakfast meal

Mean (SE) concentrations of plasma glucose (A) and serum insulin (B) before, during, and after breakfast. 15 healthy men were presented with an ad-libitum breakfast buffet from 0800 to 1100 h after 2 nights of sleep restricted to about 4 h (0245–0700 h) and of regular 8 h sleep (2245–0700 h), respectively. Breakfast intake was similar between conditions for total calorie intake (6159 [SE 507] vs 6272 [532] kJ) and composition. * $p < 0.05$. † $t < 0.10$. Modified from reference 33, by permission of the American Academy of Sleep Medicine.

Schmid et al. Lancet Diabetes Endocrinol 2015

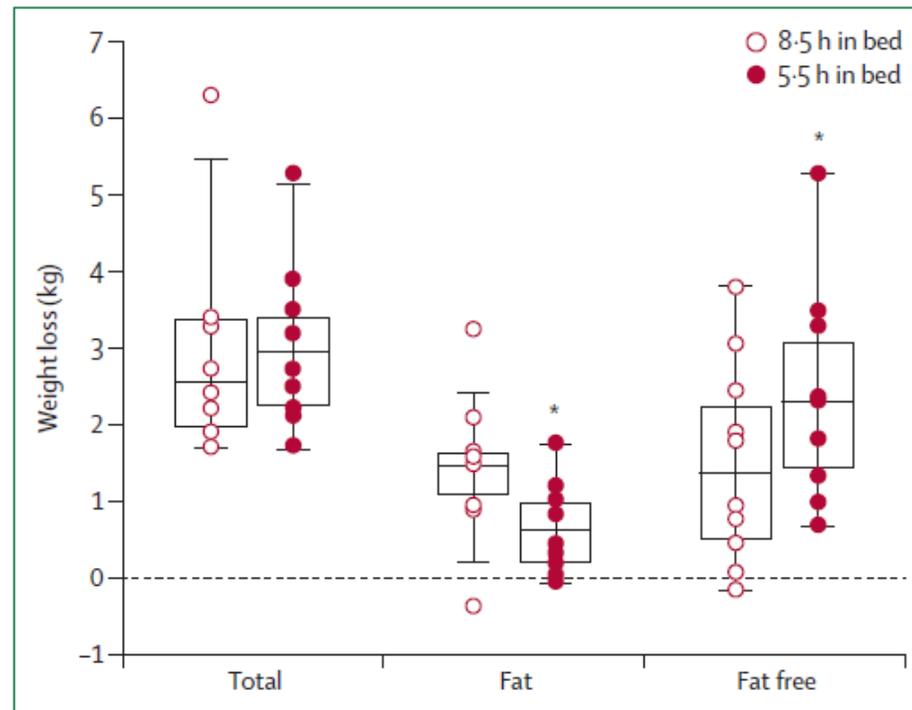


Figure 3: Changes in bodyweight and composition during dietary intervention with and without concomitant sleep restriction

Box plots show loss in bodyweight, fat, and fat-free mass in ten overweight participants (three women, mean BMI 27.4 kg/m² (SD 2.0) during 14 days of calorie restriction (to 90% of the individual resting metabolic rate at screening) accompanied by sleep restriction to 5.5 h and regular sleep of 8.5 h (time in bed; the habitual going-to-bed and getting-out-of-bed times were moved proportionally). Significant difference in loss of fat (p=0.043) and fat-free body mass (p=0.002) between conditions after study period (initial vs crossover) and pre-treatment body composition were controlled for. Adapted from reference 56, by permission of the American College of Physicians.

Schmid et al. Lancet Diabetes Endocrinol 2015

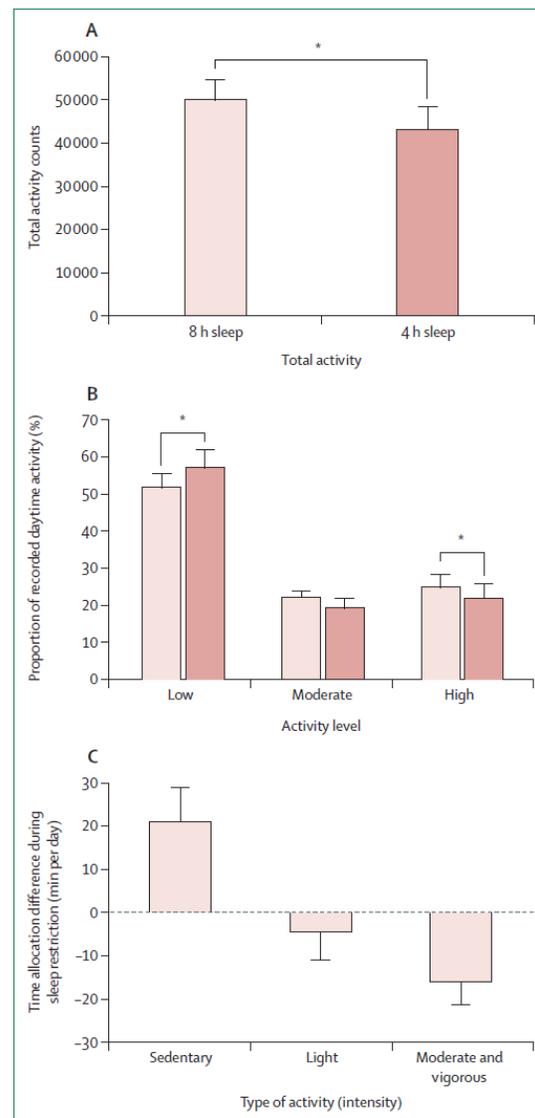


Figure 4: Effects of sleep restriction on physical activity
 Mean (SE) total activity counts (A) and distribution of activity intensities (0800 h–2000 h; B) measured by wrist-worn accelerometer under free-living conditions in 15 healthy men after 1 night of sleep restricted to roughly 4 h (right bars) and another time after 1 night of regular 8 h sleep (left bars). Panel C shows mean (SE) difference in time (min per day) allocation to distinct physical activity intensities during 7 days of 5.5 h versus 2 weeks of 8.5 h of night-time sleep opportunity in 18 healthy men and women (n=9 of each) with a parental history of type 2 diabetes. Physical activity was measured by wrist and waist accelerometry. *p<0.05. Modified from reference 7, by permission of the American Society for Nutrition (A, B), and from reference 76, by permission of the American Academy of Sleep Medicine (C).

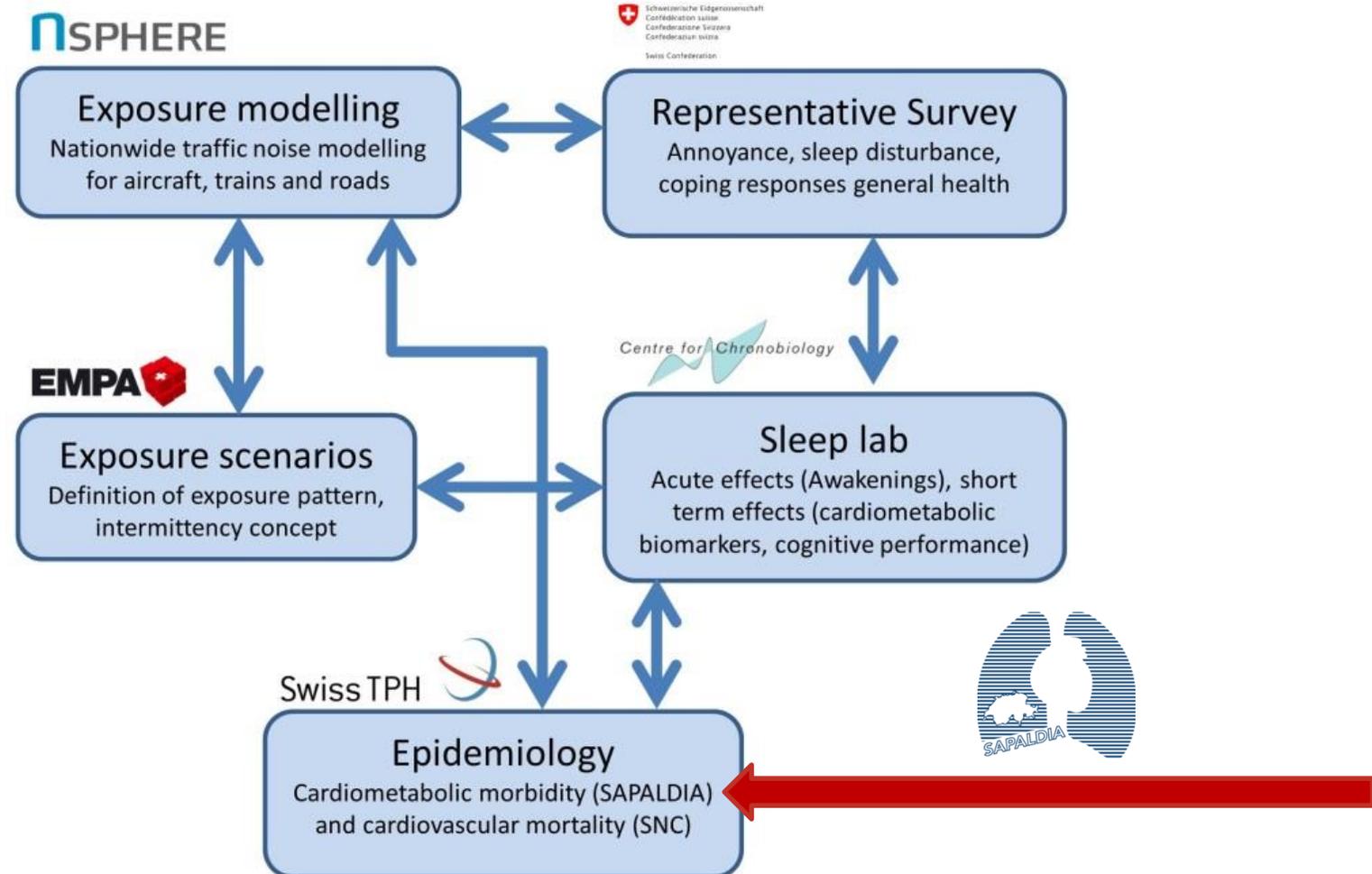
Transportation noise at night, annoyance, sleep and cardiometabolic risk: an integrated approach on acute and long term effects

Sinergia project



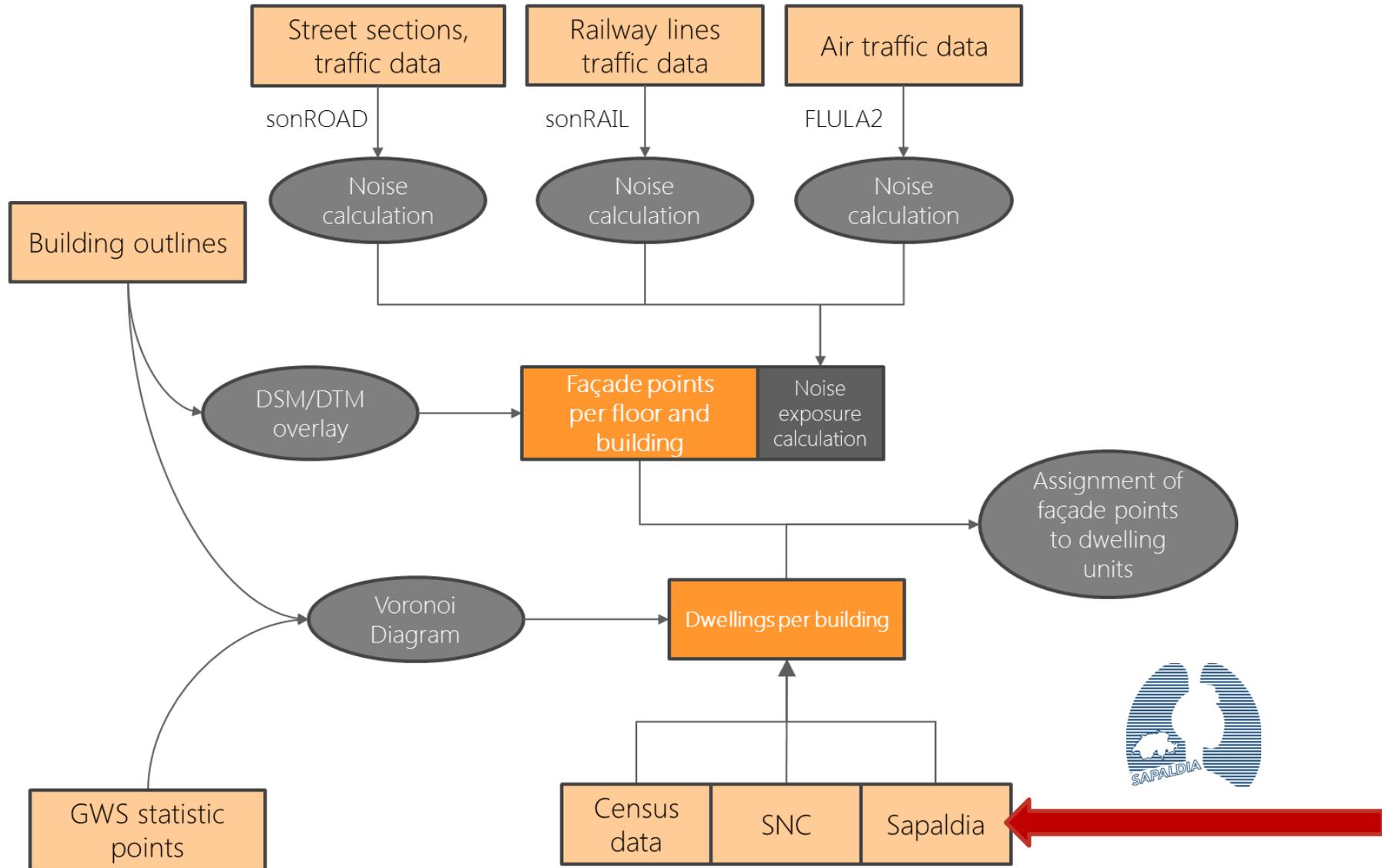
SiRENE Projekt

M. Rööslı (PI), M. Brink, JM Wunderli, C. Cajochen, N.Probst-Hensch



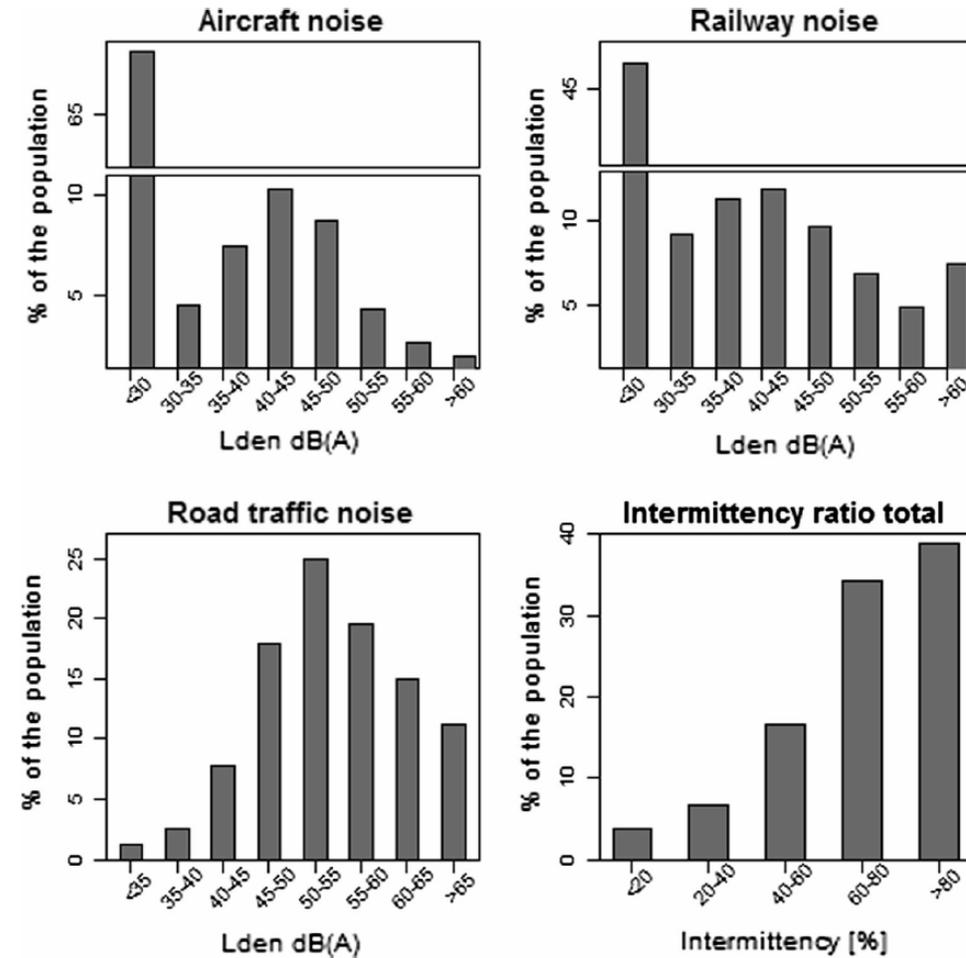
Modelling Exposition Verkehrslärm

Wunderli JM



Exposition Verkehrslärm Schweiz

Héritier et al. Eur J Epidemiol 2017





Verkehrslärm und kardiovaskuläre Mortalität

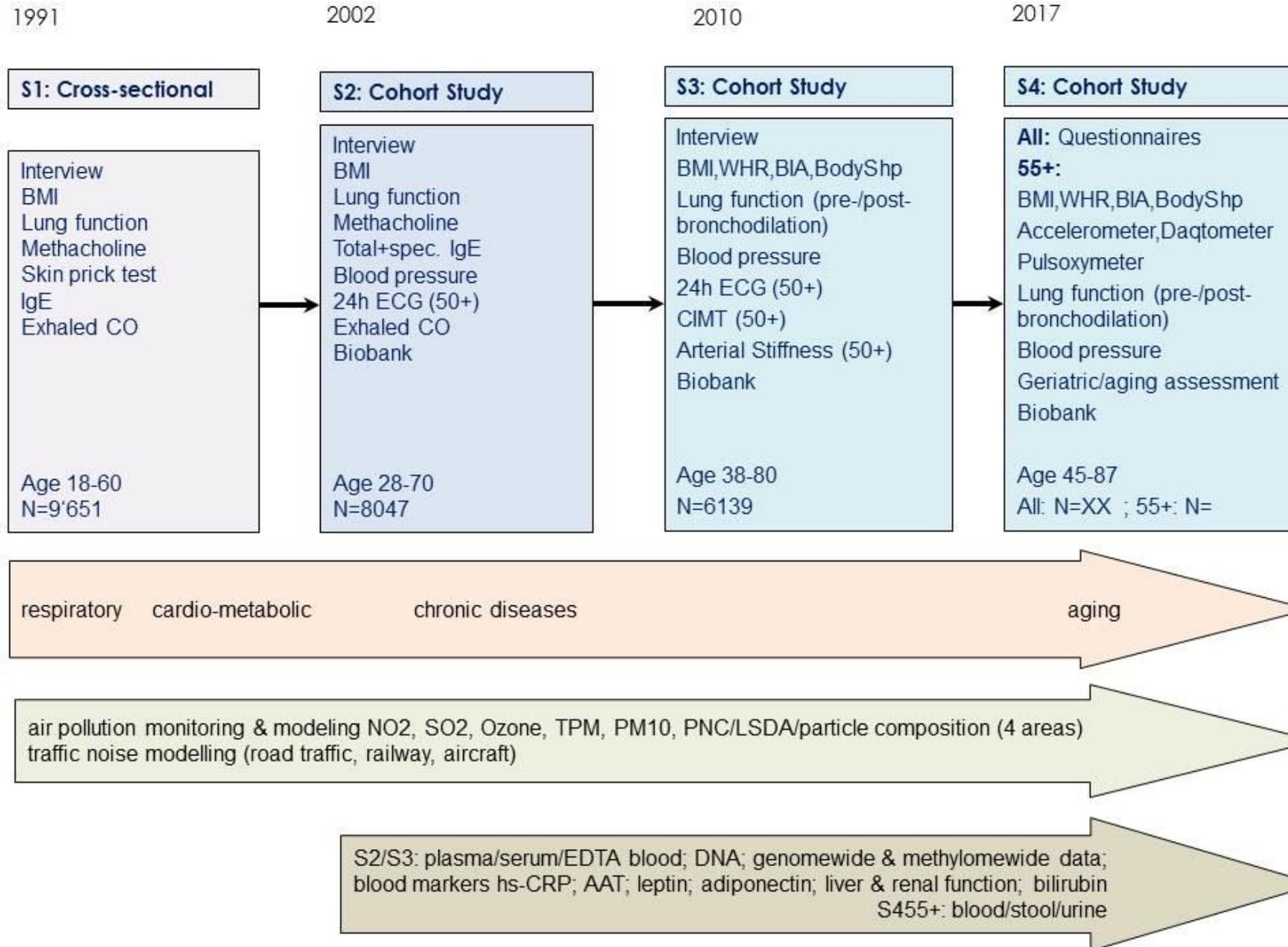
Héritier et al. Eur J Epidemiol 2017

Lärmquelle	N=142'955	HR L _{den}
Strassenverkehr		1.025 (1.018-1.032)
Zugverkehr		1.005 (1.000-1.010)
Flugverkehr		0.994 (0.985-1.002)

- konsistentester Zusammenhang mit Herzinfarkt
- Strassenverkehrslärm mit allen CVD Todesursachen assoziiert, ausser mit hämorrhagischem Schlaganfall
- Zugverkehrslärm mit MI und IHD assoziiert
- Flugverkehrslärm mit MI, Herzversagen und ischämischem Schlaganfall assoziiert

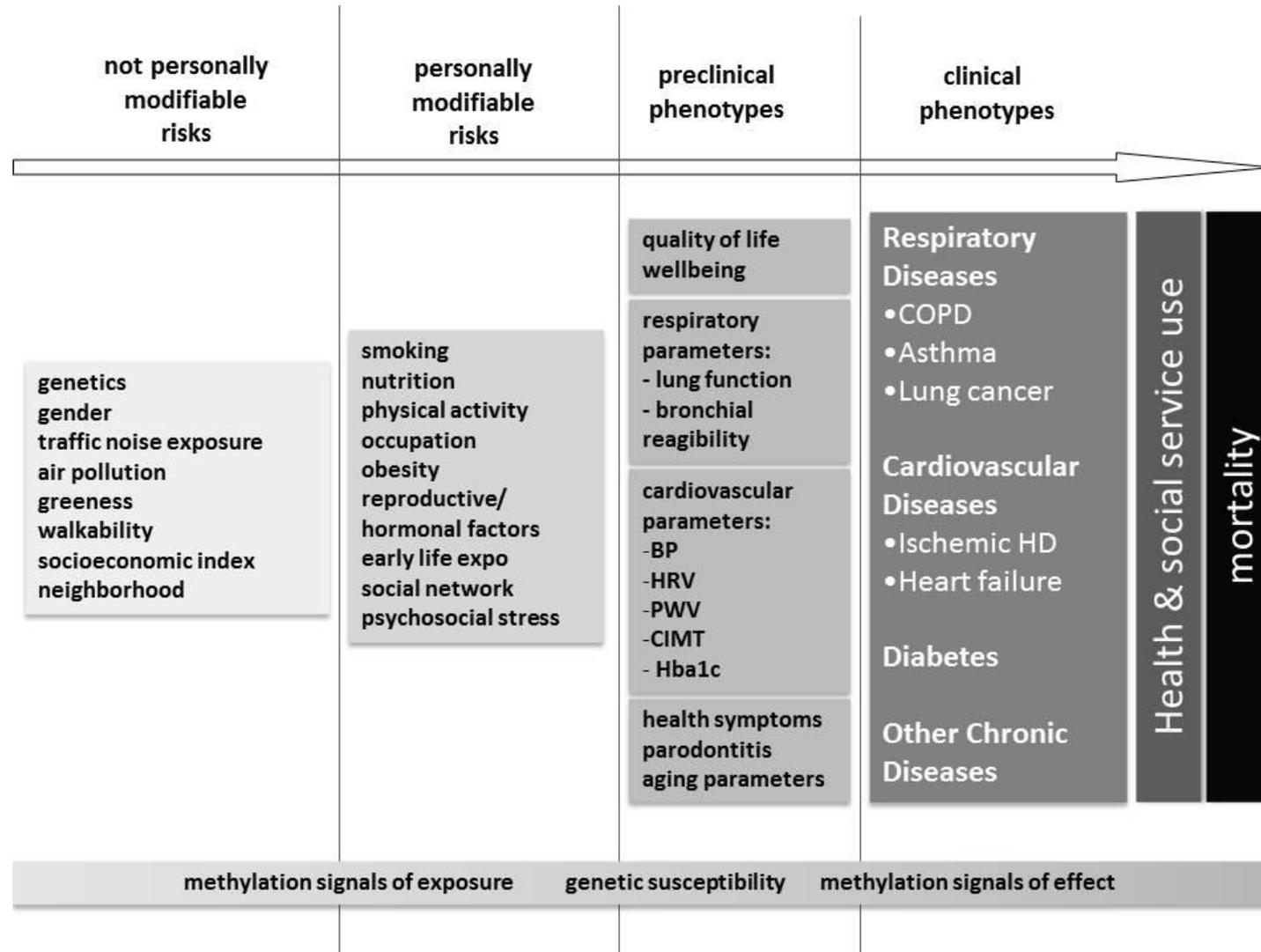


SAPALDIA Kohorte und Biobank





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The Vehicular Traffic and Obesity/Metabolic Syndrome Pathway

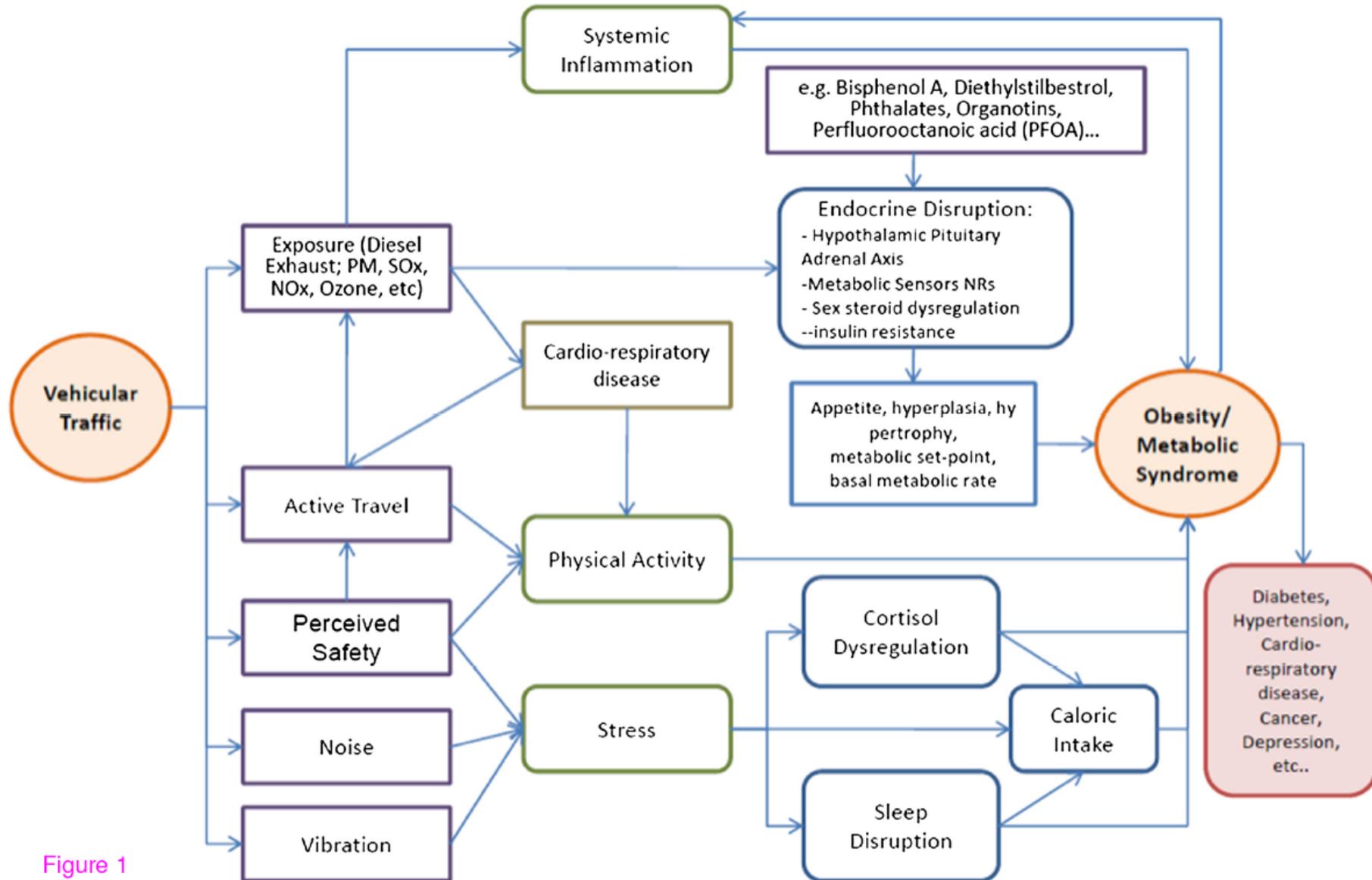
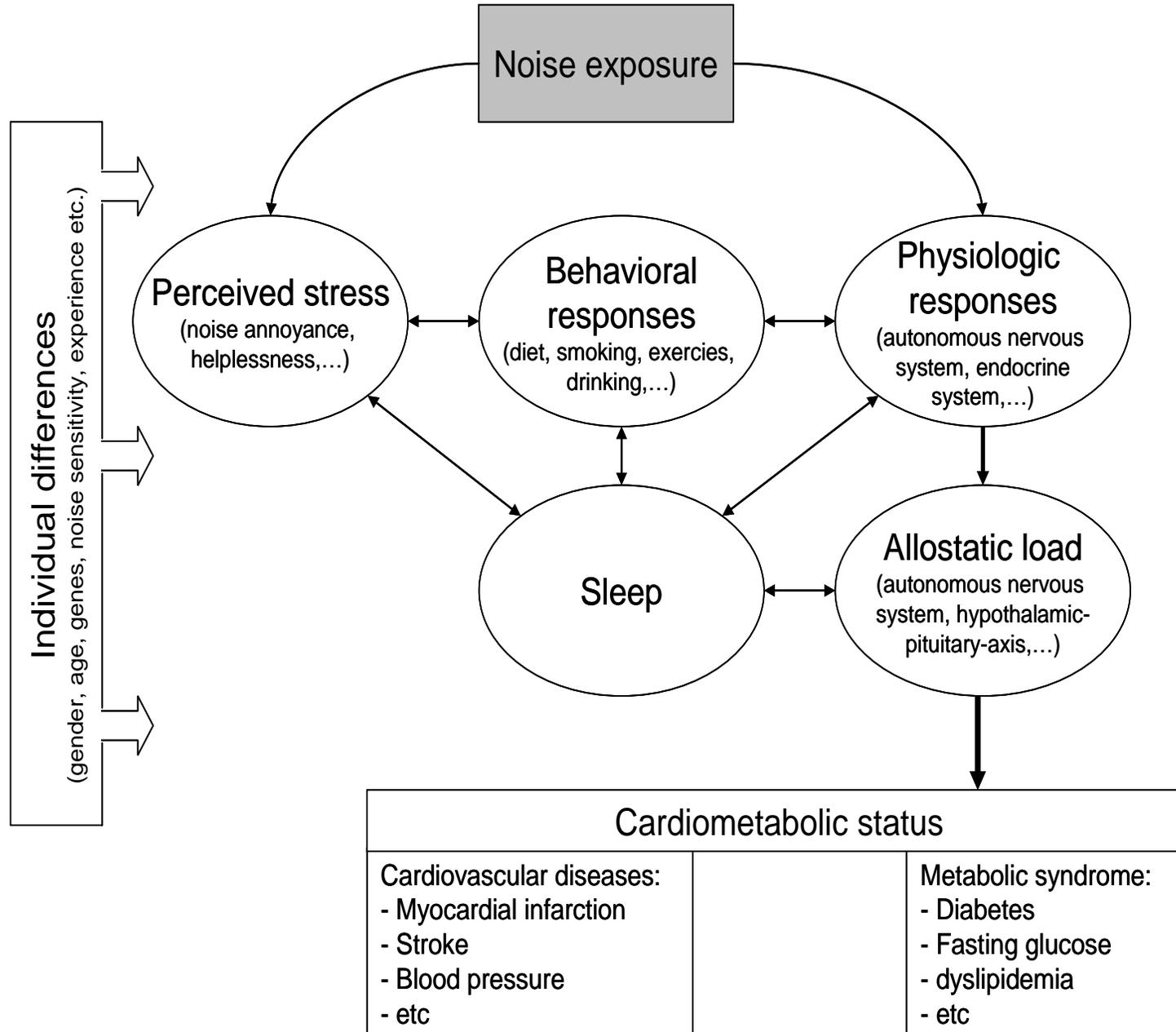


Figure 1



Verkehrslärm und körperliche Aktivität

Foraster et al. Environ Int 2016

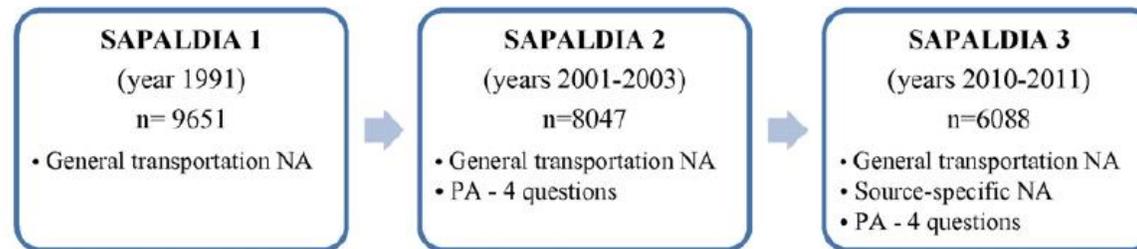
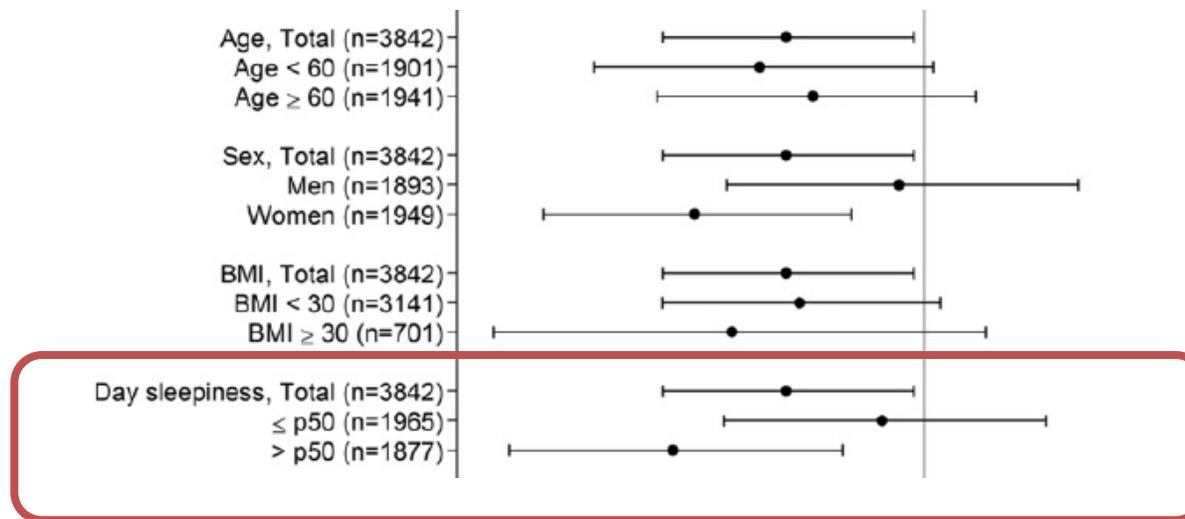
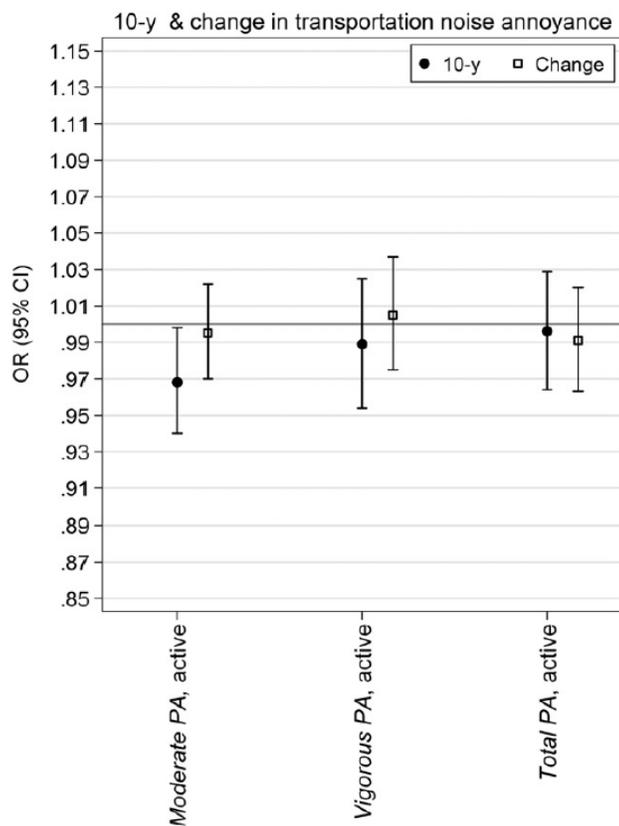
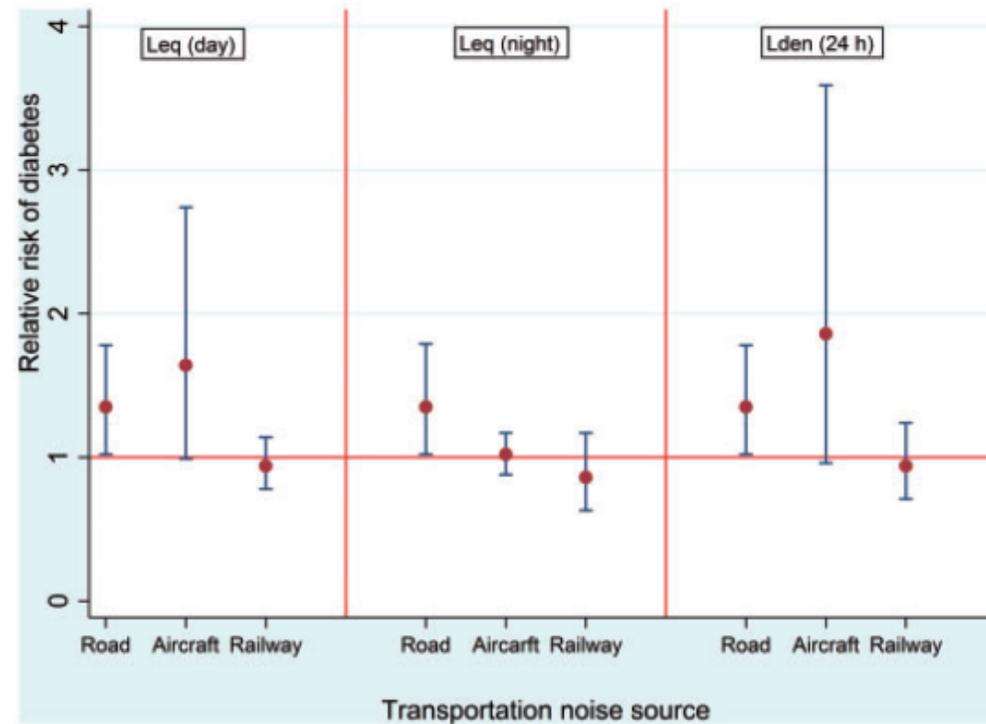


Fig. 1. Availability of information in SAPALDIA (SAP) about the outcome (physical activity: PA) and exposure (noise annoyance: NA) across the study period (baseline: SAP 1, follow-up 1: SAP 2, follow-up 2: SAP 3).



Lärm und Diabetes

Eze et al Int J Epidemiol 2017



Sleep quality

Good

2359

1.28 (0.95, 1.72)

Bad

272

2.05 (1.02, 4.12)

P-value of interaction

0.228

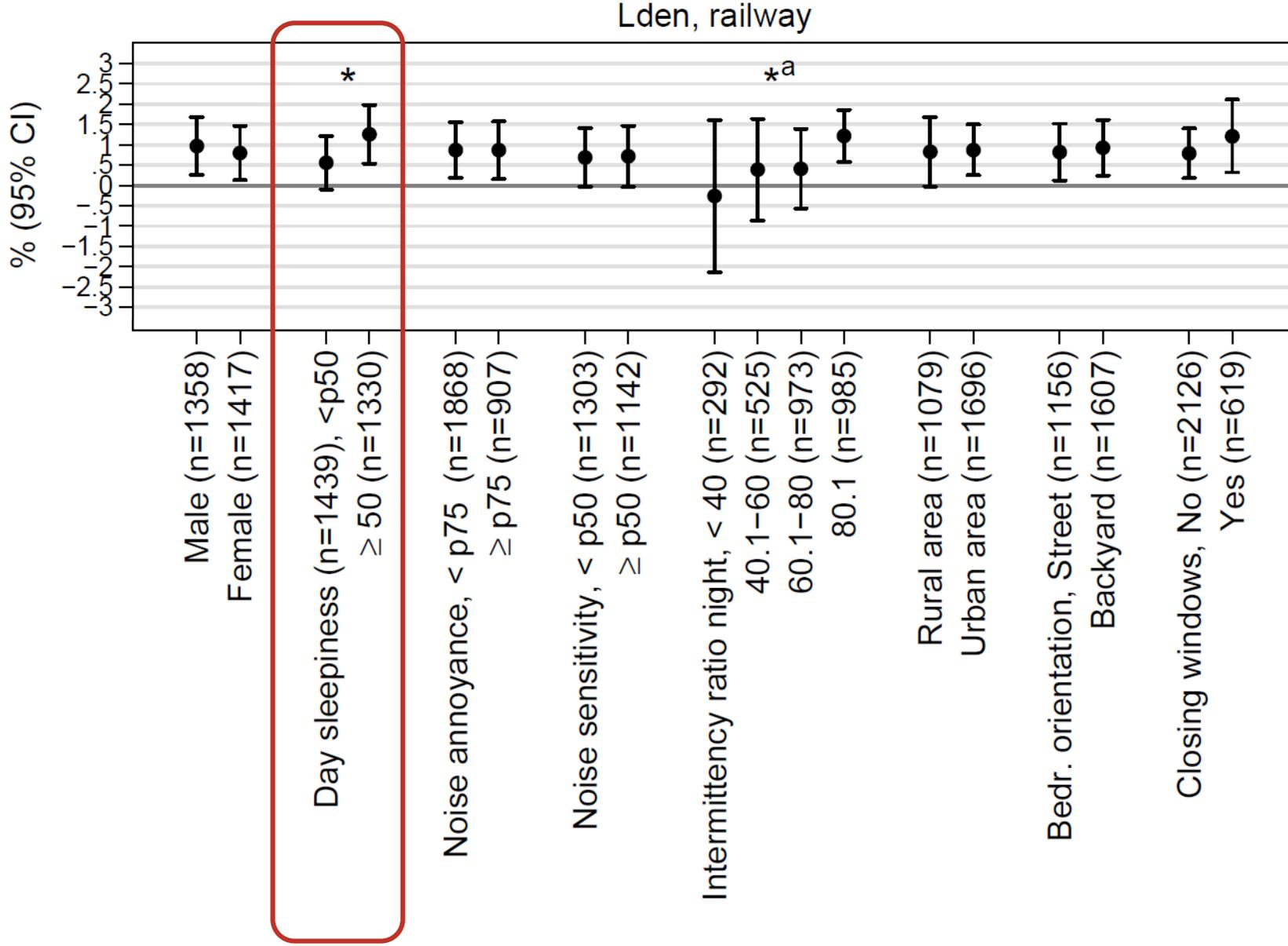
Verkehrslärm und Pulswellengeschwindigkeit

Foraster et al. Environ Health Perspectives in press

Noise indicator	Single-exposure models	Multi-exposure model A	Multi-exposure model B	Multi-exposure model C
	% (95%CI)	% (95%CI)	% (95%CI)	% (95%CI)
Lden, road	0.19 (-0.50, 0.88)	0.16 (-0.53, 0.85)	0.24 (-0.47, 0.95)	-0.59 (-1.45, 0.27)
Lden, railway	0.87 (0.31, 1.43)**	0.87 (0.31, 1.43)**	0.92 (0.35, 1.49)**	1.01 (0.44, 1.58)**
Lden, aircraft	-0.21 (-1.30, 0.88)	-0.33 (-1.43, 0.77)	-0.31 (-1.41, 0.79)	-0.26 (-1.36, 0.83)
IR _{night}	-0.05 (-0.68, 0.57)	-	-0.31 (-0.97, 0.35)	-
NE _{night} , Q1 (0-54.8)	Ref.	-	-	Ref.
NE _{night} , Q2 (55.1-122.9)	0.71 (-0.48, 1.91)	-	-	0.97 (-0.23, 2.17)
NE _{night} , Q3 (123.2-233.7)	0.89 (-0.33, 2.11)	-	-	1.42 (0.14, 2.70)**
NE _{night} , Q4 (233.8-1324.3)	1.77 (0.45, 3.09)**	-	-	2.64 (1.05, 4.22)**

Verkehrslärm und Pulswellengeschwindigkeit

Foraster, *Environ Health Perspectives* in press



Molekulare Mediation

für ein biologisches Verständnis Exposome-Phaenom

Suche nach Molekülen, welche sowohl mit Exposition als auch mit Gesundheitsparameter assoziiert sind

-

sie geben dann einen Hinweis auf Kausalität, wenn ihre Blockierung/Aktivierung den Zusammenhang zwischen Risikofaktor und Gesundheitsparameter verändern

?

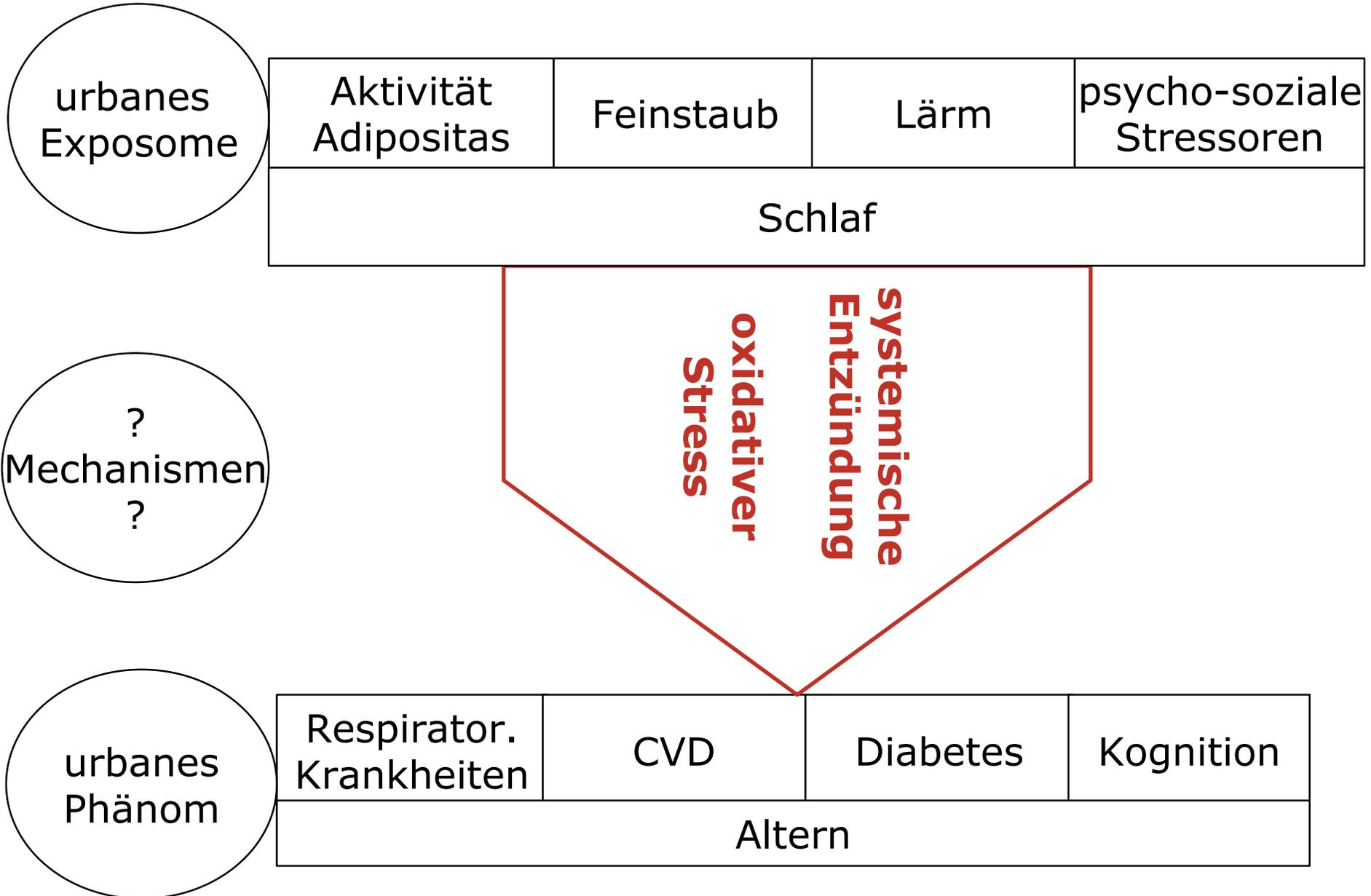
Sind systemische Entzündung/oxidativer Stress kausale Mechanismen von Public Health Bedeutung

-

sie sind mit vielen Risiken und vielen Krankheiten sowie mit Altern assoziiert und können behandelt werden (z.B. Früchtekonsum)

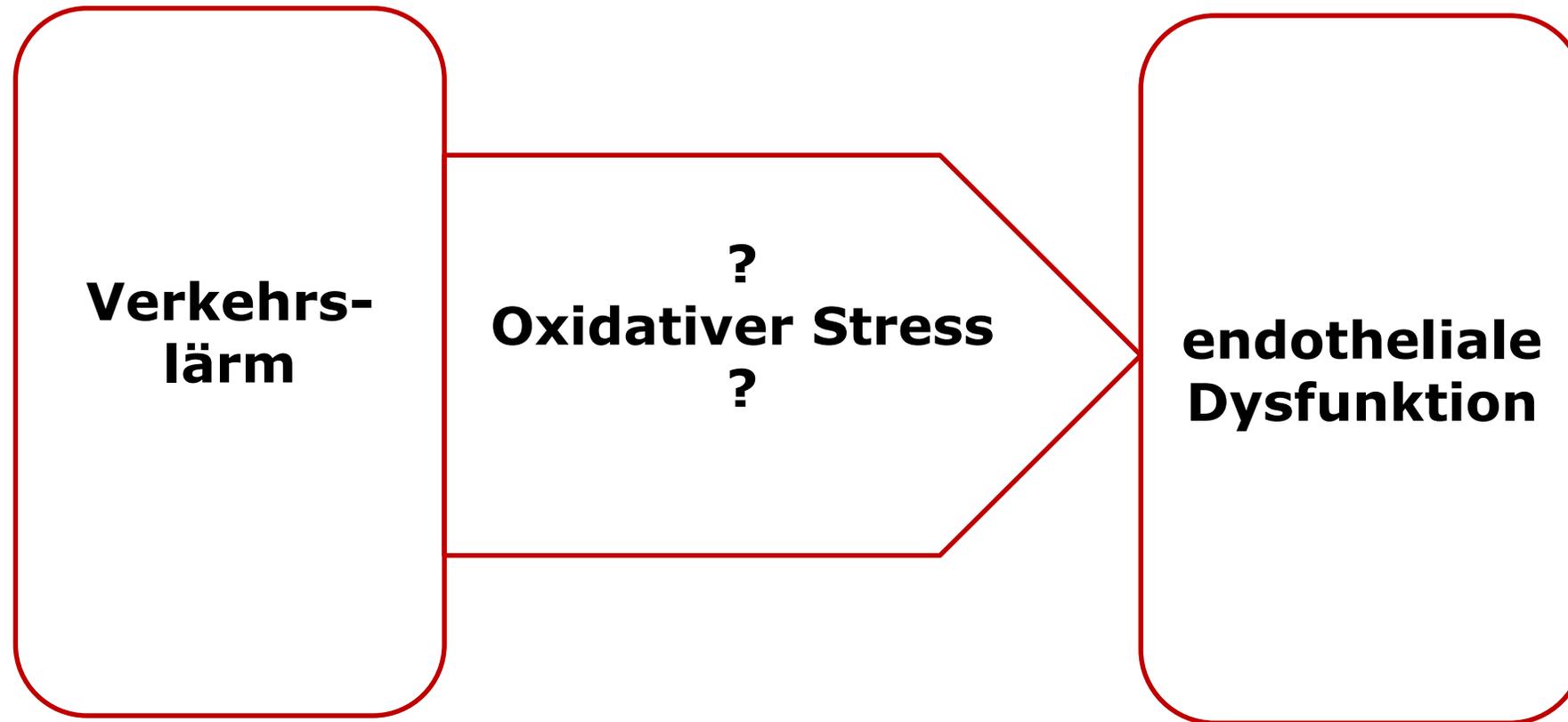
?

Public Health Relevante Mechanismen



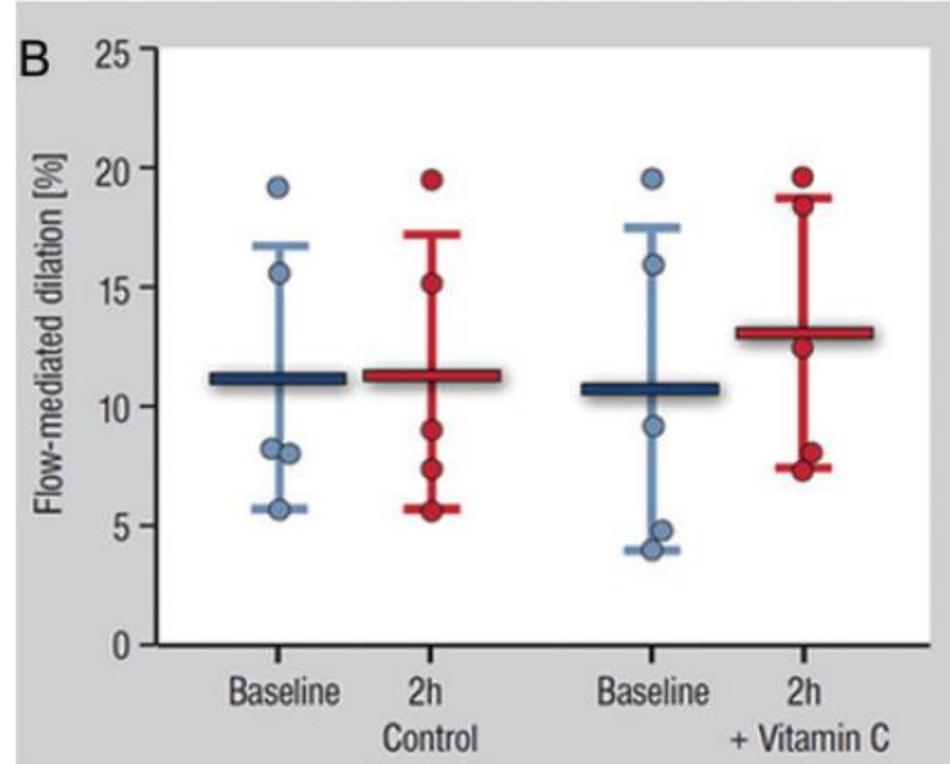
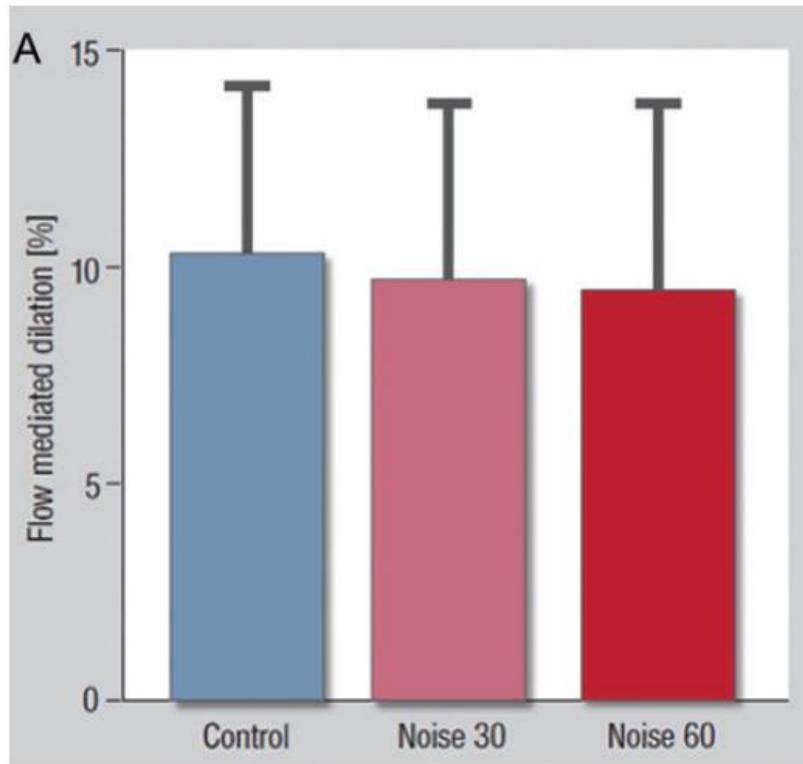


Meet-in-the-Middle – Molekulare Mediation Kandidatenansatz



Effects of noise on flow-mediated dilation

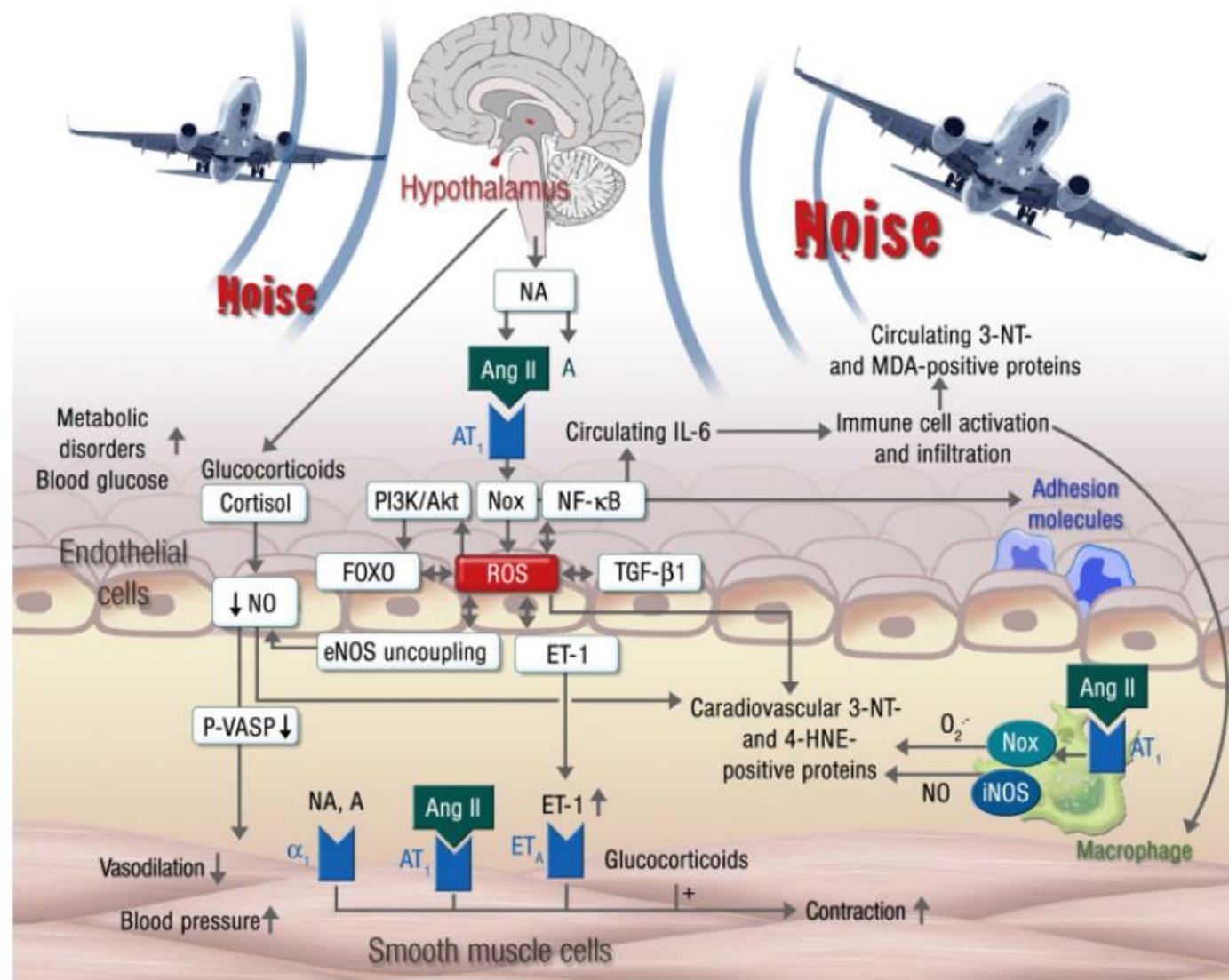
Schmidt FP et al Eur Heart J 2013



Effects of Vitamin C on FMD of the brachial artery

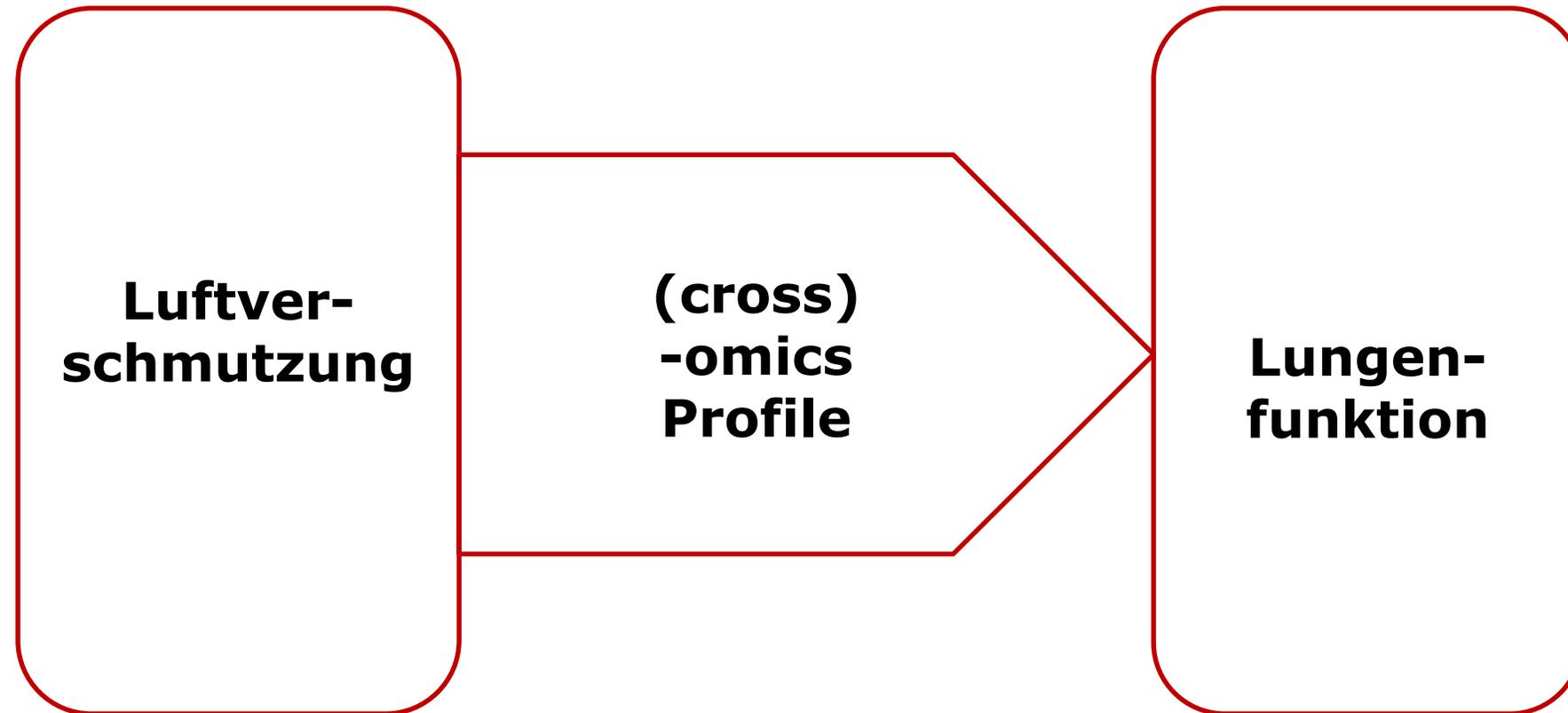
Aircraft noise exposure of mice – vascular dysfunction and oxidative stress

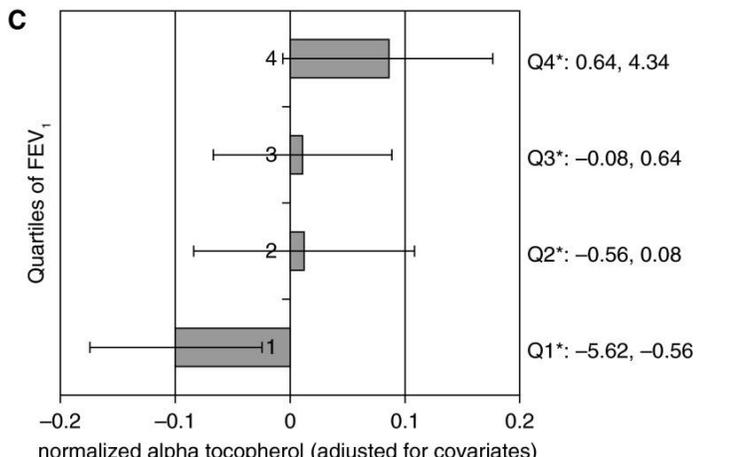
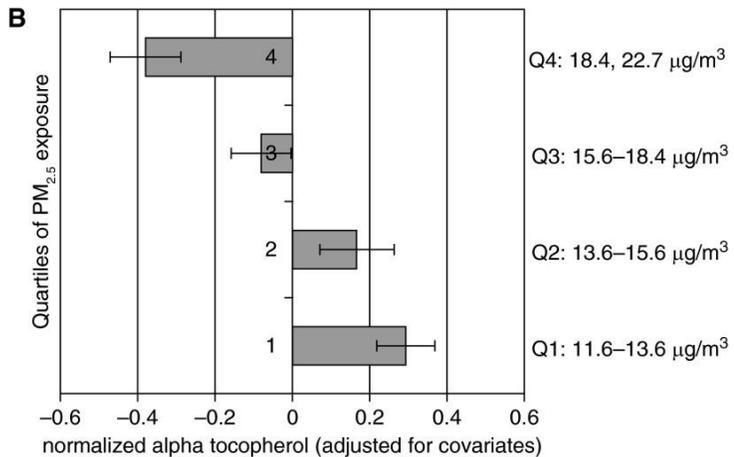
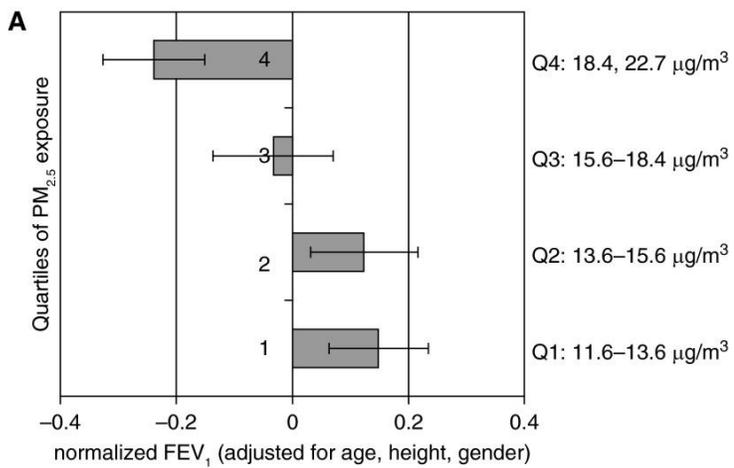
Münzel T et al. *Eur Heart J* 2017



Agnostische Interrogation der molekularen Mediation

1:1 Ansatz





alpha tocopherol – a metabolic link between ambient air pollution and lung function

Menni C et al. AJRCCM 2015;191:1203

TwinsUK Cohort

**Metabolon platform
280 metabolites**

**PM10, PM2.5
residential; dispersion model**



Acknowledgement

SAPALDIA Team



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Sirene Team



Mark Brink, Christian Cajochen, Jean-Marc Wunderli, Danielle Vienneau, Harris Héritier, Martin Röösli



Table 1 Noise metrics and their definition

SPL: The sound pressure level (SPL) is a logarithmic measure of the effective pressure of a sound relative to a reference value. It is measured in decibels (dB, see below) higher than a reference level. The reference sound pressure in air is $20 \mu\text{Pa}$ ($2 \times 10^{-5} \text{ Pa}$), which is equivalent to the human hearing threshold at a sound frequency of 1000 Hz.

dB: A logarithmic scale to measure sound pressure levels.

L_{Aeq} : The energy-equivalent average A-weighted sound pressure level (L_{Aeq}) expressed in decibels is the most commonly used noise exposure metric reflecting (energetically) averaged noise exposure over a certain time period. The A-weighting (represented by the A in L_{Aeq}) accounts for the different sensitivity of the human ear at different sound frequencies. The duration of the averaging period within the 24 h day is often amended (e.g., L_{Aeq} 16 h, usually reflecting the period from 7 a.m. to 11 p.m.). The L_{Aeq} is often calculated for long periods (e.g., over one year, the busiest 6 months of the year, etc.).

L_{night} : L_{Aeq} for the night period (usually 11 p.m. and 7 a.m.)

L_{Dn} : Weighted L_{Aeq} over a 24 h period with a 10 dB penalty for nocturnal noise exposure (usually 11 p.m. to 7 a.m.)

L_{DEN} : The 24 h L_{Aeq} with a 5 dB penalty for the evening (usually 6 p.m. to 10 p.m. or 7 p.m. to 11 p.m.) and a 10 dB penalty for the night (usually 10 p.m. to 6 a.m. or 11 p.m. to 7 a.m.). The penalties are introduced to indicate people's extra sensitivity to noise during the evening and the night. With respect to long-term health effects, these metrics are usually calculated as average annual exposure indicators.

L_{max} : Maximum noise level in a given time period (during the passing of a train). L_{max} is often better at predicting acute effects of single noise events than average noise levels. With respect to long-term health effects, however, equivalent sound levels seem more appropriate exposure metrics.

The energy-equivalent average A-weighted SPL (L_{Aeq}) as expressed in decibels is the most commonly used indicator of the noise exposure that people perceive outside and inside their homes. The A-weighting accounts for the different sensitivity of the human ear at different sound frequencies.

Münzel et al. Eur Heart J 2014