Stress biomarkører i arbejdsmiljøforskning

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Outline

- Stress historisk set
- Stressorer i arbejdet
- Måling af fysiologisk stress
- Mobning på arbejdspladsen som stressor
- Helbredseffekter af mobning på arbejdspladsen
- Natarbejde som stressor
- Allostatic load
- Stress og ulighed

Stress historisk set

1915

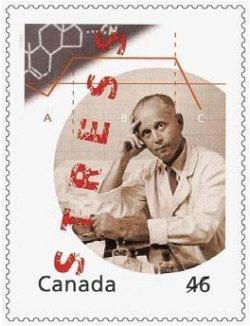
Walter B Cannon (1871-1945)

Cannon beskrev stress som den kropslige reaktion ved akut stresspåvirkning, bedre kendt som kamp eller flugt responset.
Det sympatiske nervesystem

I en presset situation bliver vi sat i et alarmberedskab, der forbereder os og mobiliserer der fornødne energi til enten at bekæmpe truslen eller flygte.

Stress historisk set

1936 1976



Hans H B Selye (1907-1982)

Selye definerede i 1936 stress som et uspecifikt fysiologisk respons på enhver udfordring eller trussel vi udsættes for.
HPA-aksen

⋯ og i 1976 om kroppens evne til at tilpasse sig.
Selye refererer hermed til den evne enhver organisme har til at fastholde stabilitet i sine vitale systemer, uanset omgivelsernes krav (homeostase)

Stress historisk set

1984

Richard Lazarus og
Susan Folkman

"*Stress er en ubalance mellem krav og ressourcer eller når presset er større end personen kan håndtere*" og refererer hermed til den transaktionelle stress model og coping

Stress historisk set

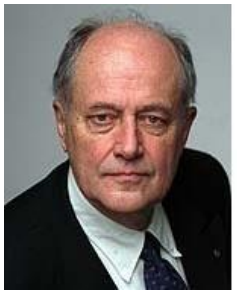
1998

Bruce McEwen

Stress fremmer tilpasning ("allostasis"), og om det varer ved fører stress over tid til slitage på kroppen ("allostatic load").

Stress historisk set

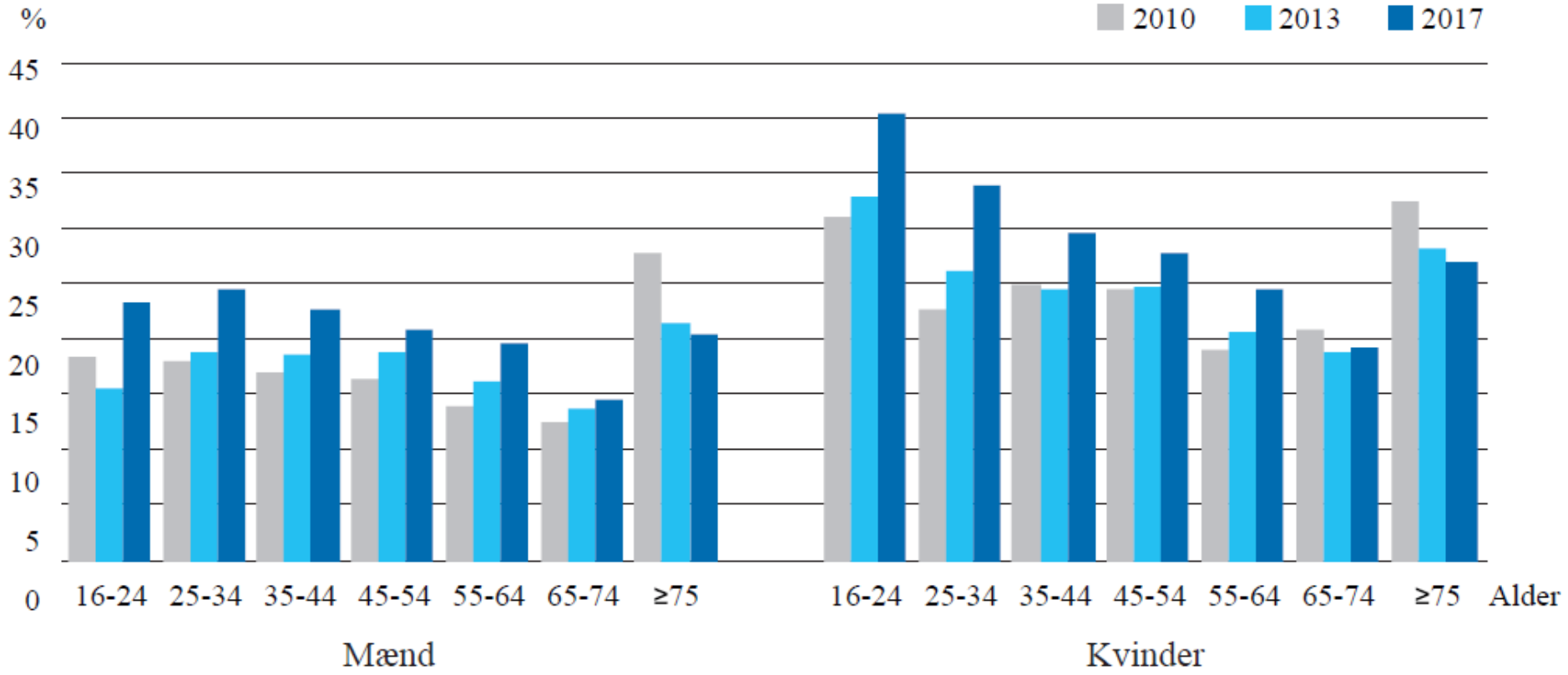
2004



Holger Ursin og Hege Eriksen

Videreudvikler den transaktionelle stress model med CATS, hvori den enkeltes kognitive vurdering af opgaven/hændelsen og egen evne til at kunne håndtere situationen afgør om det fysiologiske stressrespons bliver skadeligt.

Udvikling i selvoplevet stress fra 2010 til 2017



Der er sket en stigning på 4.3% selvrapporteret stress fra 2010 til 2017 blandt både mænd og kvinder og i næsten alle aldersgrupper

Danskernes sundhed – Den Nationale sundhedsprofil 2017

Andel der oplevet højt stress

		Procent	OR[1]	95 % sikker-hedsgrænser	Antal svarpersoner
Uddannelse	Under uddannelse	32,4			11.809
	Grundskole	33,1	2,58	(2,43;2,73)	12.861
	Kort uddannelse	24,8	1,46	(1,40;1,53)	59.600
	Kort videregående uddannelse	21,4	1,17	(1,10;1,24)	13.691
	Mellemlang videregående udd.	19,8	1		35.097
	Lang videregående uddannelse	17,5	0,82	(0,77;0,87)	18.833
	Anden uddannelse	31,2	2,15	(2,00;2,30)	7.872
Erhvervsmæssig stilling	Beskæftigede	19,4	1		83.272
	Arbejdsløse	47,0	3,60	(3,29;3,93)	3.141
	Førtidspensionister	55,6	6,07	(5,67;6,50)	5.284
	Andre uden for arbejdsmarkedet	54,6	5,55	(5,19;5,94)	7.102
	Efterlønsmodtagere	13,7			4.072
	Alderspensionister	19,8			47.612

Danskernes sundhed – Den Nationale sundhedsprofil 2017

Stress blandt mennesker i arbejde?

- 15 % af deltagere i Arbejdsmiljø og Helbred 2012 (AH2012) rapporterer, at de har følt sig stresset 'Hele tiden' eller 'Ofte' inden for de sidste 2 uger. Blandt dem angiver 43 % at kilden til stress er både arbejde og privatliv, 52% at kilden er arbejde og 5% at kilden er privatliv.

Det Nationale Forskningscenter for Arbejdsmiljø AH2012

- Indikatorer på højt stressniveau
  - Dårligt socialt netværk
  - Fysisk og psykisk belastende arbejdsvilkår
  - Storrygning
  - Fysisk inaktivitet

Nielsen et al., Ugeskrift for Læger 2004

- Ansatte fra følgende jobgrupper føler sig særligt ofte stresset:
- Psykologer
- Gymnasielærere
- Læger

Det Nationale Forskningscenter for Arbejdsmiljø AH2012
http://www.arbejdsmiljoforskning.dk/da/arbejdsmiljoedata/arbejdsmiljoe-og-helbred-20/arbejdsmiljo-og-helbred-2012/arbejdsmiljoeet-i-ord/psykisk-arbejdsmiljoe/foele-sig-stresset

Fysiske, psykiske og adfærdsmæssige tegn på stress:

Tabel 22.1. Fysiske, psykiske og adfærdsmæssige tegn på stress.

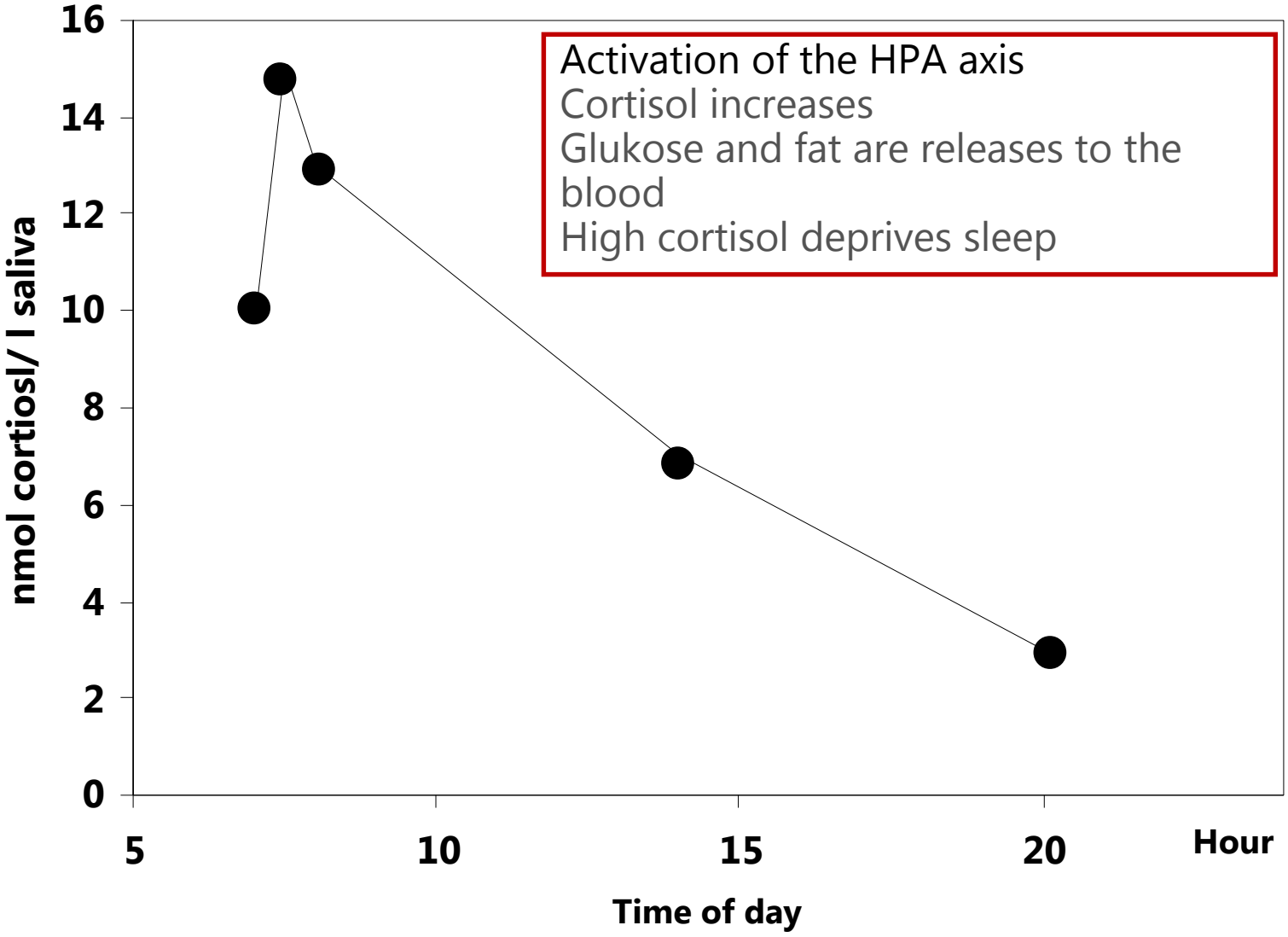
Fysiske	Psykiske	Adfærdsmæssige
Hovedpine	Ulyst	Søvnløshed
Hjertebanken	Træthed	Lav selvfølelse
Rysten på hænder	Indre uro	Hyperventilation
Svimmelhed	Hukommelsesbesvær	Følelseskulde
Tics	Koncentrationsbesvær	Indesluttethed
Mavesmerter	Rastløshed	Vrede
Hyppig vandladning	Irritabilitet	Aggressivitet
Diaré	Angst	Nedsat præstationsevne
Smerter	Nedsat humoristisk sans	Ubeslutsomhed
Nedsat potens og libido	Følelse af udmattelse	Øget brug af stimulanser
Hyppige infektioner	Depression	Appetitløshed
Forværring af kronisk sygdom		Sygefravær

Kilde: Netterstrøm, 2002.

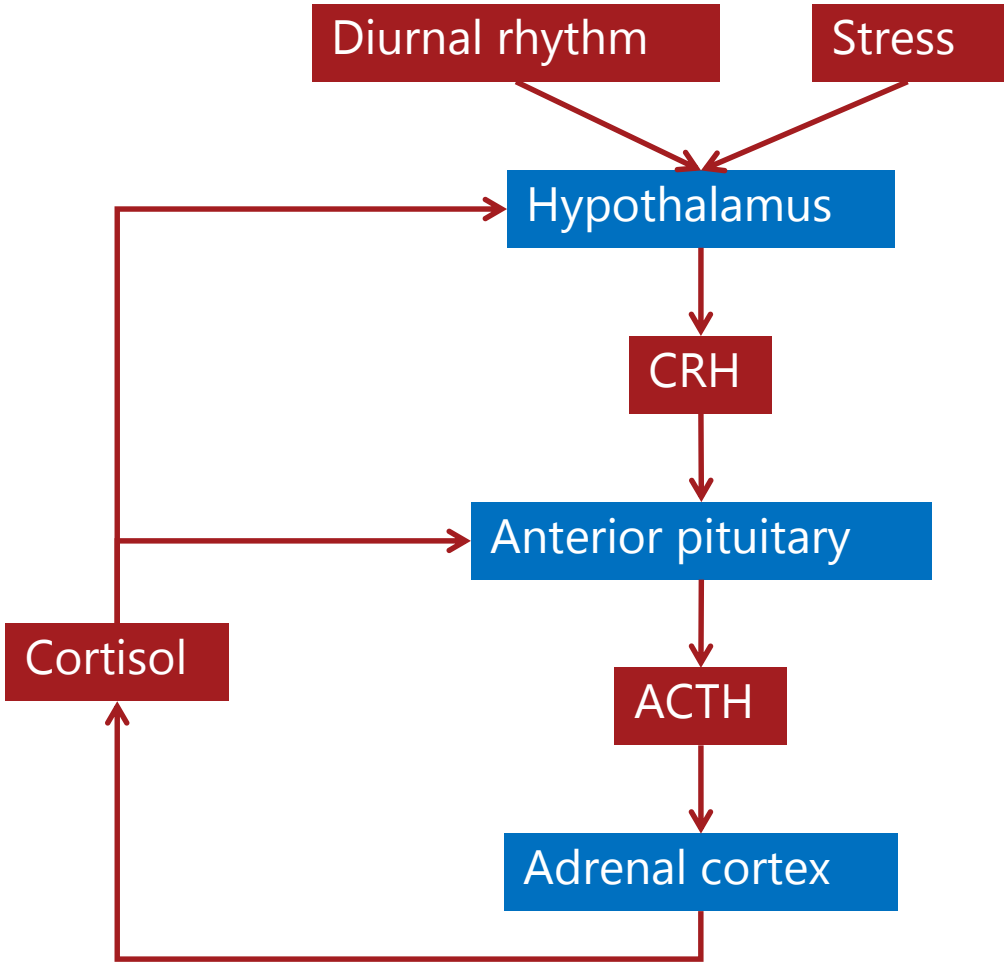
Cortisol

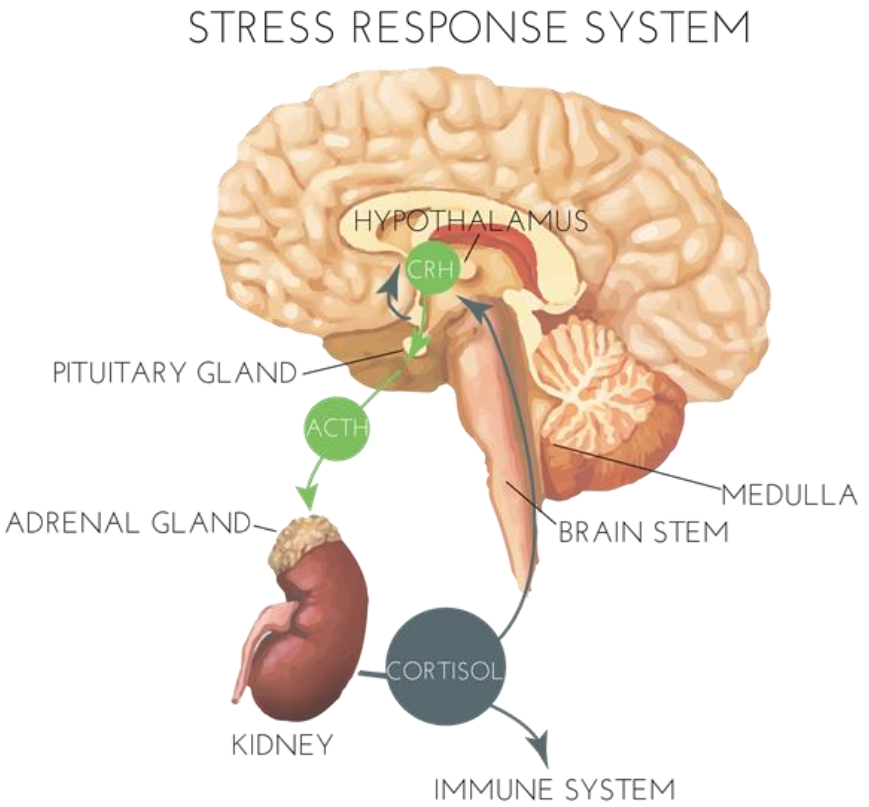
- Steroid hormone produced in the adrenal cortex regulated by a feed back mechanism
- Secreted in approx. 15 pulses during 24 hours
- Distinct diurnal variation - highest in the morning
- Effects of stressors: increase when mental exposure includes novelty and personal involvement, suppressed when mental exposure is prolonged
- Measure in saliva, blood, urine and hair

Cortisol stiger om morgenen og falder til det laveste om aftenen

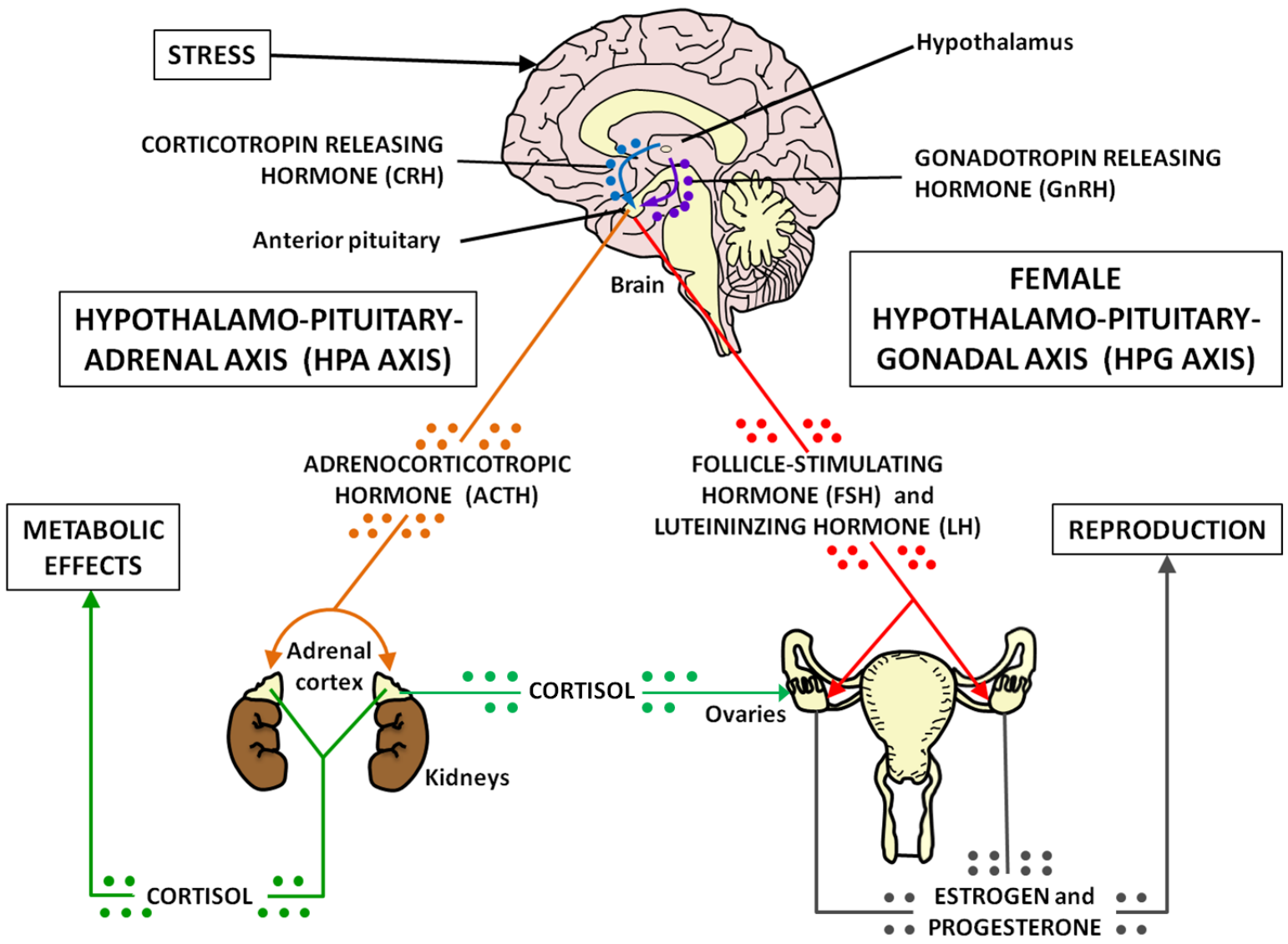


HPA-axis - negative feed back



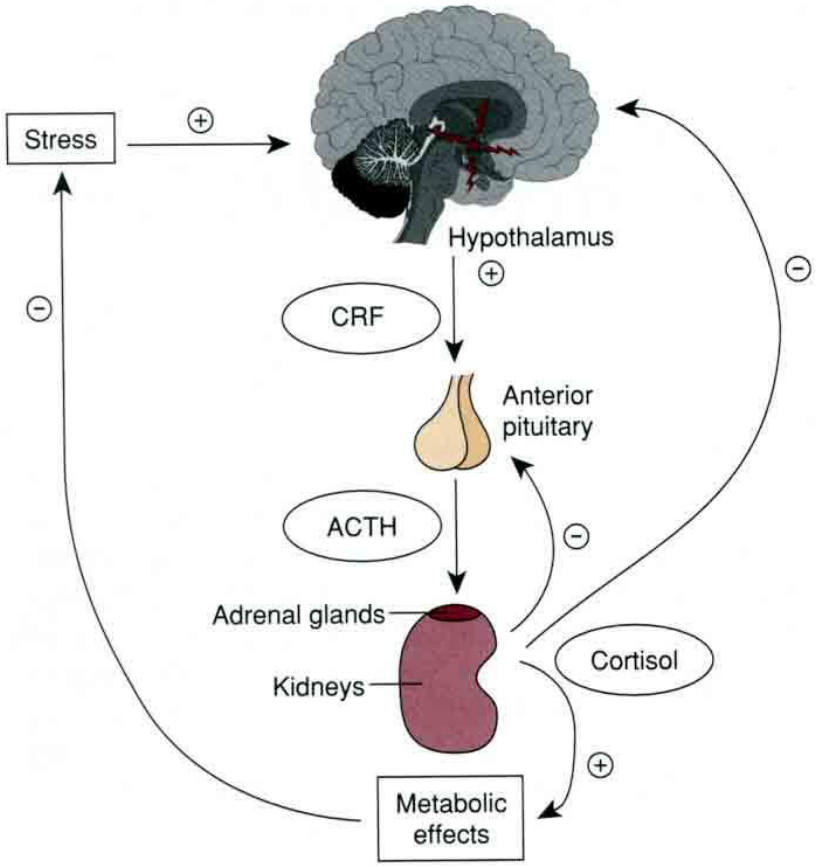


HPA axis and regulation



Wikepedia

HPA axis



- One behavioural level, for instance, depression may be interpreted as a consequence of sustained hyperactivity of the stress-system due to CRH overdrive, *hyperactivity* of the adrenergic system, and excess circulating glucocorticoid hormoner.
- Chronic *hypoactivity* of stress may lead to inertia, excessive fatigue and amotivational syndromes.

McEwen and Stellar 1993, Schulkin et al 1998

Opsummering

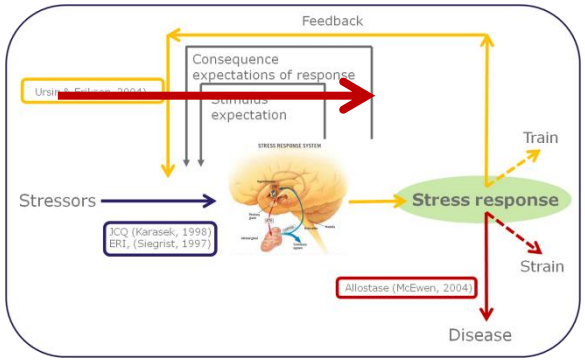
- Stress er en reaktion eller respons på ydre påvirkning (stressorer, stresspåvirkning), som manifesterer sig psykologisk og fysiologisk.
- Stressresponset er en tilpasningsmekanisme, der sikrer individet den fornødne energi og overskud, fysisk og mentalt, til at overkomme eventuelle forhindringer.
- Hverken stressorer eller stressresponset er i sin natur negativt, men gentagne eller vedvarende stresspåvirkninger, kan få helbredsmæssige konsekvenser.
  - **Kortvarig stress** gør os parate til at yde vores bedste
  - **Langvarig stress** er en tilstand af anspændthed og ulyst

Acute stress

Cardiovascular and cortisol reactivity and habituation to a virtual reality version of the Trier Social Stress Test: A pilot study.

- Peter Jönsson*, Mattias Wallergård*, Kai Österberg*, Åse Marie Hansen, Gerd Johansson*, Björn Karlson*

- *University of Lund Sweden



Jönsson et al 2010

The Trier Social Stress Test (TSST)

The VR system was a CAVE™ system with three rear projected walls (4 m 3 m), and one floor projection.

Jönsson et al 2010

Participants and methods

- Ten healthy men,
- mean age: 28.3 years (24—38 years)
- Two tests (1 week between sessions),
  - Measures: **salivary cortisol**, heart rate (HR), high frequency heart rate variability (HF-HRV, parasympathetic activity), and T-wave amplitude (TWA, suggested to be related to sympathetic influence on myocardial performance) were assessed.

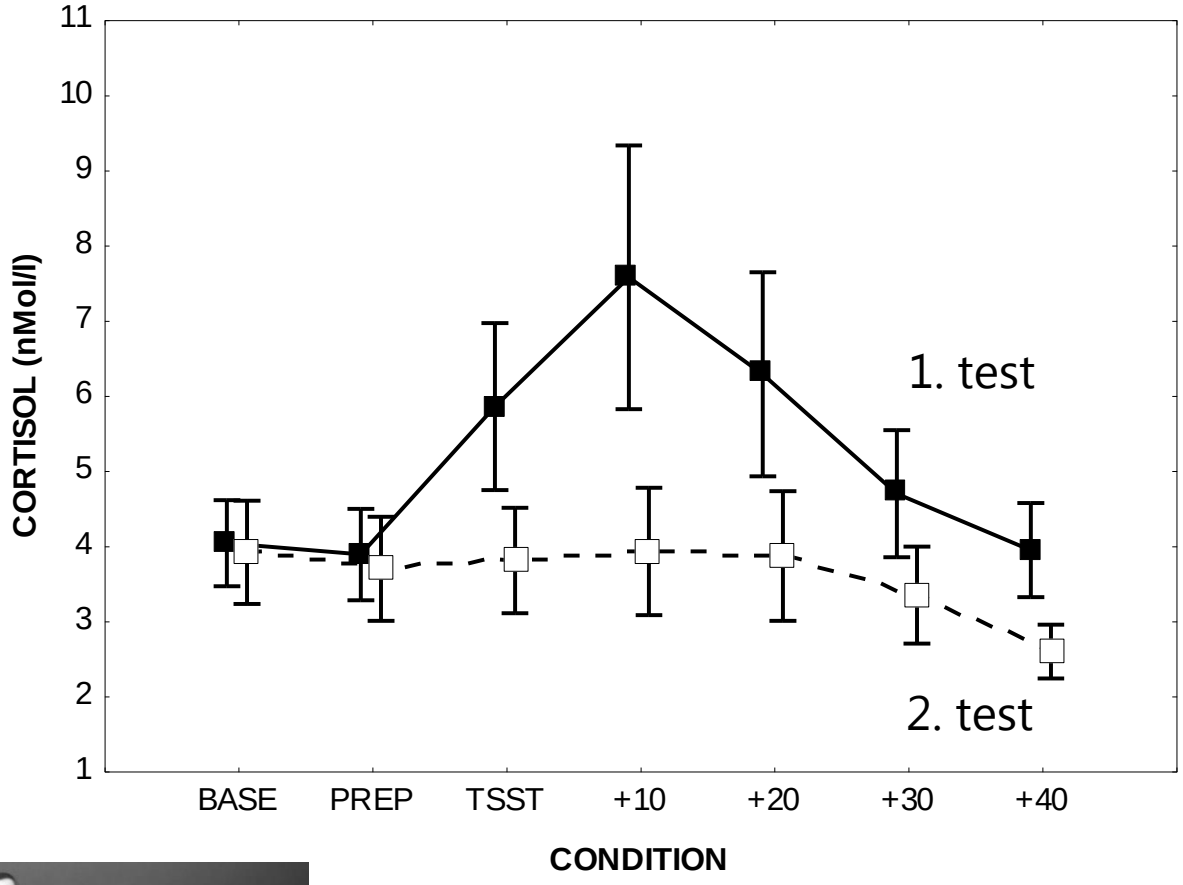
Jönsson et al 2010

Saliva sampling in the study

- Saliva cortisol was collected in sampling tubes with cotton swabs
- collected after BASE, PREP, TSST (SPEECH + MATH),
- REST + 10 min, +20 min, +30 min, and +40 min, i.e. 7 samples.

Jönsson et al 2010

Results from laboratory study



Jönsson et al 2010

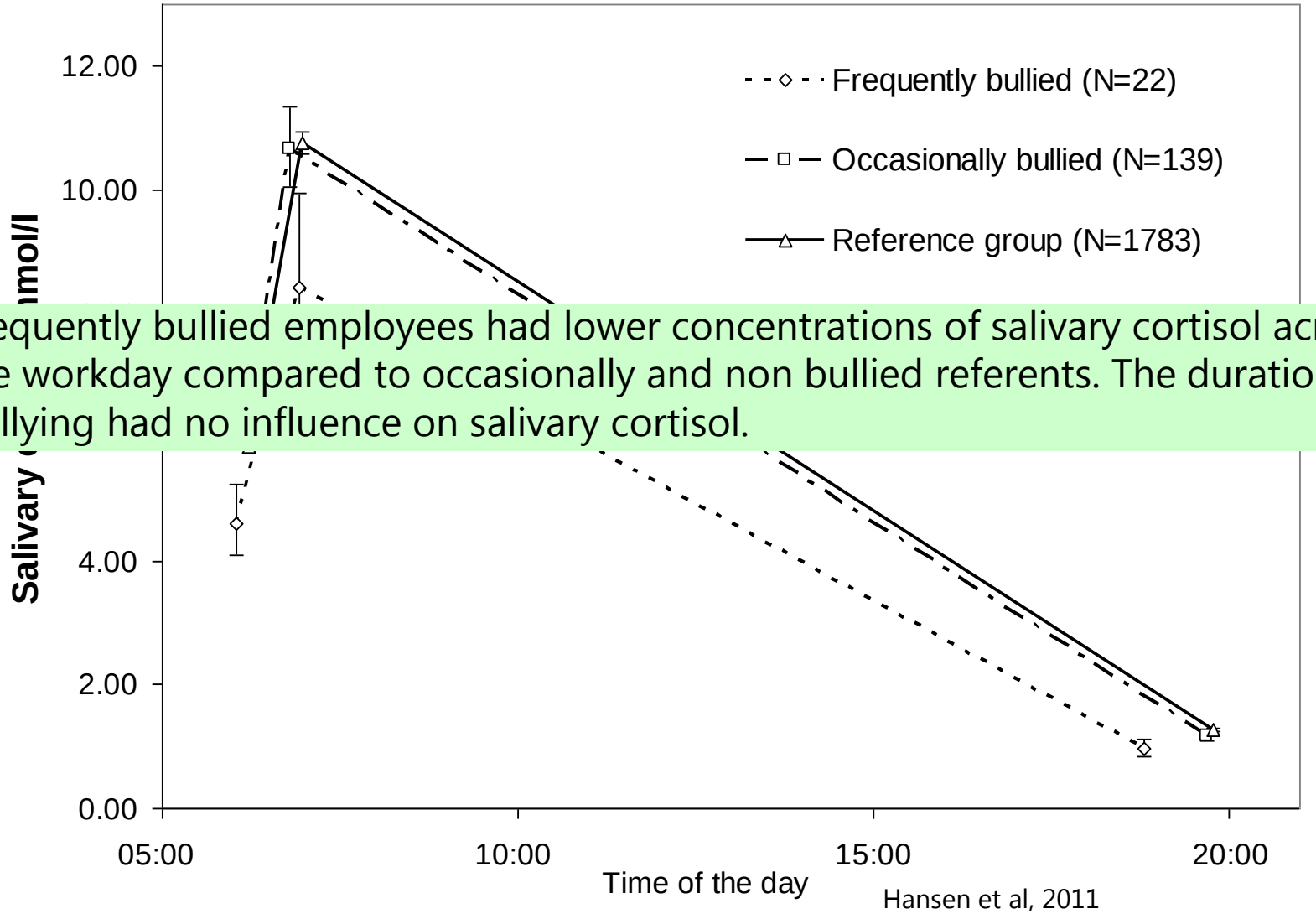
Longterm stress reactions

Mobning på Arbejdspladsen – definition

"Der er tale om krænkende handlinger, når en eller flere personer groft eller flere gange udsætter andre personer for adfærd, som af disse personer opfattes som nedværdigende. Krænkende handlinger er en samlet betegnelse for mobning, seksuel chikane og andre måder, som krænkelser kan forekomme på i arbejdet. Der kan både være tale om aktive handlinger og om at undlade at handle."

Arbejdstilsynet, Feb 2019

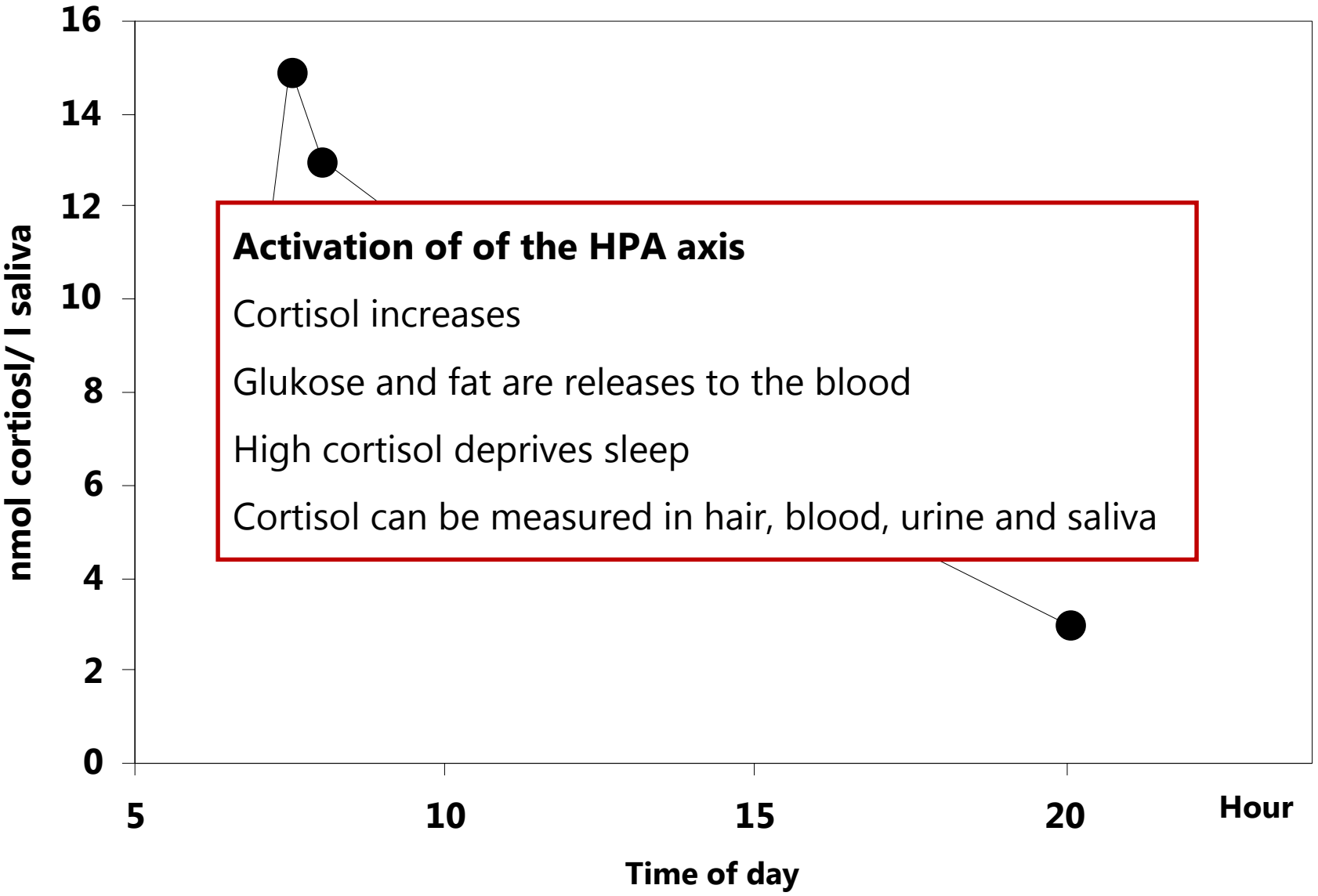
Results II. Salivary cortisol



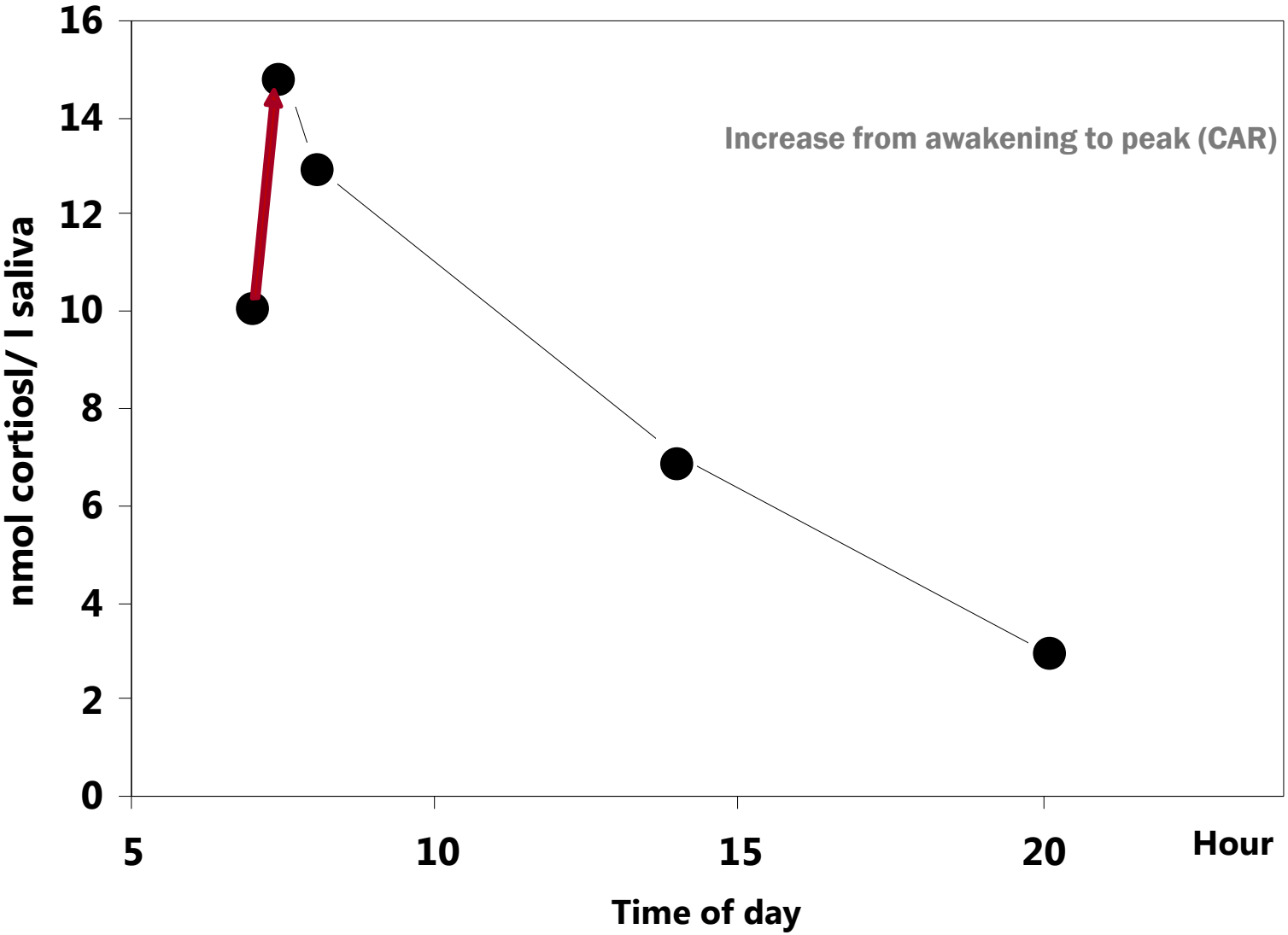
Frequently bullied employees had lower concentrations of salivary cortisol across the workday compared to occasionally and non bullied referents. The duration of bullying had no influence on salivary cortisol.

Hansen et al, 2011

Salivary cortisol, known as a stress hormone



Cortisol awakening response and derived measures of cortisol



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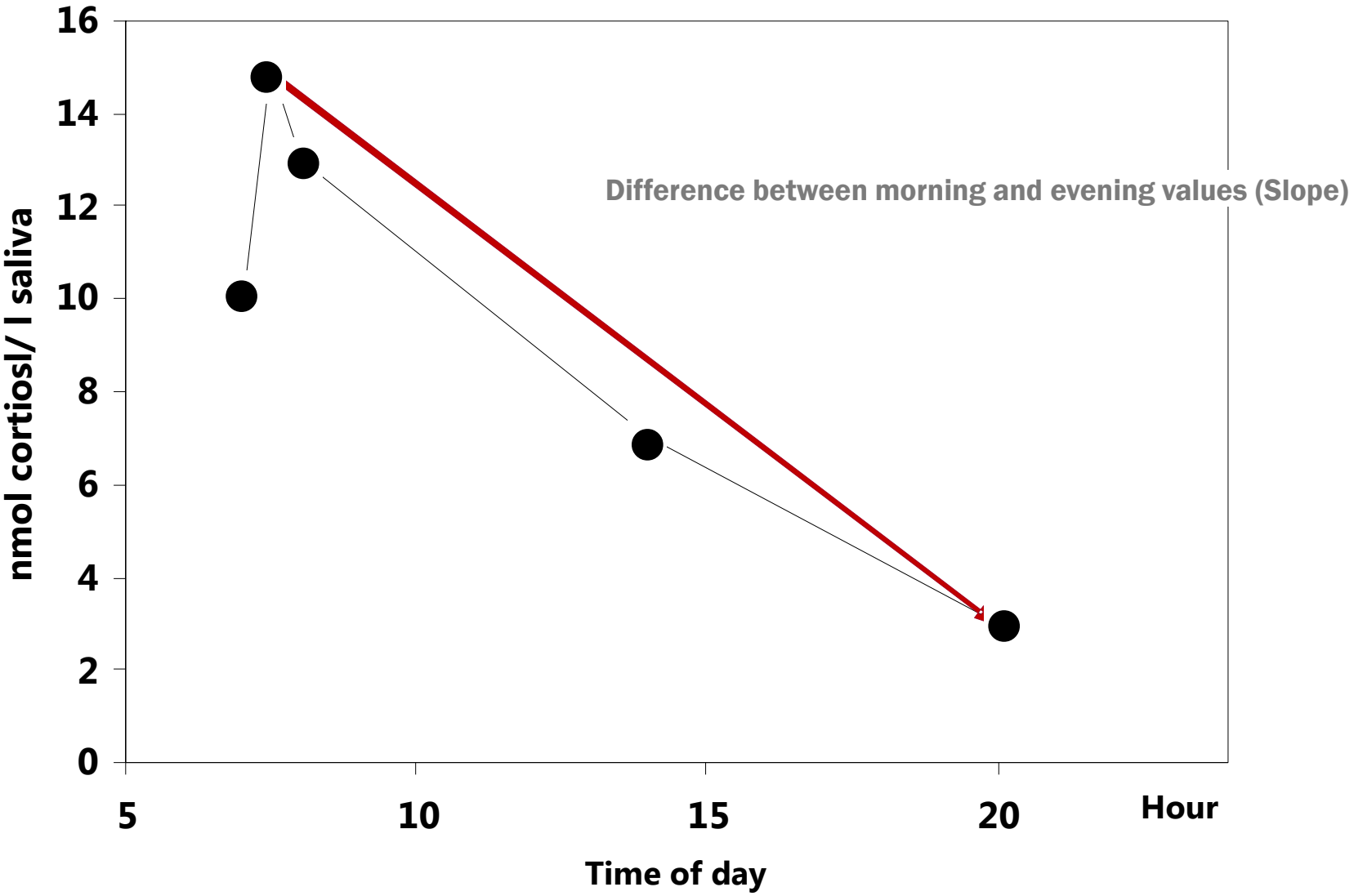
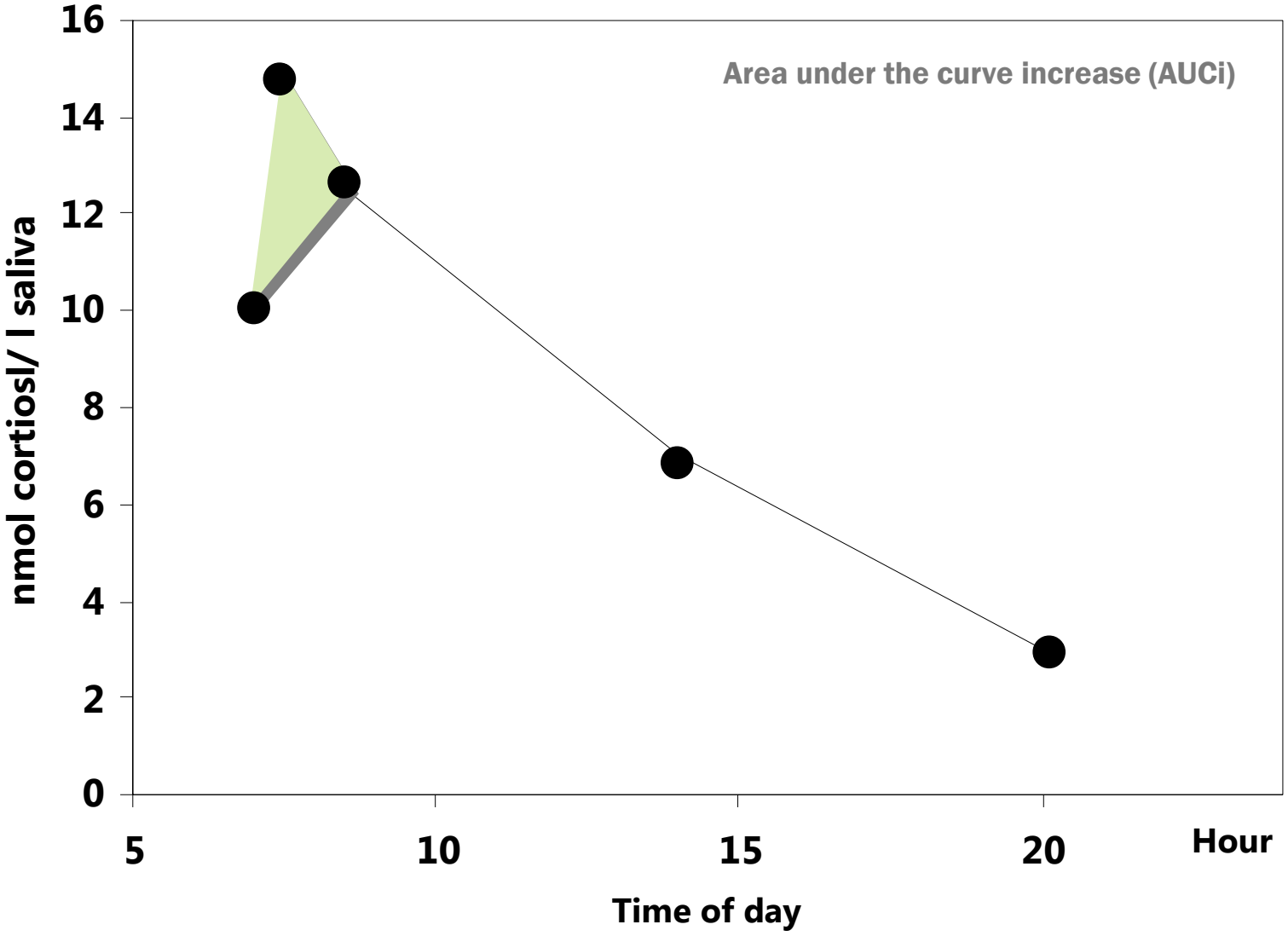
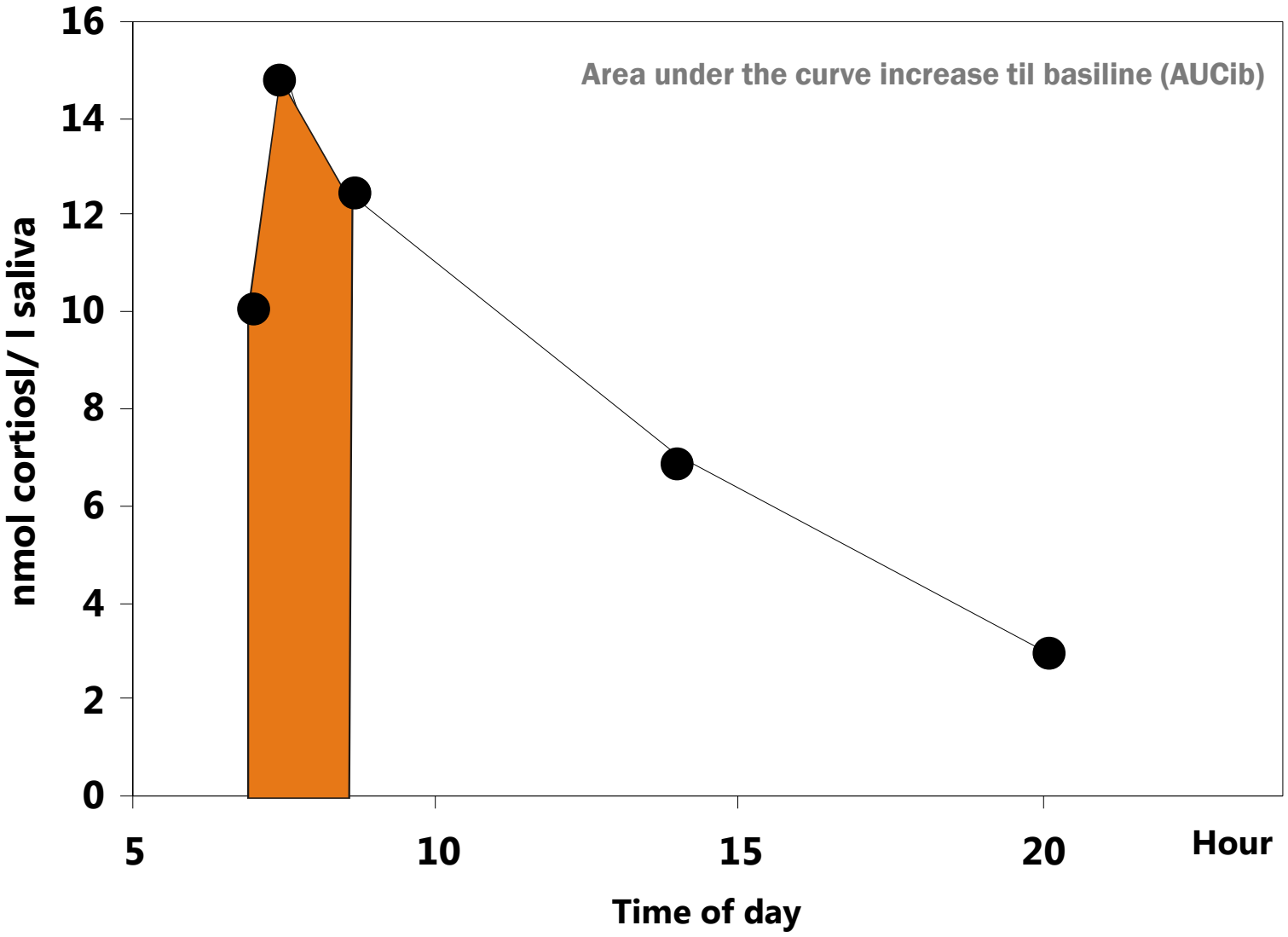


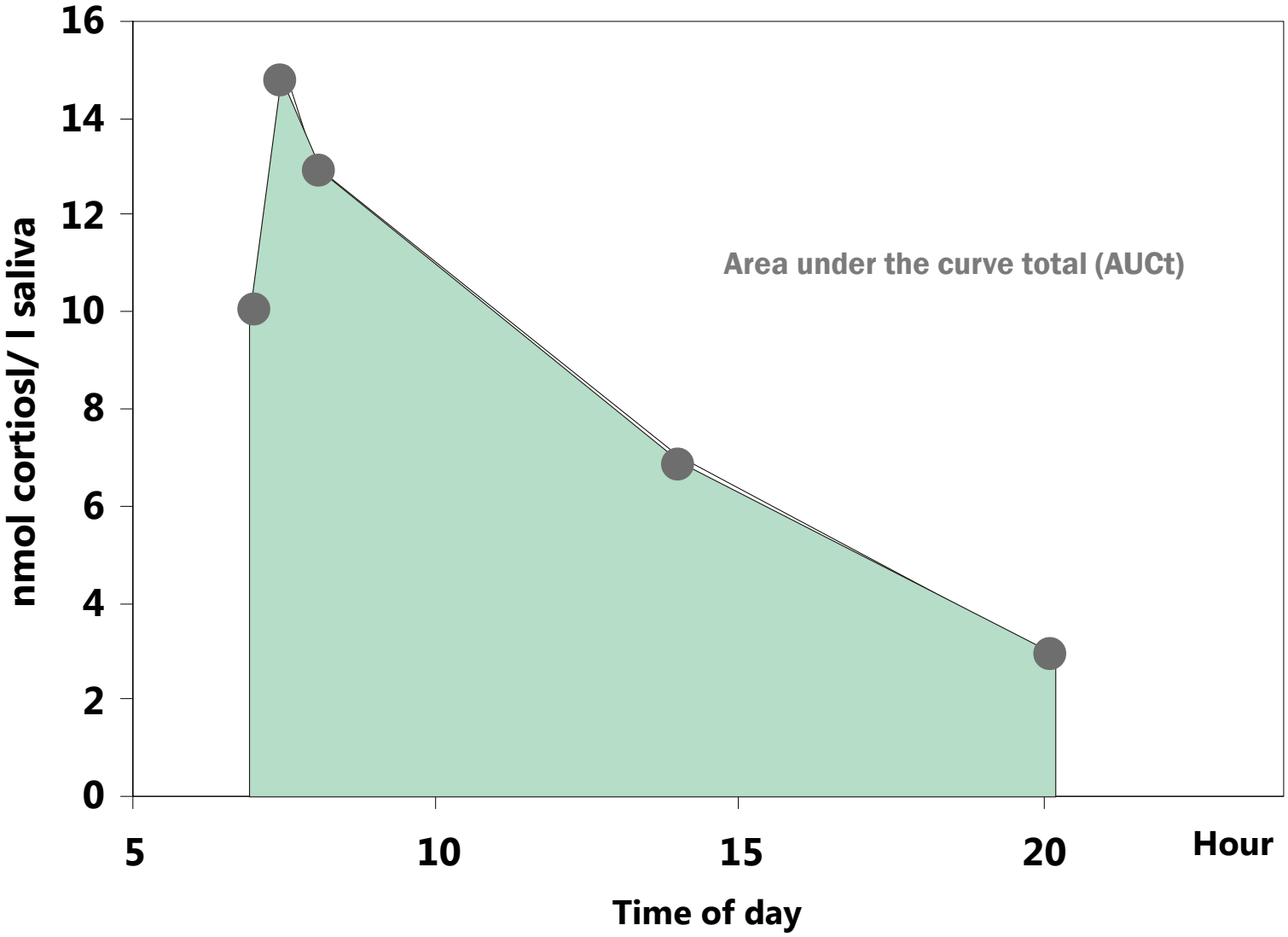
Cortisol awakening response and derived measures of cortisol



Cortisol awakening response and derived measures of cortisol



Cortisol awakening response and derived measures of cortisol



Salivary cortisol with all-cause and cardiovascular mortality

↓

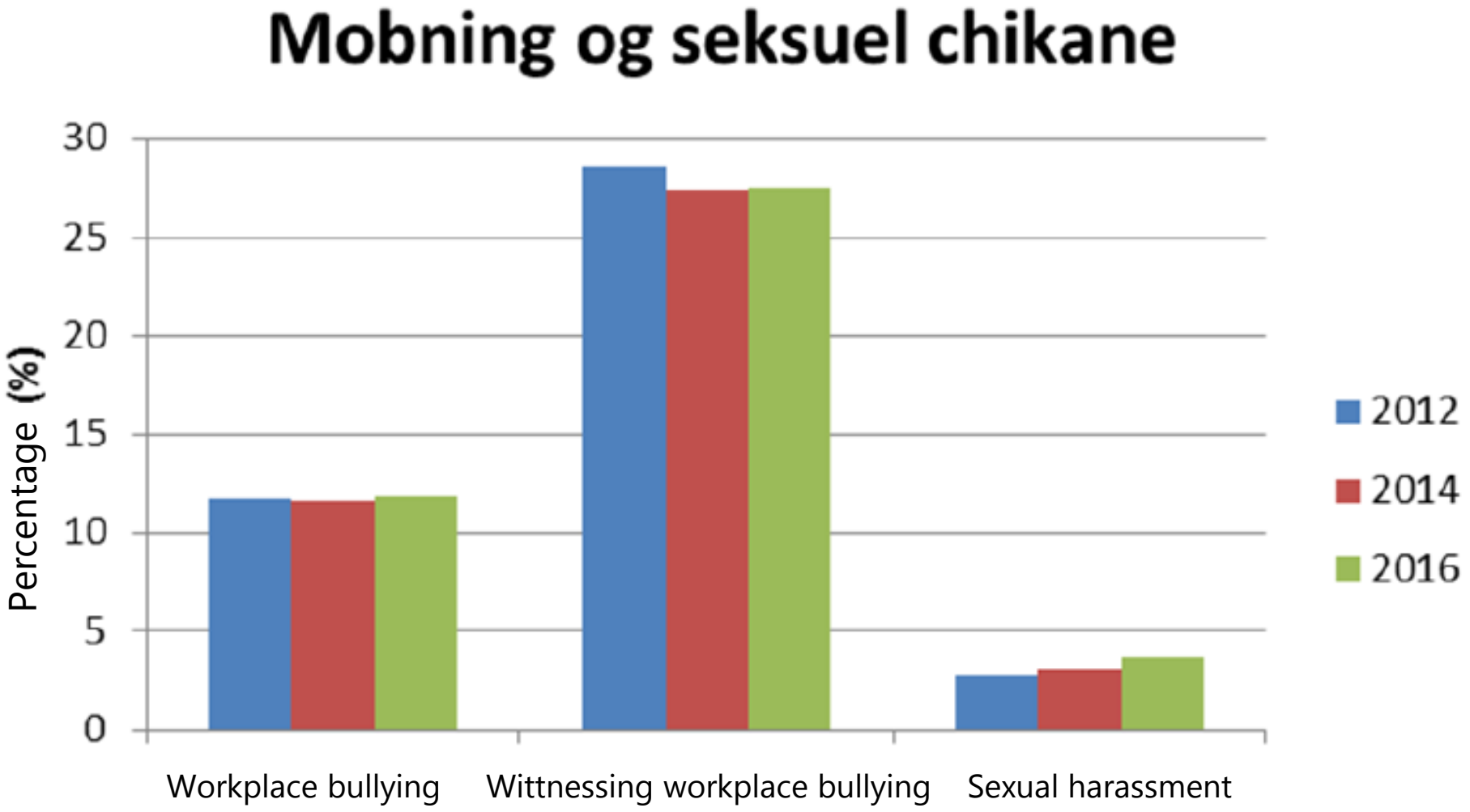
TABLE 3. HR of all-cause, cardiovascular, and noncardiovascular mortality among 4047 participants of the Whitehall II study from phase 7 (2002–2004) through to January 2010 by z-scores of measures of cortisol

	All-cause mortality	Noncardiovascular deaths	Cardiovascular deaths
Waking cortisol	0.94 (0.80–1.12)	0.93 (0.77–1.13)	0.95 (0.67–1.36)
CAR	0.94 (0.80–1.12)	0.90 (0.74–1.10)	1.12 (0.79–1.57)
Slope across the day	1.30 (1.09–1.55)	1.17 (0.96–1.43)	1.87 (1.32–2.64)
Bedtime cortisol	1.33 (1.11–1.59)	1.17 (0.96–1.44)	1.98 (1.39–2.81)

There were 139 all-cause deaths, 106 noncardiovascular deaths, and 32 cardiovascular deaths. One death from unknown cause was removed from the analysis. Numbers with bedtime cortisol were 137 all-cause deaths, 105 noncardiovascular deaths, and 32 events per 3977 total population for cardiovascular deaths. Data were adjusted for age, sex, employment grade, waking time on day of sample collection, and time of sample collection since waking at phase 7.

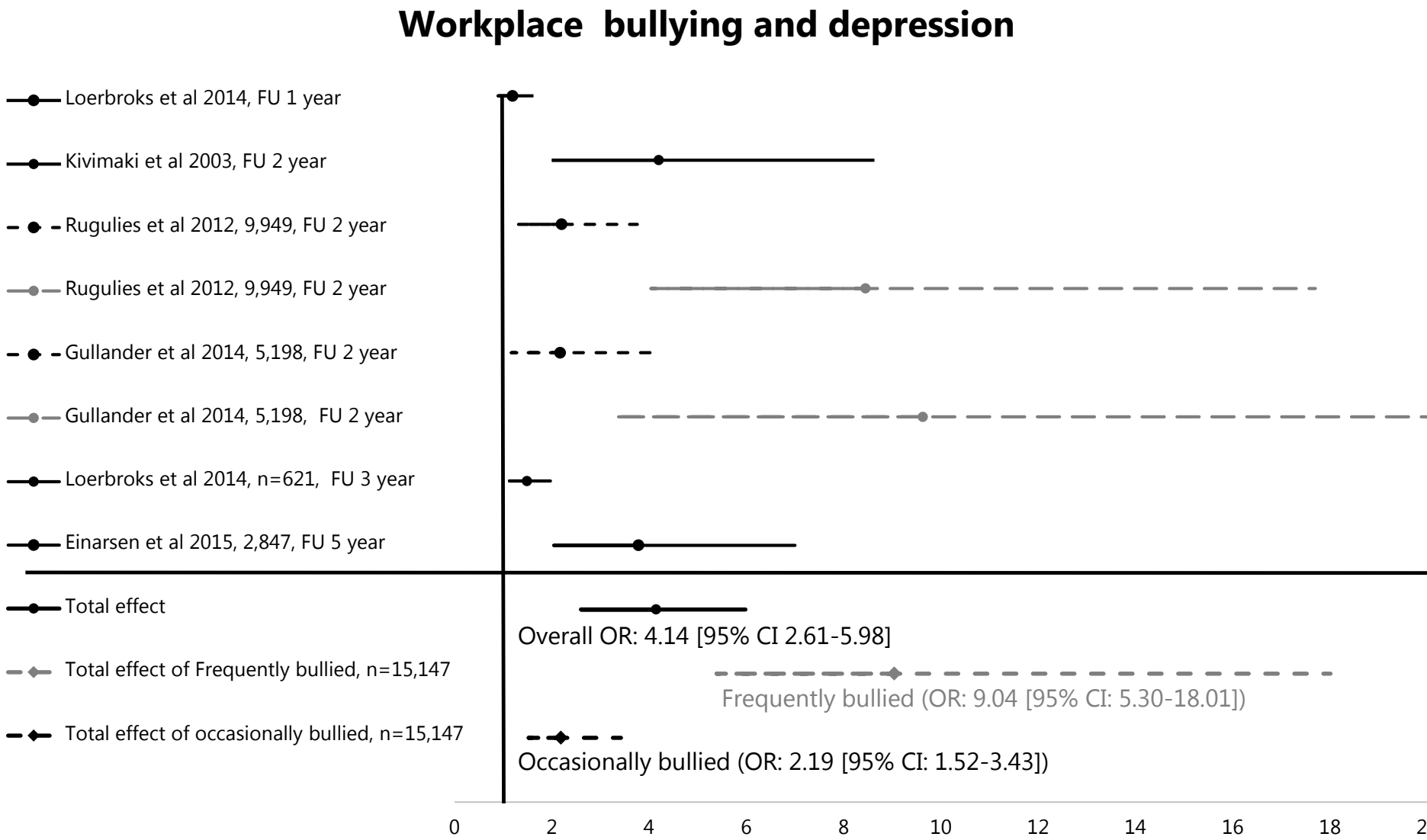
Mobning på arbejdspladsen som stressor

Arbejdsmiljø og Helbred 2012 - 2016



Work and Health Surveys, National Research Centre for the Working Environment: https://arbejdsmiljodata.nfa.dk/

Mobninpå arbejdspladsen og depression



Risk factors of workplace bullying

Organizational level

Stressful and poorly organized work environments

Agervold & Mikkelsen, 2004; Bowling & Beehr, 2006; Einarsen, Raknes, & Matthiesen, 1994;

Hauge, Skogstad, & Einarsen, 2007; Leymann, 1996; Rafnsdóttir & Tómasson, 2004.

Individual level

Negative social climate, many conflicts, lack of information

Lack social support from co-workers and supervisors

Høgh, Ortega, Giver, & Borg, 2007; Lakey, Tardiff, & Drew, 1994; Lee & Ashforth, 1996.

Measuring workplace bullying

Self-labelling item

Preceded by a definition '*Bullying takes place when employees are exposed to negative or offensive acts repeatedly over a longer period of time, which it is difficult to defend oneself against*'. Zapf et al 1995

- Have you been subjected to bullying at work within the past 6 months?

Response options:

- Yes/ No
- Never, now and then, monthly, weekly, and daily

Measuring workplace bullying

Negative acts questionnaire (22 items) Einarsen et al 2009

Examples of items:

- Someone withholding information which affects your performance
- Spreading of gossip and rumors about you
- Being shouted at or being target of spontaneous anger
- Repeated reminders of your errors or mistakes
- Persistent criticism of your work and effort

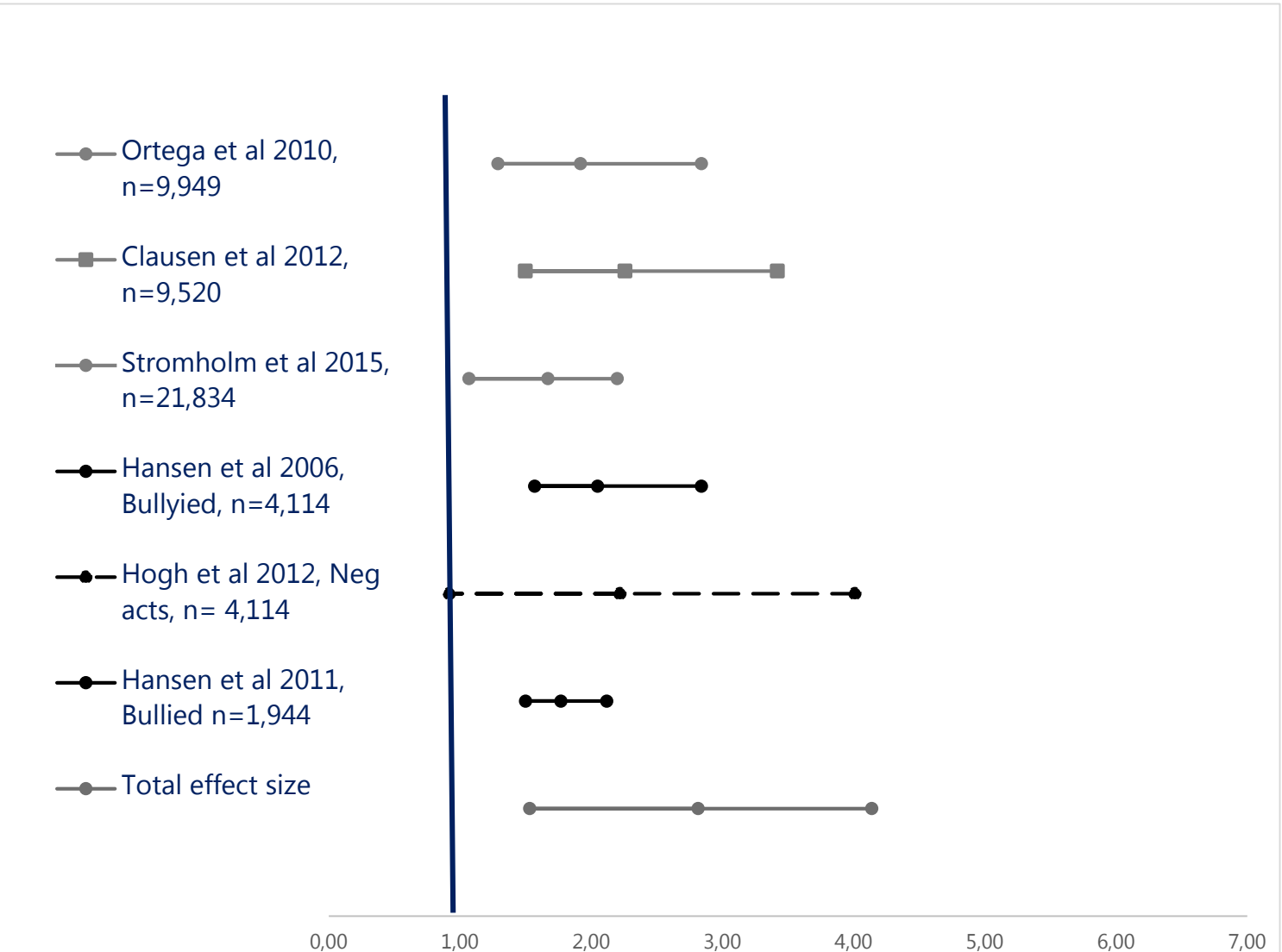
…

Response options:

Never, now and then, monthly, weekly, and daily (papers V)

- Five scales were established
  - Social isolation; Direct harassment; Intimidating behavior; Work-related acts; and Physical violence.

Workplace bullying and long-term sickness absence



Chronic stress responses

Kan medføre

- *Hyperaktivitet* af stresssystemet kan føre til overdreven cirkulerende glukokortikoidhormon (kortisol).
- *Kronisk hypoaktivitet* af stress kan føre til inerti, overdreven træthed og amotivationelle syndromer.

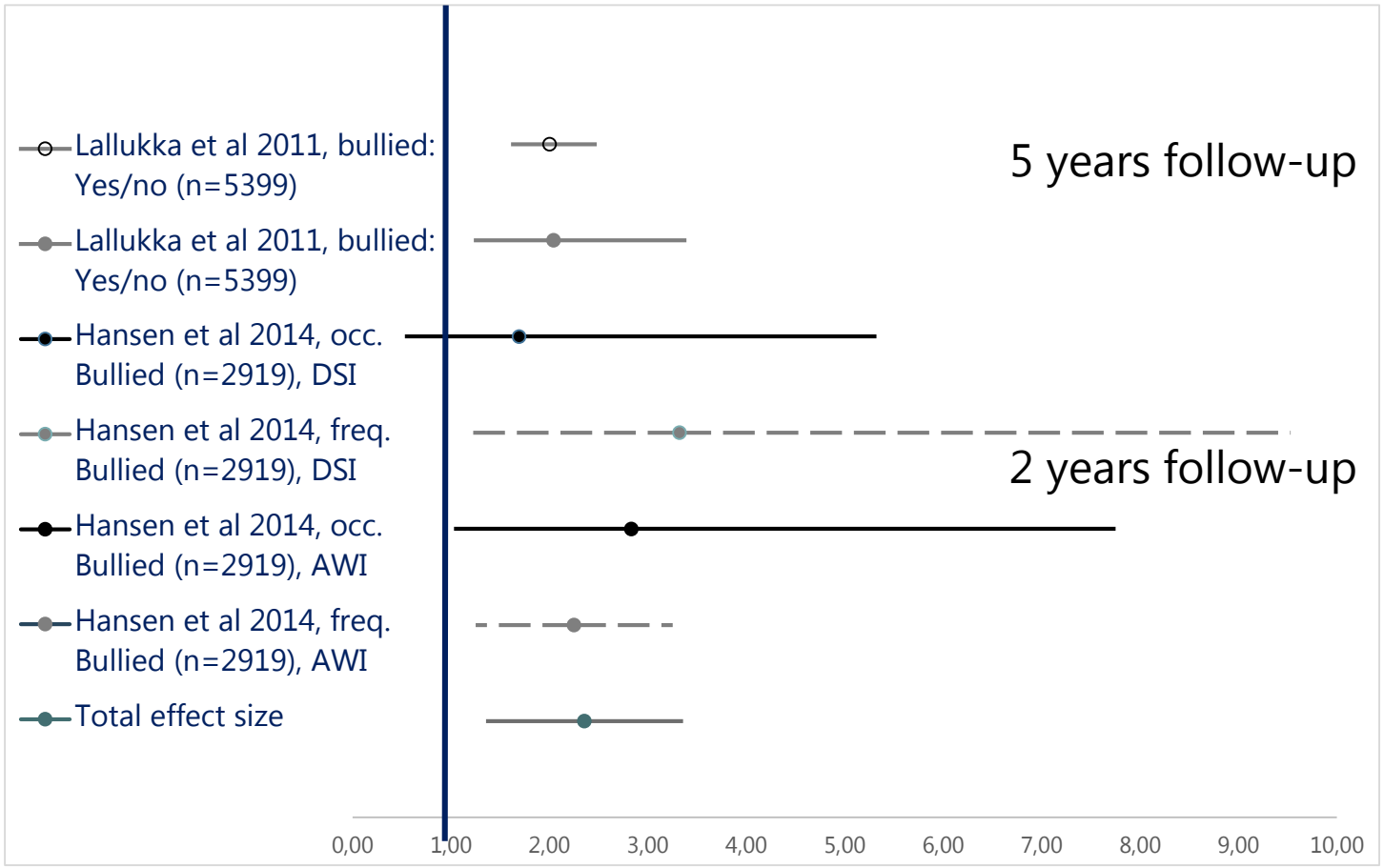
McEwen and Stellar 1993; Schulkin et al 1998; McEwen 1998.

Mobning på arbejdspladsen og kortisol i spyt

Resultaterne er ikke entydige

- Kudielka et al. 2003 finder at mobbede ansatte har lavere kotisol på en arbejdsdag sammenlignet med en fridag.
- Tre danske studier finder at ansatte der rapporterer mobning har lavere kortisol, især om morgenen (Hansen et al 2006 and 2011; Hogh et al 2012)
- Et case control studier finder ingen forskel mellem mobbede og ikke mobbede (Le Lac et al. 2012)
- Et kohorte studie finder ingen forskel mellem mobbede og ikke mobbede (Gullander et al 2015)

Mobning på arbejdspladsen og søvnproblemer i follow-up studier



OR [CI]

2.00 [1.61; 2.48]

2.04 [1.23; 3.39]

1.69 [0.53; 5.32]

3.32 [1.16; 9.53]

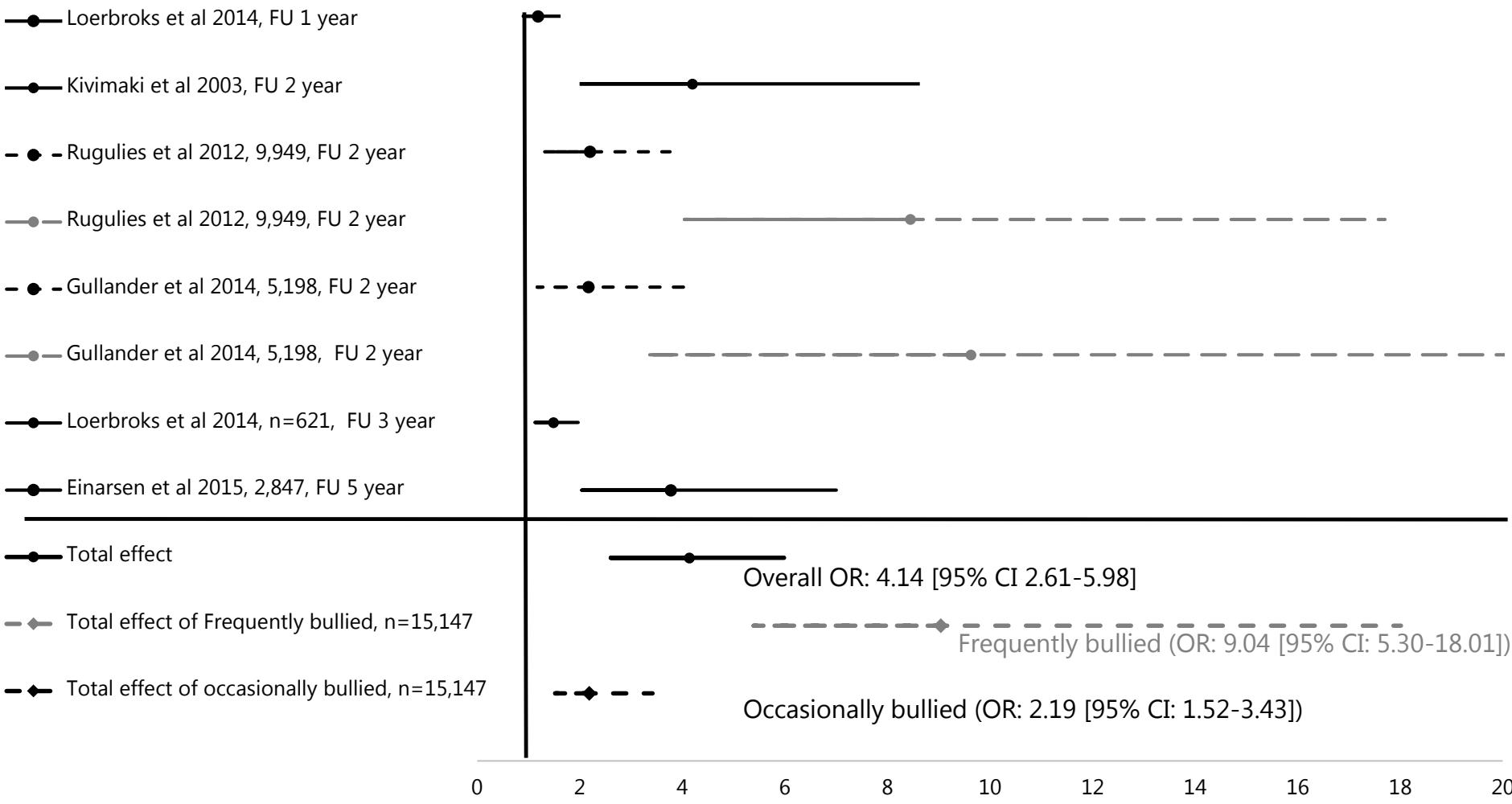
2.83 [1.03; 7.75]

2.25 [0.76; 6.61]

2.36 [1.05; 5.85]

DSI= disturbed sleep; AWI=Awakening problems

Workplace bullying and depression



Workplace bullying and CVD (HR (95% CI))

Workplace bullying and CVD in four different cohorts from Sweden and Denmark

SLOSH (N=10672)	1.27 (0.71-2.29)
DWECS (N=7992)	1.92 (1.07-3.45)
SWES95-01 (N=39252)	1.68 (1.22-2.32)
SWES07-11 (N=21039)	1.45 (0.94-2.28)
Total	1.59 (1.28-1-98)

Workplace bullying was between 7 and 13%

European Heart Journal **Xu, T. et al 2018, In press**

Workplace bullying and workplace violence as risk factors for cardiovascular disease: a multi-cohort study

Workplace bullying and type II diabetes (HR (95%CI)

Workplace bullying and type II diabetes in five Scandinavian cohorts

SWES95-01	(N=22104)	1.60 (1.11-2.30)
SWES07-95	(N=4596)	0.87 (0.46-1.65)
SLOSH	(N=7907)	1.49 (1.10-2.01)
FPS	(N=6145)	1.34 (0.90-1.99)
DWECS	(N=4995)	1.73 (1.15-2.62)
Total	(N=45647)	1.46 (1.23-1.74)

Diabetologia (2018) 61:75–83
https://doi.org/10.1007/s00125-017-4480-3

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ARTICLE

Workplace bullying and violence as risk factors for type 2 diabetes: a multicohort study and meta-analysis

Tianwei Xu[1,2] · Linda L. Magnusson Hanson[2] · Theis Lange[3,4] · Liis Starkopf[3] · Hugo Westerlund[2] · Ida E. H. Madsen[5] · Reiner Rugulies[1,5,6] · Jaana Pentti[7,8] · Sari Stenholm[7,8] · Jussi Vahtera[7,8] · Åse M. Hansen[1,5] · Mika Kivimäki[9,10,11] · Naja H. Rod[1,2]

Mobning på arbejdspladsen og arbejdsmarkeds-tilknytning

- Arbejdsløshed (Glambek et al. 2015)
- Jobskifte (Glambek et al. 2015, Hogh et al. 2011, Hogh 2012, Berthelsen et al 2011, Clausen et al. 2013, Clausen et al. 2016)
- Ønske om at skifte job (Berthelsen et al 2011, Houshmand et al. 2012, Moreno-Jimenez et al. 2012, Glamsbek et al. 2014)

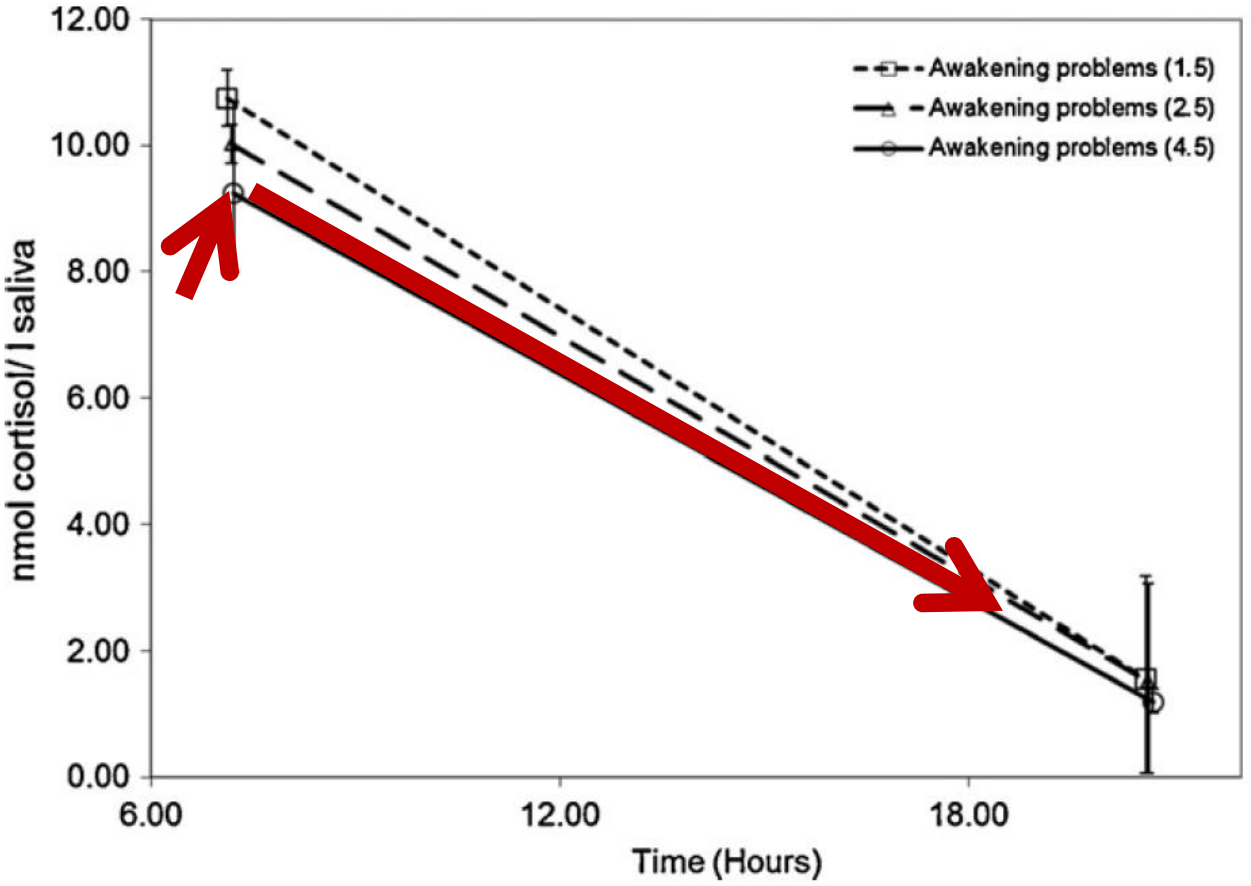
Mobning på arbejdspladsen og det fysiologiske stress response

Sleep and salivary cortisol

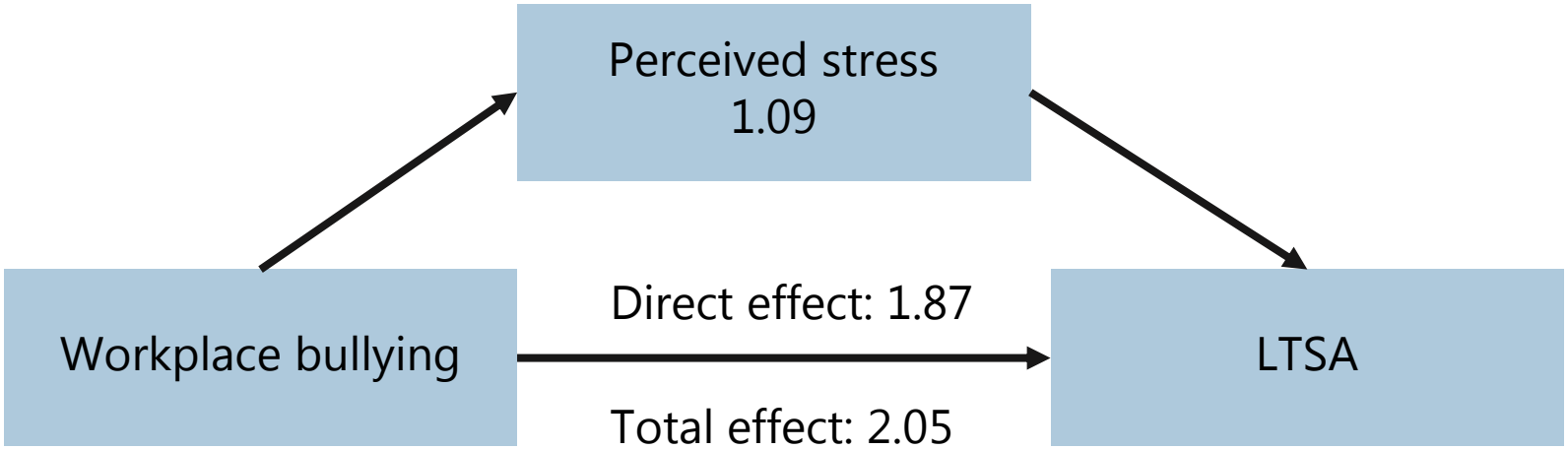
Sleep problems → Salivary cortisol

Sleep problems during the past four weeks were associated with low morning and evening saliva cortisol concentrations.

Cortisol awakening response (CAR) and slope three month later were significantly lower among participants with disturbed sleep

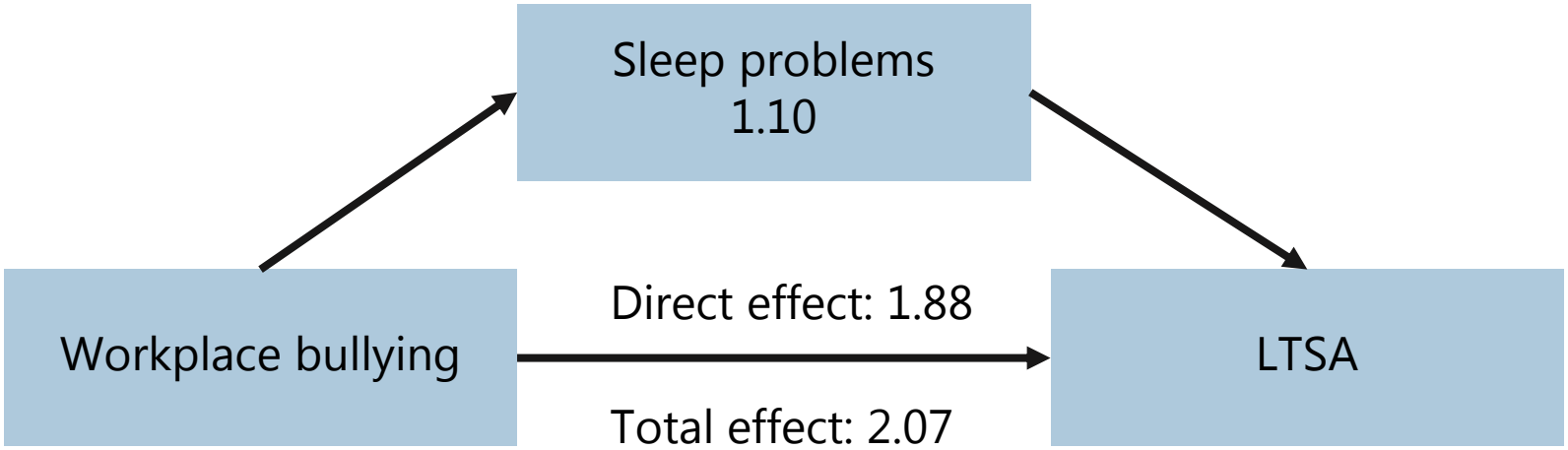


Perceived stress as a possible mechanism (Grynderup et al 2016)



Perceived stress explained 13% of the association between workplace bullying and long-term sickness absence (LTSA)

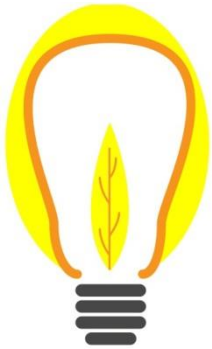
Workplace bullying, sleep and long-term sickness absence (Nabe-Nielsen et al 2017)

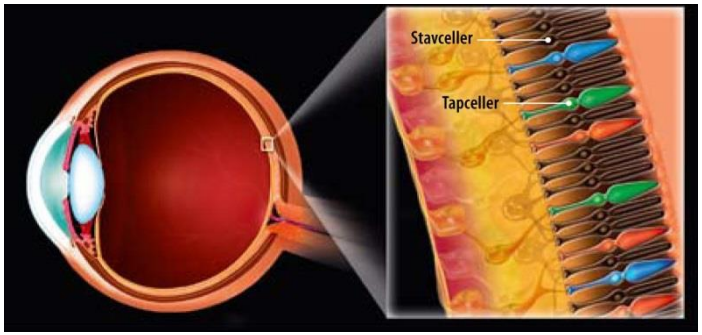


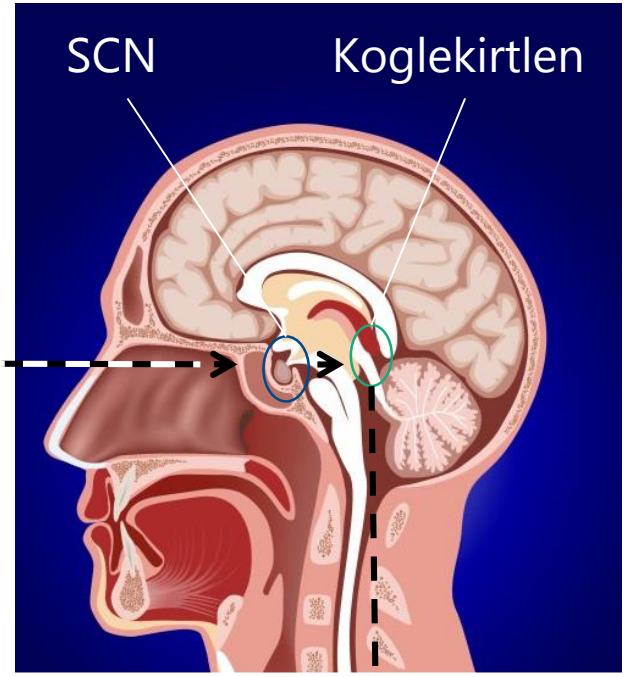
Sleep problems explained 13 % of association between workplace bullying and long-term sickness absence (LTSA)

Natarbejde som stressor

Lys og natarbejde







Lyset giver information til vores døgnrytmer

→ fx Melatonin niveauer falder

SCN – Suprachiasmatic nucleus

Døgnrytmer

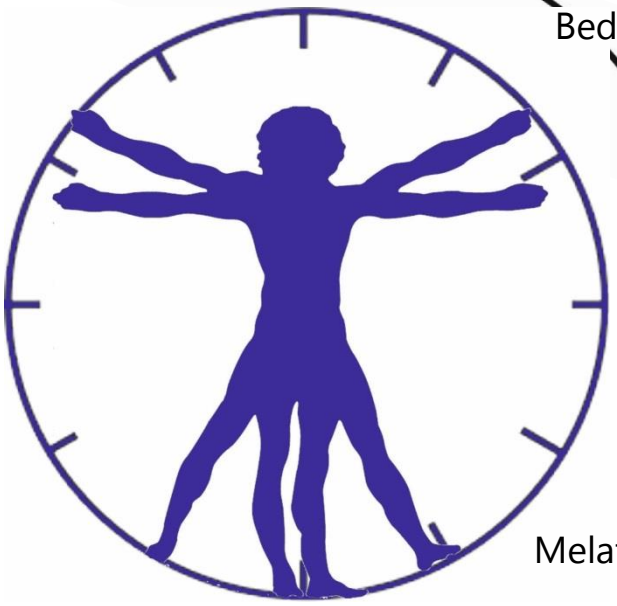
Middag

Mest alert kl. 10:00

Bedste koordination kl. 14:30

Hurtigste reaktionstid
kl. 15:30

Melatonin sekretion stopper
kl. 7:30



Laveste kropstemperatur
kl. 4:30

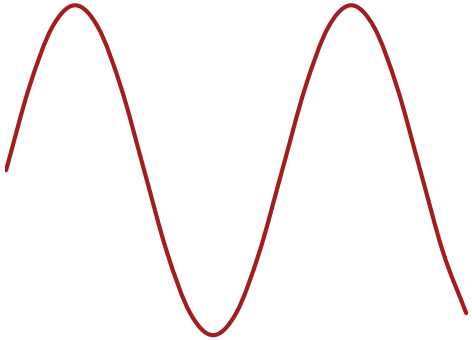
Højeste kropstemperatur
kl. 19:00

Dybeste søvn kl. 2:00

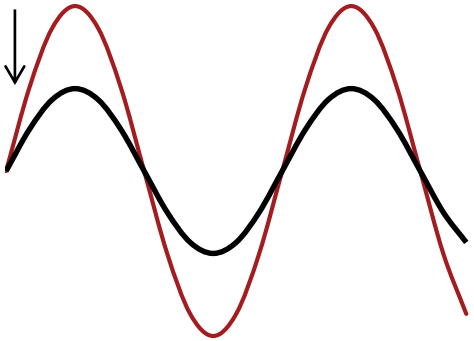
Melatonin sekretion starter kl. 21:00

Midnat

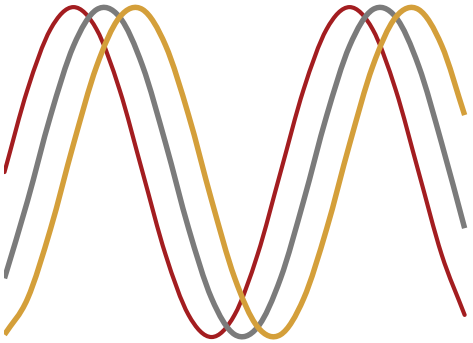
Lys om natten kan forstyrre vores døgnrytmer



Mindre amplitude



Faseforskydning



MIDT OM NATTEN

Anne Helene Garde (projektleder),
Marie Aarrebo Jensen
Åse Marie Hansen
Jesper Kristiansen
Kirsten Nabe-Nielsen

Kim Hoffmann Erichsen
Niels Hedeager
Flemming Olsen

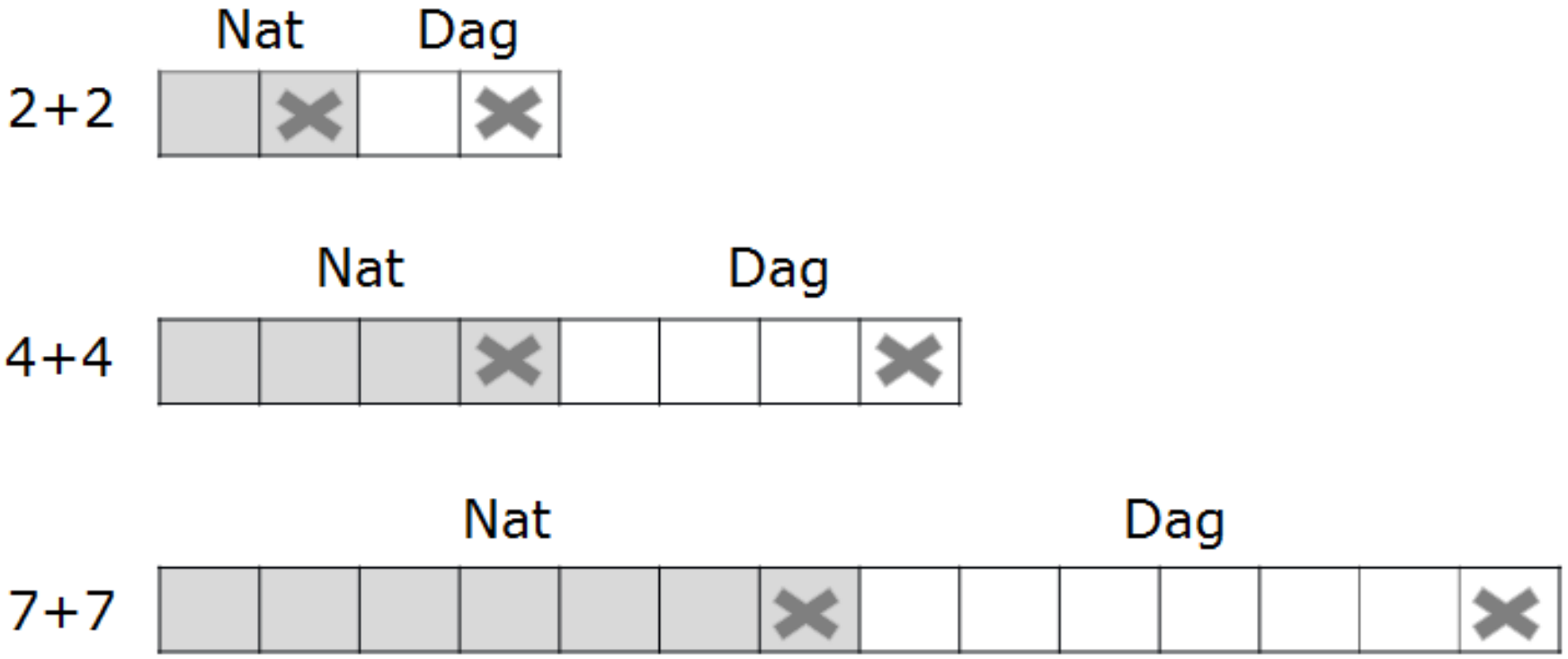
Projektet er støttet af Arbejdsmiljø-forskningsfonden og Københavns Universitet.

Formål

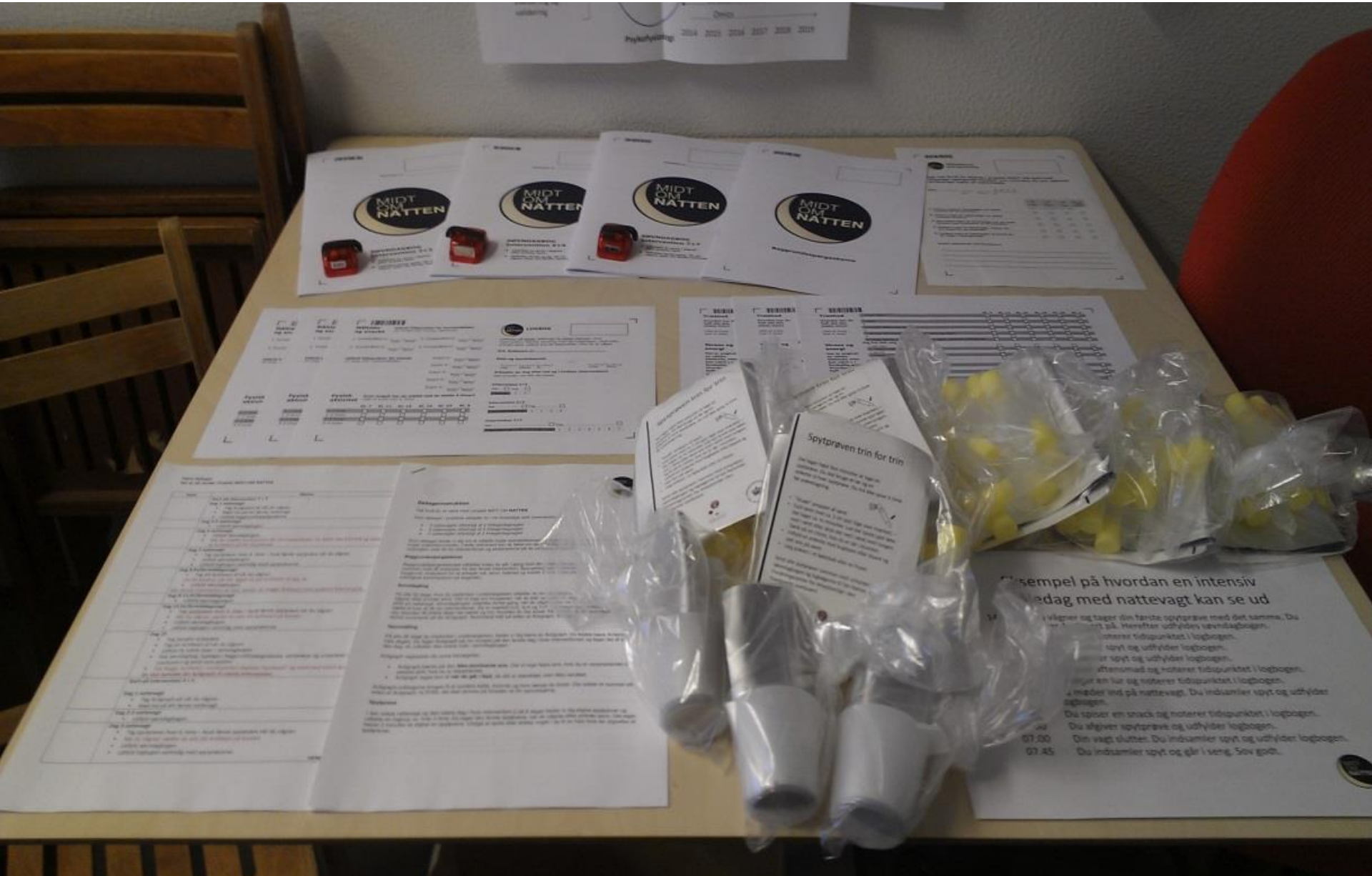
At undersøge, hvad det betyder at arbejde henholdsvis 2, 4 eller 7 nætter i træk for:

- Søvn
- Balancen i det autonome nervesystem
- Hormoner/døgnrytmer
- Præferencer

Alle deltagere har arbejdet nat på 3 forskellige måder



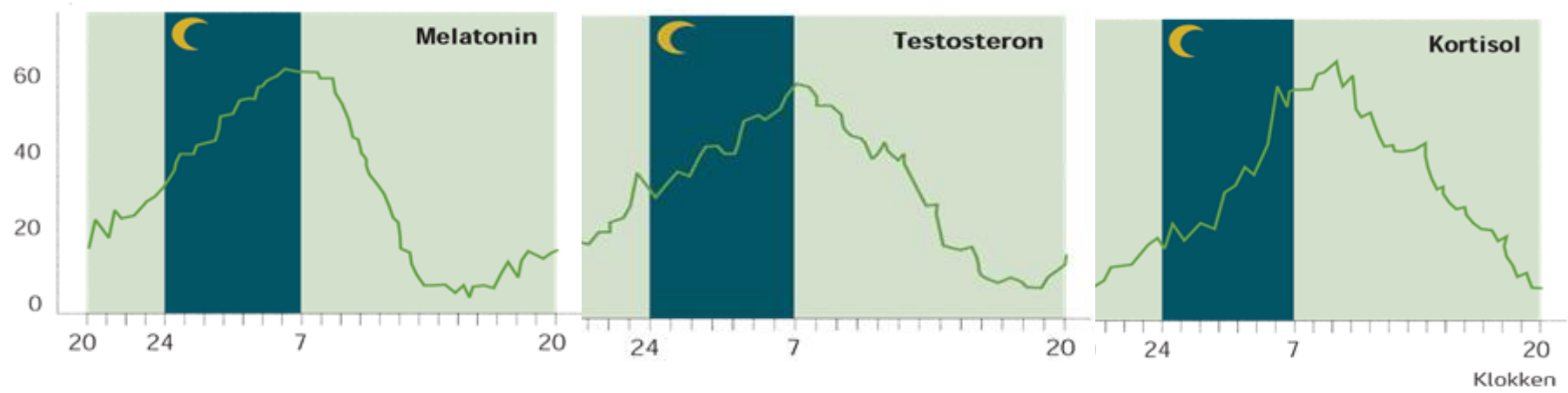
Metoder



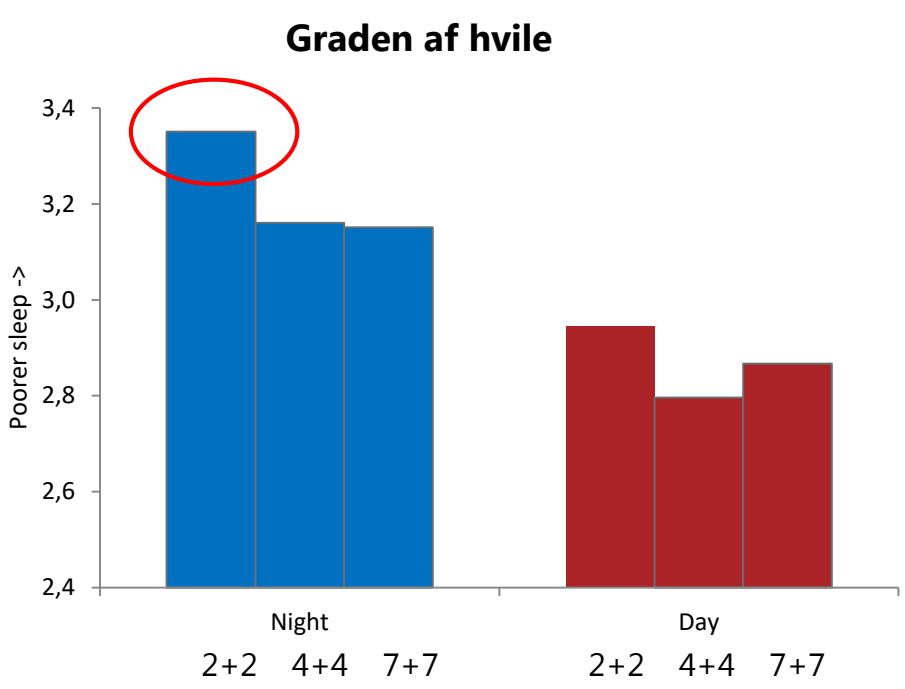
Spytprøver

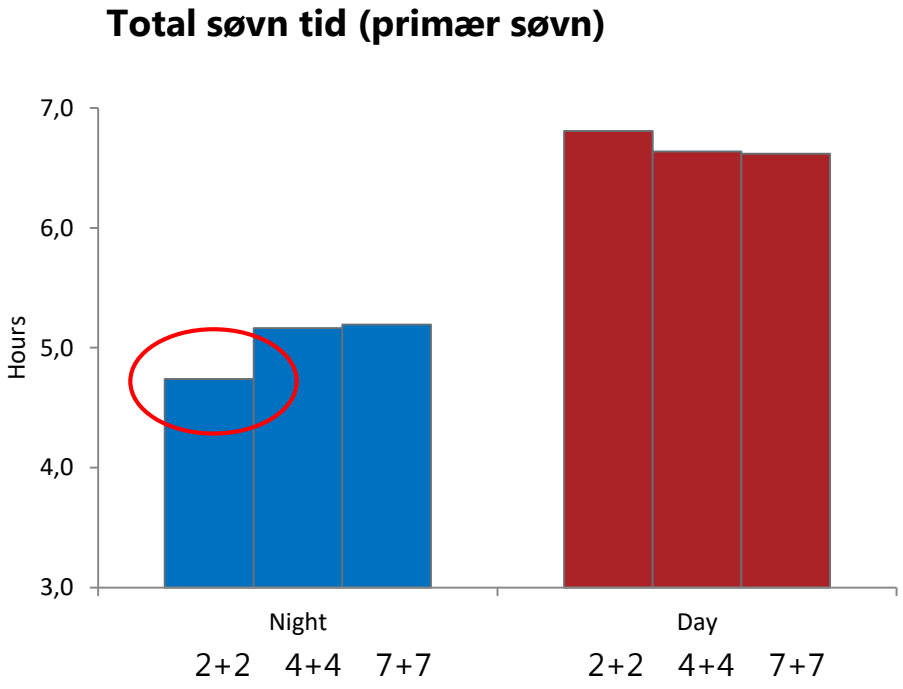
Hver 4. time, når du er vågen
(samtidigt med logbøger).

Måling af melatonin, kortisol og testosteron



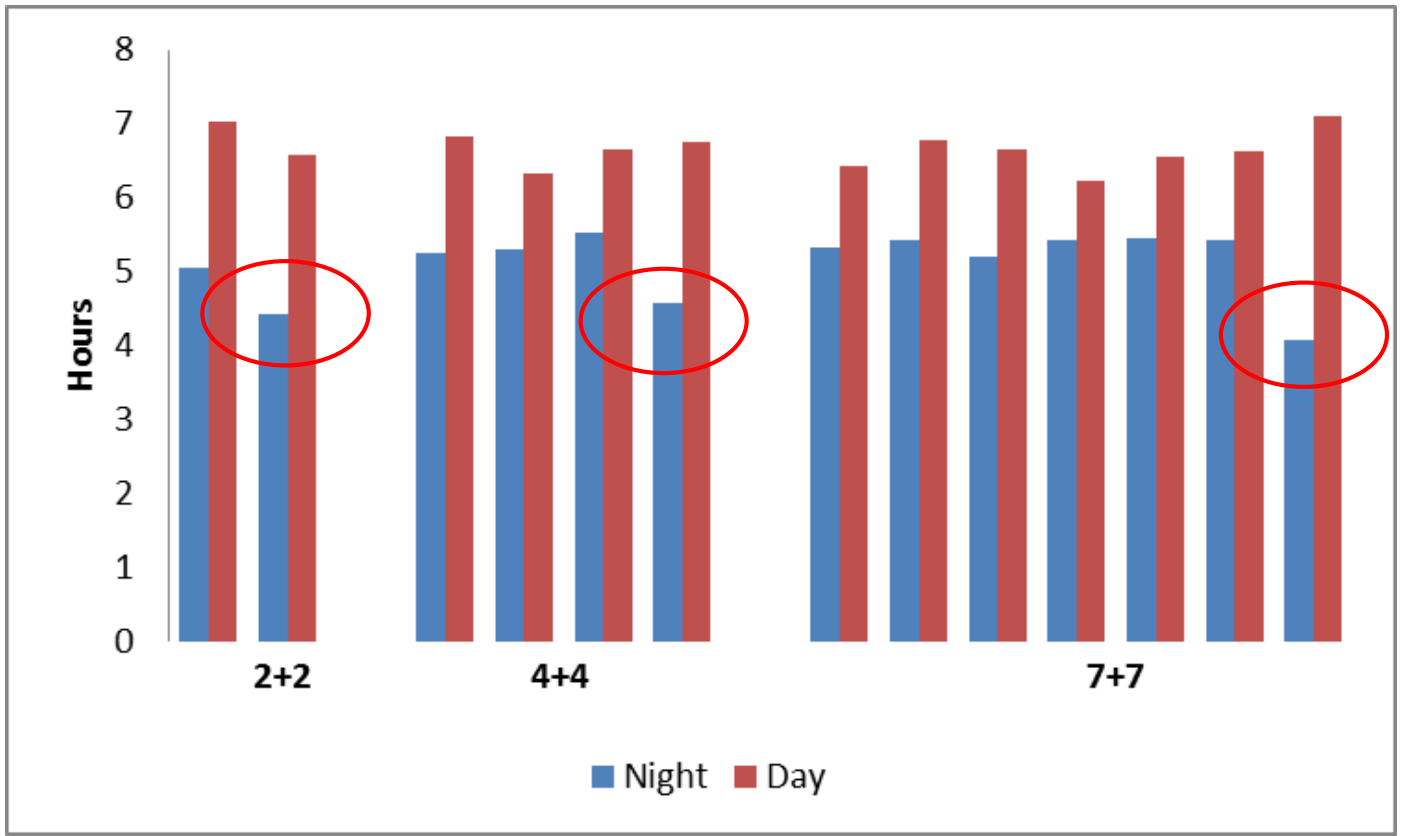
Gennemsnitlig søvn



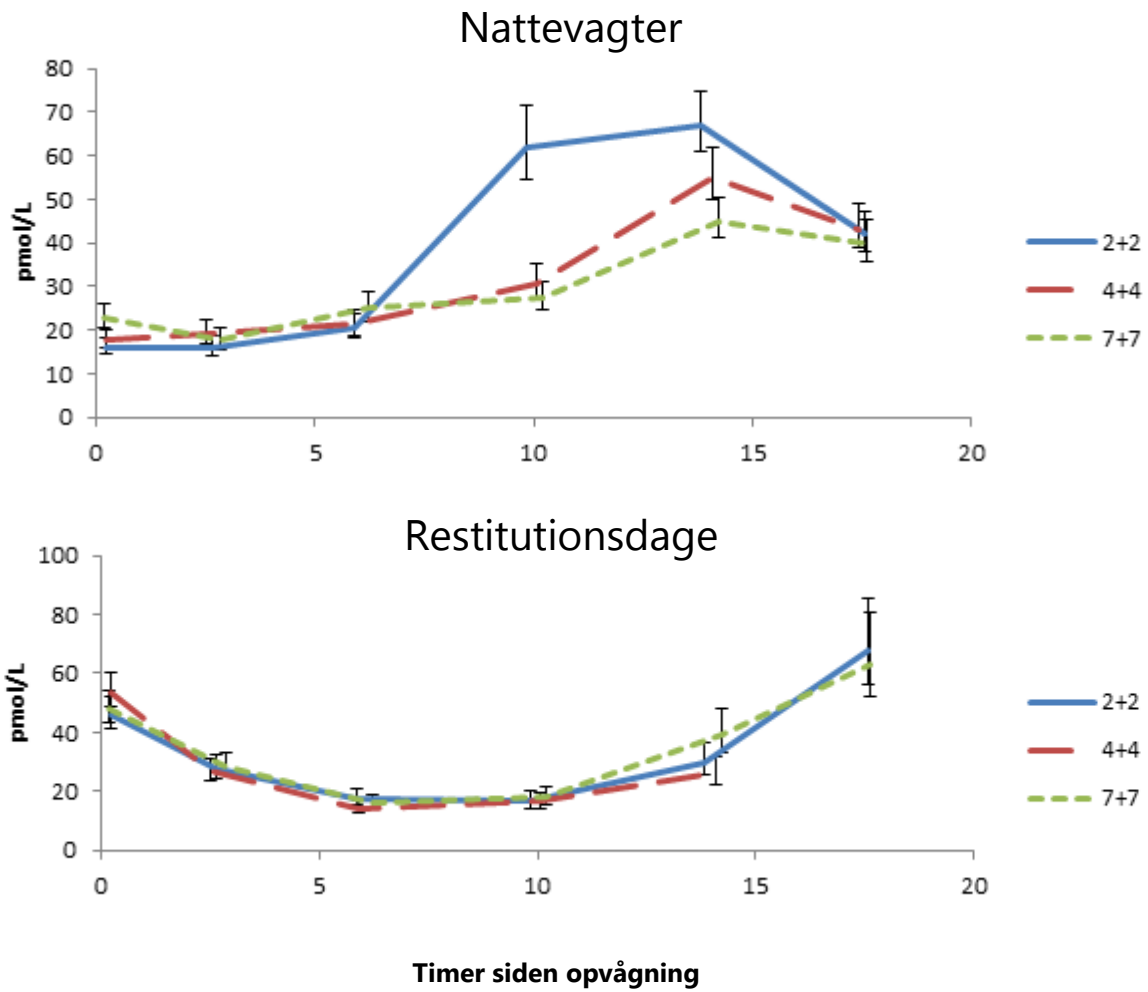


Antal dage med dårlig søvn?

- Den totale søvnlængde var kortest på den sidste dag med nattevagt
- Søvnlængden øges ikke med antallet af nattevagter i træk – det giver et øget søvnunderskud



Melatonin



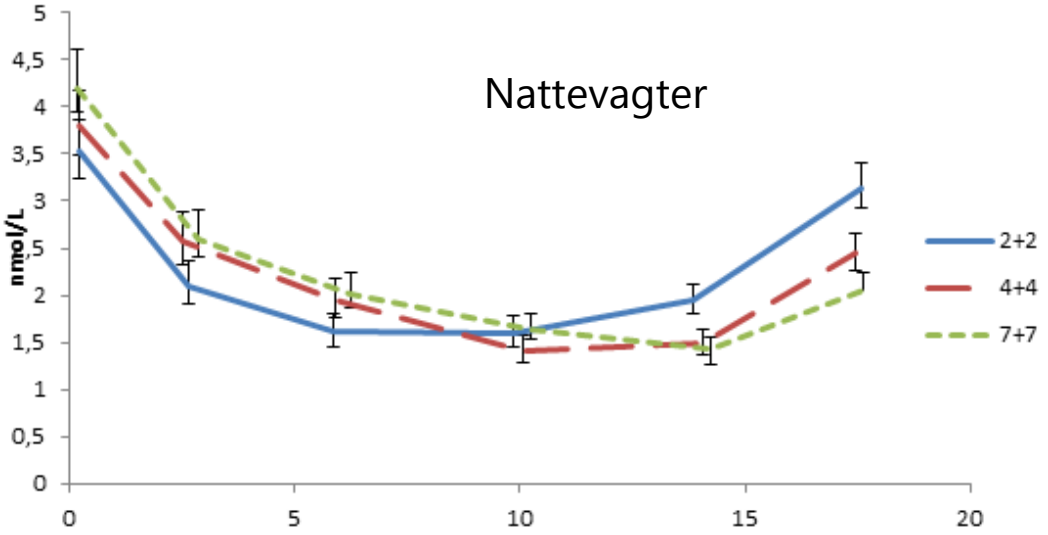
Ingen forskel på restitutionsdagene

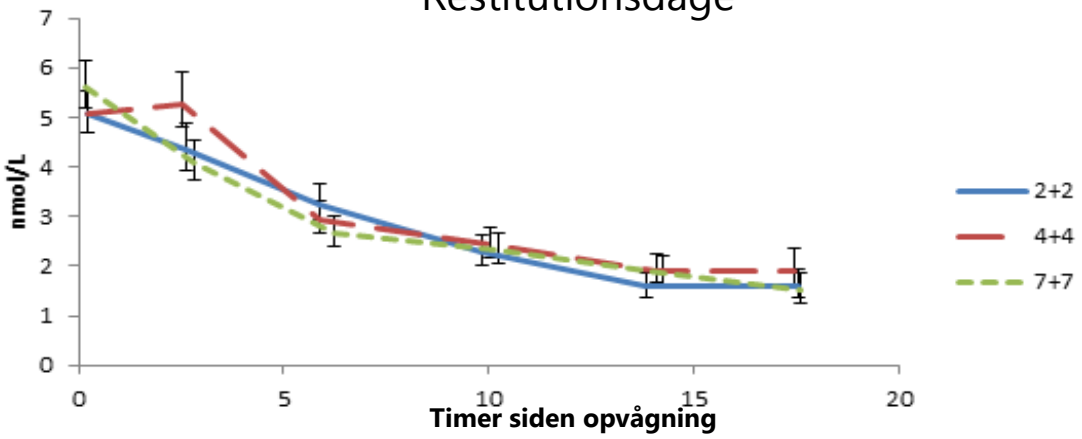
Niveauet af melatonin faldt med 4,9% per nattevagt

Melatoninrytmen blev ikke tilpasset til nattevagt efter 7 nattevagter

Jensen et al. Chronobiol. Int. (2017)

Kortisol





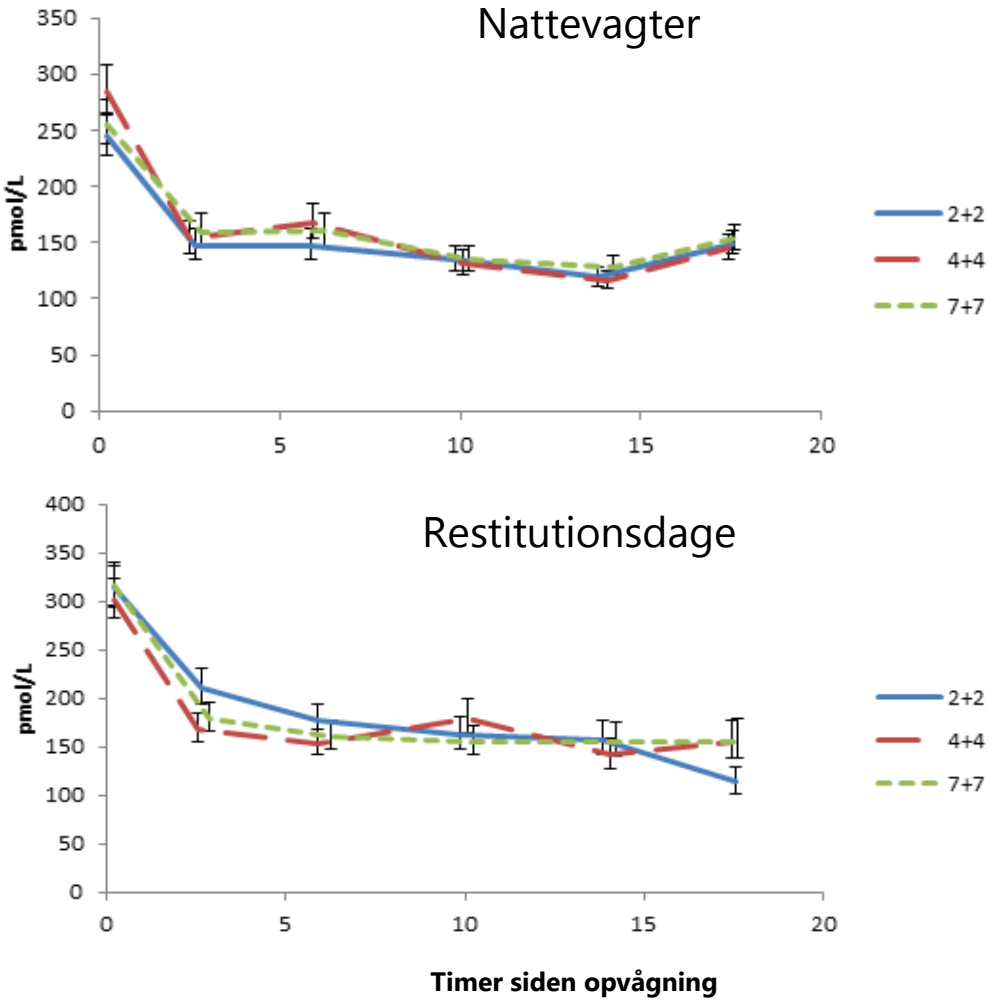
Ingen forskel på restitutionsdagene

Kortisol rytmen blev forskudt med 33 minutter per nattevagt

Kortisolrytmen blev ikke tilpasset nattevagt efter 7 nattevagter

Jensen et al. Chronobiol. Int. (2017)

Testosteron



Ingen forskel mellem interventionerne på restitutionsdage

Ingen forskel mellem interventionerne på nattevagter

Testosteronrytmen fulgte søvnen

Jensen et al. Chronobiol. Int. (2017)

De tre målte hormoner tilpasser sig forskelligt til natarbejde

Melatonin: Jo flere nattevagter jo lavere koncentration om natten

Kortisol: Jo flere nattevager jo senere opnås laveste koncentration

Testosteron: Følger søvnrytme uanset vagtskema

Døgnrytmerne er alle ude af takt med lys/mørke cyklus

Alle døgnrytmer var normaliserede ved slutningen af hver intervention

2+2 er samlet set bedst til at minimere problemerne med døgnrytme forstyrrelserne

Jensen et al. Chronobiol. Int. (2017)

Hvor mange nattevagter i træk

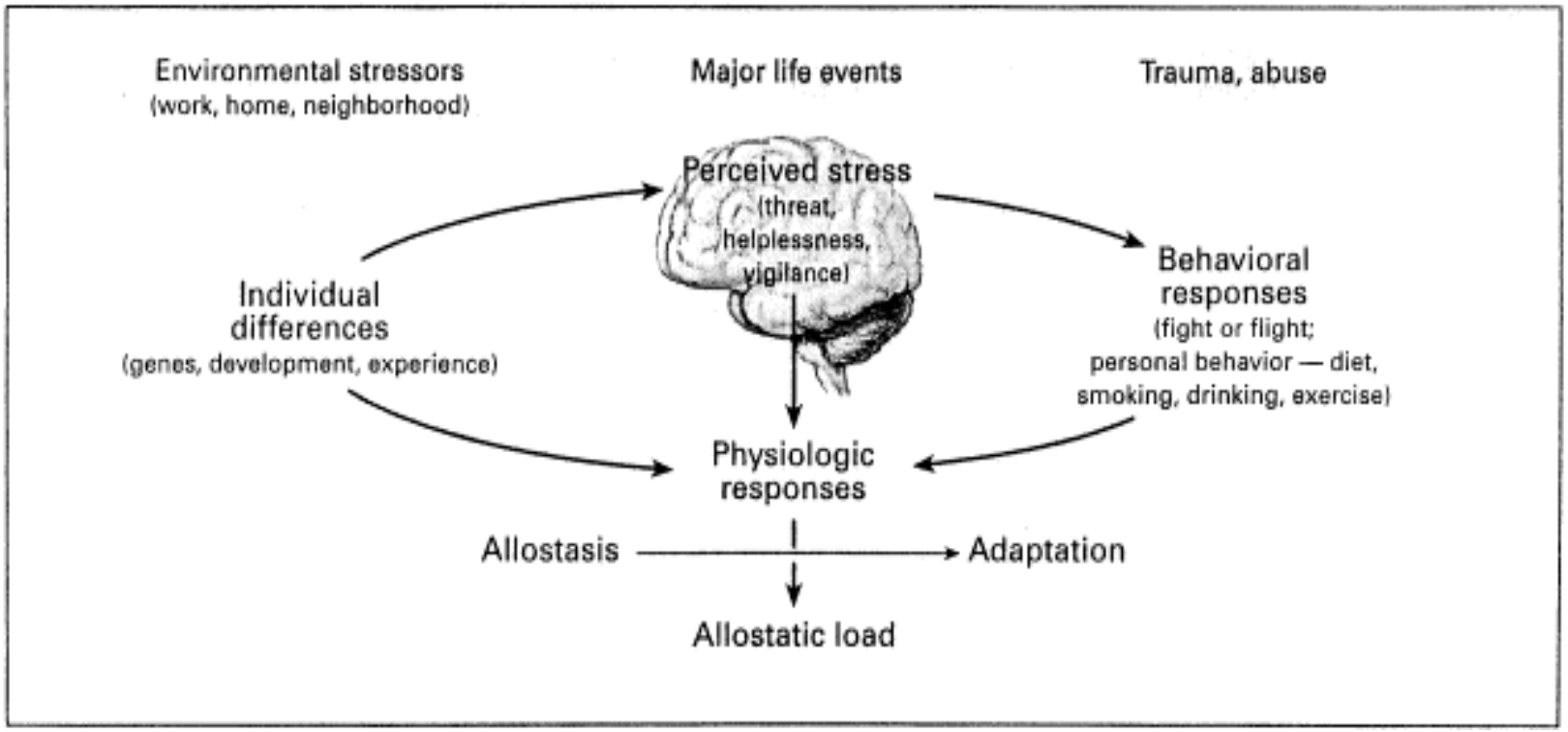
Samlet set giver resultaterne ikke anledning til at ændre på de nuværende anbefalinger om at minimereantallet af nattevagter i træk.

Dog kan det overvejes at have op til 4 nattevagter i træk som en afvejning af hensynet til døgnrytmeforstyrrelser og søvn.

Jensen et al. Chronobiol. Int. (2017)

Allostatic load som stressresponse

Allostasis and the HPA axis



Graphic adopted from McEwen, 1998.

Homeostatic processes or allo

The ability to achieve stability through change.

McEwen New England Journal of Medicine (1998)

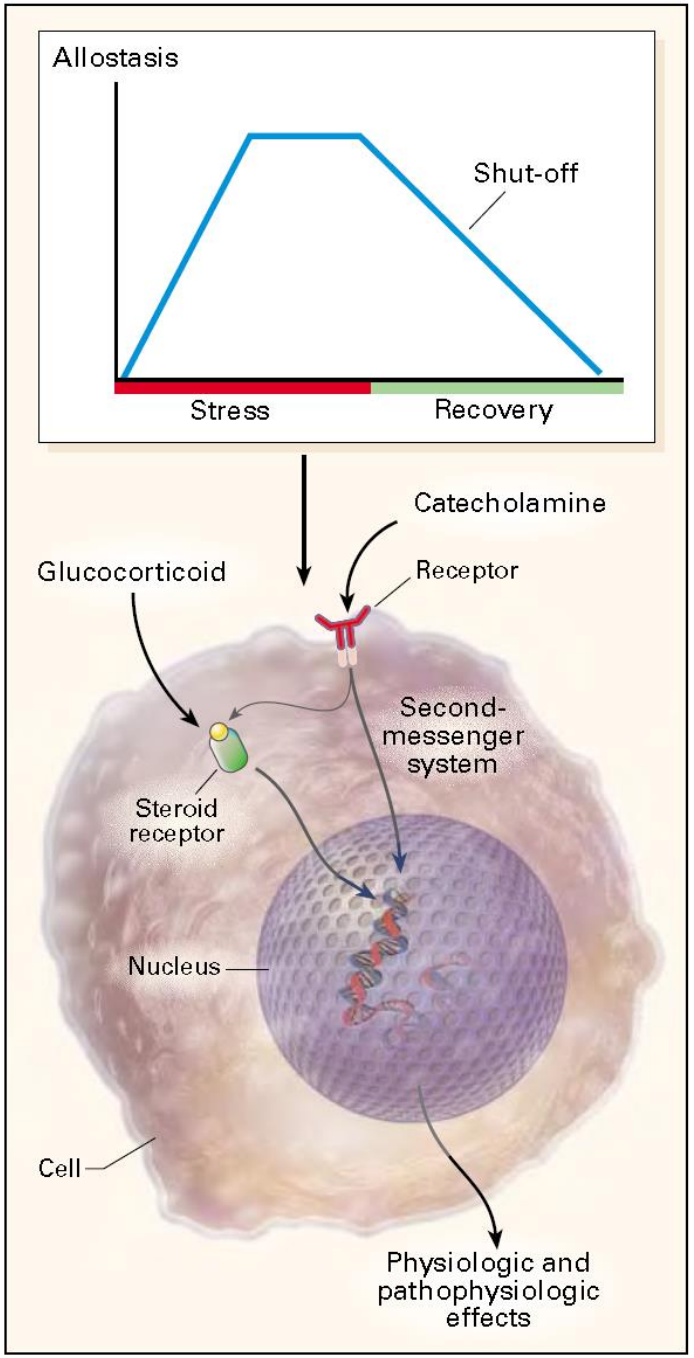
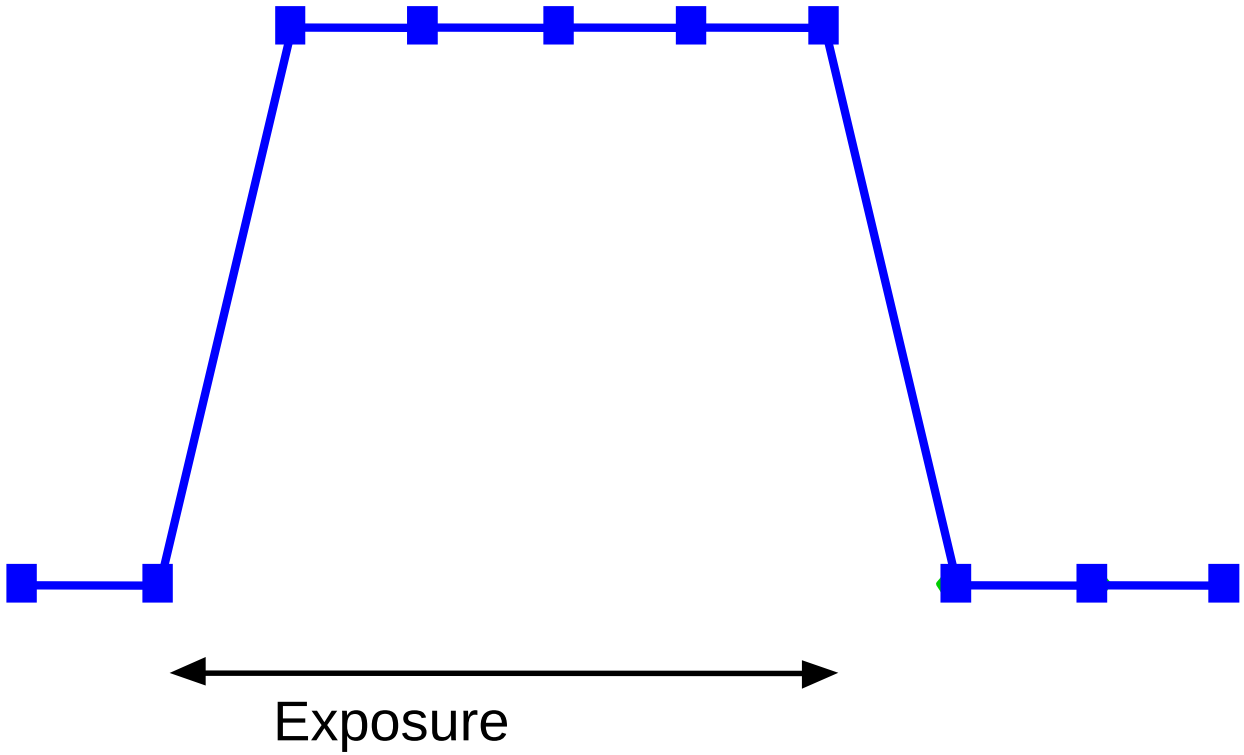
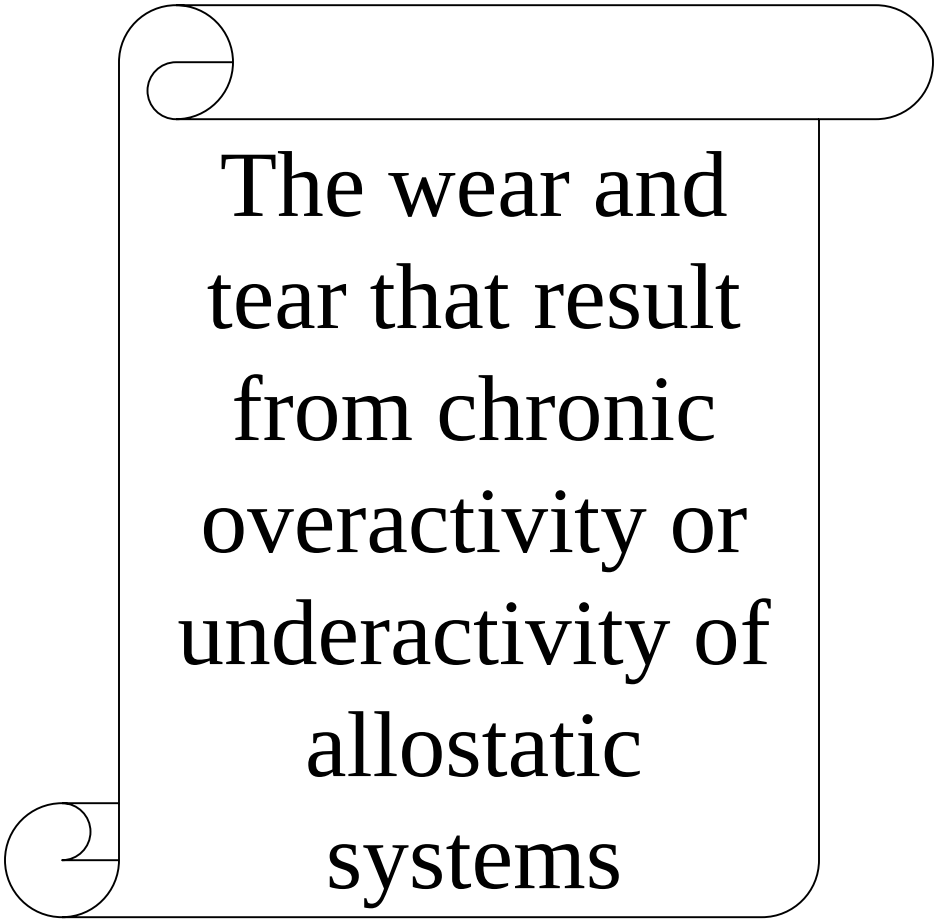


Figure 2. Allostasis in the Autonomic Nervous System and the HPA Axis.

Healthy response

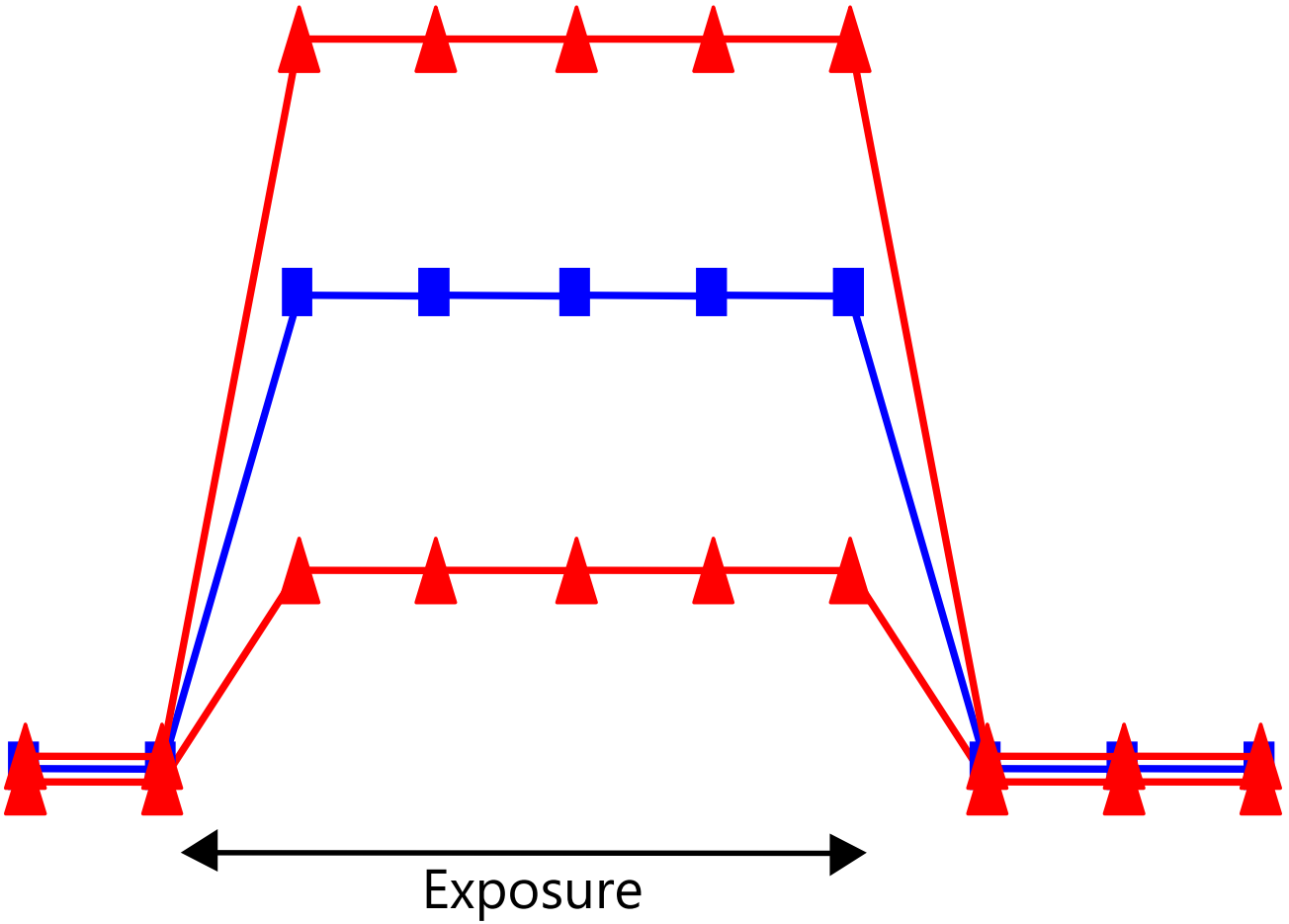


Allostatic (or homeostatic) load



McEwen New England Journal of Medicine (1998)

Size of response



This figure illustrates normal response initiated by a stressor

McEwen 1998

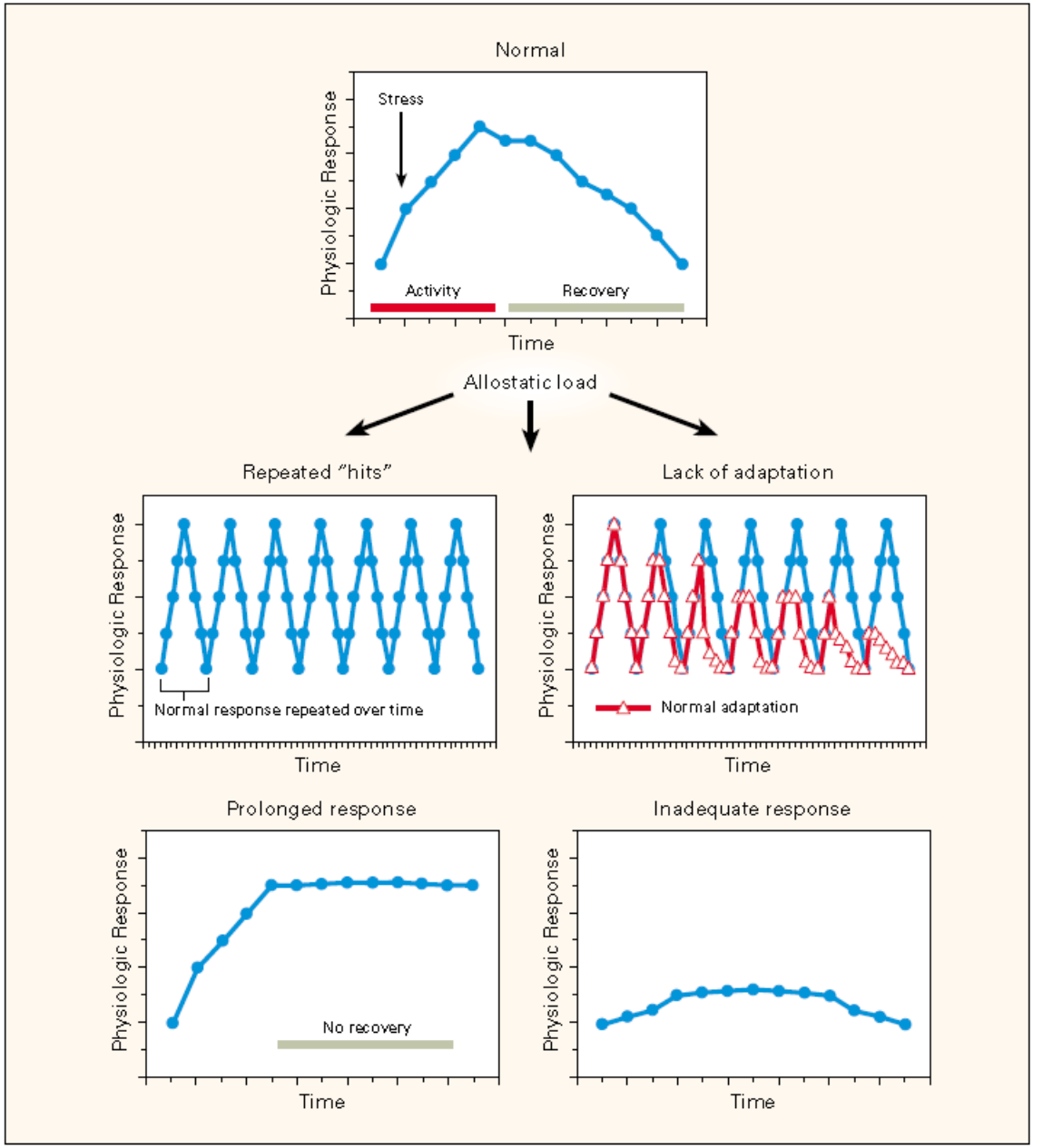


Figure 3. Three Types of Allostatic Load.

The top panel illustrates the normal allostatic response, in which a response is initiated by a stressor, sustained for an appropriate interval, and then turned off. The remaining panels illustrate four conditions that lead to allostatic load: repeated "hits" from multiple stressors; lack of adaptation; prolonged response due to delayed shutdown; and inadequate response that leads to compensatory hyperactivity of other mediators (e.g., inadequate secretion of glucocorticoids, resulting in increased concentrations of cytokines that are normally counterregulated by glucocorticoids).

Stress response

- HPA is a central part of the biological stress response
- Stress is the body's reaction to any stimuli that disturb its equilibrium (homeostasis).
- The term allostasis refers to the process whereby an organism maintains physiological stability by changing parameters of its internal milieu by matching them appropriately to environmental demands.
- Stress is a series of reactions, which may lead to a chronic individual state characterized by a combination of high arousal, aversion and negative expectation about solving the challenge.

Allostatic load (AL)

Allostatic load represents the strain that chronic stress exerts on interconnected biological systems

The allostatic load model expands the stress-disease literature by proposing a temporal cascade of multisystemic physiological dysregulations that contribute to disease trajectories.

Allostatic load index represent neuroendocrine, immune, metabolic, and cardiovascular system

Juster et al 2010, 2011

Social class and allostatic load (Hansen et al. 2015)

Copenhagen Aging and Midlife Biobank (CAMB)

- CAMB was established in 2009-2011, based on three different cohorts:

  The Metropolit cohort (MP)

  The Danish Longitudinal Study on Work, Unemployment and Health (DALWUH)

  and the Copenhagen Perinatal Study (CPC)

- Eligible cohort members were 17,937 persons living in the Eastern parts of Denmark (7,750 from MP, 4,906 from DALWUH, 5,282 from CPC)

- In total 7,191 (40%) of the invited persons answered the postal questionnaire and 5,576 (31%) participated in all parts of the study.

- Participants were examined at the National Research Centre for the Working Environment from 2009 to 2011.

Estimating Allostatic load in CAMB

Metabolic system	Diastolic blood pressure (mmhg)
	Systolic blood oressure (mmhg)
	Body mass index (kg/m^2)
	Waist-hip ratio
	Body fat (%)
	Glucose (mmol/l)
	HbA_{1c} (% of total hemoglobin)
Cardio-vasculære system	Total cholesterol (mmol/L)
	HDL-cholesterol (mmol/L)
	LDL-cholesterol (mmol/L)
	Triglycerides (mmol/L)
	hs C-reactive protein (mg/l)
Immune system	Interleukin-6 (pg/ml)
	Tumor necrosis factor-α (pg/ml)

Quartiles were estimated by calculating the 25% percentiles
The poorest quartiles were scored 1
AL= sum of the the poorest quartiles, range 0-14 (higher score indicates higher AL).

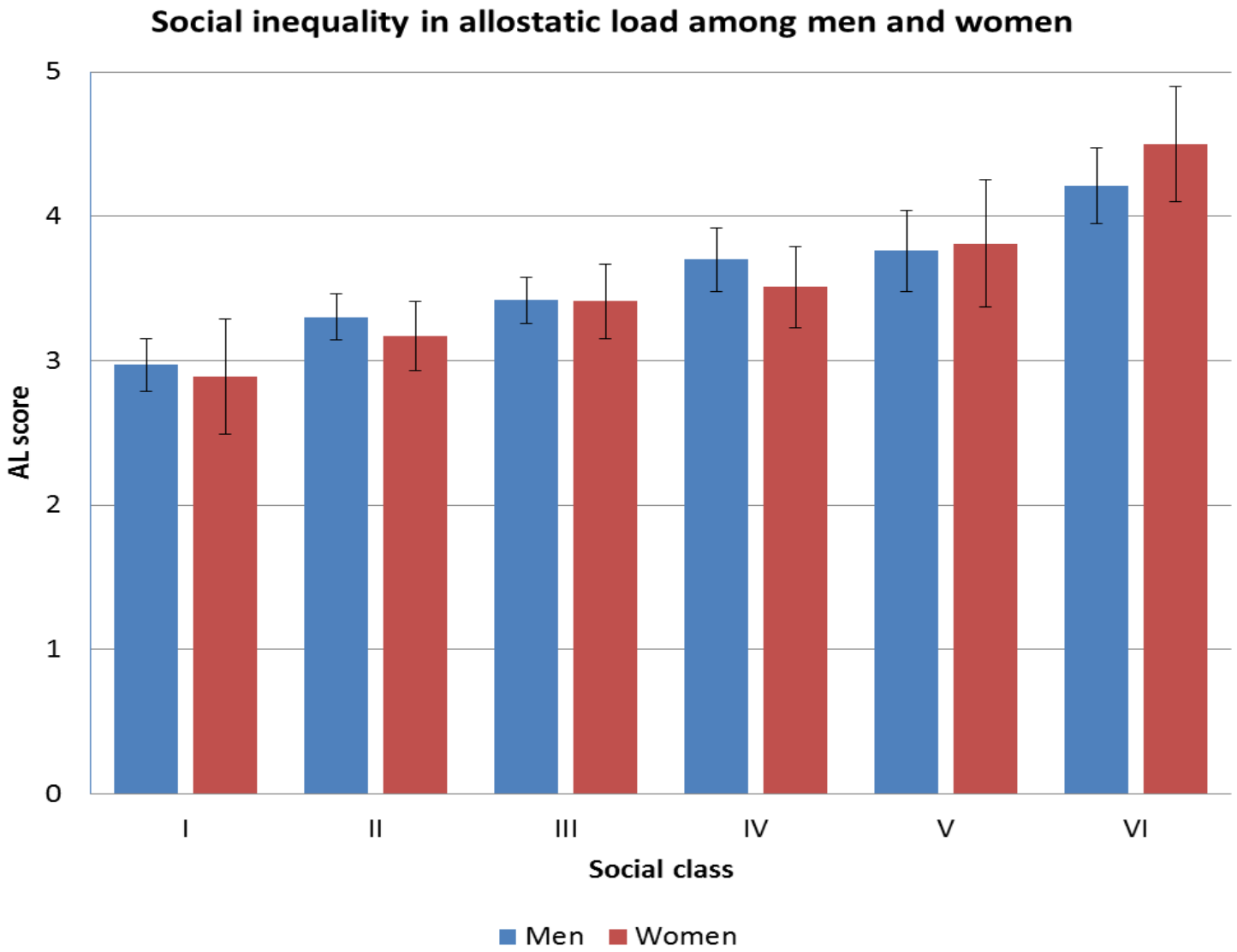
Hansen et al 2014

Measuring occupational social class

Occupational social class	
I	**> 4 years of university or a similar training**; top manager in a big company, top level civil servant, government advisor, or other executives and professionals within government, management and administration; owners of large-scale companies in both rural and urban trades with more than 50 subordinates, and self-employed with more than 20 subordinates.
II	**3 years of theoretical training** (white-collar jobs, e.g., nurse, primary school teacher, social worker, medium level civil servant, journalist; white-collar jobs which imply management responsibilities for 11 to 50 subordinates; owners of medium-scale companies (companies with 6+ employees)).
III	**1½ years of theoretical training and practical skills** (non-manual white-collar jobs e.g., accountant, police detective; (b) white-collar jobs with management responsibilities for 1 to 10 subordinates; (c) self-employed with small-scale business (e.g., small-scale farmer, self-employed craftsmen, and tradesmen with 0-5 employees).
IV	**1 year of theoretical or practical training** (manual white-collar jobs e.g., technicians, nurse assistants, office worker, sales assistant and craftsmen and tradesmen and other blue-collar workers, e.g., carpenter, bricklayer, blacksmith, plumber).
V	**Manual jobs which require little theoretical and practical training** (semi- or unskilled workers, e.g., lorry-driver, factory worker, construction worker, farm-worker).
VI	**Individuals who are economically inactive and rely primarily on transfer income** (e.g., disability pensioner, unemployed, or long-term sick).

Christensen et al 2014

Social class and allostatic load in a Danish population



We observed a statistically significant social class gradient among Danish men and women in AL ($p < .001$) with the highest AL in the lowest social class

Study population

	Men (N=3746)		Women (N=1705)	
	Mean	**SE**	**Mean**	**SE**
Age (years)	55.3	0.1	52.5	0.1
DBP (mmhg)***	93.4	0.18	88.5	0.26
SBP (mmhg)***	145.6	0.29	132.8	0.43
BMI (kg/m^2)***	26.5	0.06	25.3	0.12
WHR ***	0.95	0.001	0.85	0.002
Body fat (%)***	21.3	0.1	31.4	0.16
Glucose (mmol/l)**	5.6	0.03	5.3	0.03
HbA_{1c} (% of total hemoglobin)***	5.4	0.01	5.2	0.01
Total cholesterol (mmol/L)	6.179	0.019	6.196	0.027
HDL-cholesterol (mmol/L)***	1.4	0.01	1.7	0.01
LDL-cholesterol (mmol/L)***	3.042	0.014	2.983	0.021
Triglycerides (mmol/L)***	1.9	0.02	1.4	0.02
hsCRP (mg/l)	2.3	0.07	2.3	0.11
IL-6 (pg/ml)	3.7	0.22	3.4	0.42
THF-α (pg/ml)	6.0	0.19	5.5	0.36

Hansen et al, 2015

Occupational social class

- Social class was classified by occupation and coded into social class I-VI and two supplementary groups, according to the standards of the Danish occupational social class classification and described by (Christensen et al. (2013).
- According to this classification social class I-V encompass economically active individuals ranging from professional occupation in social class I to unskilled occupation in social class V.
- 81 participants did not respond to the item of occupation and were consequently excluded.
- Social class VI represents people on transfer income, including sickness benefits and disability pension.
- For the present study we included economically active individuals (social class I-V) and individuals on transfer income (social class VI).
- 8 individuals who were economically active but without sufficient job information (social class VII) and altogether 29 students and housewives (social class VIII) were also excluded from further analysis.
- In total 5420 participants were included.

Estimering af Allostatic load i CAMB -

Quartiles were estimated by calculating the 25% percentiles
The poorest quartiles were scored 1
AL= sum of the the poorest quartiles, range 0-14 (higher score indicates higher AL).

	Cut-off value (Men)	Cut-off value (Women)
DBP (mmhg)	>96.0	>90.8
SBP (mmhg)	>148.8	>135.3
BMI (kg/m^2)	>28.5	>27.47
WHR	>0.99	>0.89
Body fat (%)	>24.9	>35.8
Glucose (mmol/l)	>6.0	>5.7
HbA_{1c} (% of total hemoglobin)	>5.68	>5.47
Total cholesterol (mmol/L)	>6.90	>6.87
HDL-cholesterol (mmol/L)	<1.13	<1.41
LDL-cholesterol (mmol/L)	>3.59	>3.5
Triglycerides (mmol/L)	>2.33	>1.75
hsCRP (mg/l)	>2.4	>2.3
IL-6 (pg/ml)	>3.05	>2.65
THF-α (pg/ml)	>5.76	>5.34

Hansen et al, 2015

Social klasse og AL blandt kvinder og mænd i Danmark

Social class	I Reference	II	III	IV	V	VI
N (Men)	687	945	856	555	326	377
N (Women)	165	476	410	350	139	165
	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
AL (Men)	2.70 (0.17)	3.12* (0.16)	3.28*** (0.16)	3.48*** (0.18)	3.58*** (0.19)	4.21*** (0.19)
AL (Women)	3.26 (0.35)	3.62* (0.31)	3.85*** (0.32)	4.00*** (0.31)	4.44*** (0.36)	5.20*** (0.35)

We observed a statistically significant social class gradient among Danish men and women in AL ($p < .001$) with the highest AL in the lowest social class

Hansen et al, 2015