



# Obstruktiv Søvnepnø (OSA) og kardiovaskulære risikofaktorer

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Maxillofacial  
Ear Nose and Throat  
Research



# Agenda

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Introduktion til Søvn, OSA og AFLI

Formål

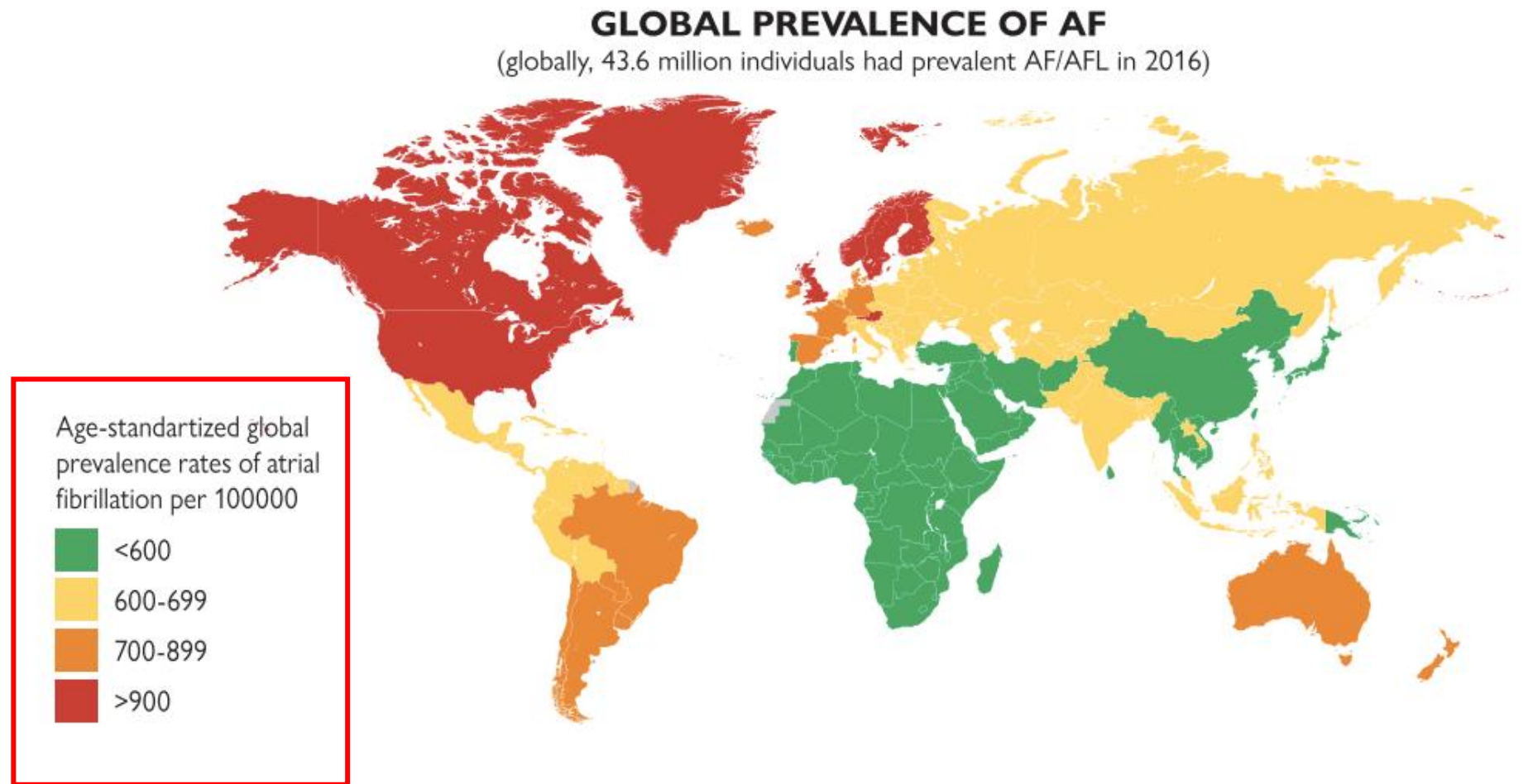
Studie 1

Studie 2

Konklusioner fra studier

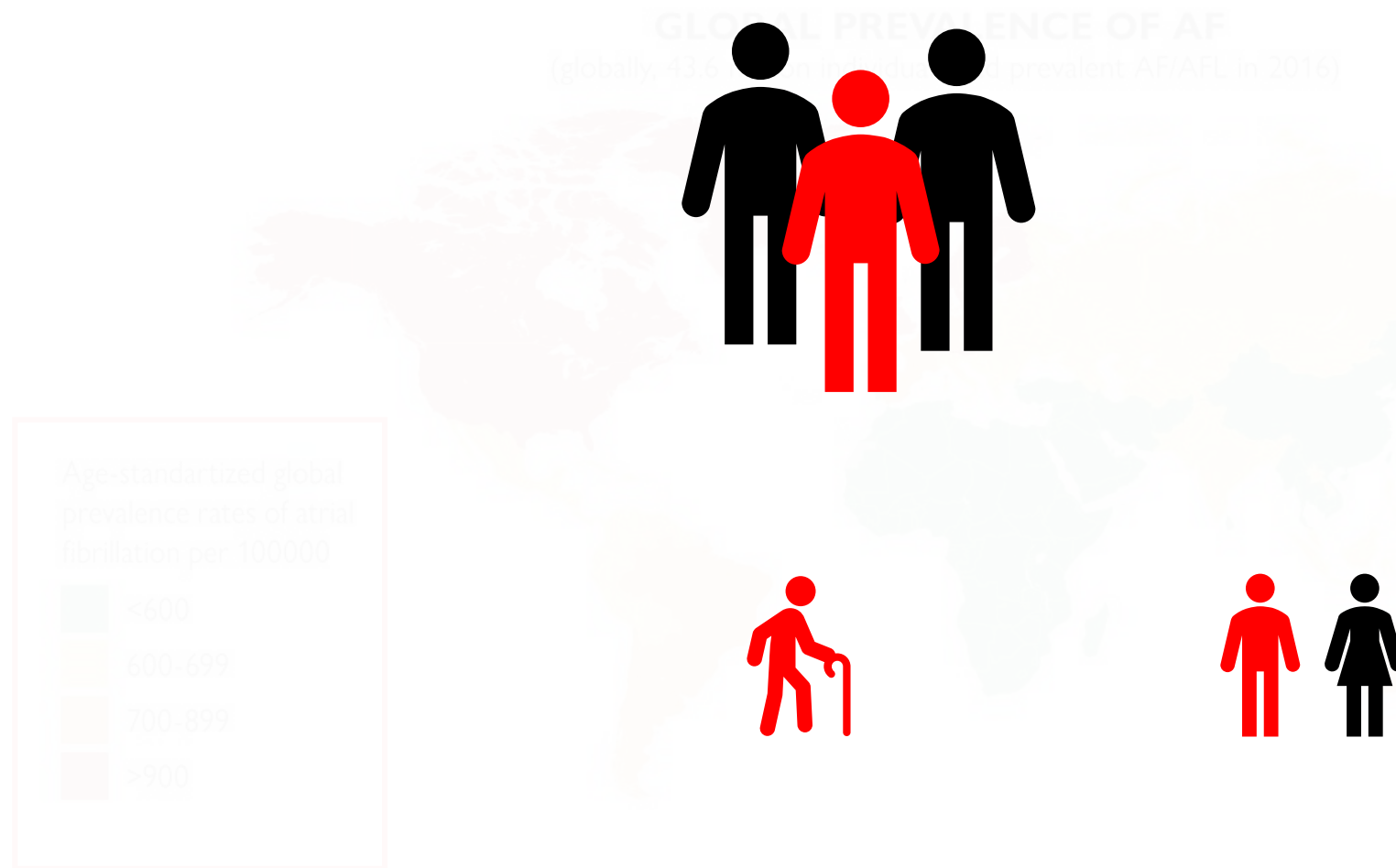
Klinisk relevans og fremtidsperspektiver

# Forekomst af atrieflimmer (AF)





# Livstidsrisiko for AF er 1:3<sup>1</sup>



<sup>1</sup>Europeans at index-age of 55, 37 % [34.3-39.6%]

Staerk L, Wang B, Preis SR, Larson MG, Lubitz SA, Ellinor PT, McManus DD, Ko D, Weng LC, Lunetta KL, Frost L, Benjamin EJ, Trinquart L. Lifetime risk of atrial fibrillation according to optimal, borderline, or elevated levels of risk factors: cohort study based on longitudinal data from the Framingham Heart Study. *BMJ* 2018;361:k1453.

the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*

# “Stum” atrieflimmer (AF)



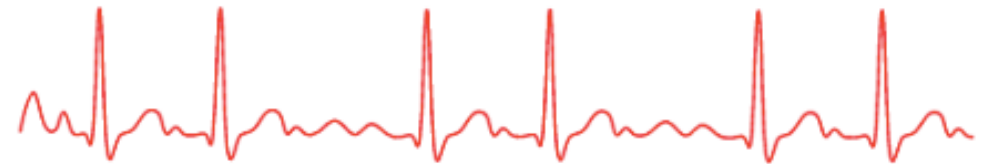
Asymptomatisk eller klinisk “stum” AF ca. 1/3 af alle tilfælde AF<sup>1</sup>



Hurtigere progression fra paroxystisk til persisterende(vedvarende) AF ved stum AF<sup>1</sup>



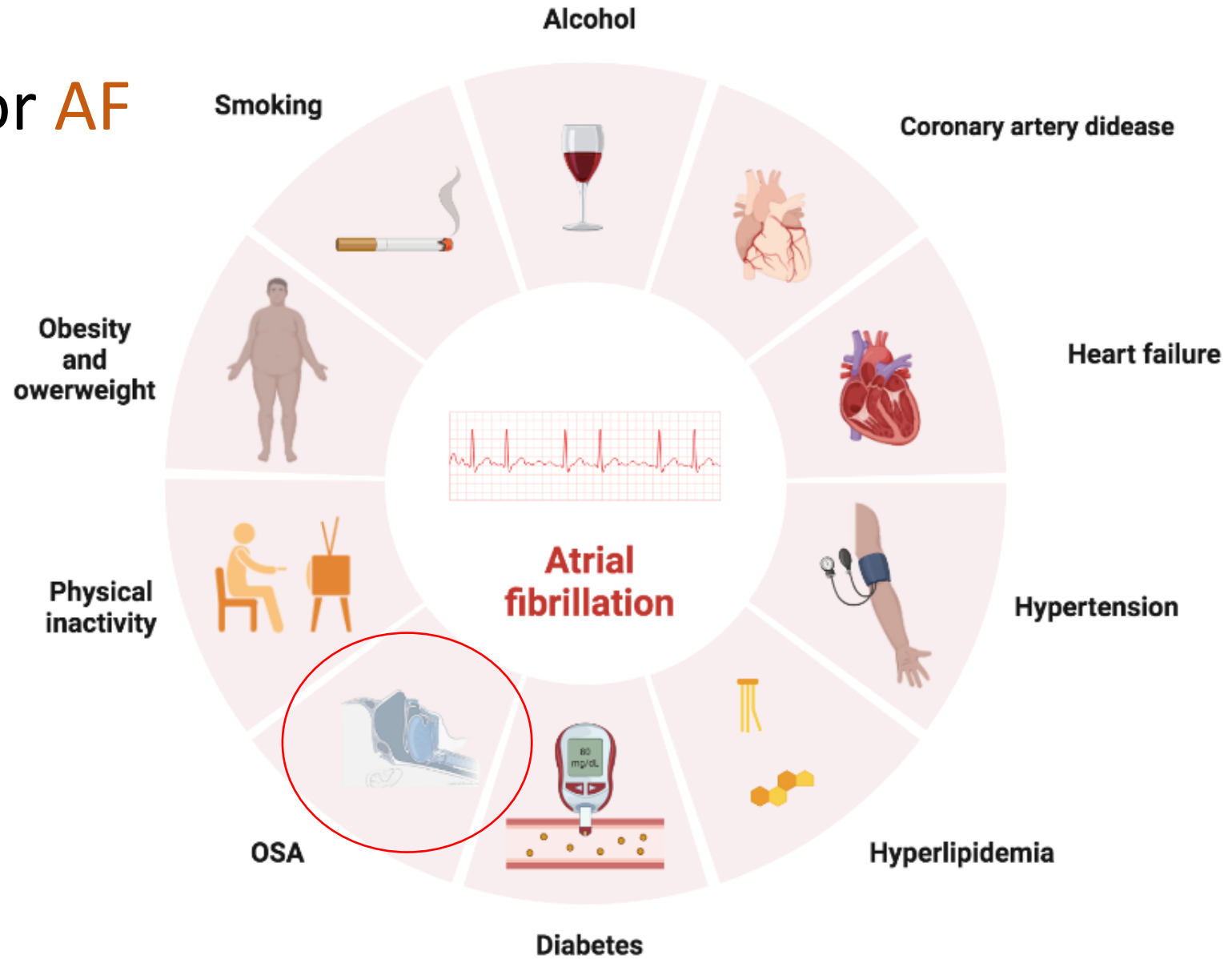
Højere mortalitet og risiko for stroke<sup>2</sup>



<sup>1</sup>Dilaveris PE, Kennedy HL. Silent atrial fibrillation: epidemiology, diagnosis, and clinical impact. Clin Cardiol. 2017;40(6):413-418.

<sup>2</sup>Healey JS, Connolly S, Gold MR, Israel CW, Van Gelder IC, Capucci A et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012;366:120–9

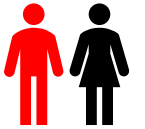
# Risiko faktorer for AF



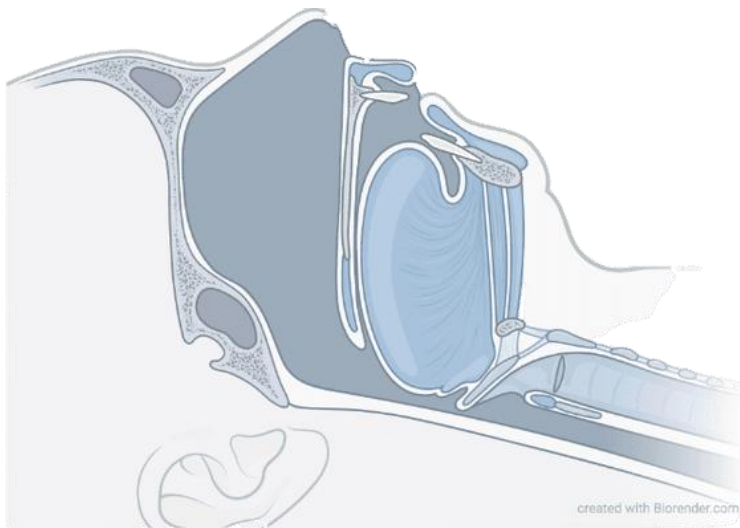


# Obstruktiv søvnapnø (OSA)

Gentagne **kollaps af pharynx** under søvn der medfører **hypoksi** (fald i blodets iltmætning) og **søvnfragmentering** (hyppige opvågninger/mikro-opvågninger, der afbryder søvncyklussen og dermed forringer søvnkvaliteten)



Global forekomst: **FLERE** end 100 millioner personer



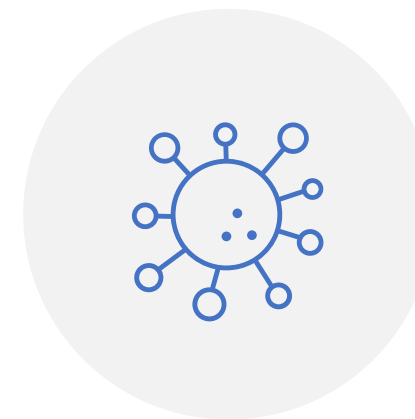
# Hvorfor sover vi ?



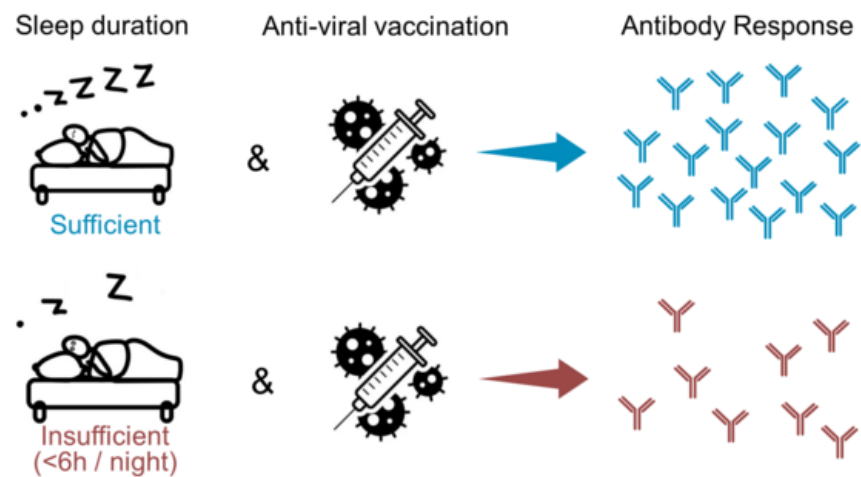
HVOR MEGET SKAL MAN SOVE?



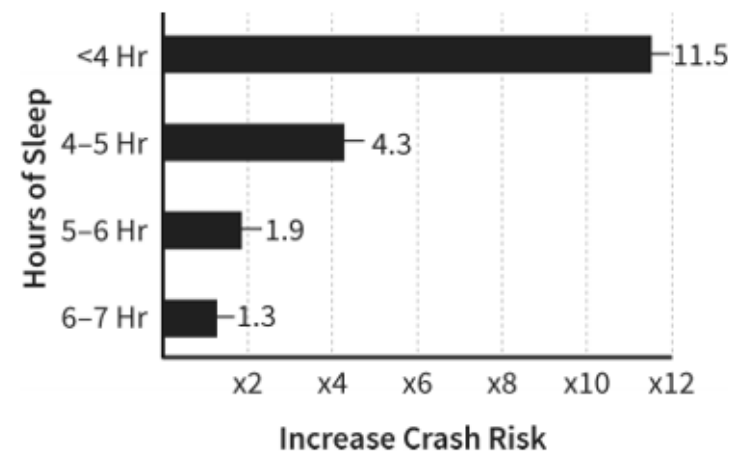
HVAD SKER DER NÅR VI IKKE  
SOVER NOK?



HVILKEN BETYDNING HAR SØVN  
FOR IMMUNFORSVARET?

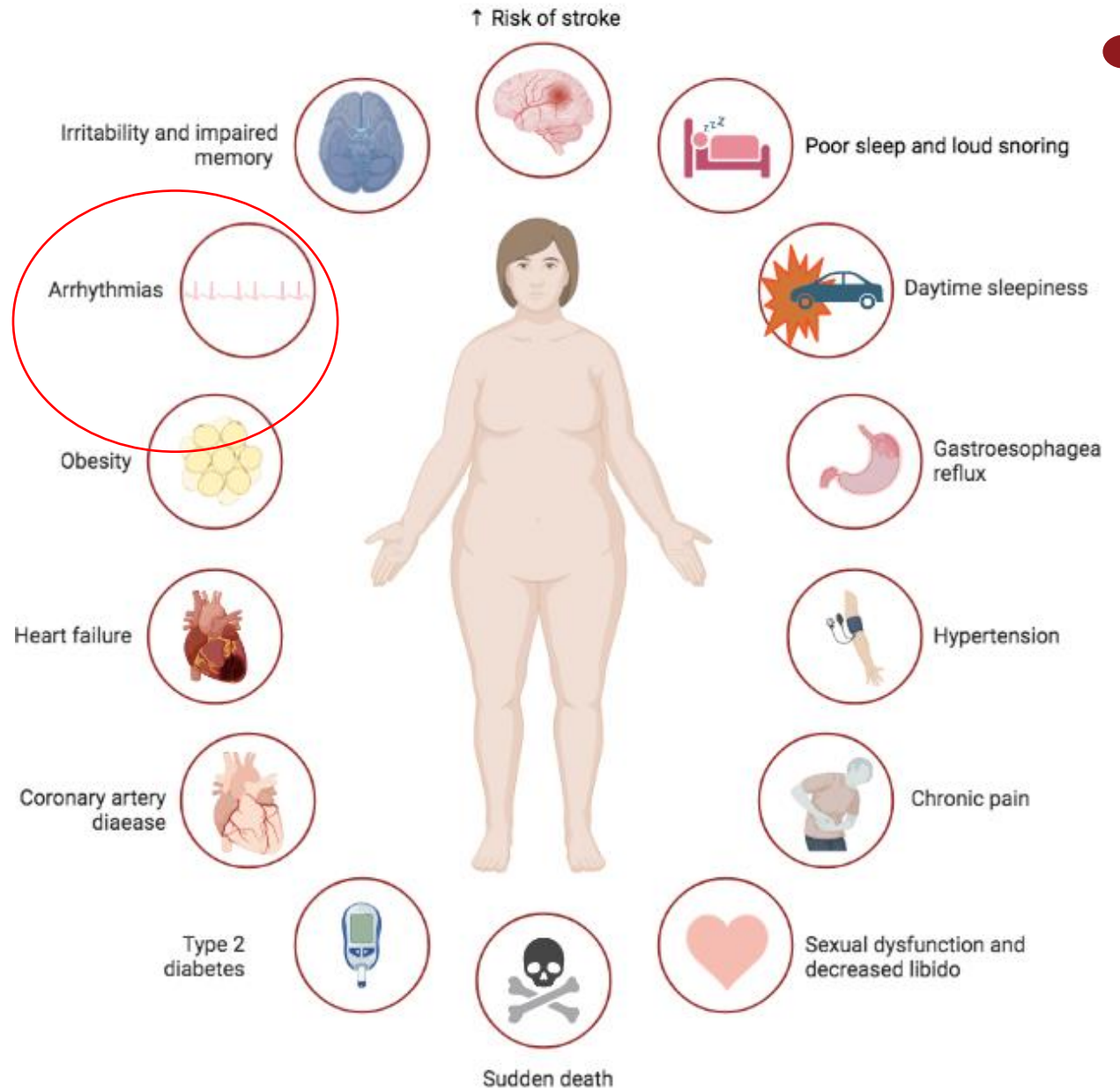


**Insufficient sleep around the day of vaccination is associated with a lower antibody response**



**Figure 12: Sleep Loss and Car Crashes**

# OSA og risikofaktorer





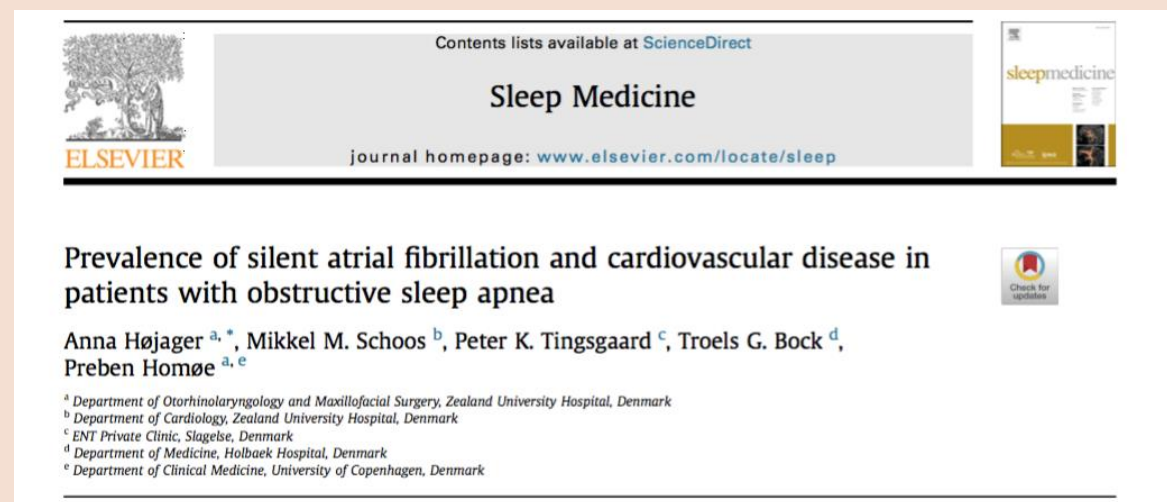
# Studie I - formål

## Studie I

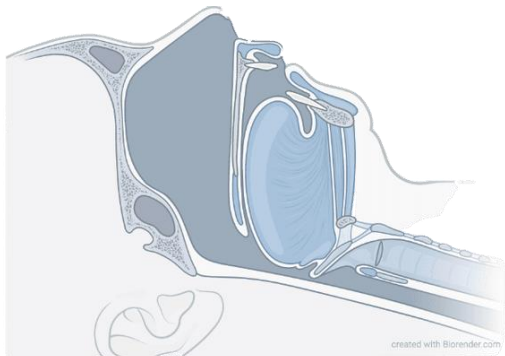
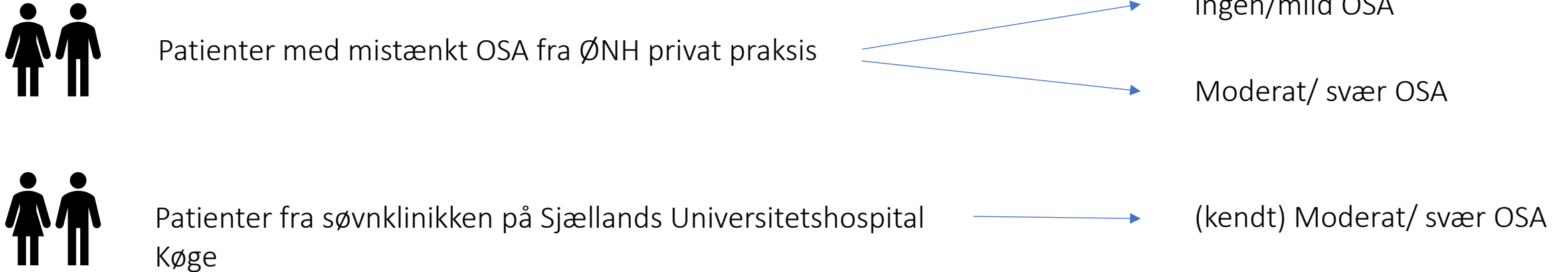
At bestemme **prævalens/forekomst af "stum" AF** I en kohorte af patienter med varierende grader af OSA ved brug af ELR (ekstern loop recorder) til hjemme-monitorering

Desuden at **identificere associerede risikofaktorer** der kan finde kandidater til **screening + tidlig antikoagulationsterapi** I forhold til at forebygge fremtidig *stroke*

**identificere IKKE tidligere erkendt**  
diabetes, prediabetes, hypertension,  
og  
hyperkolesterolæmi



# Studie I - Metode og studie-design

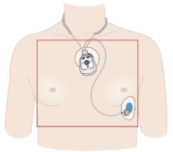




# Studie I og II - Metode og studie-design



1 nat med hjemme-søvnmonitorering med type 3 device (NOXt3)



7 dage hjemme-monitorering med event-triggered external loop recorder (ELR)



Standard blodprøver (p- hæmoglobin, p- Hb1Ac, p-blodsukker, p-creatinine, eGFR, u-albumin, p-TSH)



Blodtryk og puls



12-aflednings' ECG



Information om andre *kendte* komorbiditeter (diabetes, kardiovaskulær sygdom, medicin)

Event- triggered loop recorder (ELR)



R.Test Evolution 4®, NorDiaTech, Paris, France\*

# Studie I - Resultater



69.9%



56.4 år



66%



31.6 kg/m<sup>2</sup>



11.8% (HbA1c 42-47mmol/L)



15.8% (kun type 2 diabetes)



70 %\*

## Patient baseline- karakteristika i studie I and II

|                                                | All Patients<br>(n =303) | Patients with AHI<br><15 (n= 65) | Patients with AHI<br>15- <30 (n=93) | Patients with AHI<br>≥30 (n =145) | p-value |
|------------------------------------------------|--------------------------|----------------------------------|-------------------------------------|-----------------------------------|---------|
| Male, n (%)                                    | 208 (69.6)               | 37 (56.9)                        | 61 (65.6)                           | 110 (75.9)                        | 0.018   |
| Age, years, mean (SD)                          | 56.4 (12.4)              | 50.2 (13.1)                      | 57.6 (11.5)                         | 57.6 (11.9)                       | <0.001  |
| Hypertension, n %                              | 200 (66)                 | 28 (43.1)                        | 60 (64.5)                           | 112 (77.2)                        | <0.001  |
| Hypertension, dysregulated, n %                | 83 (27.7)                | 9 (13.8)                         | 23 (24.7)                           | 51 (35.2)                         | 0.005   |
| Hypertension, unknown, n %                     | 78 (25.7)                | 12 (18.5)                        | 25 (26.9)                           | 41(28.3)                          | 0.31    |
| Undertreated hypertension, n %                 | 161 (53)                 | 21(32.3)                         | 48 (51.6)                           | 92 (63.5)                         | <0.001  |
| Dyslipidaemia, n %                             | 235 (77.6)               | 44 (67.7)                        | 73 (78.5)                           | 118 (81.4)                        | 0.086   |
| Dyslipidaemia, unknown n, %                    | 151 (49.8)               | 31(47.7)                         | 48 (51.6)                           | 72 (49.7)                         | 0.89    |
| Treatment with oral cholesterol lowering drugs | 83 (27.4)                | 13 (20)                          | 25 (26.9)                           | 45 (31)                           | 0.25    |
| BMI, kg/m2, mean (SD)                          | 31.6 (6.6)               | 29.6 (5.6)                       | 31.0 (6.6)                          | 32.9 (6.8)                        | 0.002   |
| Type 2 diabetes, n %                           | 48 (15.8)                | 4 (6.2)                          | 13 (14.0)                           | 31 (21.4)                         | 0.017   |
| Type 2 diabetes unknown, n %                   | 9 (2.9)                  | 1 (1.5)                          | 2 (2.2)                             | 6 (4.1)                           | 0.51    |
| Prediabetes, n % (HbA1c 42-47mmol/L)           | 36 (11.8)                | 2 (3.1)                          | 13 (14.0))                          | 21 (14.5)                         | 0.046   |
| Diabetes duration, years, (SD)                 | 4.7 (7.8)                | 2.2 (2.0)                        | 7.7 (12.6)                          | 3.7 (4.9)                         | 0.26    |
| History of prior ischemic stroke, n %          | 11 (3.6)                 | 1 (1.5)                          | 2 (2.2)                             | 6 (4.1)                           | 0.51    |
| History of prior UAP, n %                      | 3 (1)                    | 1 (1.5)                          | 1 (1.1)                             | 1 (0.7)                           | 0.84    |
| History of prior stable AP, n %                | 12 (3.9)                 | 1 (1.5)                          | 2 (2.2)                             | 9 (6.2)                           | 0.16    |
| Prior AMI, n %                                 | 10 (3.3)                 | 1 (1.5)                          | 4 (4.3)                             | 5 (3.5)                           | 0.93    |
| IHD, n %                                       | 11 (3.6)                 | 1 (1.5)                          | 3 (3.2)                             | 7 (4.8)                           | 0.48    |
| History of CABG, n %                           | 4 (1.3)                  | 0                                | 2 (2.2)                             | 2 (1.4)                           | 0.51    |
| Family history of IHD, n (%)                   | 74 (24.4)                | 12 (18.5)                        | 19 (20.4)                           | 43 (30.0)                         | 0.12    |
| Pack-years, cigarettes, mean, (SD)             | 13.9 (17.5)              | 7.6 (9.7)                        | 15.3 (18.1)                         | 15.9 (19.2)                       | 0.004   |
| Active smokers, n, %                           | 81 (26.7)                | 13 (20)                          | 25 (26.9)                           | 43 (29.7)                         | 0.34    |
| Thyroid disease, n %                           | 10 (3.3)                 | 1 (1.5)                          | 3 (3.2)                             | 6 (4.1)                           | 0.62    |
| HbA1c mmol/mol, mean, (SD)                     | 40.0 (10.2)              | 36.8 (11.4)                      | 38.7 (7.5)                          | 42.3 (10.6)                       | <0.001  |
| Triglyceride, mmol/L, mean (SD)                | 2.2 (1.5)                | 1.8 (1.4)                        | 2.1 (1.2)                           | 2.4 (1.7)                         | 0.019   |
| Total cholesterol mmol/L, mean (SD)            | 5.2 (1.1)                | 5.9 (5.9)                        | 5.2 (1.1)                           | 5.1 (1.0)                         | 0.14    |
| LDL cholesterol mmol/L, mean (SD)*             | 2.9 (0.9)                | 3.1 (1.0)                        | 2.9 (0.9)                           | 2.8 (1.0)                         | 0.07    |
| LDL cholesterol mmol/L, mean (SD)**            | 2.9 (0.9)                | 3.1 (1.1)                        | 2.9 (0.9)                           | 2.8 (1.0)                         | 0.13    |
| HDL cholesterol mmol/L, mean (SD)              | 1.3 (0.4)                | 1.4 (0.5)                        | 1.4 (0.4)                           | 1.2 (0.4)                         | 0.043   |
| Waist/hip ratio, mean, (SD)                    | 1.0 (0.1)                | 0.9 (1.2)                        | 1.0 (0.1)                           | 1.0 (0.1)                         | <0.001  |
| Systolic blood pressure, mmHg, mean (SD)       | 143.7 (19.9)             | 134.9 (17.6)                     | 144.5 (18.3)                        | 147.3(20.9)                       | <0.001  |
| Diastolic blood pressure, mmHg, mean (SD)      | 88.2 (11.8)              | 87.3 (10.3)                      | 85.6 (10.4)                         | 90.3 (12.9)                       | 0.009   |
| Heart-rate, mean (SD)                          | 72.4 (12.8)              | 70.8 (14.2)                      | 68.8 (11.3)                         | 75.6 (12.5)                       | <0.001  |
| Metabolic syndrome, n %                        | 212 (70)                 | 28 (43.0)                        | 70 (75.3)                           | 114 (78.6)                        | <0.001  |
| Central apneas, mean (SD)                      | 10.3 (26.3)              | 2.1 (3.3)                        | 6.0 (8.1)                           | 16.8 (36.4)                       | <0.001  |
| Epworth Sleepiness Scale, score, mean (SD)     | 9.9 (4.8)                | 9.5 (4.1)                        | 9.9 (4.9)                           | 10.1 (5.1)                        | 0.73    |

AHI: apnea-hypopnea-index, Dysregulated hypertension: patients treated pharmacological for hypertension with blood pressure at consult >140 systolic and/or 90 diastolic mmHg measured 3 times at resting state. Dyslipidemia: Treatment with oral cholesterol-lowering drugs or total cholesterol >5mmol/L or triglycerides > 2.6mmol/L. OSA: obstructive sleep apnea. SD: standard deviation

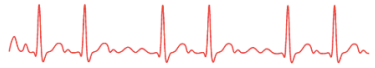
\*Missing blood samples from 20 patients due to very high triglycerides, the formula of Friedewald is not used on these patients.

\*\*Calculated LDL in all 303 patients using Friedewald's formula.

Metabolic syndrome; Central obesity (waist circumference > 94 cm for men and >80 cm for women) and two of the following; triglycerides >1.7 mmol/L, or treatment; HDL > 1.0 for men and > 1.3 for women; resting fasting blood glucose > 5.6 or previously diagnosed with type 2 diabetes; blood pressure > 130/85 or treatment for hypertension (International Diabetes Federation(IDF) guidelines



# Study I - Resultater og primært outcome



*Forekomst af AF i patienter moderat og svær OSA (AHI  $\geq 15$ ) (n=238) var 8.8 %  
versus*

*1.5 % (patienter med mild OSA (n=65, AHI  $< 15$ ))*

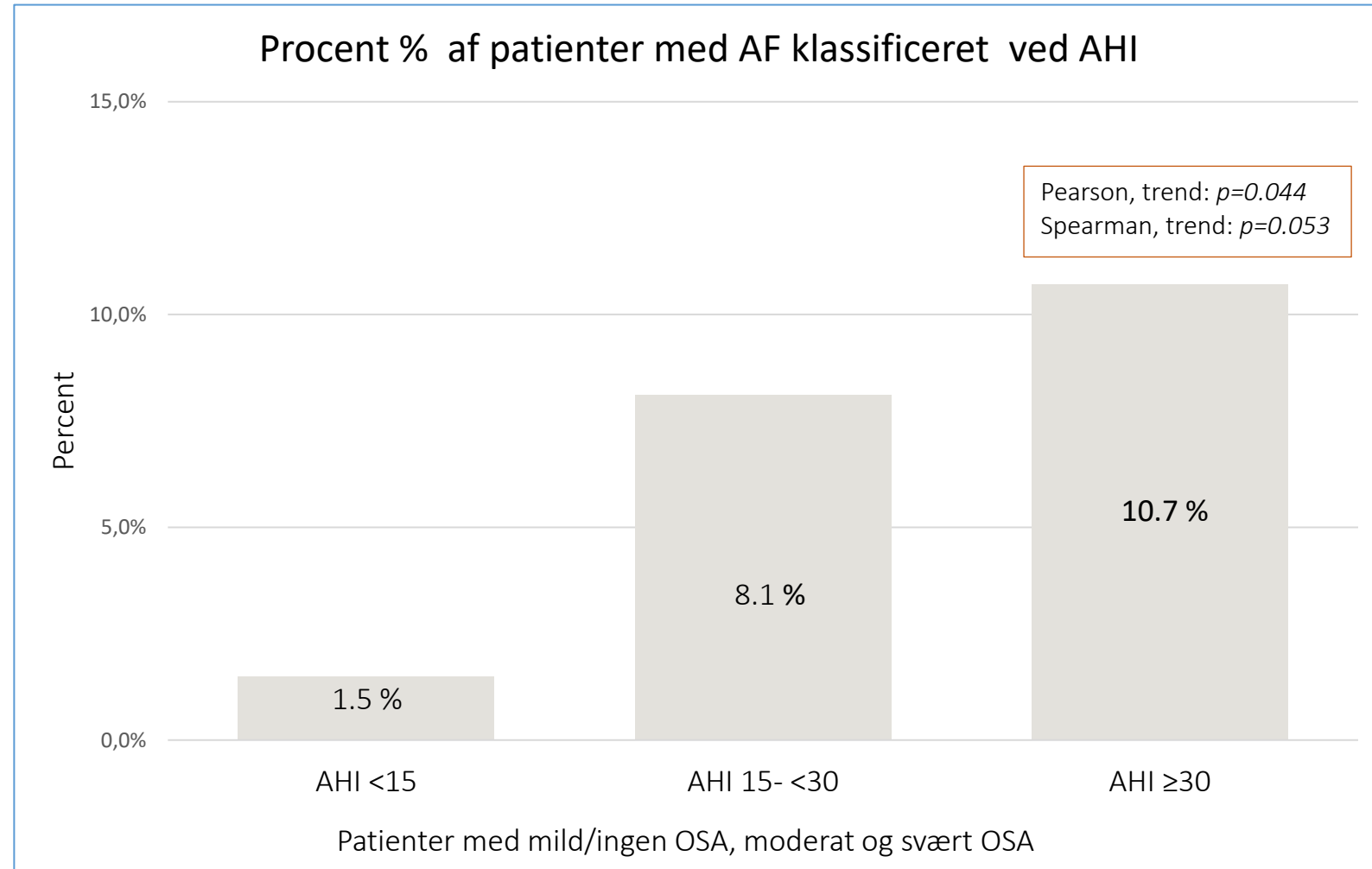
*21 af 22 patienter med AF havde moderat/svær OSA (AHI  $\geq 15$ ) ( $p=0.045$ )*



# Studie I - Resultater

Gennemsnitlig AHI (alle patienter) var

34.2 (0.2-115.8)



Percent of patients with AF > 30 seconds (n=22) among all patients (n=303) stratified by AHI. AHI <15 (n=1 af 65 patients), AHI 15-30 (n=7 of 93 patients), AHI > 30 (n= 14 of 145 patients)

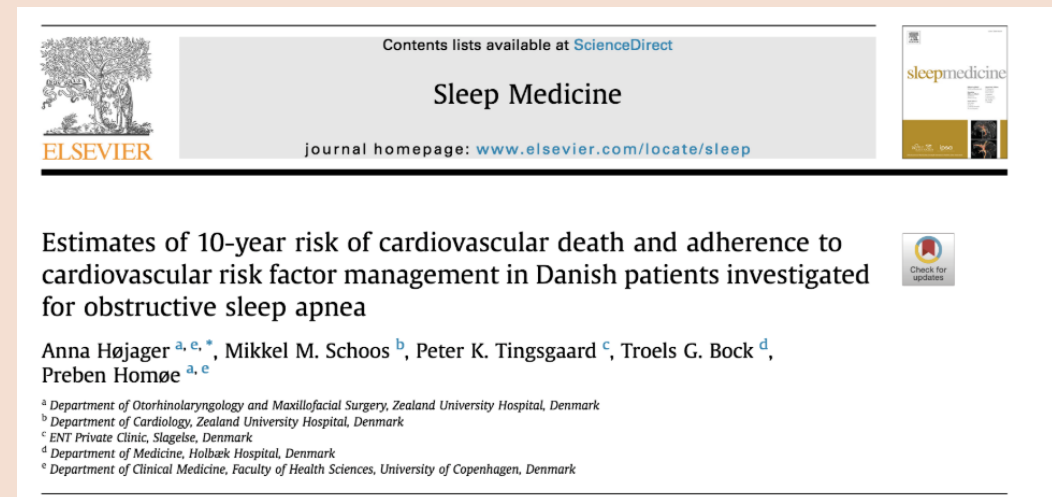


## Study II -Formål

Formålet var at *bestemme 10-års risiko for hjertedød* hos patienter med *mild/moderat/ svær OSA*

Ved brug af 2019 (ESC/EAS) *scorings-redskab* “Systematic Coronary risk Evaluation (SCORE) samt indikationen for *håndtering af risikofaktorer*.

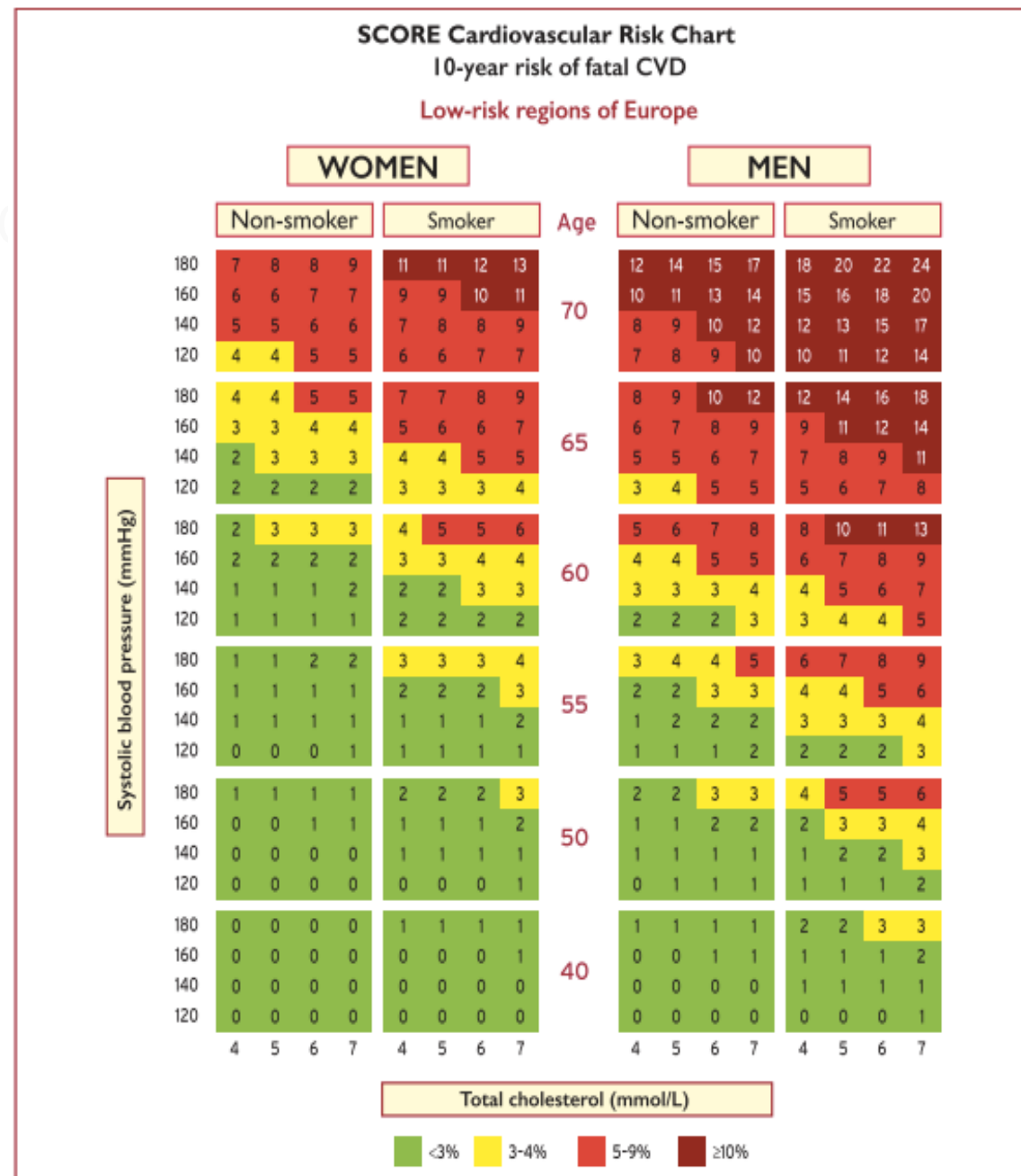
Desuden at undersøge *indikationen* for *præventiv, lipidsænkende farmakologisk behandling* hos patienter med OSA



Højager A, ET al. Estimates of 10-year risk of cardiovascular death and adherence to cardiovascular risk factor management in Danish patients investigated for obstructive sleep apnea. *Sleep Med.* 2023;104:22-28. doi:10.1016/j.sleep.2023.02.009

# Study III - Methods and data

2019 ESC/EAS SCORE risiko-scorings værktøj for 10-års risiko for hjertedød<sup>1</sup>



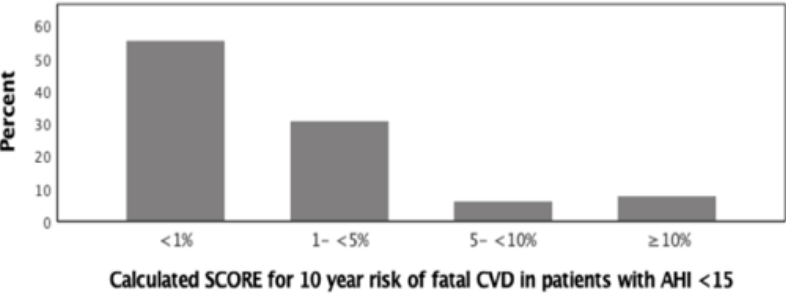
<sup>1</sup>Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111-188. doi:10.1093/eurheartj/ehz455

# Studie II - Resultater

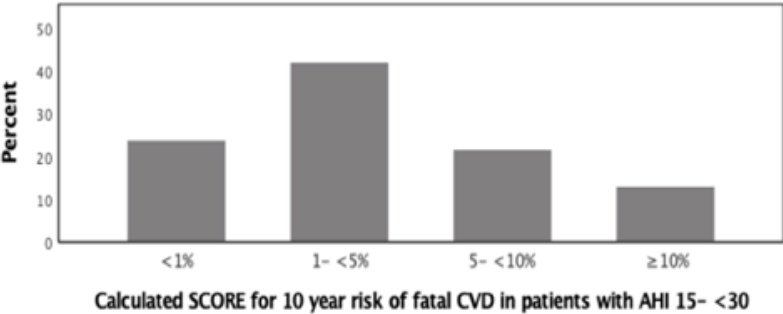




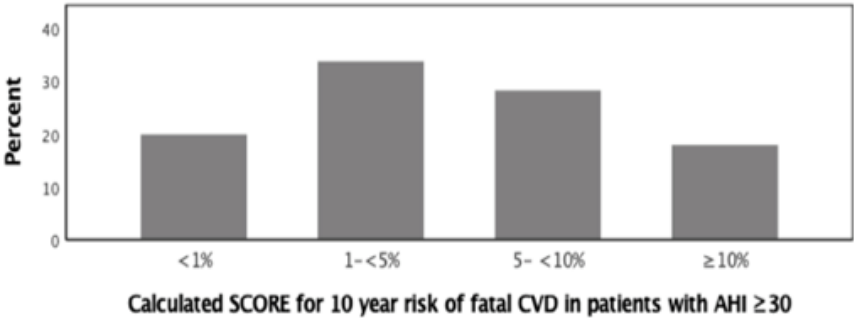
Calculated SCORE for 10-year risk of fatal CVD stratified by severity of OSA  
Procentsats svarende til 10-års risiko for hjertedød



Mild/ingen OSA



Moderat OSA



Svær OSA

AHI: apnea-hypopnea index. CVD: cardiovascular disease. OSA: obstructive sleep apnea. SCORE: systematic coronary risk estimation. Percent was for the total population (n=303)



# Studie II - forhøjet kolesterol og underbehandlet hypertension



Færre end 1/3 fik medicin mod forhøjet kolesterol (27.4%) af alle patienter

ESC  
European Society  
of Cardiology

European Heart Journal (2020) 41, 111–188  
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES



2019 ESC/EAS Guidelines for the management  
of dyslipidaemias: lipid modification to reduce  
cardiovascular risk

Statin-behandling var indiceret hos **yderligere 54 patienter** (17.8%) af alle 303 patienter

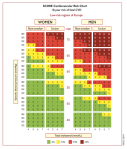
28.3% blandt patienter med moderat/svær OSA + forhøjet kolesterol



Underbehandlet hypertension\* hos 53% af alle patienter

\* Both patients with dysregulated hypertension in patients with known hypertension and unknown hypertension

# Studie II – primære fund og konklusion



10 års risikoen for hjertedød steg med mængden af kardiovaskulære risiko faktorer+ sværhedsgrad af OSA



Hos patienter ubehandlede for hyperkolesteolæmi med både OSA and dyslipidæmi

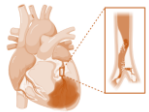
Var FLERE end 1 af 4 kandidater til kolesterolsænkende behandling



# Study I, II and III – overall conclusions



Stum og ikke-erkendt AF er hyppigt forekommende blandt patienter med OSA



Associerede kardiovaskulære komorbiditeter hos OSA-patienter er underbehandlede og der er et stort forebyggelses-potentiale



# Klinisk relevans og fremtids-perspektiver

Screening for (stum) atrieflimmer bør overvejes præventivt hos patienter med OSA

Screening og behandling af komorbiditeter hos patienter med *moderat* eller *svær* OSA bør **standardiseres nationalt** da der (for nuværende) ikke er **en national eller international guideline** til screening for komorbiditeter ved OSA

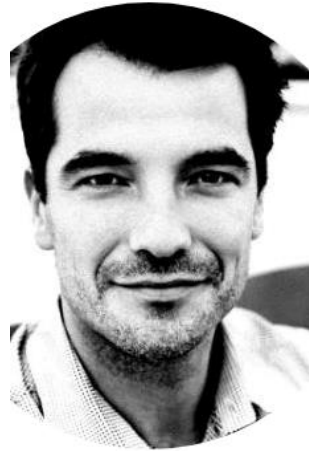
En mere **ensrettet behandling/udredning af patienter med OSA** er nødvendig tværsektorielt og regionelt i Danmark



# Many thanks



Professor, MD, P.h.D., *DMSc*  
Preben Homøe



Associate Professor, MD, Ph.D  
Mikkel Malby Schoos



MD, *DMSc*  
Troels G. Bock



MD, PhD  
Peter Koefoed Tingsgaard & team



Fonden for Faglig Udvikling af  
Speciallægepraksis

TOYOTA · FONDEN

Poul Traun-Pedersens mindelegat

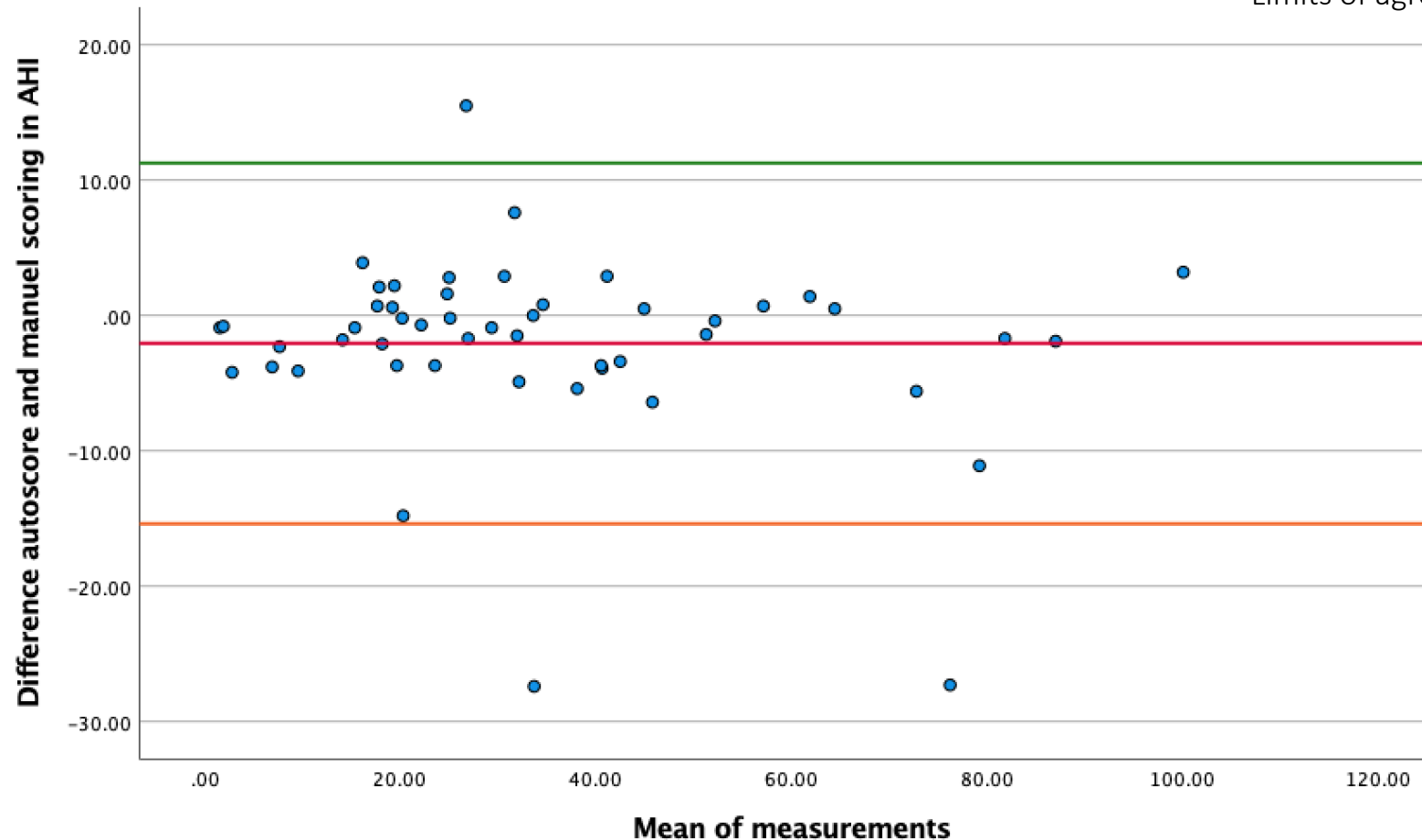
Region Sjællands Sundhedsvidenskabelige Forskningsfond (RSSF)





## Study II - validating autoscore NoxT3

Mean difference: -2.06 [95% CI:-3.99,-0.13].  
Limits of agreement: -15.38 and 11.26.



Bland-Altman plot of 50 samples

## Study II and III - Methods

Nox T3 sleep monitoring device



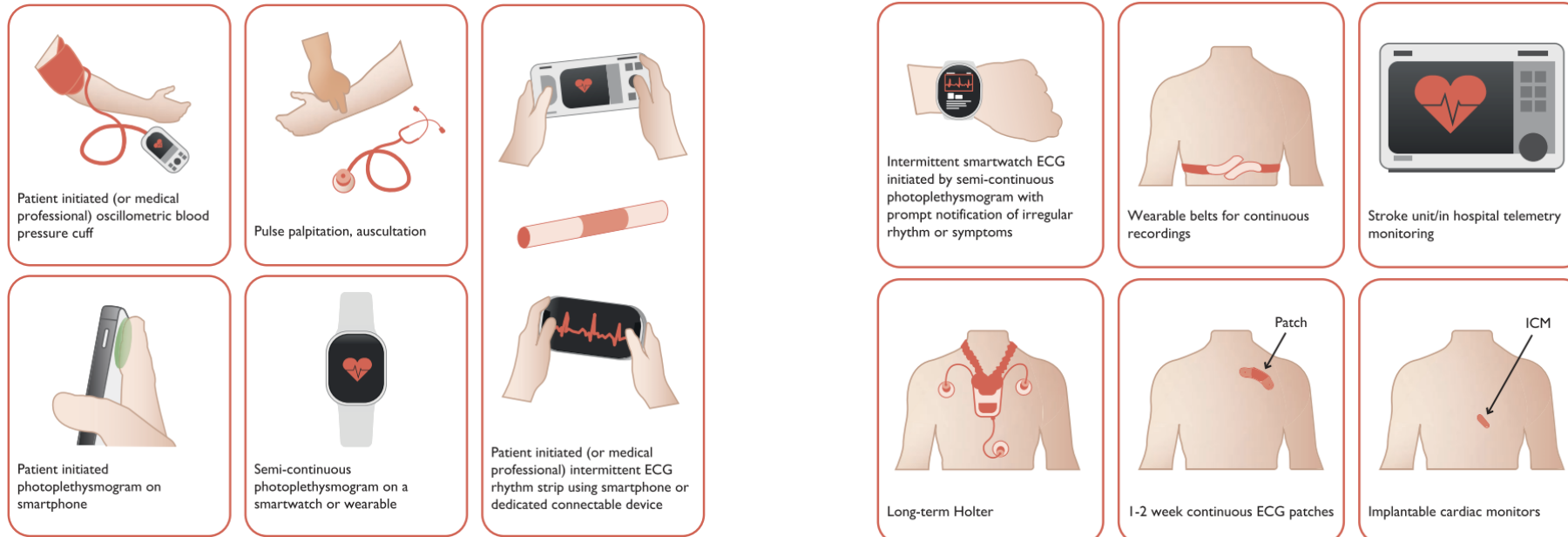
(Nox Medical Inc., Reykjavik, Iceland)

|        | No. of channels | Description                                                                                                                                                                                                                                                                                    |
|--------|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Type 1 | $\geq 7$        | In- laboratory polysomnography (PSG). Gold standard                                                                                                                                                                                                                                            |
| Type 2 | $\geq 7$        | Full un-attended PSG.<br>Portable                                                                                                                                                                                                                                                              |
| Type 3 | 4-7             | Channels typically including 2 respiratory variables (e.g. resp. movement, airflow), a cardiac variable (e.g. heart-rate or ECG) and arterial oxygen saturation. Other variables includes audio, body position and activity.<br>No signals to determine sleep stages or disruption<br>Portable |
| Type 4 | 1-2             | 1-2 channels, typically arterial oxygen saturation and airflow<br>Portable                                                                                                                                                                                                                     |

# Screening for AF and stroke prevention



Early identification of patients eligible for **anticoagulation therapy**





# Diagnosing OSA

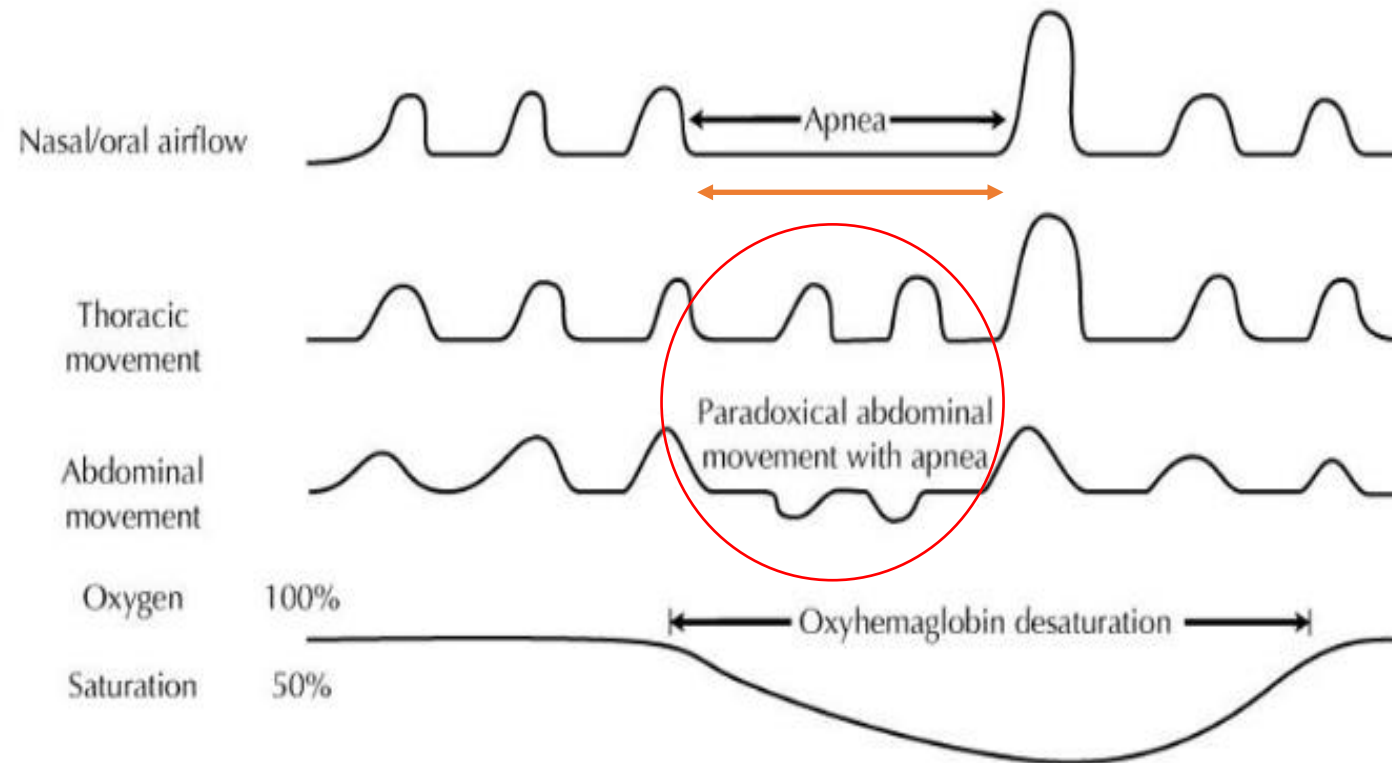
Severity of OSA is measured by the **apnea-hypopnea-index (AHI)** (mean number of apneas/hour sleep)

AHI 5- <15 mild OSA

Treatment of OSA is offered in Denmark

AHI 15- <30 moderate OSA

AHI  $\geq 30$  severe OSA







Extra slides



# Beta-blockers and AF

- No data on Beta-blockers/ $\text{Ca}^{2+}$  antagonist treatment (antiarrhythmics) or potassium-antagonist's such cordarone
- Therefore it might be possible that some patients might be prone to AF but did not present that



# Echocardiography findings

Echocardiography was not performed or interpreted by the same operator

Unfortunately, in echocardiography, interrater variability is significantly different with different operators.



## Echocardiography findings in patients with atrial fibrillation, study II

| Patient no: | LV                   | LVEF    | Valvular disease                                                                                        | Atrium sizes             | Other findings           |
|-------------|----------------------|---------|---------------------------------------------------------------------------------------------------------|--------------------------|--------------------------|
| 1           | Mild hypertrophic LV | Normal  | Mild aortic insufficiency                                                                               | Normal                   | -                        |
| 2           | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 3           | Normal               | 50 %    |                                                                                                         | LA moderately dilated    | Mildly dilated RV        |
| 4           | Normal               | Normal  |                                                                                                         | Normal                   | Mildly dilated RV        |
| 5           | Mild hypertrophic LV | 40 %    | -                                                                                                       | Moderate dilated atriums | -                        |
| 6           | Normal               | Normal  | Mild mitral insufficiency+ mild tricuspid insufficiency                                                 | LA mildly dilated        | -                        |
| 7           | Mild hypertrophic LV | Normal  | Mild tricuspid insufficiency                                                                            | Normal                   | Mildly dilated aorta asc |
| 8           | Normal               | 40 %    | Mild mitral insufficiency                                                                               | RA+LA dilated            | -                        |
| 9           | Mild hypertrophic LV | Normal  | -                                                                                                       | Normal                   | Moderate aortic ectasia  |
| 10          | Normal               | Normal  | Mild mitral insufficiency                                                                               | Normal                   | -                        |
| 11          | Mild hypertrophic LV | 45-50 % | -                                                                                                       | Normal                   | -                        |
| 12          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 13          | Mild hypertrophic LV | Normal  | Mild mitral insufficiency + sclerotic mitral valve +mild mitral insufficiency                           | LA severely dilated      | -                        |
| 14          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 15          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 16          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 17          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 18          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |
| 19          | Normal               | Normal  | Mild aortic stenosis                                                                                    | Normal                   | -                        |
| 20          | Normal               | > 55 %  | Sclerotic and mildly insufficient tricuspid valve +mild aortic insufficiency+ mild mitral insufficiency | Normal                   | -                        |
| 21          | Mild hypertrophic LV | 45 %    | -                                                                                                       | Normal                   | -                        |
| 22          | Normal               | Normal  | -                                                                                                       | Normal                   | -                        |

LA: left atrium.LV: left ventricle. LVEF: left ventricle ejection fraction. RA: right atrium. RV: right ventricle



## Study II, ELR recordings of patients with AF

| Time to first episode of AF, hours | Total AF burden, hh:min:sec | Number of episodes | Monitoring time dd:hh:min | Other findings                               |
|------------------------------------|-----------------------------|--------------------|---------------------------|----------------------------------------------|
| 1                                  | 00:37:00                    | 19                 | 06:16:56                  | EAT, PSVT                                    |
| 47                                 | 00:02:00                    | 1                  | 06:20:52                  | PVC in bigeminy, trigeminy, non-sustained VT |
| 0                                  | 30:18:00                    | 1053               | 06:01:01                  | -                                            |
| 36                                 | 00:06:00                    | 4                  | 06:06:11                  | -                                            |
| 1                                  | 84:54:00                    | 904                | 07:01:44                  | -                                            |
| 135                                | 00:02:00                    | 1                  | 06:19:40                  | PVC in bigeminy                              |
| 153                                | 00:04:00                    | 4                  | 08:07:53                  | -                                            |
| 0                                  | 140:21:00                   | 91                 | 06:15:16                  | non-sustained VT                             |
| 39                                 | 03:59:00                    | 75                 | 06:23:20                  | -                                            |
| 36                                 | 27:26:00                    | 240                | 06:14:24                  | -                                            |
| 120                                | 00:02:00                    | 2                  | 06:14:40                  | Non-sustained VT                             |
| 19                                 | 00:23:00                    | 7                  | 06:20:16                  | PSVT, non-sustained VT                       |
| 141                                | 00:00:30                    | 1                  | 06:15:00                  | PSVT, non-sustained VT                       |
| 23                                 | 05:38:00                    | 167                | 06:20:56                  | -                                            |
| 134                                | 00:08:00                    | 1                  | 06:00:14                  | -                                            |
| 28                                 | 00:36:00                    | 21                 | 05:18:00                  | -                                            |
| 46                                 | 06:35:00                    | 120                | 07:02:41                  | PSVT                                         |
| 66*                                | 00:11:00                    | 2                  | 06:23:20                  | -                                            |
| 39                                 | 00:31:00                    | 10                 | 06:20:16                  | -                                            |
| 34                                 | 13:03:00                    | 291                | 07:04:04                  | EAT                                          |
| 5                                  | 00:05:00                    | 3                  | 07:04:32                  | -                                            |
| 98                                 | 05:45:00                    | 40                 | 07:11:13                  | -                                            |



# Study I - other arrhythmia's

- 14 (7%) Non-sustained ventricular tachycardia (non-sus VT >3 complexes)
- 5 (2.5%) pauses at night of >2.5 seconds
- 1 (0.5) Ectopically multifocal tachycardia
- 5 (2.5%) bradycardia at night



## Study II - other arrhythmia's

- 69 (22.8%) paroxysmal supraventricular tachycardia/ PSVT/SVT
- 24 (7.9%) Non-sustained ventricular tachycardia (non-sus VT >3 complexes)
- 5 (1.7%) AF <30 seconds
- 5 (1.7%) pauses at night of 2.2 -9.6 seconds
- 4 (1.3%) Ectopically multifocal tachycardia
- 1 Wolff-Parkinson Whites syndrome (WPW) + SVT

# Statistics – study I

Exact logistic regression was used in models with controlling for either age or both age and gender.

All variables with a  $p < 0.1$  from univariate analysis were entered in the model with one exception of the  $\text{CHA}_2\text{DS}_2\text{VAS}_\text{c}$ -score, as the variable was incorporated in the inclusion criteria.

Cumulative incidence rates (time to first detection) of AF are presented as cumulative incidence curves.

Normality was checked by histograms and residual plots (q-q plots) (study I, II and III).

# Sample size calculations –study I

In an effort to estimate the sample size and number of events, a power analysis was performed based on several previous studies of AF among patients with diabetes ~detection rate of 4% prevalence of AF.

In a risk-enriched diabetes population with at least one additional CHA2DS2VASC risk factor and with longer monitoring for AF than in the previous studies, we hypothesized that we might identify twice as many AF events and with a power of 80% and an alpha of 0.05.

A sample-size calculation of 110 to 230 patients would be able to provide a significantly higher than previously reported prevalence of an 8 to 10 % of AF in this diabetes population.

# Statistics- study II

A **logistic regression analysis with backward elimination** to assess risk of AF association with risk factors. Variables with a  $p < 0.1$  from univariate analysis were entered in the model.

## Sample size calculations (study II and III)

The **power analysis** was performed based on various previous studies of AF among patients with OSA. The analysis gave an expectation of a detection rate of unknown AF among these patients of **approximately 4%**.

With a longer monitoring time, we hypothesized the detection rate could be **approximately 8%**. With a power of 80% and an alpha of 0.05%, the sample size calculation **estimated a study group of 230 patients** to be able to provide a significantly higher prevalence of AF among patients with OSA as previously reported.

# Statistics –study III

10-year risk of fatal CVD estimated with the (SCORE) risk chart based on variables:

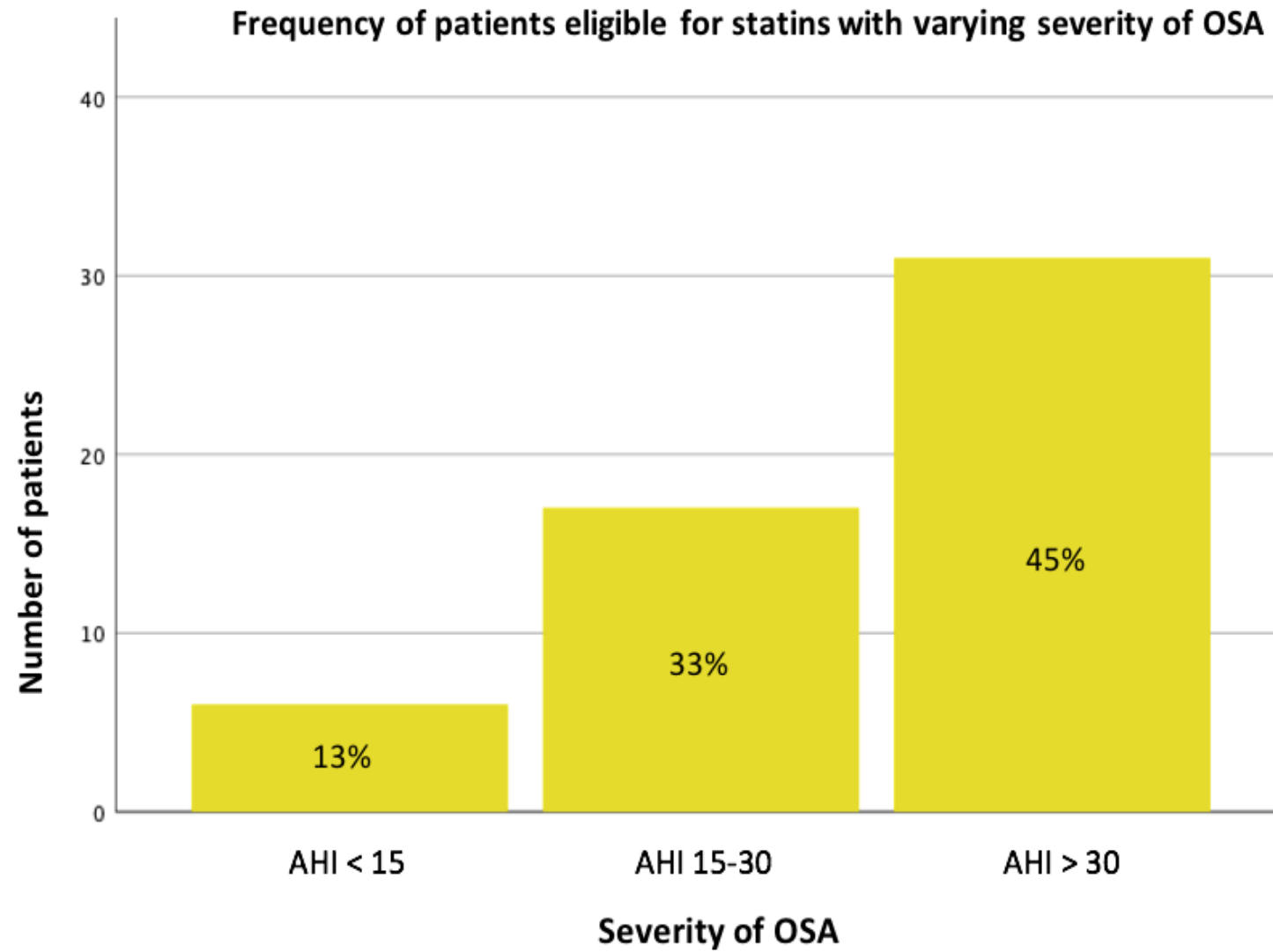
- age,
- Sex
- systolic blood pressure measurements
- blood-sample analysis (p-total cholesterol and p-LDL),
- active smokers yes/no
- diabetes,
- documented arteriosclerotic CVD,
- severe chronic kidney disease (CKD)
- familial hypercholesterolemia.

Patients were allocated in risk categories of *low*, *moderate*, *high* and *very high* risk.

## Statin eligibility

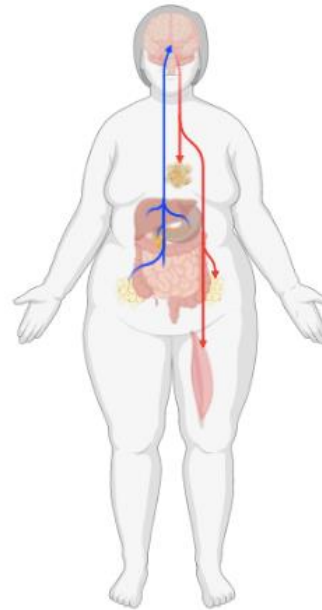
- Assessed based on to the Class 1/A recommendation for statins of the EAC/EAS 2019 guideline for the management of dyslipidaemias

## Study III



# Metabolic syndrome

(international diabetes federation, IDF)



**Table 2.** IDF Metabolic Syndrome World-wide Definition.

**CENTRAL OBESITY**

Waist circumference\*– ethnicity specific (Table 2)

Plus any two of the following:

- **RAISED TRIGLYCERIDES:**  
≥ 150mg/dl (1.7 mmol/l)  
or specific treatment for this lipid abnormality
  - **REDUCED HDL-CHOLESTEROL**  
< 40 mg/dl (1.03 mmol/l) in males  
< 50 mg/dl (1.29 mmol/l) in females  
or specific treatment for this lipid abnormality
  - **RAISED BLOOD PRESSURE**  
Systolic : ≥ 130 mmHg  
or Diastolic: ≥ 85 mmHg  
or treatment of previously diagnosed hypertension
  - **RAISED FASTING PLASMA GLUCOSE\*\***  
Fasting plasma glucose ≥ 100 mg/dl (5.6 mmol/l)  
or previously diagnosed type 2 diabetes  
If above 5.6 mmol/l or 100 mg/dl, OGTT is strongly recommended but is not necessary to define presence of the syndrome.
- \* If BMI is > 30 kg/m<sup>2</sup> then central obesity can be assumed, and waist circumference does not need to be measured. Ethnic specific waist circumference are listed in table 2.
- \*\* In clinical practice, IGT is also acceptable, but all reports of the prevalence of the metabolic syndrome should use only the fasting plasma glucose and presence of previously diagnosed diabetes to assess this criterion. Prevalences also incorporating the 2 hour glucose results can be added as supplementary findings.

# Polysomnography vs. Type III portable device

## PSG:

- Sleep expert analyzes all data (often >4hours) after strict guidelines of American Academy of Sleep Medicine (AASM)
- Noticing ALL beginnings and endings of periods with disrupted breathing
- Expensive
- Uncomfortable
- Time-consuming (both analyst's and patient)

## Nox T3:

- Clinically validated against PSG
- 7 Channels
- Automatic detection and analyzing software
- More patient friendly
- Less expensive
- Less time-consuming for trained analyst

|        | No. of channels | Description                                                                                                                                                                                                                                                                                    |
|--------|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Type 1 | $\geq 7$        | In- laboratory polysomnography (PSG). Gold standard                                                                                                                                                                                                                                            |
| Type 2 | $\geq 7$        | Full un-attended PSG.<br>Portable                                                                                                                                                                                                                                                              |
| Type 3 | 4-7             | Channels typically including 2 respiratory variables (e.g. resp. movement, airflow), a cardiac variable (e.g. heart-rate or ECG) and arterial oxygen saturation. Other variables includes audio, body position and activity.<br>No signals to determine sleep stages or disruption<br>Portable |
| Type 4 | 1-2             | 1-2 channels, typically arterial oxygen saturation and airflow<br>Portable                                                                                                                                                                                                                     |

# Apneas

## Obstructive apneas

- Drop in airflow of at least 90% lasting for a minimum of 10 seconds w + ongoing respiratory effort (paradox respiration)

## Hypopneas

- Drop of airflow of at least 30% in 10 seconds + followed by a drop of oxygen saturation of minimum 3 % *or EEG arousal*

## Mixed apneas

- Components of both obstructive and central sleep apnea

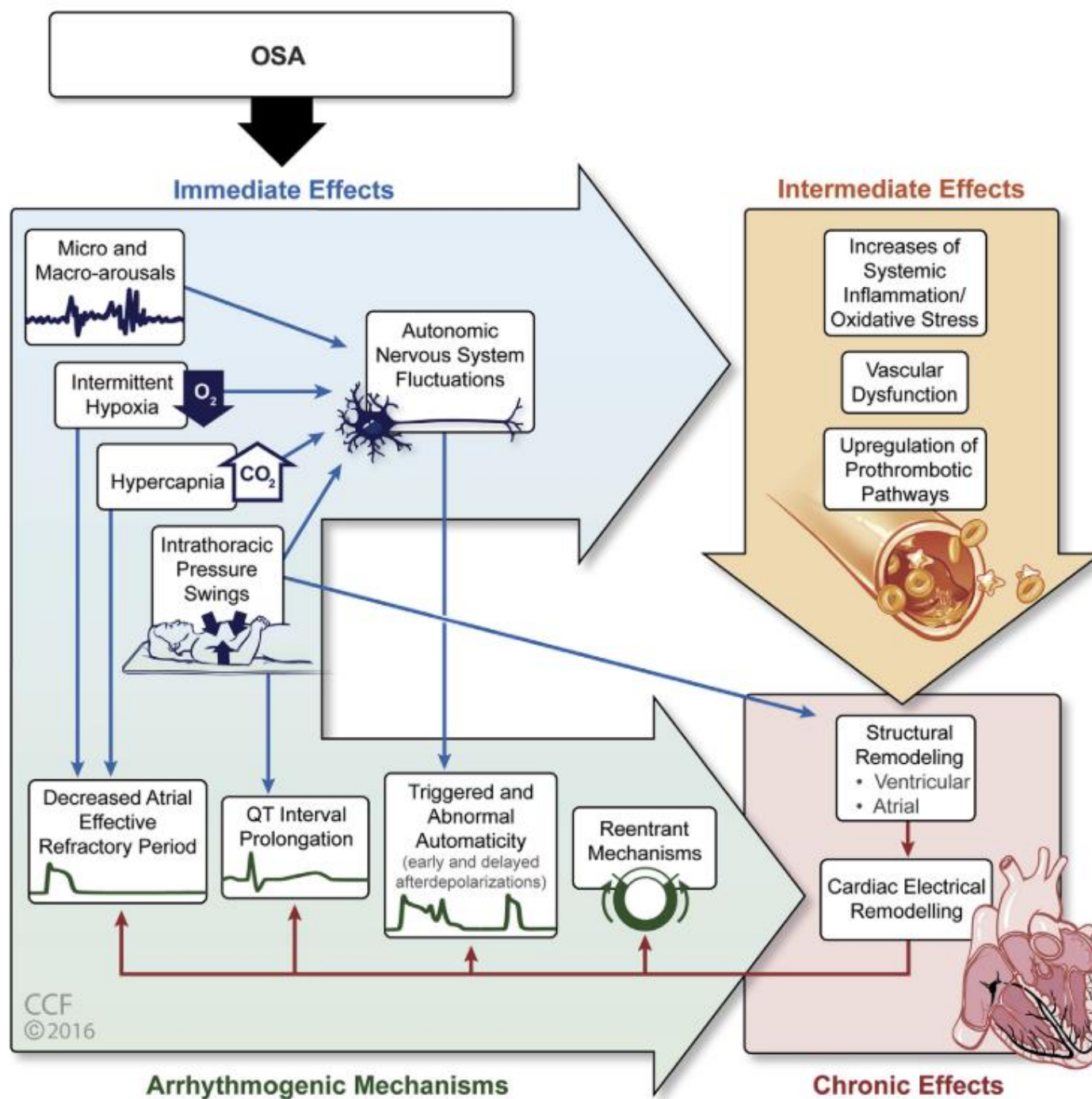
## Central sleep apneas

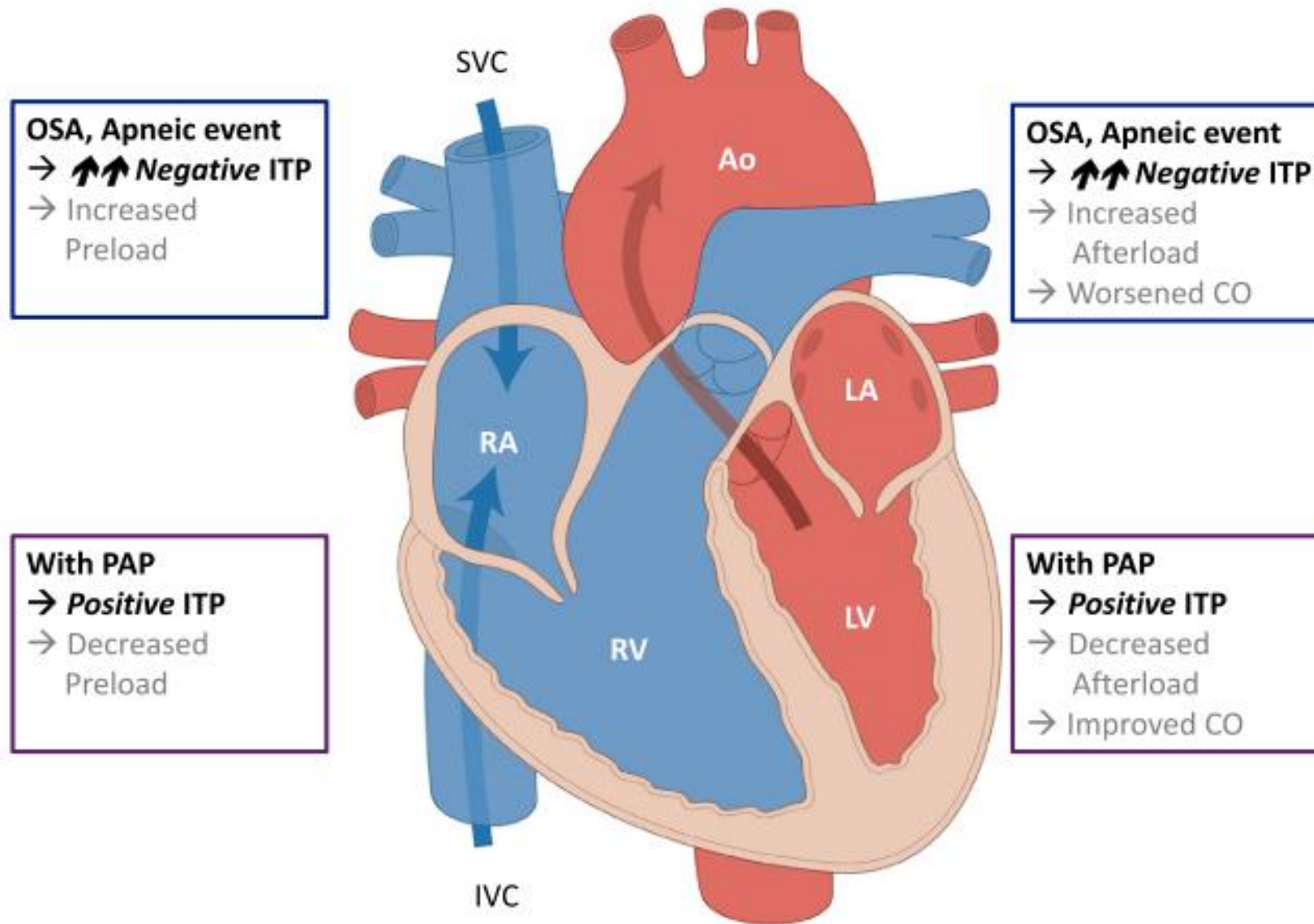
- 10 seconds pause in airflow with *no respiratory effort* throughout the apnea

Table 2. Summary of treatment recommendations in adherence to the American Academy of Sleep Medicine

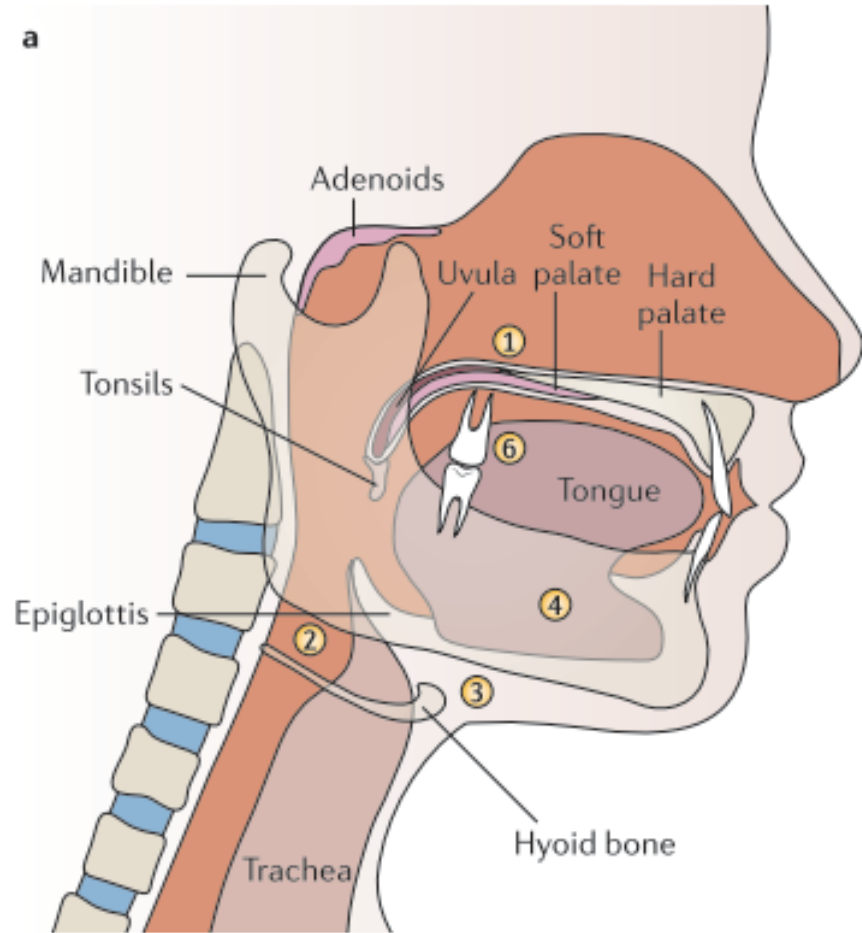
|                                                                          | Recommendations                                                                                                                                                                                                  |
|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CPAP positive airway pressure                                            | Verified AHI of 15 or above: Clinicians use CPAP compared to no therapy in adults with; excessive sleepiness (strong), impaired quality of life (conditional), comorbid hypertension (conditional) <sup>65</sup> |
| Oral appliances (mandibular advancement device, tongue retaining device) | Clinicians consider use oral appliances rather than no treatment in adult patients with verified OSA who are intolerant of CPAP or prefer alternative treatment <sup>66</sup>                                    |
| Upper airway surgery                                                     | Clinicians consider surgical therapy when CPAP or oral appliance is <u>ineffective<sup>a</sup></u> or declined <sup>67</sup>                                                                                     |
| Weight loss                                                              | Weight loss and exercise should be recommended to all patients with verified OSA who are overweight or obese <sup>64</sup> .                                                                                     |

<sup>a</sup> At least 3 months trial of therapy





Patient without OSA



OSA patient

