



Kantonsspital Aarau



HK HormoKine GmbH
Nachhaltige Medizin & Spitalmanagement

Endokrinologie 2033 – Clinical reasoning besser als Artificial Intelligence?

Essen Sie weniger und trinken Sie mehr !

Mediterrane Kost gegen Alzheimer-Demenz !

Beat Müller, M.D.

Argovia Professor

Medical Faculty University of Basel



2013

Frau K.K. wird 58, pensioniert, will nun «gesund leben»



Diagnosen:

- **Metabolisches Syndrom** mit
 - Adipositas (BMI 37 kg/m²)
 - Diabetes mellitus Typ II
 - Dyslipidämie
 - Arterielle Hypertonie
 - pos. Familienanamnese
- **Atherosklerose** mit
 - Mikroangiopathie mit Mikroalbuminurie
 - Vd. Subklinische Makroangiopathie bei Nikotin (20pyrs, gestoppt vor 10J)
- **Rezidivierende HWIs seit Menopause**

„Clinical Reasoning“ → Therapie

- **Weniger Essen & mehr Bewegung**
- **Salzarme Kost & „viel Trinken“**
- **Medikamentös** unterstützt
 - Metformin & GLP-1 Agonist? (wenn erhältlich...)
 - Zestoretic 20/12.5mg
 - Rosuvastatin 20mg
 - E2 Vaginal-Supp.

2033! (78J), Notfall mit Fieber, Dyspnoe & Husten



Hauptdiagnose: „Poly-Morbidität“

- **Pneumonie? COVID-33?** DD: **COPD** Exacerbation
 - **Atherosklerose** mit KHK & CHF
 - Nikotin (20pyrs, stop vor 30J.)
 - Arterielle Hypertonie, Dyslipidemia, pos. FH
 - **Hyponatriämie**
 - **M. Parkinson** mit rezidivierenden Stürzen
 - **Polyarthrose & Osteoporose** mit Schmerzen
 - **Malnutrition** mit Sarkopenie, BMI 24m/kg²
-
- **Mildes kognitives Defizit**
 - **Sozial:** Wittwe,
3 Kinder, erfolgreiche Wissenschaftler (USA)

Lebt zu Hause

8 Medikamente = **14 Tabletten jeden Tag . . .**

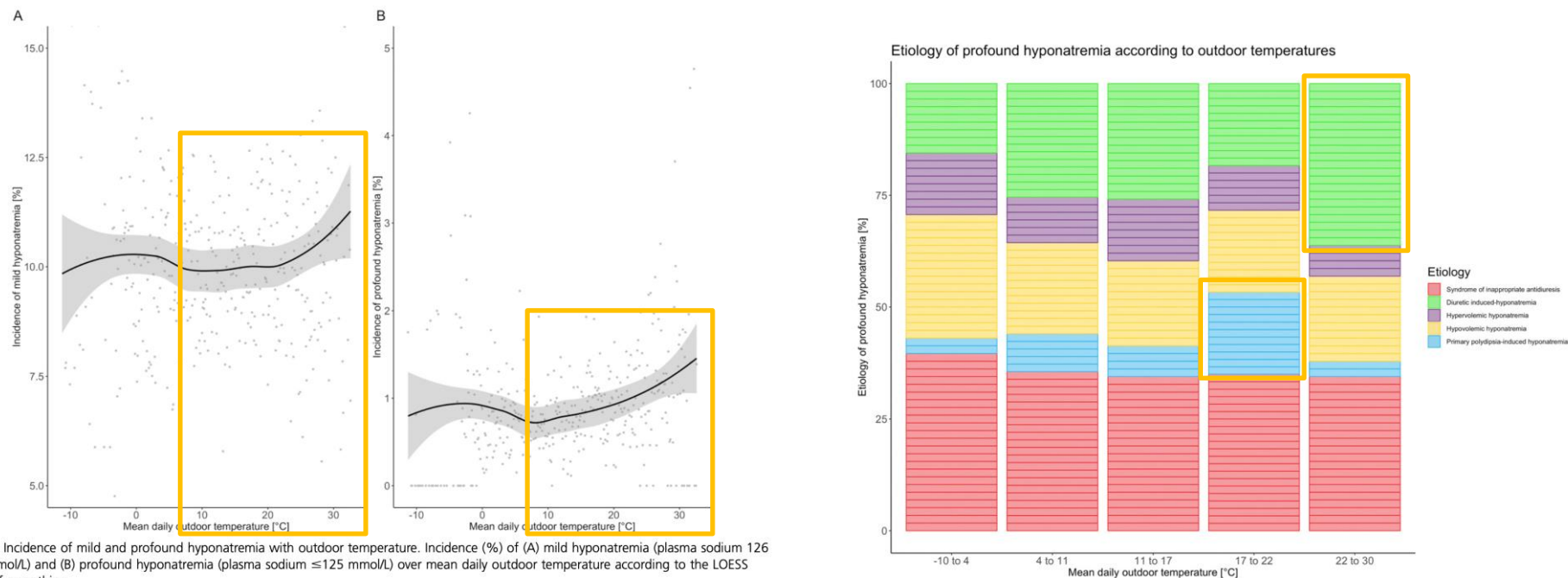
Ziel des Vortrages ist ihr Handeln vor 2033 zu verbessern, indem sie lernen, dass „gute“ Ratschläge für eine rüstige 58-Jährige, für 78-jährige polymorbide PatientInnen tödlich sein können.

Viel Trinken im Sommer – Zuviel des Guten ?

CLINICAL RESEARCH ARTICLE

Influence of Outdoor Temperature and Relative Humidity on Incidence and Etiology of Hyponatremia

Clara O. Sailer,^{1,2*} Bettina Winzeler,^{1,2*} Nicole Nigro,¹ Luca Bernasconi,³ Beat Mueller,⁴ and Mirjam Christ-Crain^{1,2}



Conclusions: Higher outdoor temperature, but not relative humidity, seems to be associated with the incidence of profound hyponatremia. Our data suggest that diuretics should be used with caution during hot weather. (*J Clin Endocrinol Metab* 104: 1304–1312, 2019)

Artificial Intelligence heute ?

ChatGPT

HA

I am 75 years old and on diuretic treatment due to arterial hypertension with impaired kidney function. It is summer and very hot. How much water should I drink per day ?



I'm not a doctor, but I can offer some general guidance. Staying properly hydrated is crucial, especially in hot weather and when you're on diuretic medication. However, your specific water intake needs can vary based on individual factors, so it's essential to discuss this with your healthcare provider. They can provide personalized recommendations based on your medical history, medications, kidney function, and overall health.



Artificial Disclaimer !

ChatGPT

1. **Consult Her Healthcare Provider:** Your mother's doctor can provide specific guidance based on her medical history, medications, and overall health. They can assess her individual fluid needs and may adjust her medication dosage if necessary.
2. **Encourage Regular Hydration:** Remind your mother to drink fluids regularly throughout the day. Encourage her to have a glass of water or other hydrating beverages at set intervals.
3. **Monitor for Signs of Dehydration:** Keep an eye out for signs of dehydration, such as dark urine, dry mouth, dizziness, weakness, or confusion. If any of these symptoms occur, it's crucial to address them promptly.
4. **Hydrating Foods:** Some foods have a high water content and can contribute to hydration. Encourage your mother to consume fruits like watermelon, oranges, and berries, as well as vegetables like cucumber and celery.
5. **Limit Caffeine and Alcohol:** These substances can have diuretic effects, potentially increasing fluid loss. While moderate consumption is generally acceptable, it's best to avoid excessive intake, especially in hot weather.
6. **Electrolyte Balance:** If she sweats heavily due to the heat, she may lose not only water but also important electrolytes like sodium and potassium. Encourage her to eat foods rich in electrolytes or speak to her doctor about the need for electrolyte supplements.
7. **Use a Reusable Water Bottle:** Having a reusable water bottle with her throughout the day can serve as a visual reminder to stay hydrated and make it convenient to sip water regularly.
8. **Stay Cool:** Avoiding excessive heat exposure can reduce the risk of dehydration. Encourage her to stay in a cool environment during the hottest parts of the day and wear light, breathable clothing.
9. **Medication Timing:** Ensure she takes her hypertension medication as prescribed. Some medications may affect fluid balance, so follow her doctor's instructions closely.

Remember that individual hydration needs can vary, and it's crucial to tailor recommendations to your mother's specific circumstances. Her healthcare provider is the best source of guidance regarding her fluid intake, especially considering her age, health status, and medications.

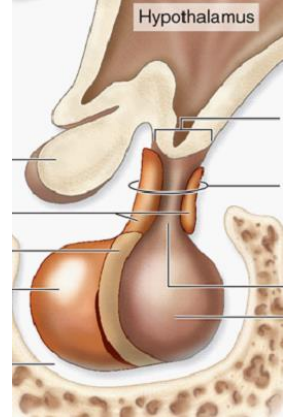


«Clinical Reasoning» heute

Anti-Diuretisches Hormon = Arginin-Vasopressin

ADH = AVP = 3 Funktionen

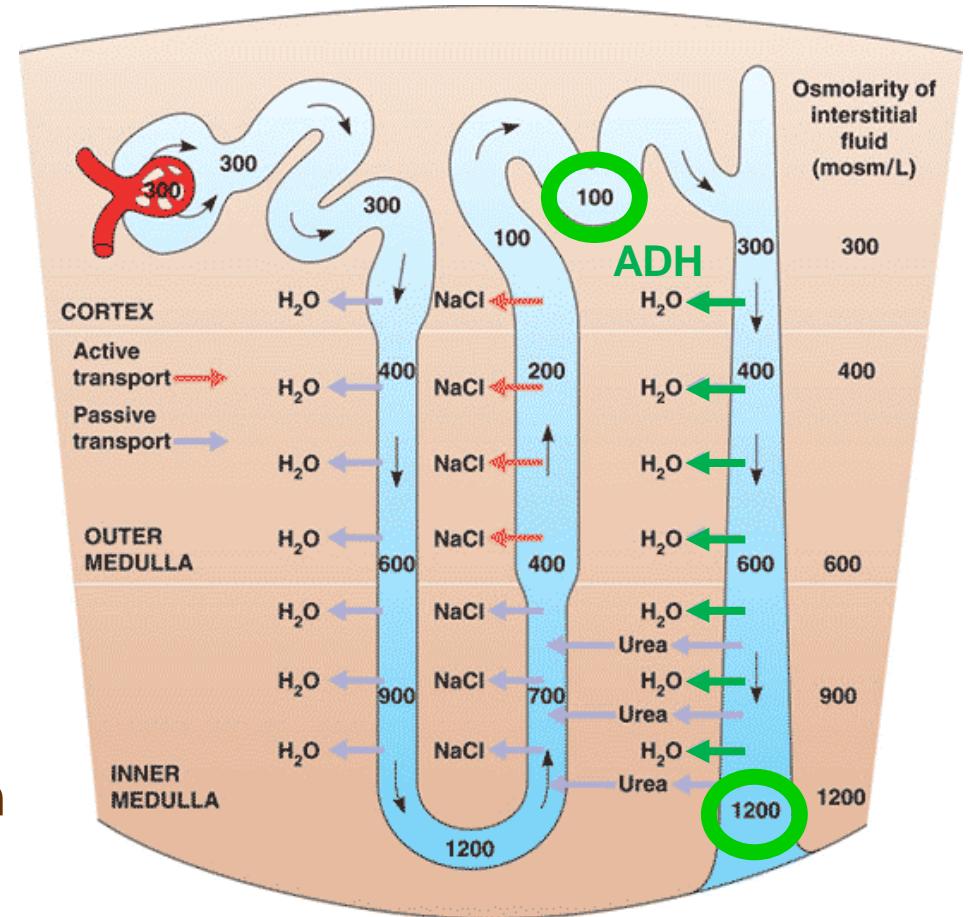
1) Wasser- (& so indirekt auch Salz-) Haushalt



Anti-Diuretisches Hormon & Niere

Plasma: 280 – 295 mosm/kg
↓ADH↑

- **ADH** bindet an V2-Rezept.
- Steigerung der **H₂O-Permeabilität** in distalen Tubuli/ Sammelrohren
- H₂O - Rückresorption↑
- Urinkonzentration ↑
- Angewiesen auf **renalen Gradienten !**
- **Um diesen Gradienten aufzubauen, braucht es Salz im Primärharn (← im Essen !)**



Urin: 100 – 1200 mOsm/kg



24. Wasser & Salz

Ce qui est important en médecine, c'est de comprendre avant d'apprendre.

INTAKE

EXCRETION

Salt in Food



NaCl
12g/d

Salt in „Water“ (g/L)

Sea 30g/L

mOsm

Shark 

1000

Blood 


100



Lake
Tapwater
Tea, Juice
Beer . . . 1-2g/L

Distilled 0g/L

10



Insens. Losses
Lung

1

30g/L
ADH

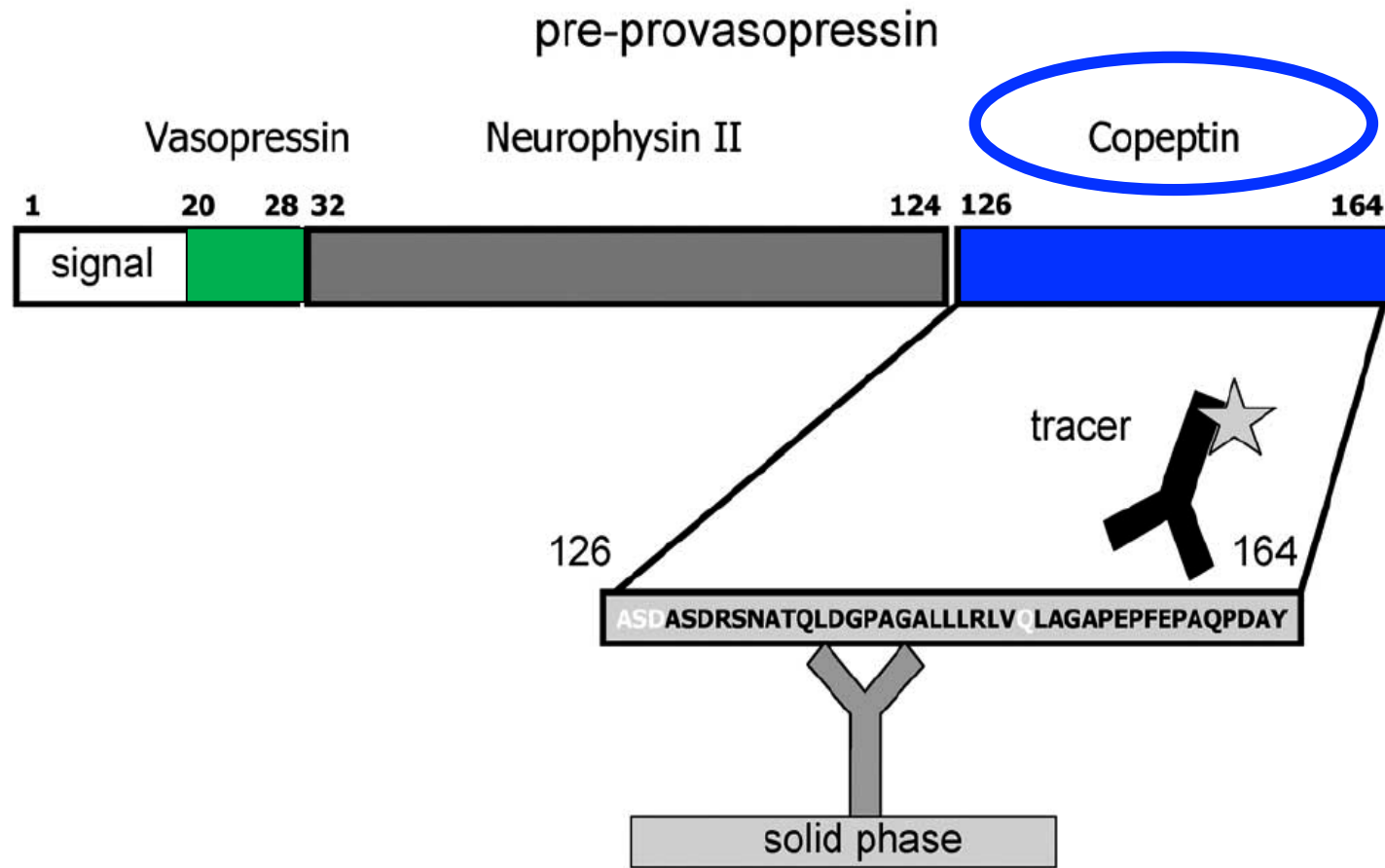
Urine

(ADH)
2g/L



Sweat
(5g/L)

... and then came Copeptin !



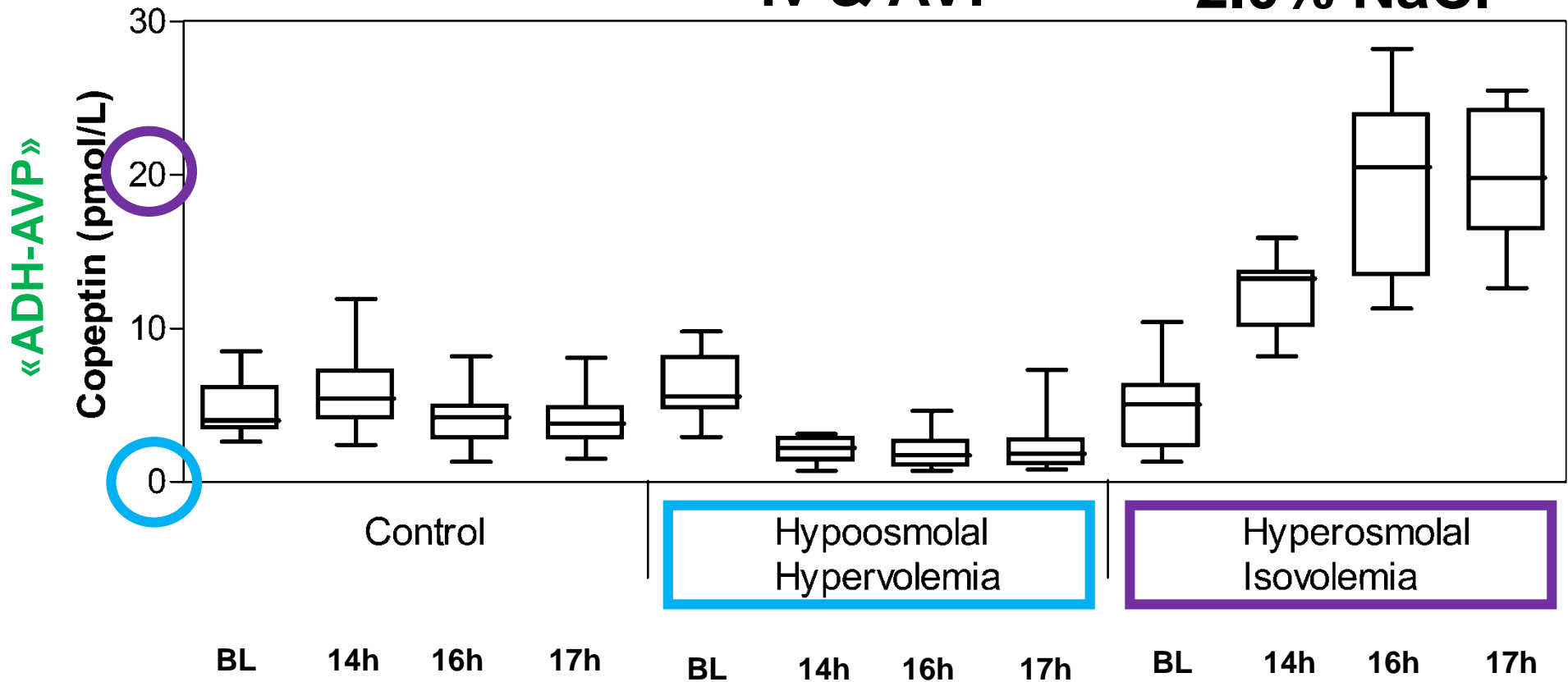
ADH/AVP - precursor can now be measured!

ADH-Produktion & Osmolarität

Freies Wasser

Freies Wasser
iv & AVP

Dursten &
2.0% NaCl

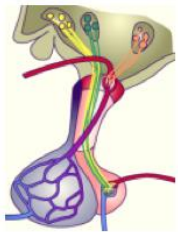


Polyuria / Polydipsia Syndrome

Definition: Polyuria > 50ml/kgBW/24h, Polydipsia



„ADH Deficiency“
Central
Diabetes insipidus (DI)

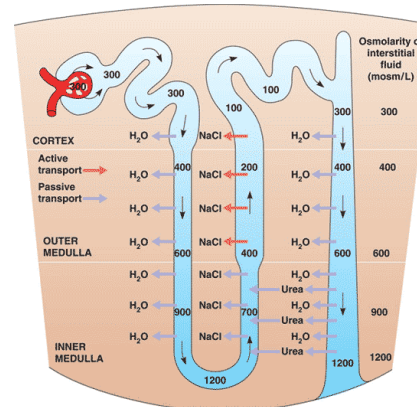
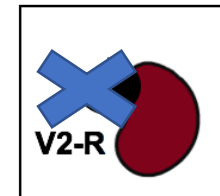
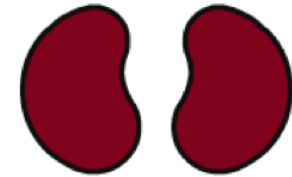


DD ?

Primary
Polydipsia (PP)



„ADH Resistance“
Nephrogenic
Diabetes insipidus



Exzessives Trinken von H₂O
→ “Ausschwemmen” renalen
Salzgradient (1200 → 300 mOsm)
→ Urin kann nicht mehr
konzentriert werden !
→ “pseudo-renaler D.i.”

Baseline Copeptin
>21.4pmol/l

A Copeptin-Based Approach
in the Diagnosis of Diabetes Insipidus

W. Fenske, J. Refardt, I. Chifu, I. Schnyder, B. Winzeler, J. Drummond,
A. Ribeiro-Oliveira, Jr., T. Drescher, S. Bilz, D.R. Vogt, U. Malzahn, M. Kroiss,
E. Christ, C. Henzen, S. Fischli, A. Tönjes, B. Mueller, J. Schopohl,
J. Flitsch, G. Brabant, M. Fassnacht, and M. Christ-Crain



A Central Diabetes Insipidus vs. Primary Polydipsia

B Complete or Partial Central Diabetes Insipidus vs. Primary Polydipsia

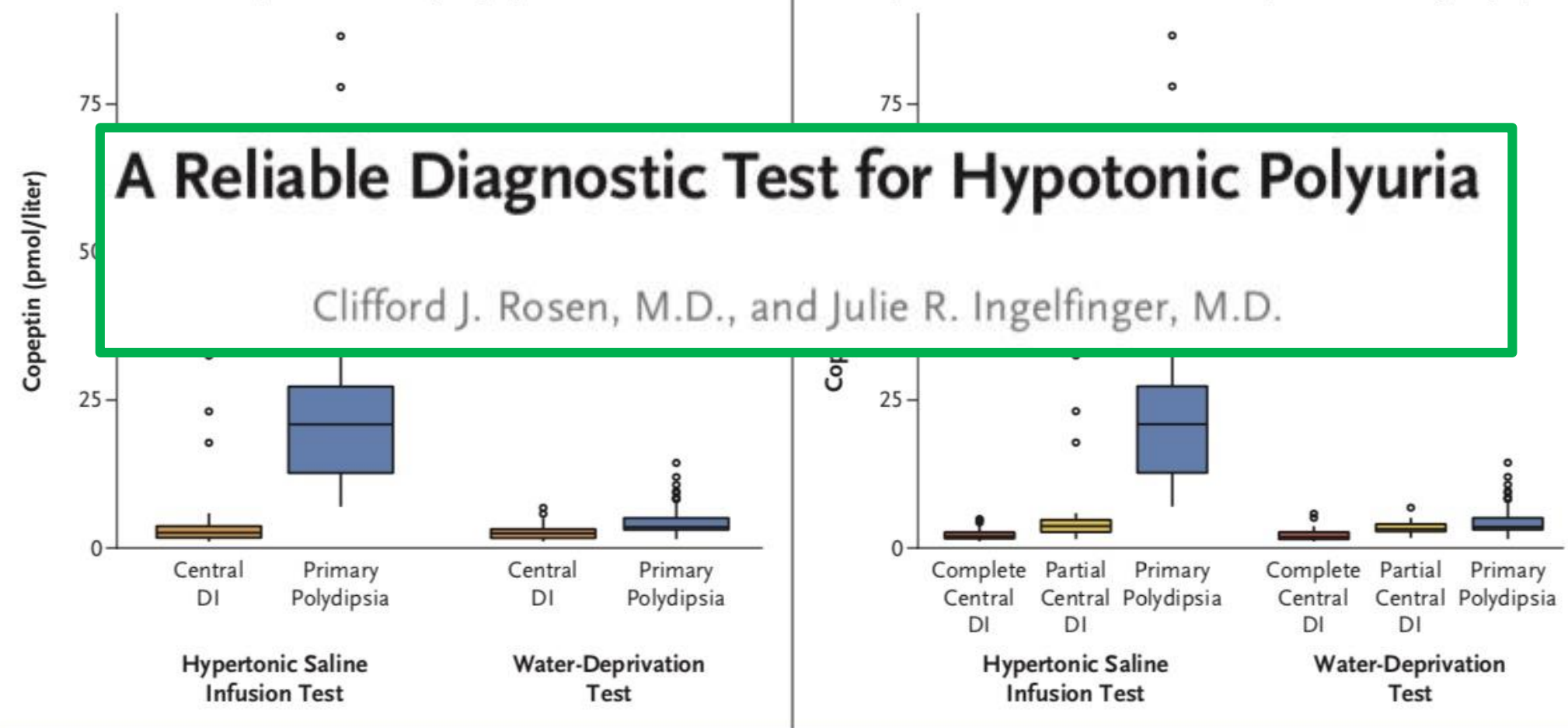
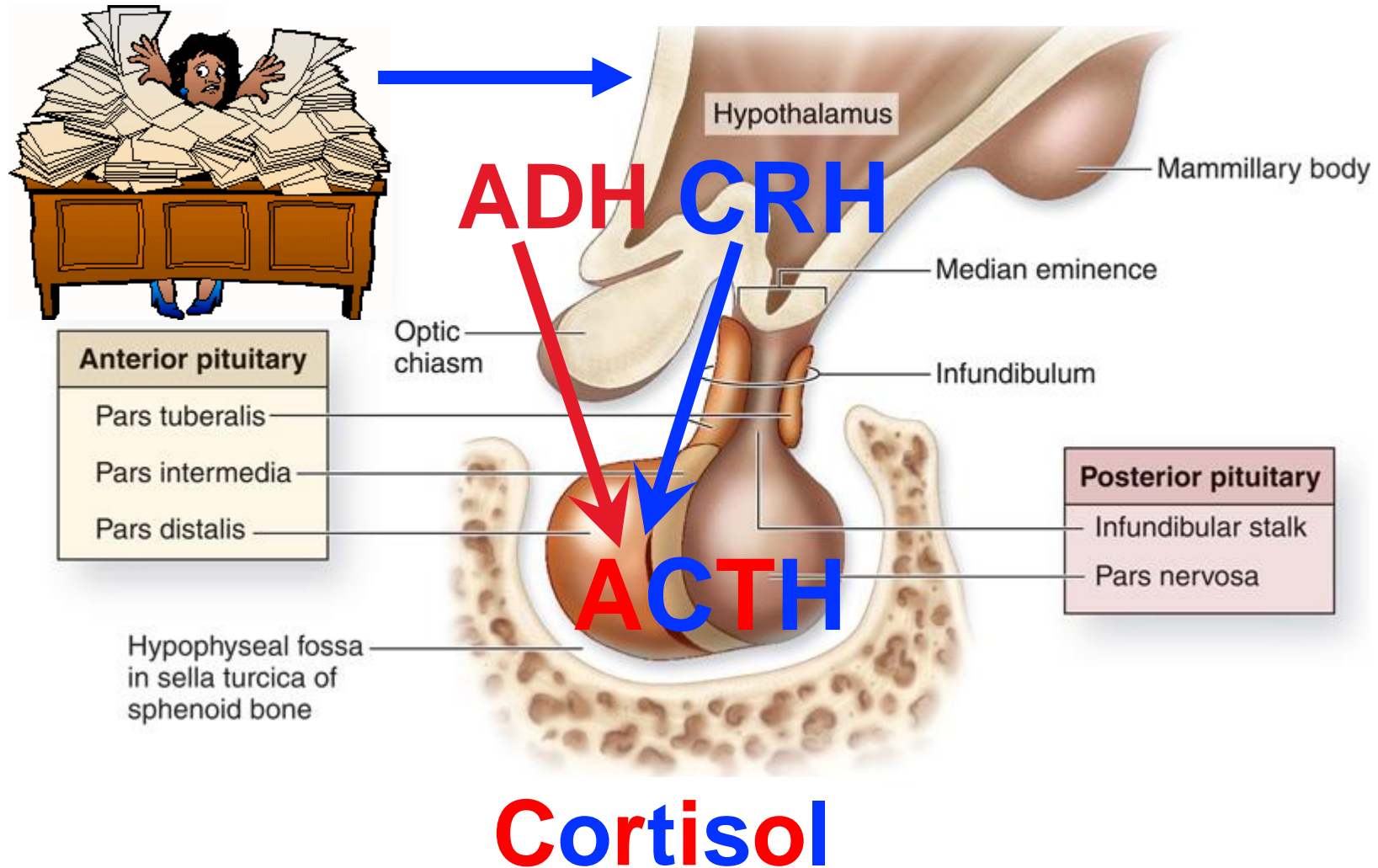
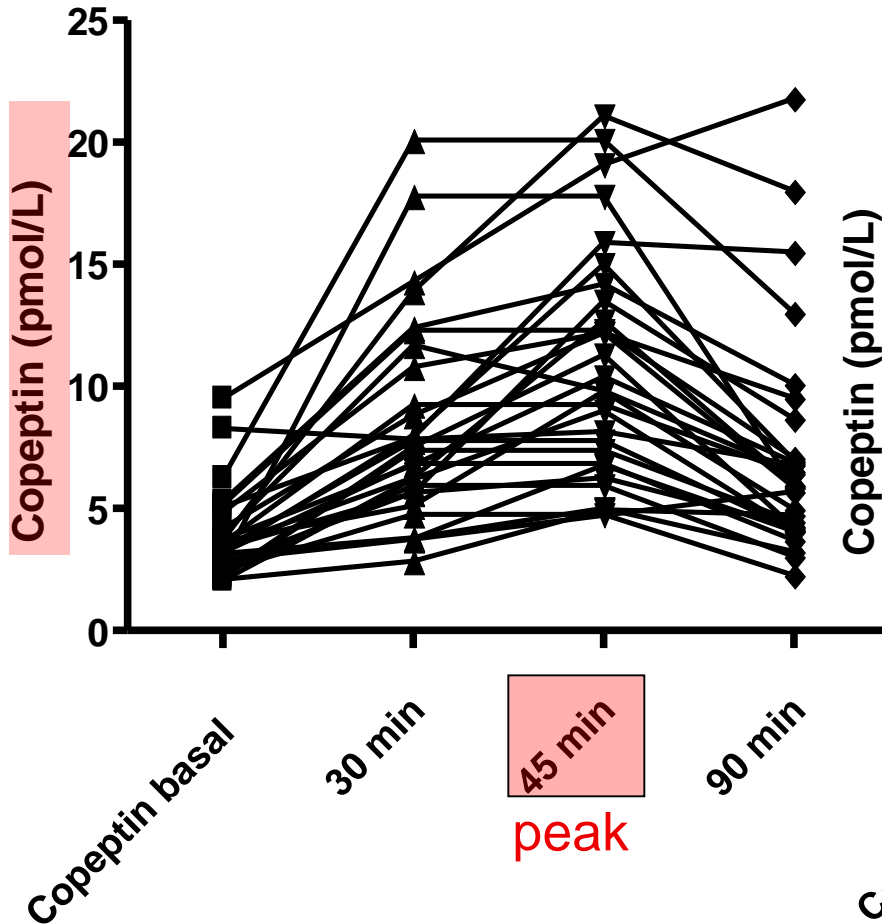


Figure 1. Stimulated Copeptin Levels in Response to the Hypertonic Saline Infusion and Water-Deprivation Tests in Patients with Hypotonic Polyuria. Fenske W., et al., New Engl J Med 2018

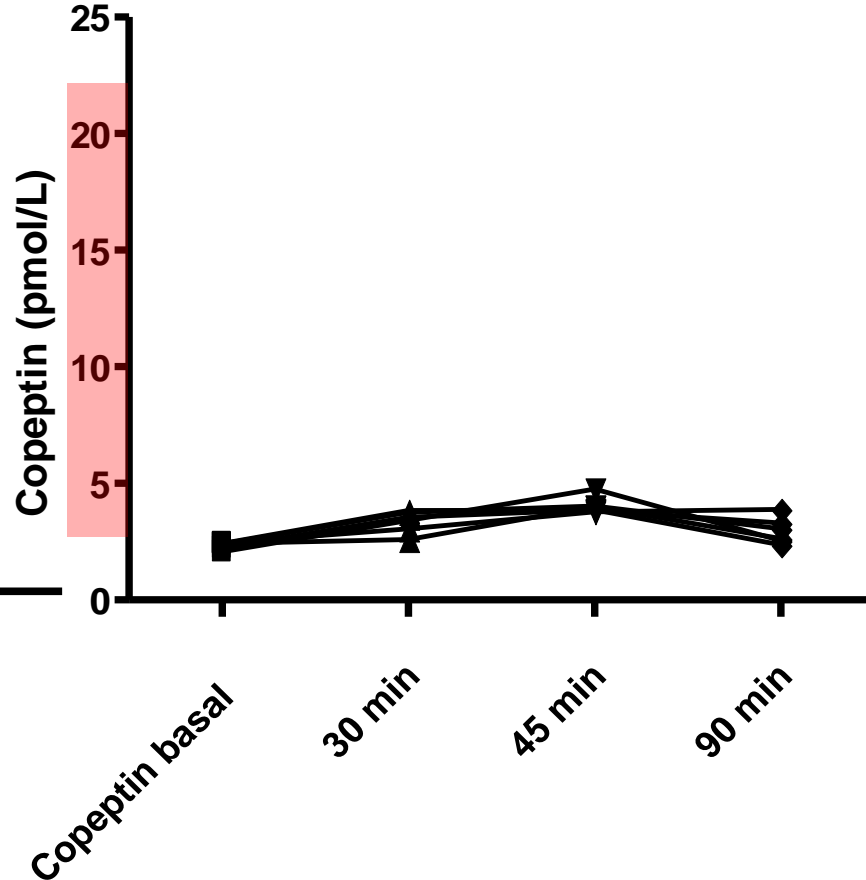
ADH/AVP is a „STRESS Hormone“: ACTH-dependent cortisol secretion



ADH/AVP & Insulin-Hypoglykämie-Test



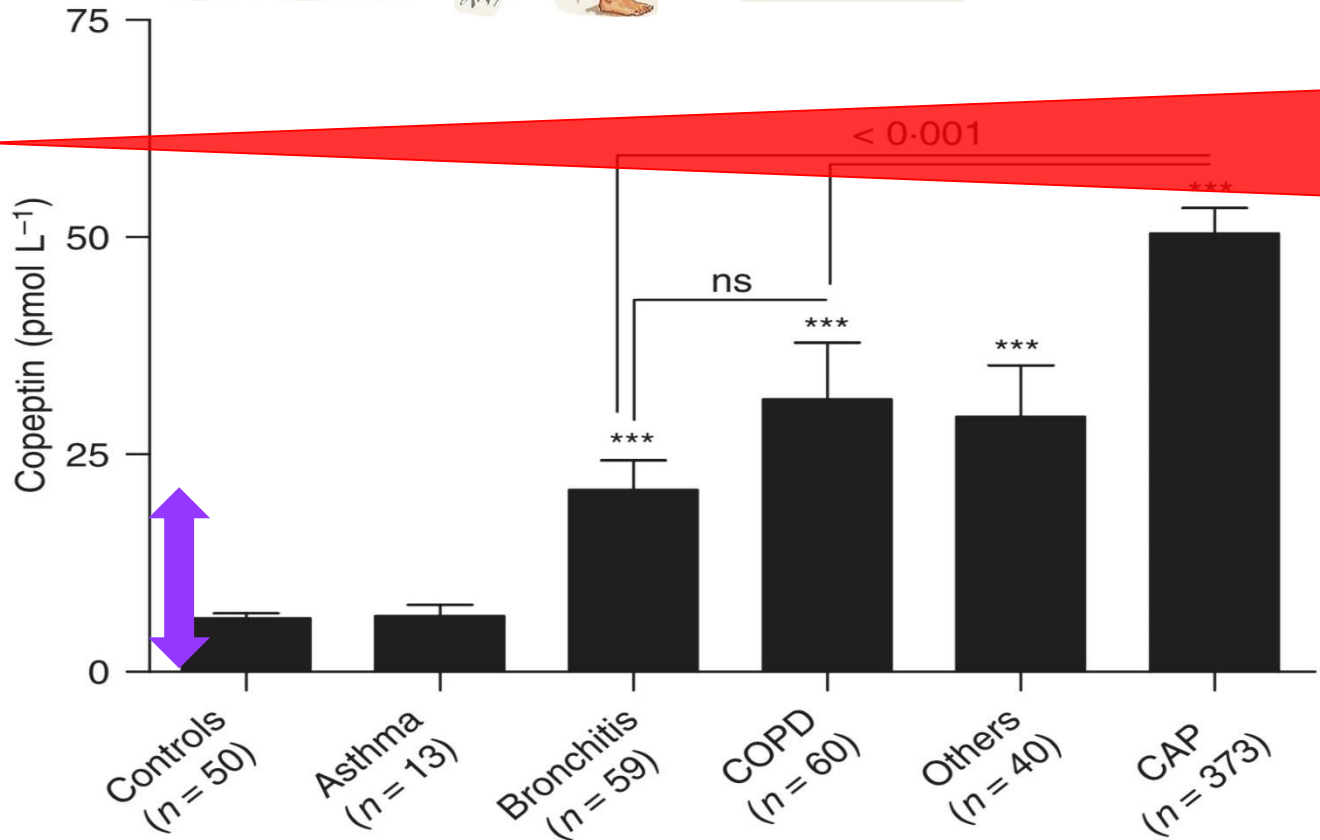
intakte posteriore Hypophyse
Signifikanter Anstieg
⇒ 45 min. 11.1 ± 4.8 pM



Zentraler Diabetes insipidus
⇒ 45 min. 4.0 ± 0.4 pM

Copeptin (aka ADH/AVP)

correlates with disease stress severity in LRTI



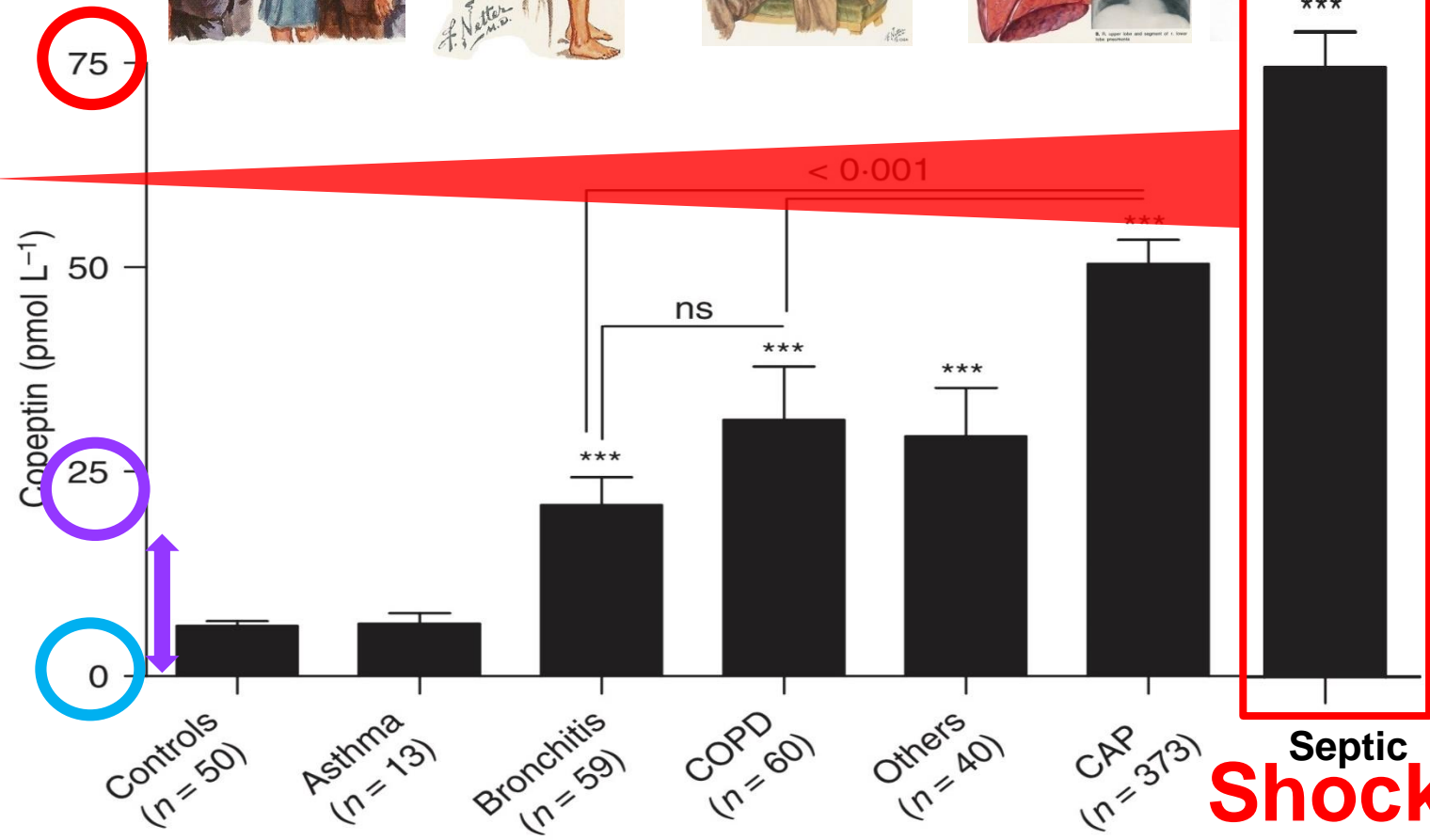
Copeptin (aka ADH/AVP)

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Stresslevel

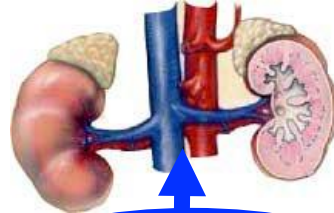
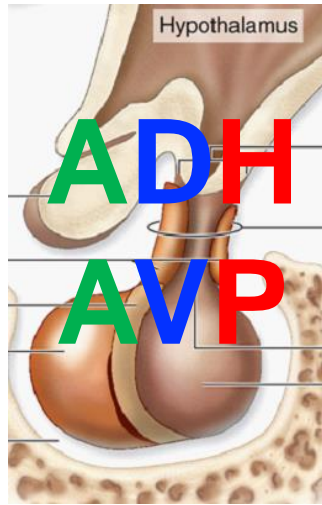
Hydration
Dysnatremia



«Clinical Reasoning» heute

Anti-Diuretisches Hormon = Arginin-Vasopressin

ADH = AVP = 3 Funktionen



Cortisol



Clinical Reasoning in Hospitalized Patients

INTAKE

EXCRETION

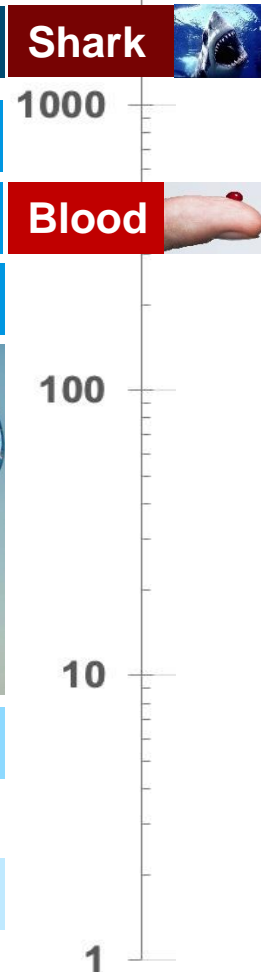
Salt in Food

Salt in „Water“ (g/L)

mOsm



Sea	30g/L
3% NaCl	25g/L
0.9% NaCl	8g/L
Bouillon	4-8g/L
Lake Tapwater Tea, Juice Beer . . .	1-2g/L
5% Glc	0g/L
Distilled	0g/L



Sweat (5g/L)

Insens. Losses Skin & Lung

30g/L
ADH
Urine
(ADH)
2g/L

ADH
ADH
Diuretics

Renal Insuff. (Alter)



2023 ! 78J. kommt auf NF mit Fieber & Husten



Hauptdiagnose: „Poly-Morbidität“

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 - **Malnutrition** mit Sarkopenie, BMI 24m/kg²

 - **Mildes kognitives Defizit**, depressiv
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 - Kinder erfolgreiche Wissenschaftler (USA)
- 8 Medikamente = 14 Tabletten jeden Tag . . .**

**Die arme Frau hat eine „Wasservergiftung“
weil**

- Sie pflichtbewusst alle Tbl einnahm (Diuretika für Hypertonie)**
- Krankheit = Stress = ADH-AVP-Tonus stark erhöht („SAAD“)**
- Alle (auch „Al“!) meinen „Staying properly hydrated is crucial ...“**
- Sie wegen Appetitlosigkeit nichts mehr ass (trank Honig-Tee...)**

2023! 78J. kommt auf NF mit Fieber & hustet



Hauptdiagnose: „Poly-Morbidität“

- **Pneumonie?** **COVID!??** DD: **COPD** Exacerbation
 - **Atherosklerose** mit KHK, CHF
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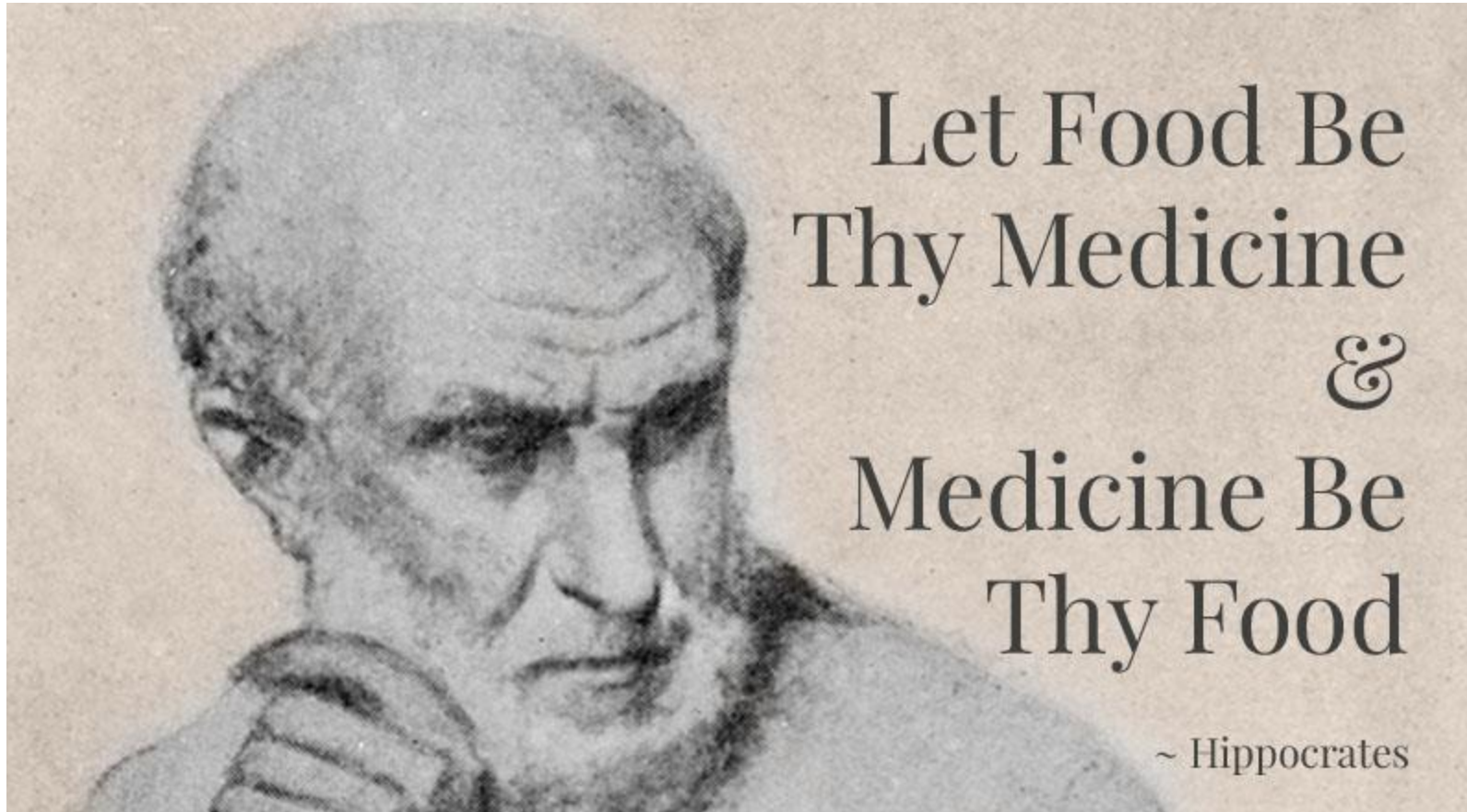
 - **Mildes kognitives Defizit**, depressiv
 - **Sozial**: Wittwe, lebt zu Hause
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- 8 Medikamente = 14 Tabletten jeden Tag . . .**

But, but wait....there is more

Sie hat keinen Appetit !

Sollte man sie “zwingen“ zu essen ?

Clinical Reasoning in der Antike



Artificial Intelligence heute ?

ChatGPT

HA

I am 75 years old with pneumonia and have not appetite. Should I force myself to eat a normal meal ?



I'm not a doctor, but I can offer some general guidance. If you're 75 years old and have pneumonia, it's essential to prioritize your health and recovery. Pneumonia can weaken your immune system and make it harder for your body to fight off infections. While nutrition is crucial for recovery, it's also important to listen to your body.

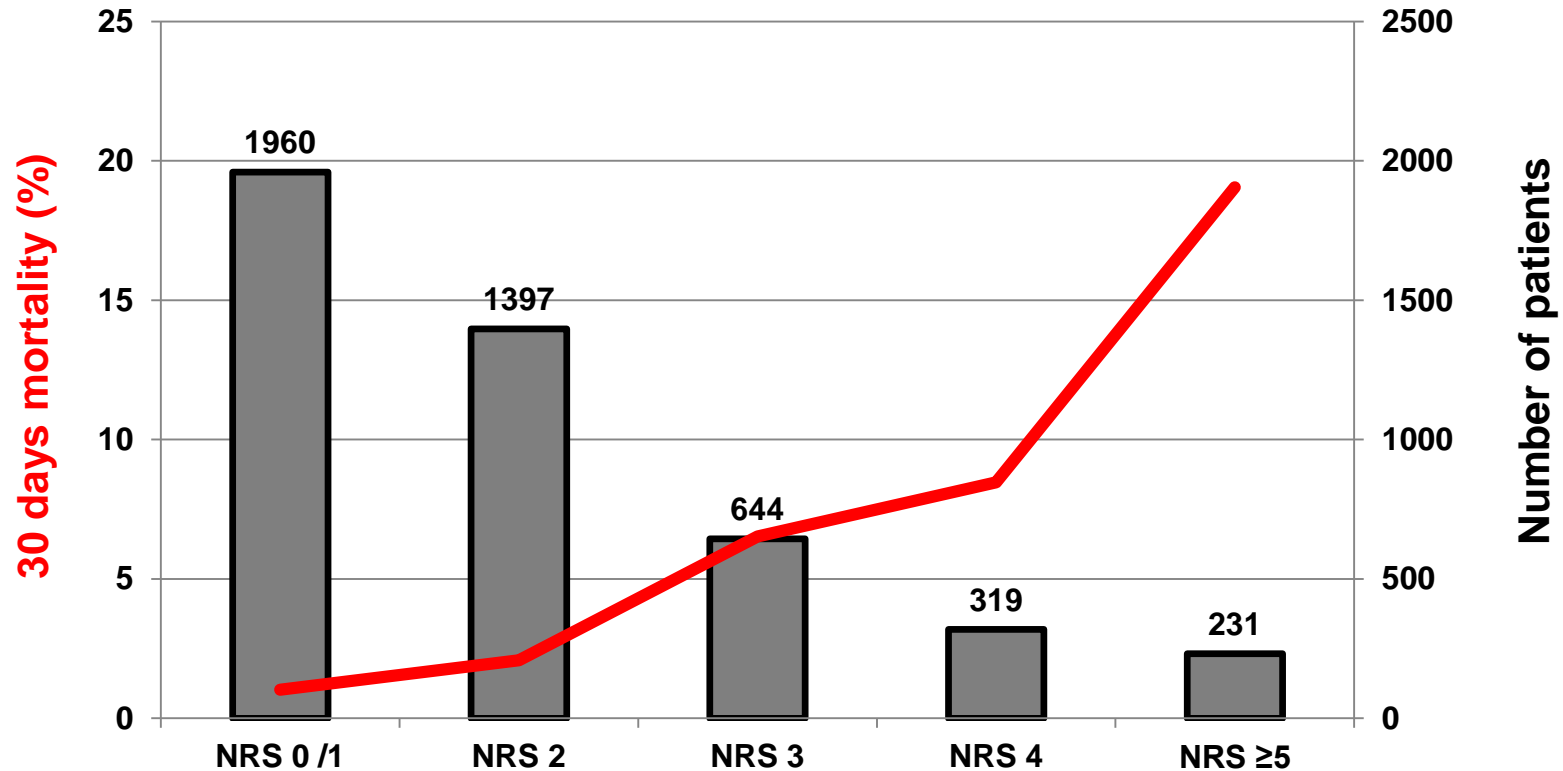


Malnutrition and Mortality

Kantonsspital Aarau,

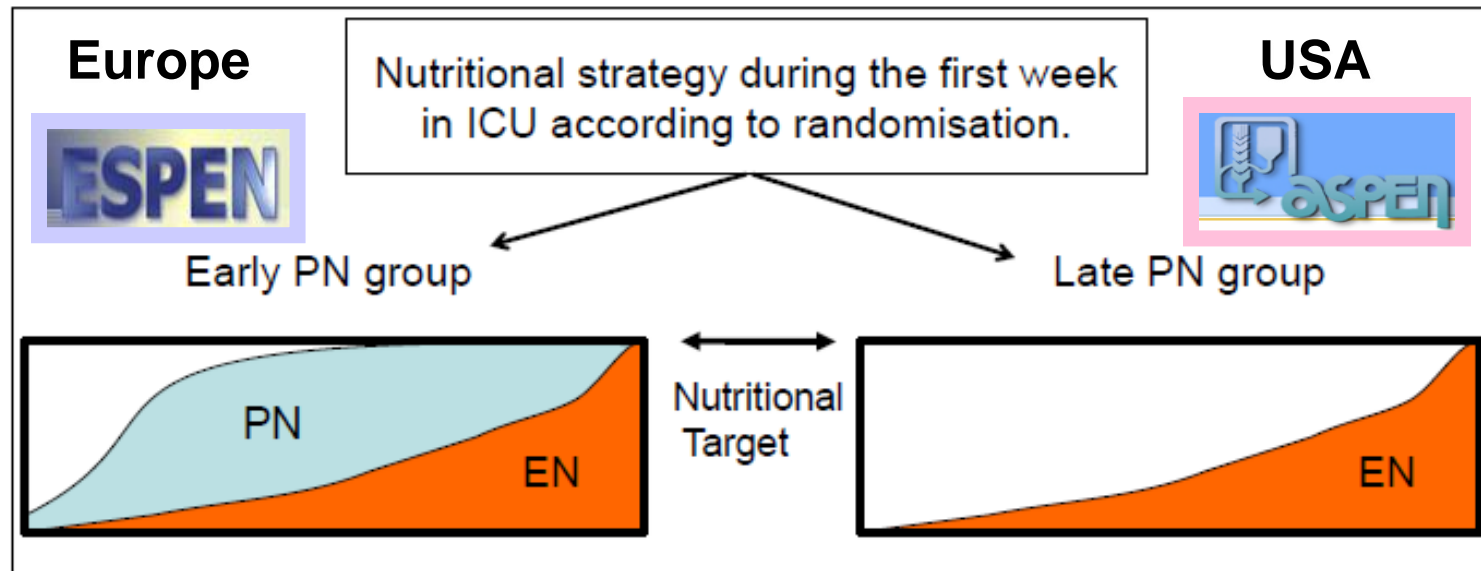
6 month observation (04/2013-10/2013)

4000 patients, ~ 30% at risk for malnutrition (NRS \geq 3 points)

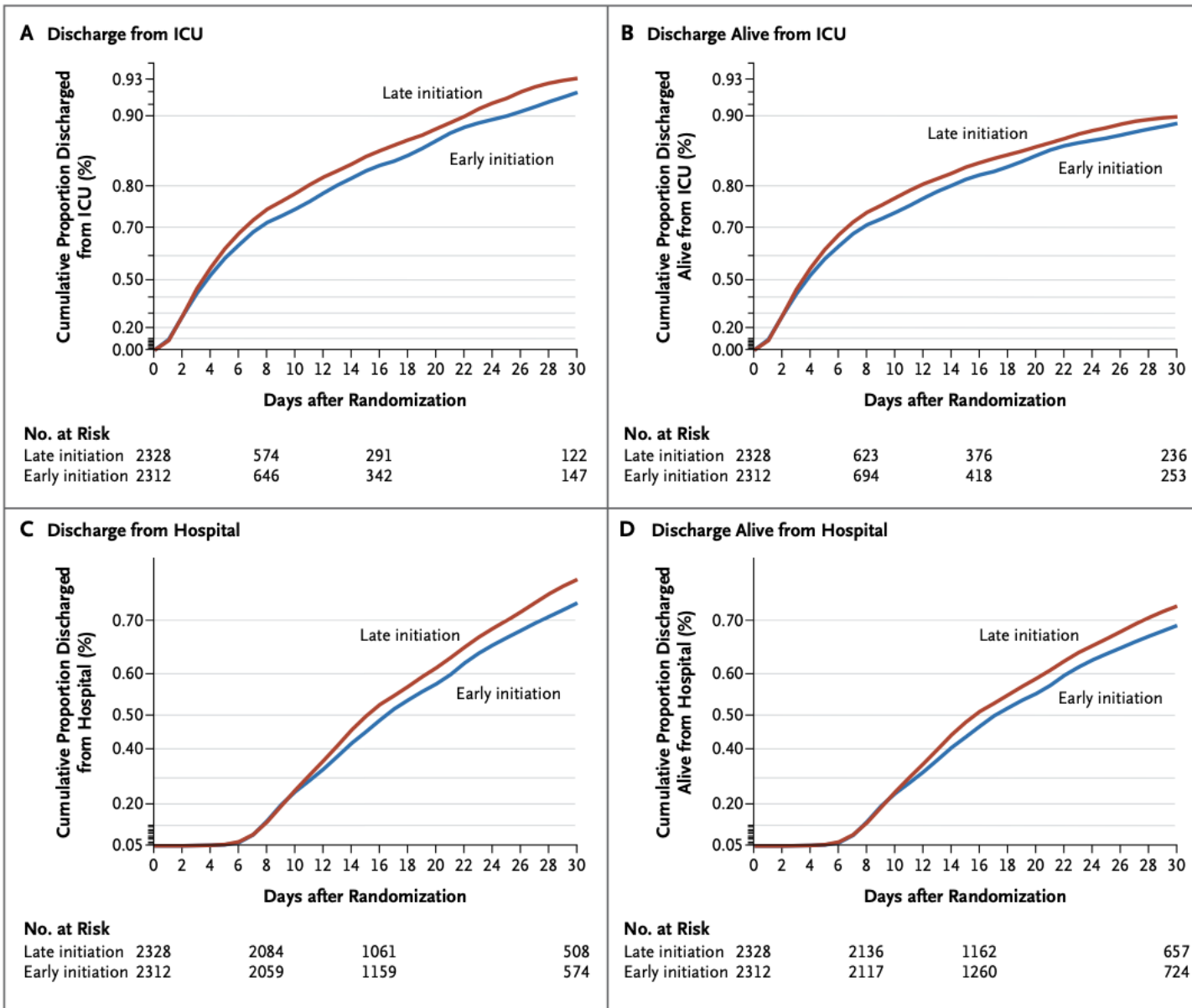


Nutritional Risk score (NRS)

What is Best Way to Reduce Caloric Deficits?



What is Best Way to Reduce Caloric Deficits **on the ICU?**



feeds better than



Hospitalized patients

< 5% on ICU

> 95% on wards !

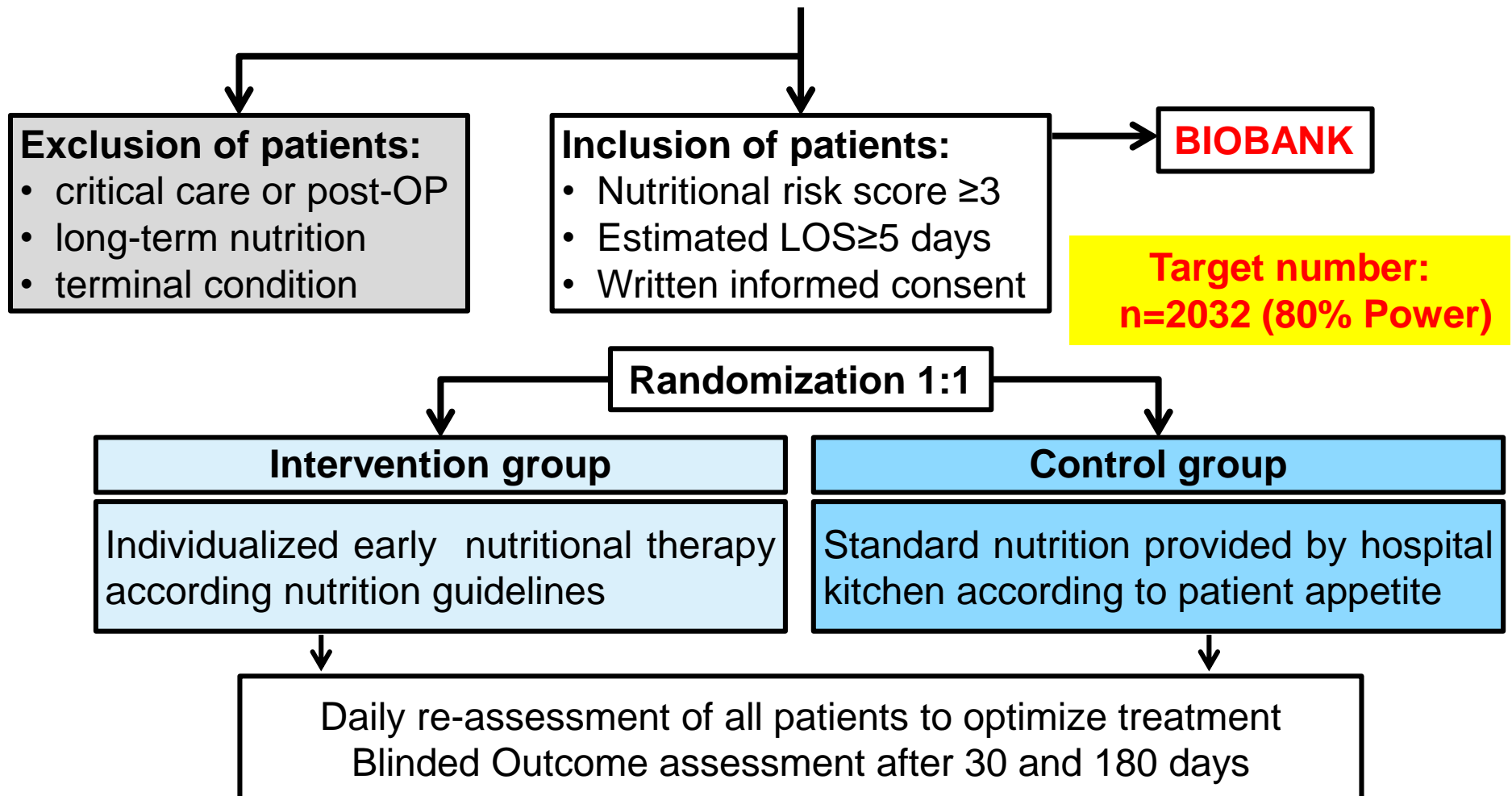
**same, same
but different ?**

Figure 3. Kaplan–Meier Estimates of the Time to Discharge from the Intensive Care Unit (ICU) and from the Hospital.

The EFFORT trial - study flow diagram

DANKE ENDO-TEAM KSSG !

Nutritional screening of consecutive medical inpatients



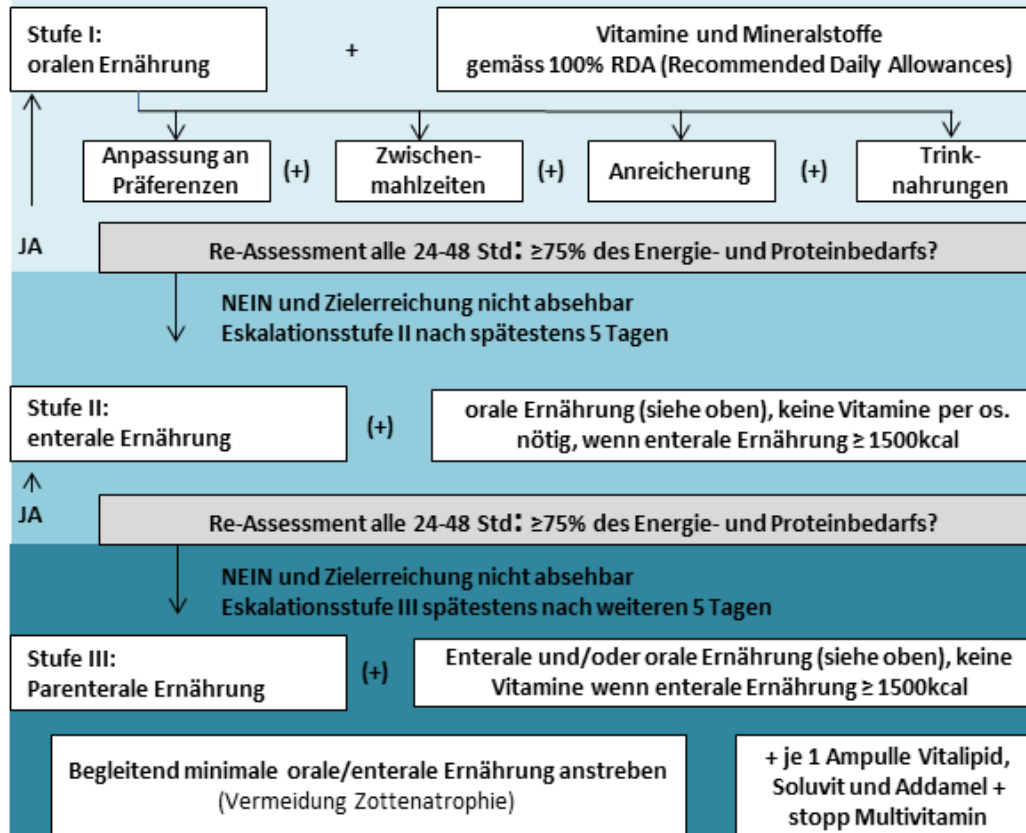
Nutrition Risk Screening (NRS) innerhalb 24-48Std. nach Spitaleintritt

wenn $NRS \geq 3$ Punkte \rightarrow individuelles Assessment des Patienten
Malnutrition vorhanden? Ernährungstherapie gewünscht und sinnvoll?
wenn Ja \rightarrow Festlegung einer Strategie zur Erreichung von individuellen Ernährungszielen

Ernährungsziele

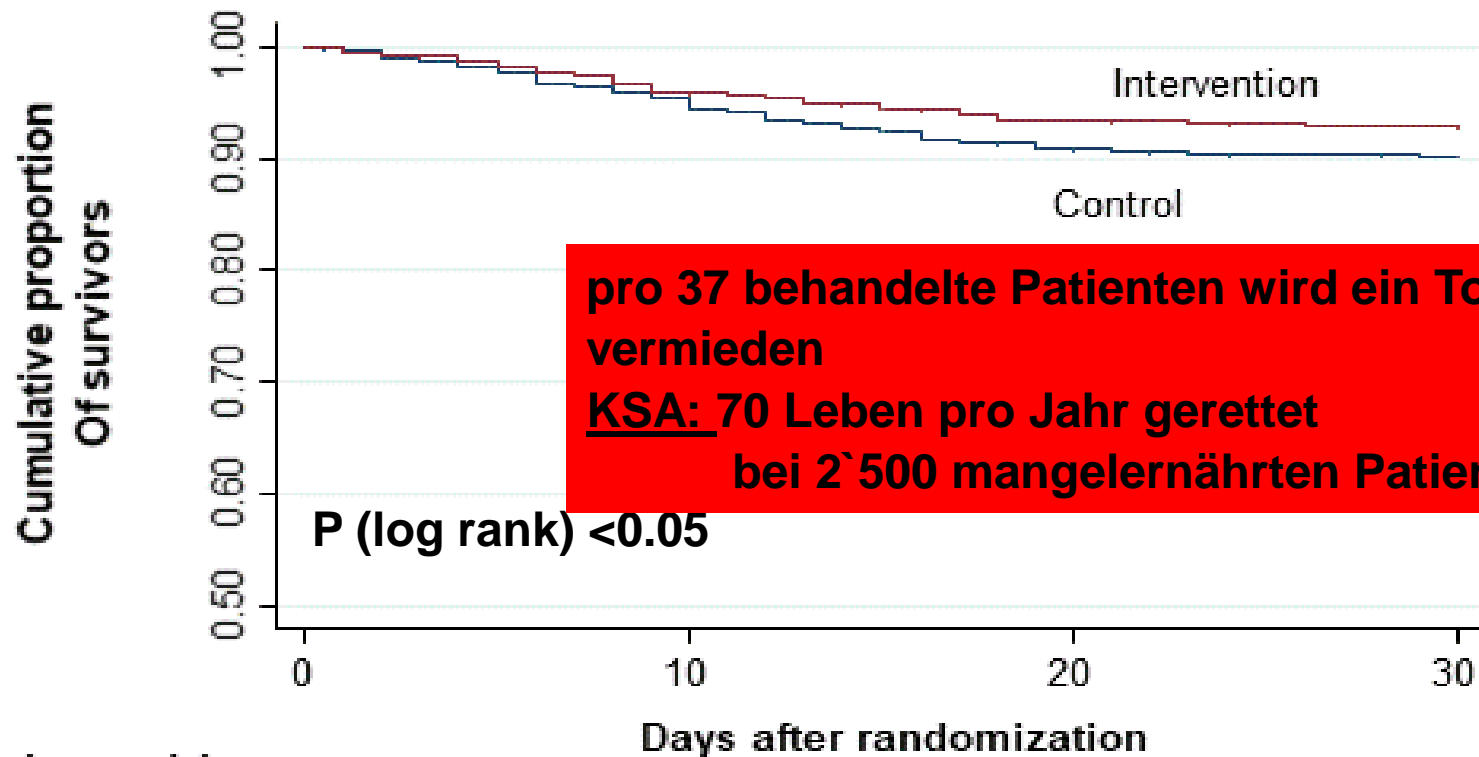
Kalorienbedarf	Proteinbedarf	Mikronährstoffe	Spezielle Ziele
Harris Benedict mit adjustiertem Gewicht <u>oder</u> ind. Kalorimetrie	1.2-1.5g/kgKG/Tag (0.8 bei schwerer Niereninsuffizienz ohne Dialyse)	Multivitamin Präparat, andere Mikronährstoffe gemäss Labor	Krankheits-spezifische Anpassungen ¹

Ernährungsstrategie zum Erreichen der Ernährungsziele



Time to DEATH

9.9% (Controls) vs 7.2% (Intervention)
Number needed to treat (NNT): 37



Number at risk

Control 1013

967

922

913

Intervention 1015

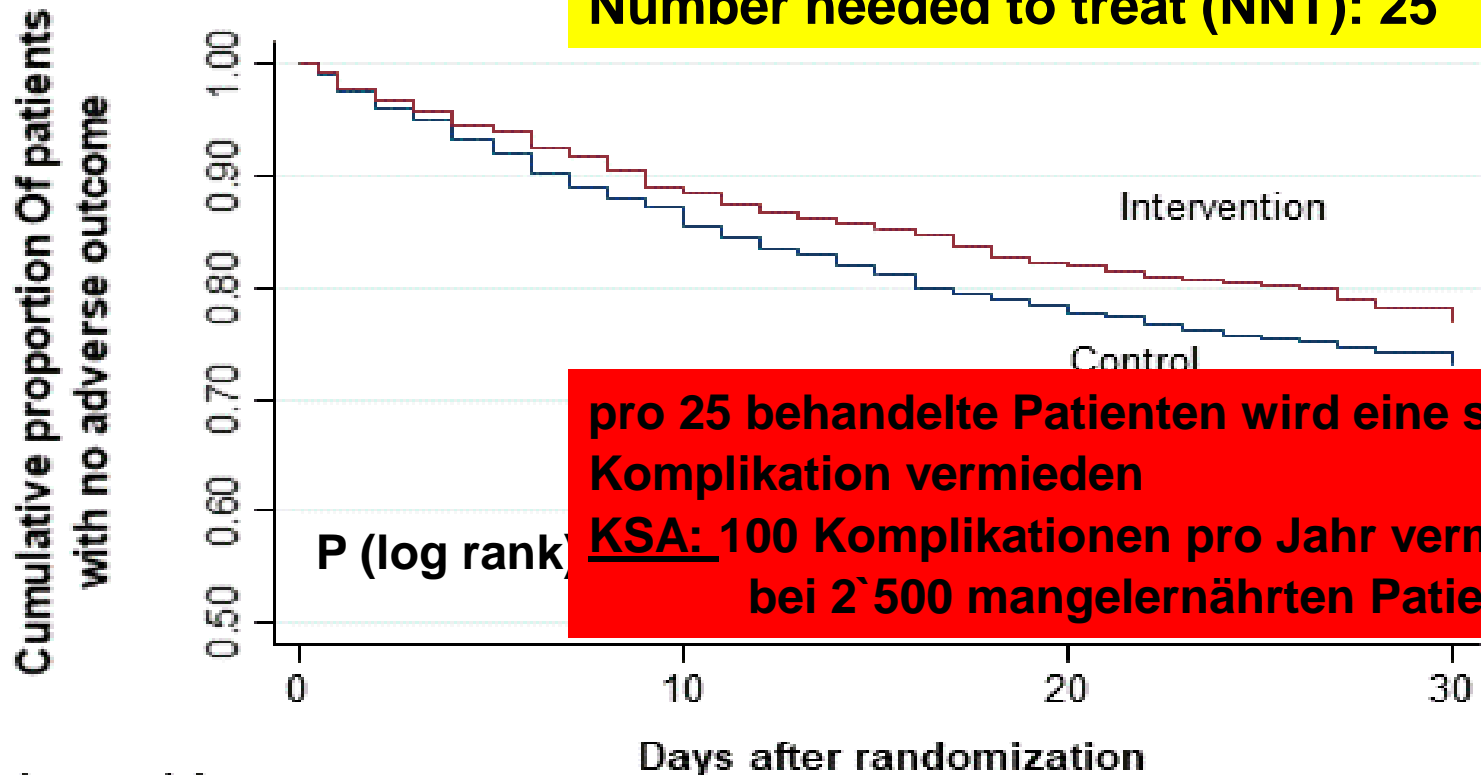
975

949

943

Time to **ADVERSE OUTCOME**

**26.9% (Controls) vs 22.9% (Intervention)
Number needed to treat (NNT): 25**



**pro 25 behandelte Patienten wird eine schwere
Komplikation vermieden
KSA: 100 Komplikationen pro Jahr vermieden
bei 2`500 mangelernährten Patienten**

Number at risk		Days after randomization			
Control	1013	882	791	749	
Intervention	1015	895	825	786	

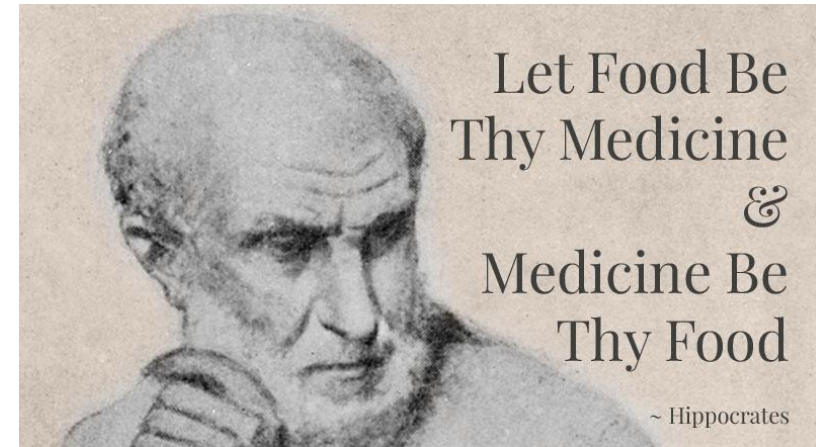
THE LANCET

Volume 393 · Number 10188 · Pages 2275-2358 · June 8-14, 2019

www.thelancet.com

“EFFORT has provided 21st century evidence to substantiate the aphorism of Hippocrates: ‘The patient ought likewise to be consider’d, whether he is able to hold out with the prescribed diet, even in the height of the disease; for if the diet is not sufficient, the patient will grow too faint, and be overcome by the disease.’”

See Comment page 2278



Editorial

Plan S: the final out
See page 2276

Articles

Upadacitinib as monotherapy
in rheumatoid arthritis with
inadequate response to
methotrexate
See page 2301

Articles

Individualised nutritional
support in medical inpatients
at nutritional risk
See page 2312

Articles

Restrictive strategy for
cholecystectomy in patients
with gallstones and
abdominal pain
See page 2322

Review

Novel paradigms in systemic
lupus erythematosus
See page 2344

«Clinical Reasoning» heute

*AT***Kearney**

Request a briefing

Personalized Nutrition

It's time to
**personalize
nutrition.**





Original Investigation | Nutrition, Obesity, and Exercise

Association of Baseline Inflammation With Effectiveness of Nutritional Support Among Patients With Disease-Related Malnutrition

A Secondary Analysis of a Randomized Clinical Trial

Meret Merker, MD; Martina Felder, BMSc; Louise Gueissaz, BMSc; Rebekka Bolliger, MD; Pascal Tribolet, MSc; Nina Kägi-Braun, MD; Filomena Gomes, PhD; Claus Hoess, MD; Vojtech Pavlicek, MD; Stefan Bilz, MD; Sarah Sigrist, MD; Michael Brändle, MD; Christoph Henzen, MD; Robert Thomann, MD; Jonas Rutishauser, MD; Drahomir Aujesky, MD; Nicolas Rodondi, MD, MAS; Jaques Donzé, MSc; Zeno Stanga, MD; Beat Mueller, MD; Philipp Schuetz, MD, MPH

Abstract

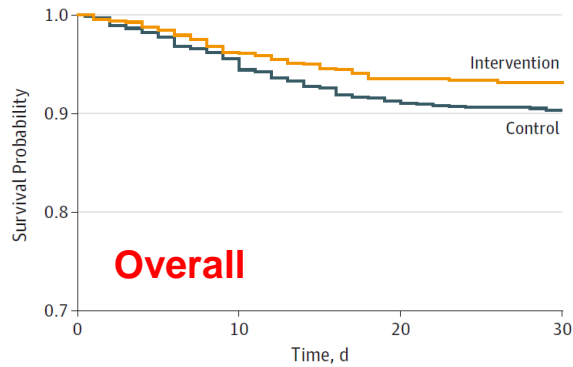
IMPORTANCE Inflammation is a key driver of malnutrition during illness and is often accompanied by metabolic effects, including insulin resistance and reduction of appetite. However, it still remains unclear if inflammation influences the response to nutritional support among patients with disease-related malnutrition.

Key Points

Question Does nutritional support have a similar effect on 30-day mortality among patients with high inflammation compared with patients with low or moderate inflammation?

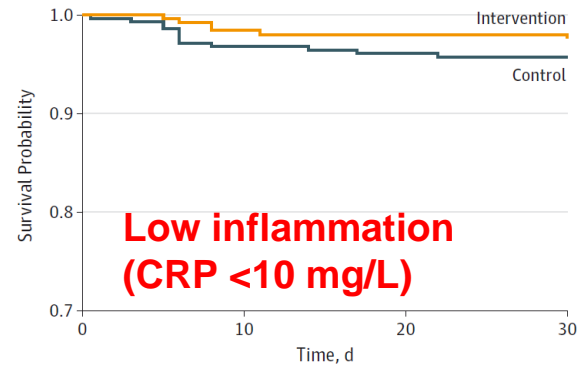
Figure 2. Kaplan-Meier Estimate for Time to Death Within 30-Days According to Inflammatory Status

A 30-Day mortality in overall population



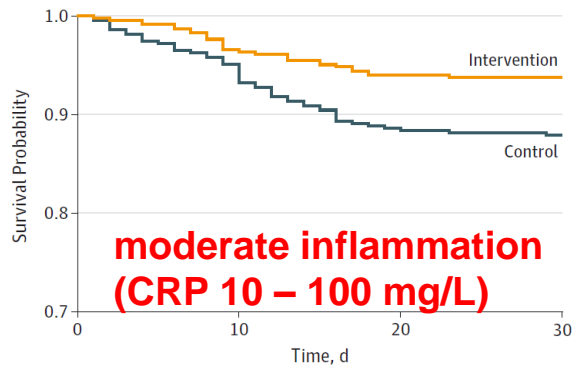
No. at risk				
Control	972	929	887	878
Intervention	978	941	915	911

B 30-Day mortality among patients with low inflammation



No. at risk				
Control	281	272	270	269

C 30-Day mortality among patients with moderate inflammation

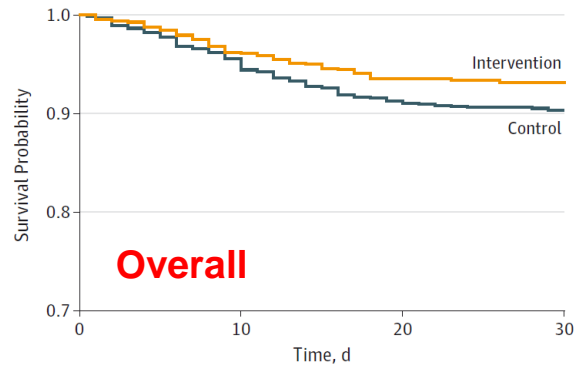


No. at risk				
Control	429	408	380	377
Intervention	465	449	437	436

intervention	261	244	231	228
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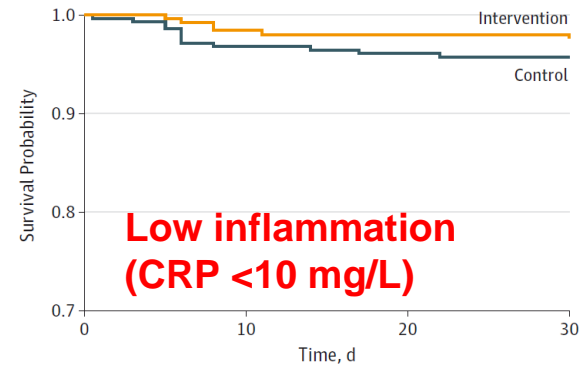
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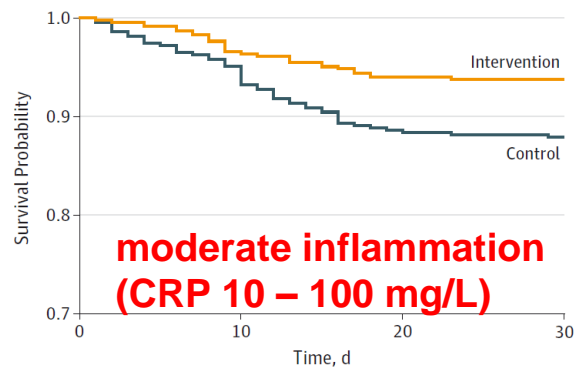
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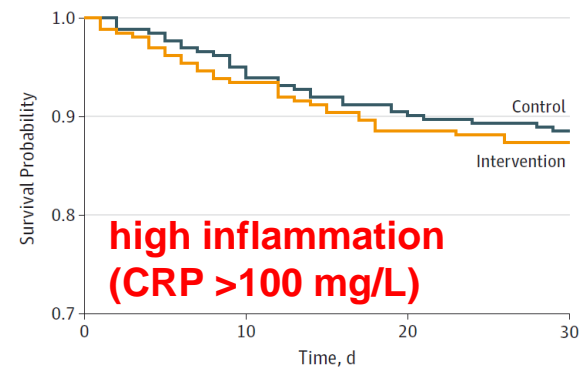
No. at risk				
Control	281	272	270	269
Intervention	252	248	247	247

C 30-Day mortality among patients with moderate inflammation



No. at risk				
Control	429	408	380	377
Intervention	465	449	437	436

D 30-Day mortality among patients with high inflammation



No. at risk				
Control	262	249	237	232
Intervention	261	244	231	228

ICU ?

Sie wird 58, pensioniert, will nun «gesund leben»



Ok, das hat sie verstanden.
Aber Sie hat sie noch eine letzte Frage:
Ihre Freundin, Aerztin & Professorin,
schwört auf mediterrane Kost um
ihre Demenz zu verzögern. Hilft das ?
Sie fragen Chat-GPT !

Artificial intelligence heute ?

ChatGPT

HA

Does mediterranean Diet protects from dementia ?



The Mediterranean diet has been associated with several health benefits, including potential protection against cognitive decline and dementia. While it's not a guarantee, research suggests that adhering to a Mediterranean-style diet may contribute to a lower risk of dementia. Here are some reasons why this diet is thought to be beneficial for brain health:



Artificial reasoning !

ChatGPT

1. **Rich in Antioxidants:** The Mediterranean diet emphasizes fruits, vegetables, and whole grains, which are high in antioxidants. Antioxidants help protect brain cells from oxidative stress, which is thought to be a contributing factor in neurodegenerative diseases like dementia.
2. **Healthy Fats:** This diet is rich in healthy fats, particularly monounsaturated fats found in olive oil and omega-3 fatty acids found in fish. Omega-3 fatty acids have been linked to improved cognitive function and a reduced risk of cognitive decline.
3. **Low in Saturated Fat:** The Mediterranean diet is relatively low in saturated fats, which are associated with an increased risk of heart disease and may also have negative effects on brain health.
4. **Moderate Alcohol Consumption:** Some versions of the Mediterranean diet include moderate consumption of red wine, which has been associated with a lower risk of dementia when consumed in moderation.
5. **Balanced Macronutrients:** This diet promotes a balance of carbohydrates, fats, and proteins, providing a steady source of energy for the brain.
6. **Reduced Risk of Vascular Issues:** The Mediterranean diet is known to support heart health, reducing the risk of vascular problems that can affect blood flow to the brain. Healthy blood flow is essential for cognitive function.
7. **Anti-Inflammatory Effects:** The diet's emphasis on foods like fruits, vegetables, and fatty fish may have anti-inflammatory effects, which can be beneficial for brain health.



Fr. K.K. wird 58, pensioniert, will nun «gesund leben»



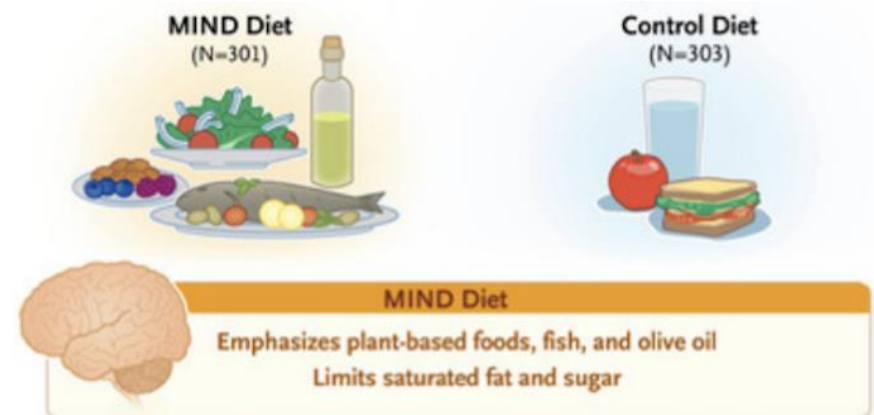
Ok, das hat sie verstanden.
Aber Sie hat sie noch eine Frage:
Ihre Freundin, Aerztin & Professorin,
schwört auf mediterrane Kost um
M. Alzheimer zu verzögern. Hilft das ?
Was tun Sie „clinically reasonable“?

Sie suchen EVIDENZ aus randomisierten (RCT) Studien !

Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons

CLINICAL PROBLEM

Observational studies have suggested that dietary patterns might affect cognitive decline, but clinical findings are limited. Most clinical trials of dietary interventions have focused on cardiovascular health outcomes that might affect the occurrence of dementia, rather than focusing directly on cognitive function.



Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons

CLINICAL TRIAL

Design: A two-site, randomized, controlled trial assessed the effects of a 3-year dietary intervention on cognitive decline and brain imaging markers of dementia and Alzheimer's disease in older adults without cognitive impairment but with a family history of dementia.

Intervention: 604 adults ≥65 years of age who were overweight, had suboptimal diets, and had a family history of Alzheimer's dementia were assigned to follow the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet (a hybrid of the Mediterranean diet and the Dietary Approaches to Stop Hypertension diet) with mild caloric restriction or a control diet with mild caloric restriction for 3 years. All participants received counseling regarding adherence to their assigned diet and support to promote weight loss. The primary end point was the change from baseline in a global cognition score (higher scores indicate better cognitive performance).

RESULTS

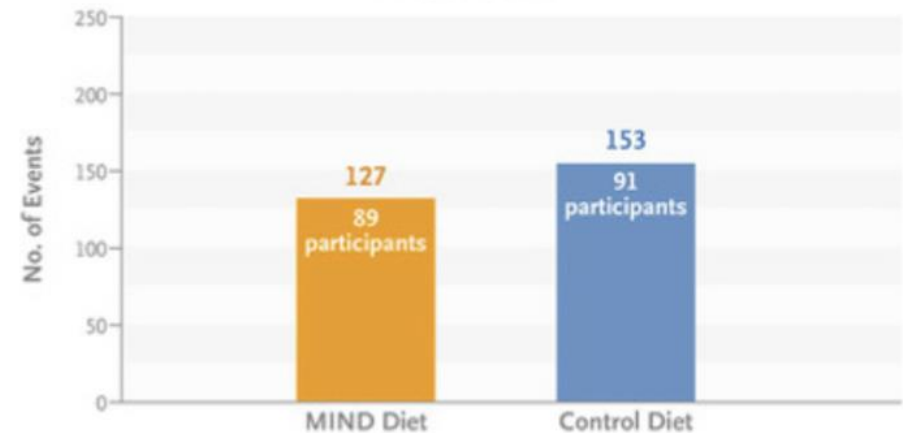
Efficacy: Global cognition scores improved from baseline to year 3 in both the MIND-diet group and the control-diet group but without a significant between-group difference.

Safety: The incidence of adverse events was similar in the two groups. The most common events were cardiovascular and musculoskeletal.

Change in Global Cognition Score at 3 Yr



Adverse Events

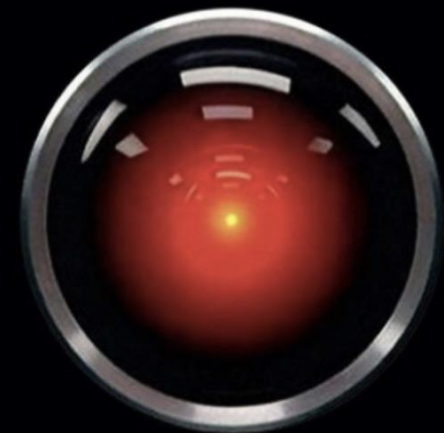


Clinical Reasoning 2033 ?

- Prognosen sind schwierig.
Vor allem betreffend der Zukunft.
- Wir glauben Hormone & Ernährung sind wichtig
- Glaube macht selig.
In der Medizin manchmal früher als nötig !
- “Clinical reasoning” macht Sinn
und wird immer Sinn machen.
- *Medicine is the science of uncertainty
and the art of probability.*
William Osler, 1902 (!)
- “Artificial intelligence” kann und wird
unsere Medizin verbessern, aber nur
falls “clinically reasonable” angewendet !



I'M SORRY, DAVE



I'M AFRAID I CAN'T DO THAT

2001: A Space Odyssey by Stanley Kubrick, 1967

**DAS
WARS**