Società Medico Chirurgica di Ferrara dal 1846

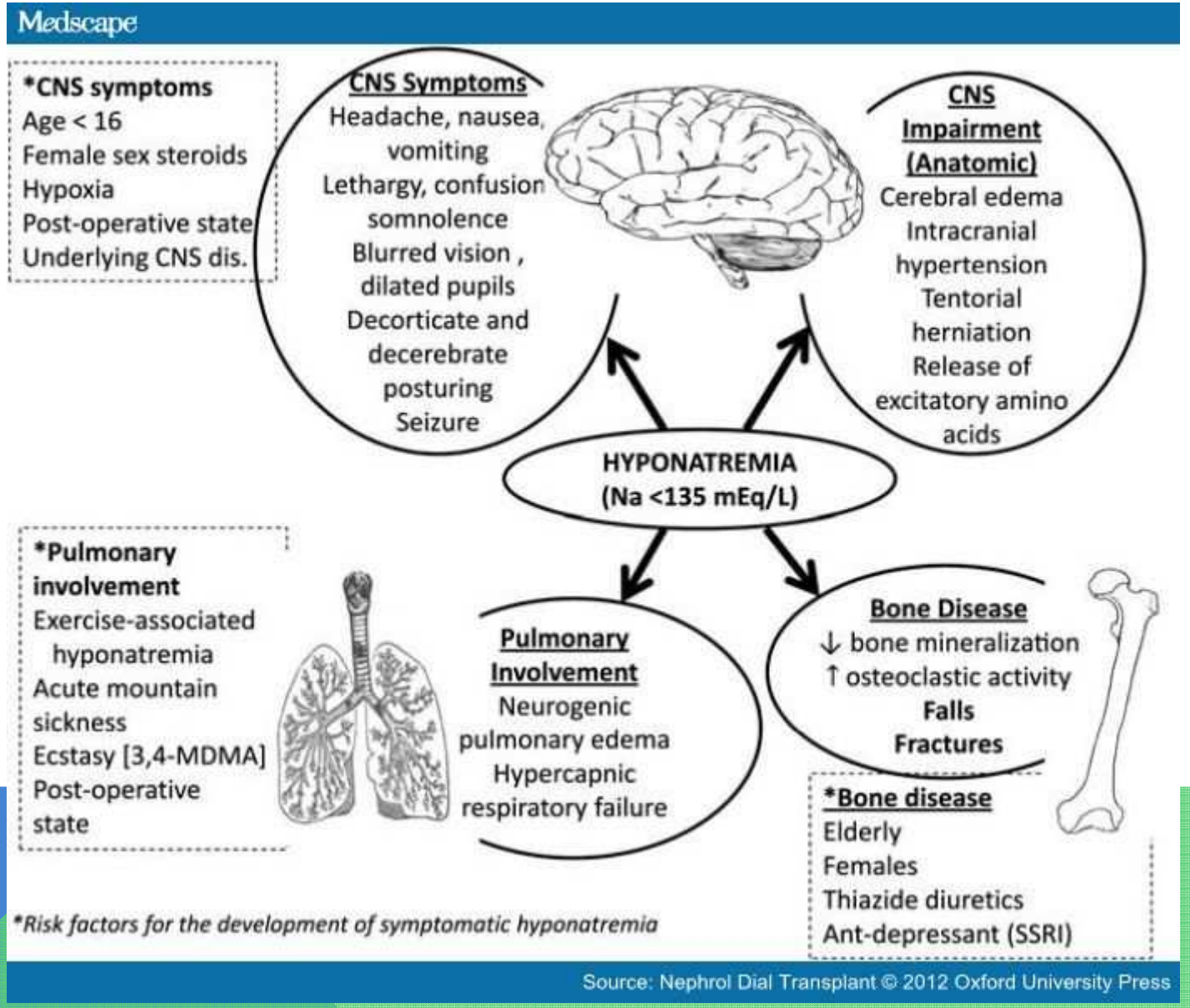

REMDICONTO
DELLE ADUNANZE
dell' Accademia
MEDICO-CHIRURGICA
DI FERRARA
DEGLI ANNI
1846 – 1847 – 1848 – 1849

LA GESTIONE CLINICA DEL PAZIENTE CON IPONATREMIA

Sabato 17 ottobre 2015

Aula Magna Nuovo Arcispedale S. Anna

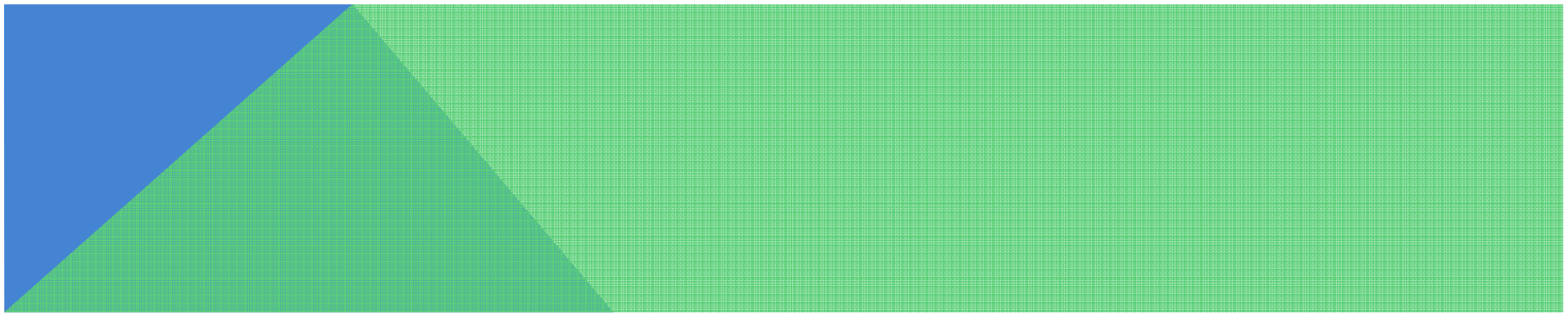
Iponatremia in Medicina Interna.

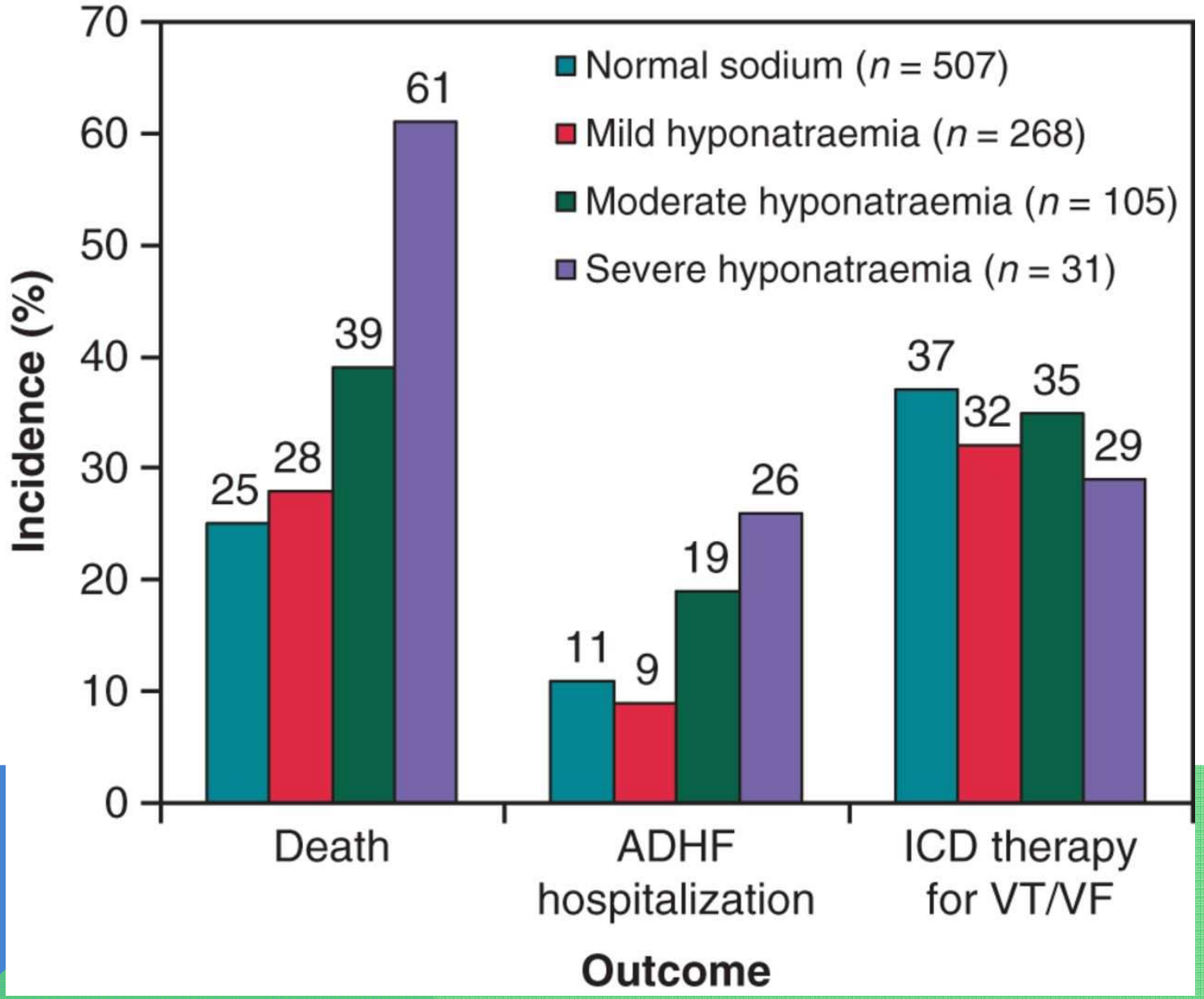

Medscape
*CNS symptoms
Age < 16
Female sex steroids
Hypoxia
Post-operative state
Underlying CNS dis.
CNS Symptoms
Headache, nausea, vomiting
Lethargy, confusion somnolence
Blurred vision , dilated pupils
Decorticate and decerebrate posturing
Seizure
CNS Impairment (Anatomic)
Cerebral edema
Intracranial hypertension
Tentorial herniation
Release of excitatory amino acids
HYPONATREMIA (Na <135 mEq/L)
*Pulmonary involvement
Exercise-associated hyponatremia
Acute mountain sickness
Ecstasy [3,4-MDMA]
Post-operative state
Pulmonary Involvement
Neurogenic pulmonary edema
Hypercapnic respiratory failure
Bone Disease
↓ bone mineralization
↑ osteoclastic activity
Falls
Fractures
*Bone disease
Elderly
Females
Thiazide diuretics
Ant-depressant (SSRI)
*Risk factors for the development of symptomatic hyponatremia
Source: Nephrol Dial Transplant © 2012 Oxford University Press

PROGNOSIS

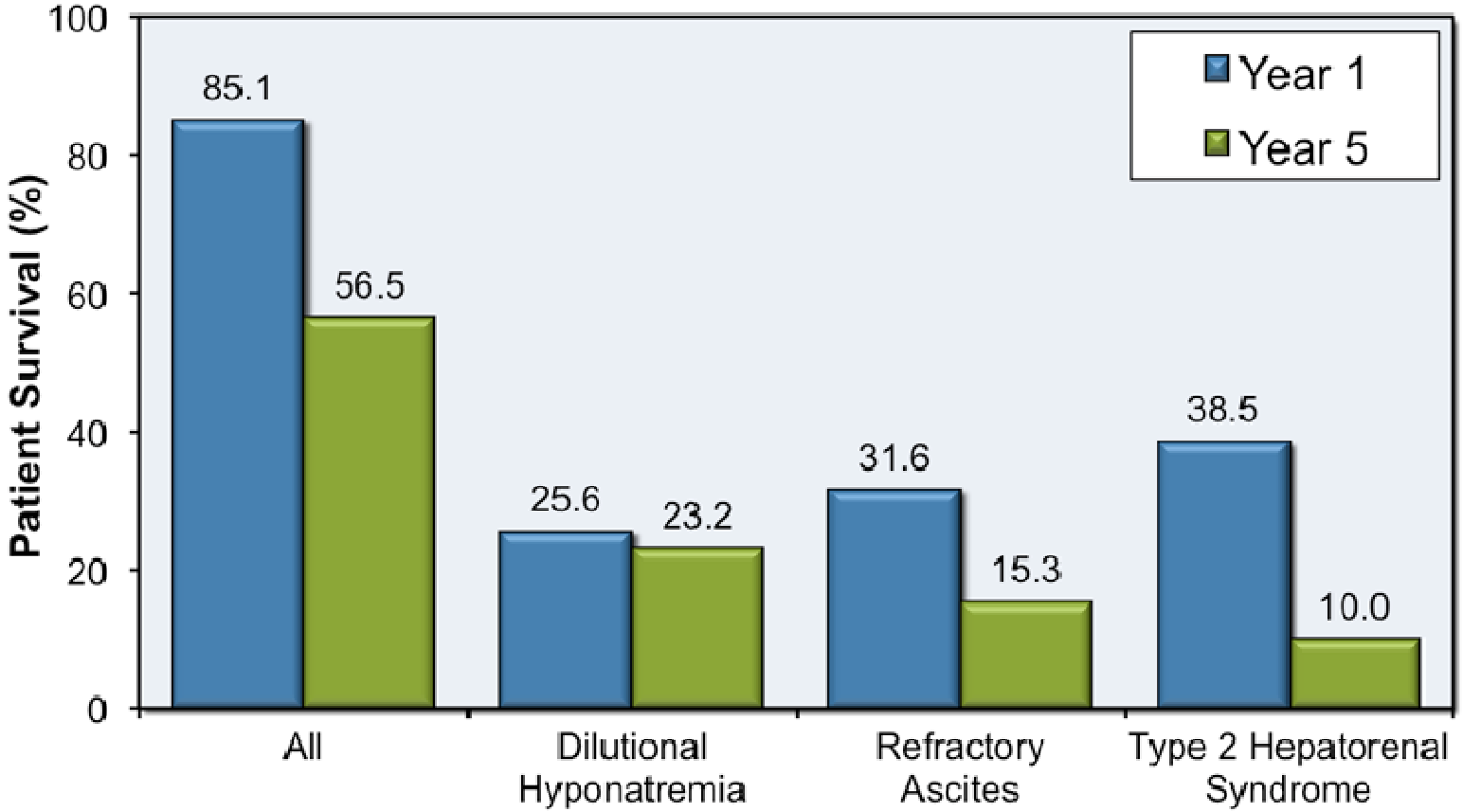
Mortality rates as high as 18-30% are reported for hyponatremic patients.

High mortality rates reflect the severity of underlying conditions and are not influenced by treatment of hyponatremia (Hochman I, et al. *Isr J Med Sci.* 1989;25:73-6).

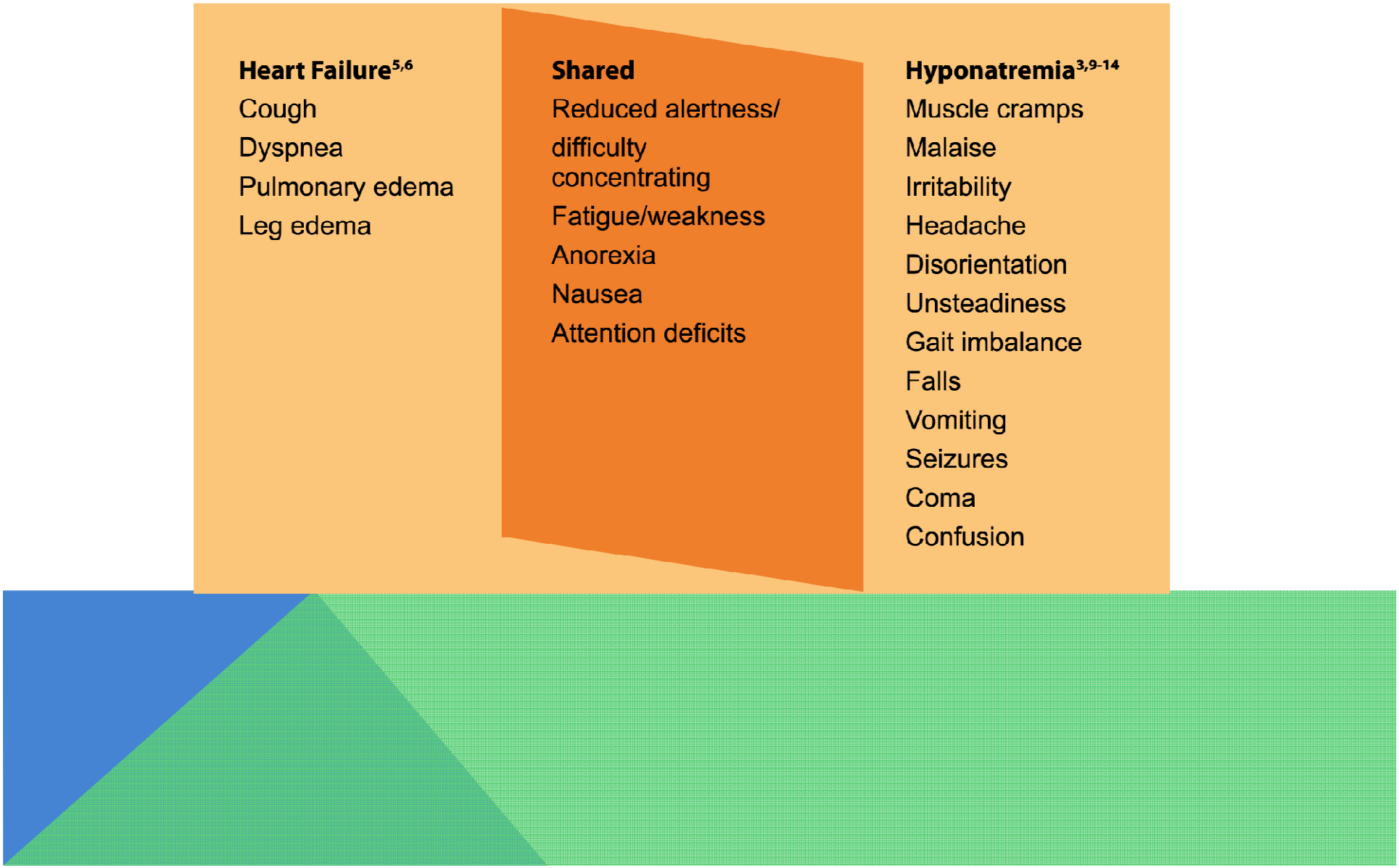



Normal sodium (n = 507)
Mild hyponatraemia (n = 268)
Moderate hyponatraemia (n = 105)
Severe hyponatraemia (n = 31)
Incidence (%)
70
60
50
40
30
20
10
0
25
28
39
61
11
9
19
26
37
32
35
29
Death
ADHF hospitalization
ICD therapy for VT/VF
Outcome

NATURAL HISTORY AND SURVIVAL OF PATIENTS WITH ASCITES. PATIENTS WHO DO NOT DEVELOP COMPLICATIONS HAVE MARKEDLY BETTER SURVIVAL THAN THOSE WHO DEVELOP DILUTIONAL HYPONATREMIA, REFRACTORY ASCITES, OR HEPATORENAL SYNDROME.



HYPONATREMIA AND HEART FAILURE HAVE SEVERAL OVERLAPPING SYMPTOMS.



Nephrology (Carlton). 2015 Oct 1. doi: 10.1111/nep.12634. [Epub ahead of print]

Association of serum sodium levels with all-cause and cardiovascular mortality in chronic kidney disease: Results from a prospective observational study.

Chiu DY[1,2], Kalra PA[1,2], Sinha S[1,2], Green D[1,2].

Author information

Abstract

AIMS: The prevalence of hyponatraemia in the out-patient setting has not been thoroughly explored and little is known about the prognostic implication of dysnatraemia in chronic kidney disease (CKD) patients, in particular accommodating the effect of concurrent medications.

METHODS: This is a prospective observational study of non-dialysis dependent CKD patients managed in a nephrology clinic. Patients enrolled between 2002-2012 in the Chronic Renal Insufficiency Standards Implementation Study (CRISIS) were assessed. Survival analyses were performed using baseline sodium and twelve-month time-averaged sodium, with adjustment for comorbid diseases, laboratory findings, and concurrent medications.

RESULTS: At baseline (n = 2093), mean eGFR was 32.8 ± 15.9 ml/min/1.73 m^2 , median age 67 (Interquartile range 56-75) years, median serum sodium concentration was 140 (138-142) mmol/l. After a follow up of 41 (18-67) months, there were 684 deaths; 174 from cardiovascular causes. 1925 time-averaged sodium values were analysed. In the cox multivariate adjusted regression, baseline hyponatraemia, but not hypernatraemia, was independently associated with all cause mortality (HR 1.35, 95% CI 1.02-1.78, p = 0.04 and HR 1.15, 95% CI 0.84-1.57, p = 0.39 respectively). This was similarly the case for time-averaged hyponatraemia and hypernatraemia (HR 2.15, 95% CI 1.59-2.91, p < 0.01 and HR 1.47, 95% CI 0.93-2.38, p = 0.10 respectively). However, the association of baseline and time-averaged hyponatraemia with cardiovascular mortality were not significant.

CONCLUSION: Hyponatraemia in the ambulatory setting is associated with all-cause but not cardiovascular mortality in CKD, independent of concomitant medications and co-morbidities. This article is protected by copyright. All rights reserved.

KEYWORDS: ambulatory patients; cardiovascular disease; chronic kidney disease; hyponatraemia; mortality

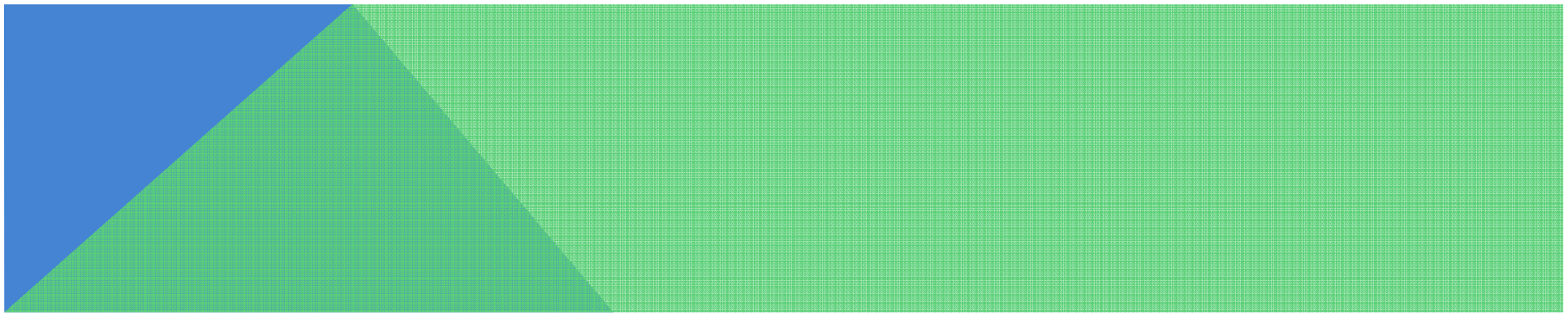
PREVALENCE

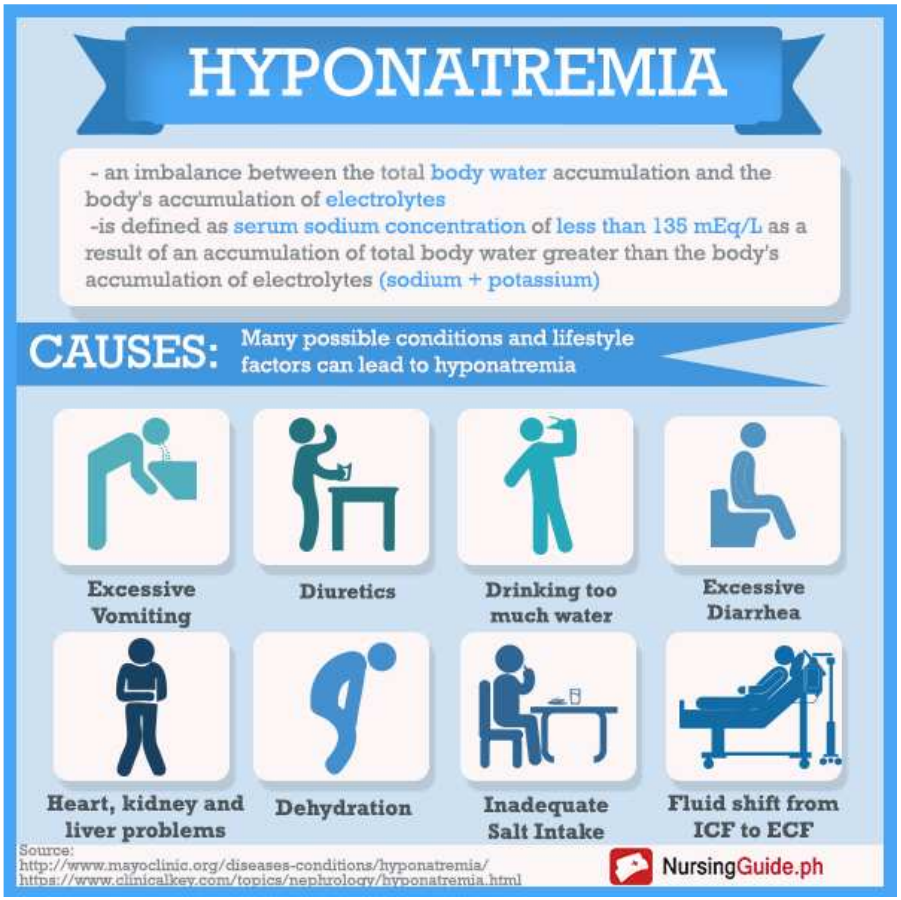
Most common electrolyte disorder encountered in hospitalized patients.

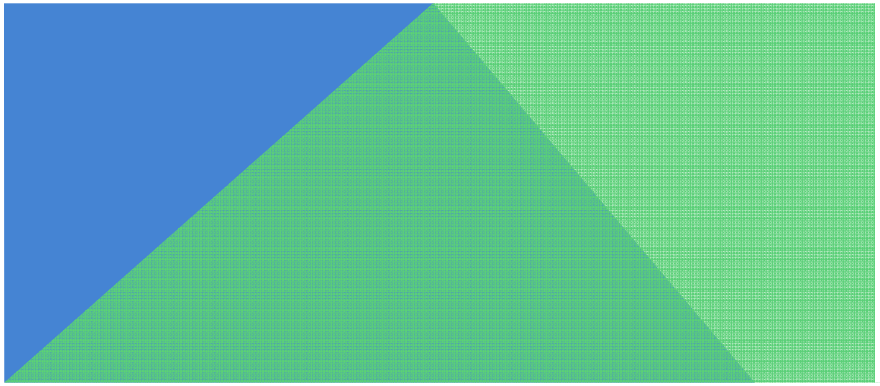
Prevalence at initial presentation to acute care setting reported as high as 28% (Hawkins RC. *Clin Chim Acta* 2003;337:169-72).

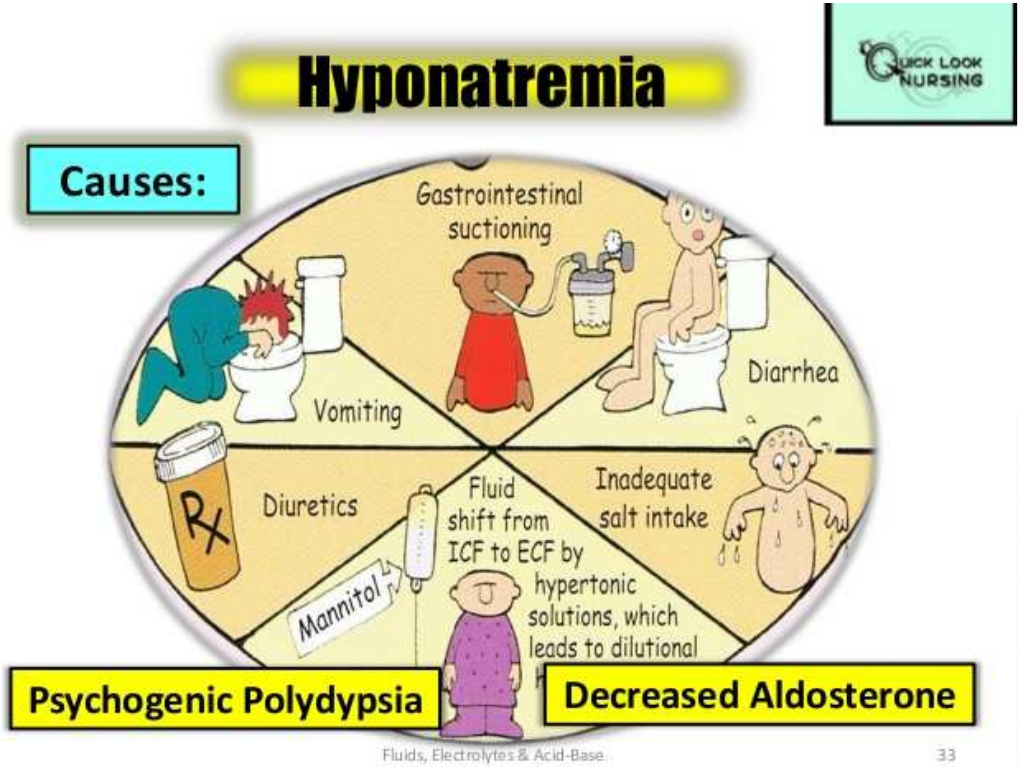
Prevalence of hyponatremia in hospitalized patients has been reported as 15-18%.

Common in nursing home residents (18% prevalence).




HYPONATREMIA
- an imbalance between the total body water accumulation and the body's accumulation of electrolytes
-is defined as serum sodium concentration of less than 135 mEq/L as a result of an accumulation of total body water greater than the body's accumulation of electrolytes (sodium + potassium)
CAUSES:
Many possible conditions and lifestyle factors can lead to hyponatremia
Excessive Vomiting
Diuretics
Drinking too much water
Excessive Diarrhea
Heart, kidney and liver problems
Dehydration
Inadequate Salt Intake
Fluid shift from ICF to ECF
Source:
http://www.mayoclinic.org/diseases-conditions/hyponatremia/
https://www.clinicalkey.com/topics/nephrology/hyponatremia.html
NursingGuide.ph

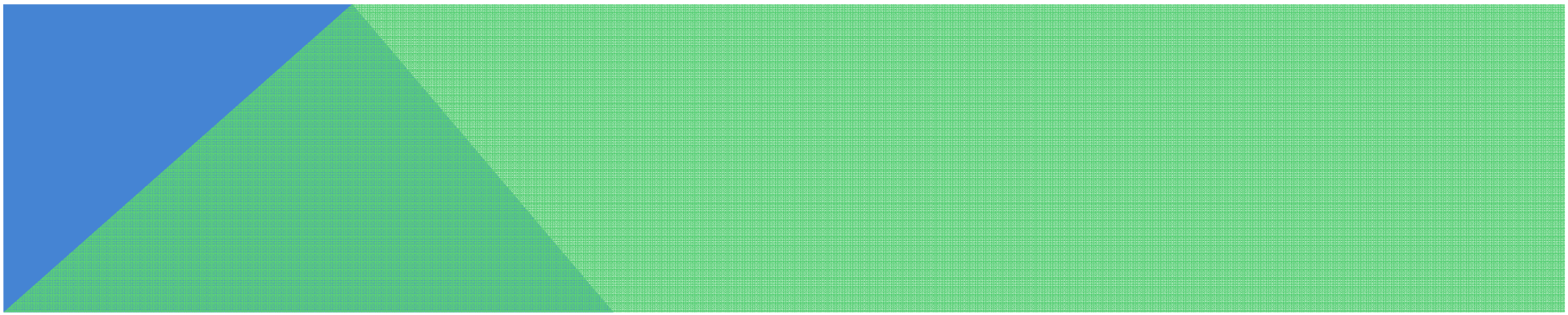



Hyponatremia
QUICK LOOK NURSING
Causes:
Gastrointestinal suctioning
Vomiting
Diarrhea
Diuretics
Rx
Fluid shift from ICF to ECF by hypertonic solutions, which leads to dilutional
Mannitol
Inadequate salt intake
Psychogenic Polydypsia
Decreased Aldosterone

A 76-YEARS LADY RESIDING IN A NURSING HOME

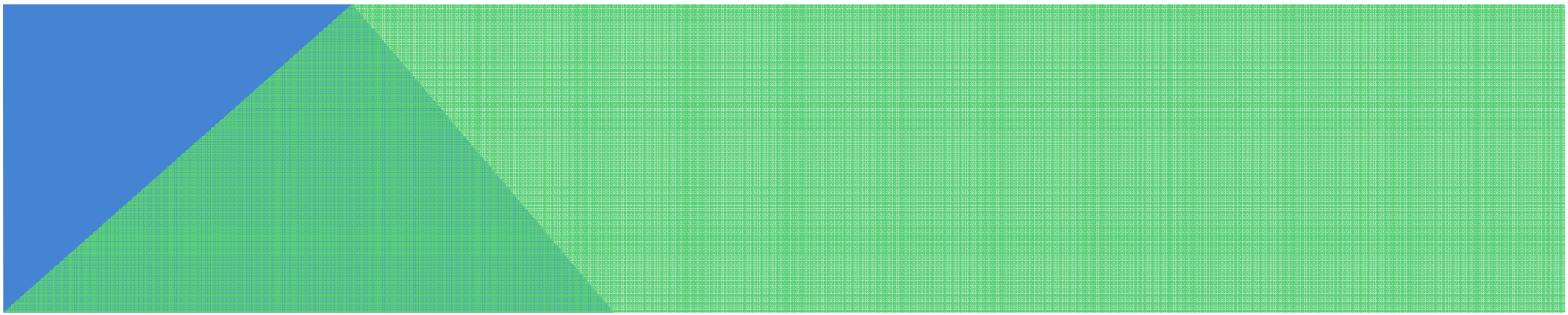
She was seen by general practitioner (GP) because of high blood pressure (BP 165/85 mmHg).

In her history no particular medical problems were recorded, although she was treated with low dose aspirin.



GP diagnosed mild hypertension and prescribed hydrochlorthiazide (25 mg/day). Moreover the lady was advised to reduce “as much as possible” her dietary salt intake.

Six weeks later her BP went down to 135/80 mmHg, however some changes in her mental status were recorded.



SYMPTOMS

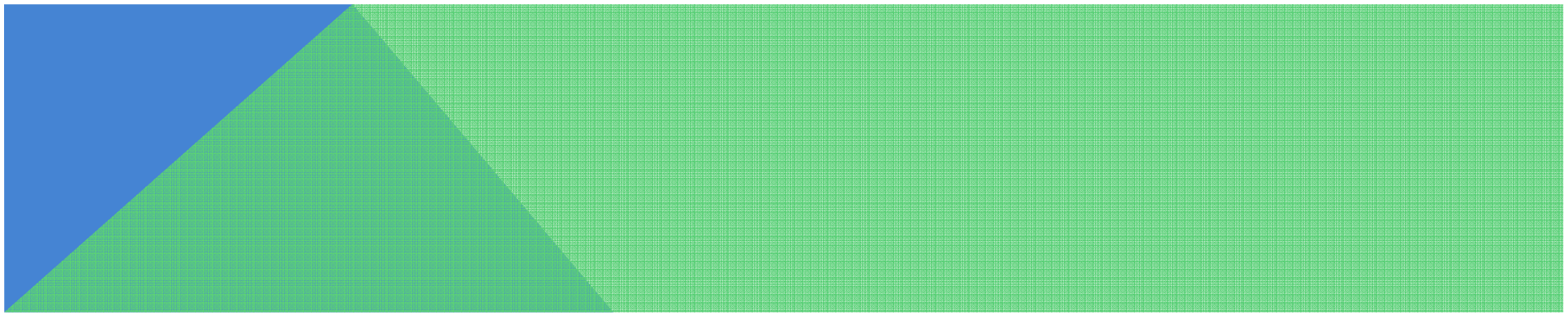
She was less alert

She had difficulties in concentrating

Her appetite decreased, she could only drink fluids

She had increasing gait instability

She suffered a fall, fortunately without any fractures



PHYSICAL EXAMINATION

Normal skin turgor (it is not easy to evaluate skin turgor in older adults)

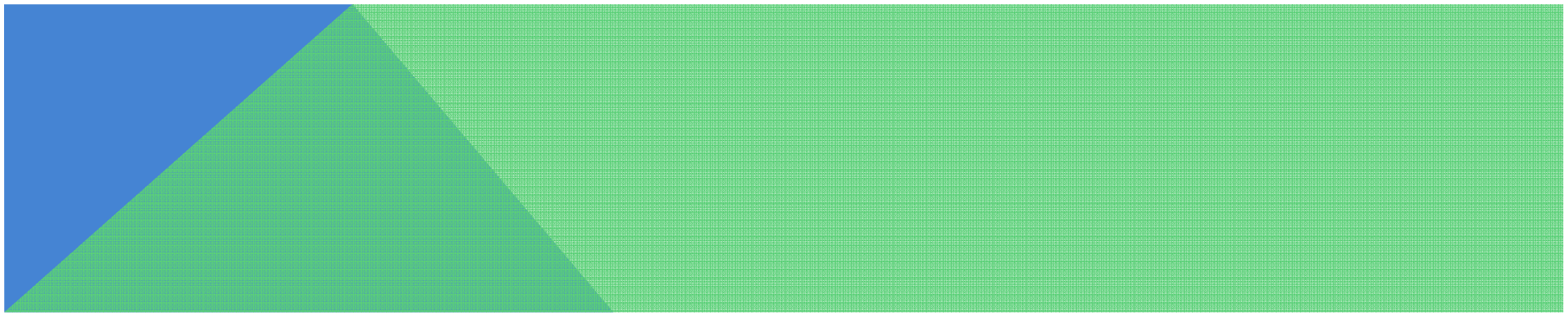
No orthostatic fall in BP or acceleration of the pulse

BP 125/80 mmHg

No focal neurological findings

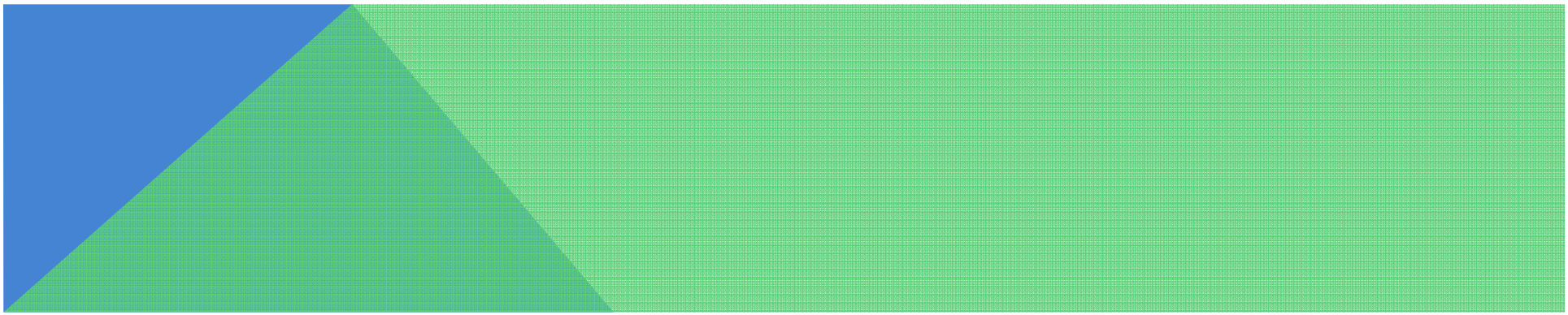
Evident gait disturbance that necessitated a walker for ambulation

Body weight stable around 58 Kg



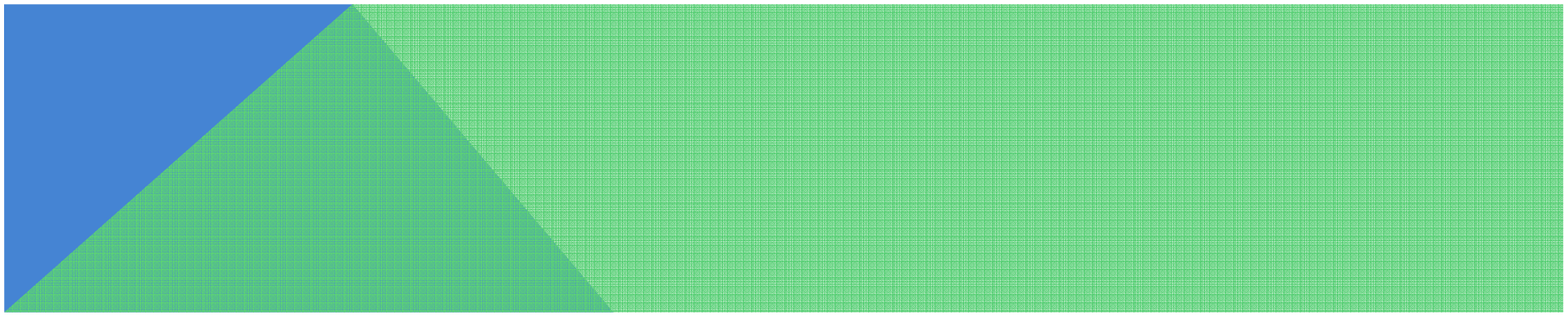
LABORATORY TESTS

	PLASMA		URINE	
Na	116		65	mmol/l
K	2.8		60	mmol/l
Cl	74		60	mmol/l
HCO3		30		
SCr		1.4 mg/dl		
Osmolality		244	340 mOsm/Kg water	
Uric acid		4.9 mg/dl		



CALCULATIONS

Glomerular filtration rate	39 ml/min/m^2
Fractional excretion of uric acid	9%



DIAGNOSIS

Acute renal failure

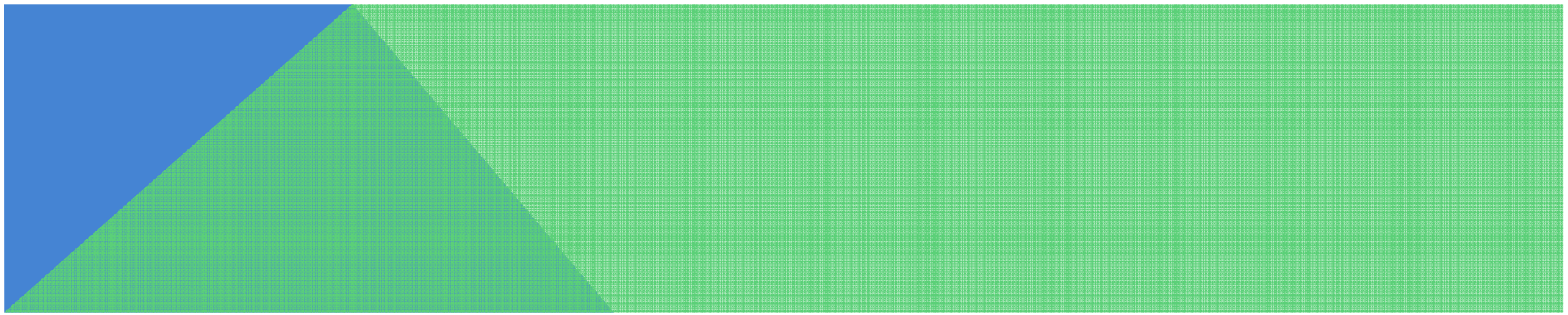
Hyponatremia (hypotonic)

Hypokaliemia

Mild metabolic alkalosis

Gait disturbance

Normal total body water



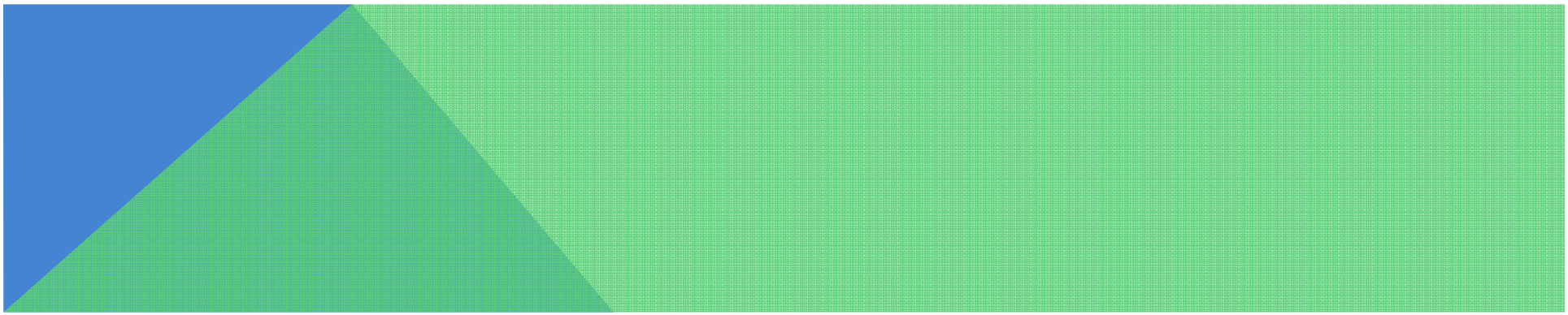
KEY POINTS

IS HYPONATREMIA REALLY HYPOTONIC?

A decrease in serum Na reflects a state of hypotonicity. Both Na and osmolality are low

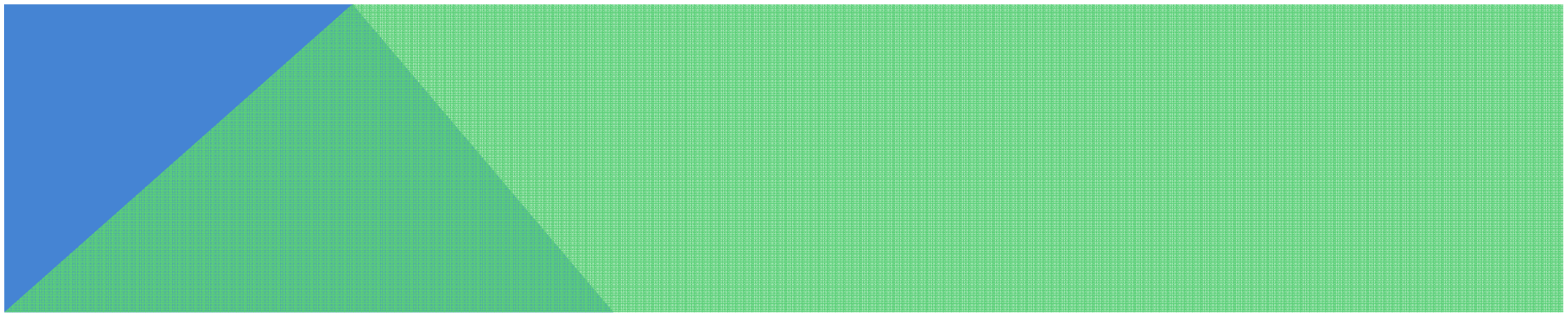
Consider concentration of solutes that do not cross the cell membrane

- ✓ glucose
- ✓ mannitol
- ✓ lipid
- ✓ protein



IS THERE AN EMERGENCY PRESENT ON ADMISSION NECESSITATING ACUTE THERAPEUTIC ACTION TO IMPROVE THE ELECTROLYTE DISTURBANCE?

Symptoms pointed to chronic hyponatremia. Acute hyponatremia usually develops in 48 hours



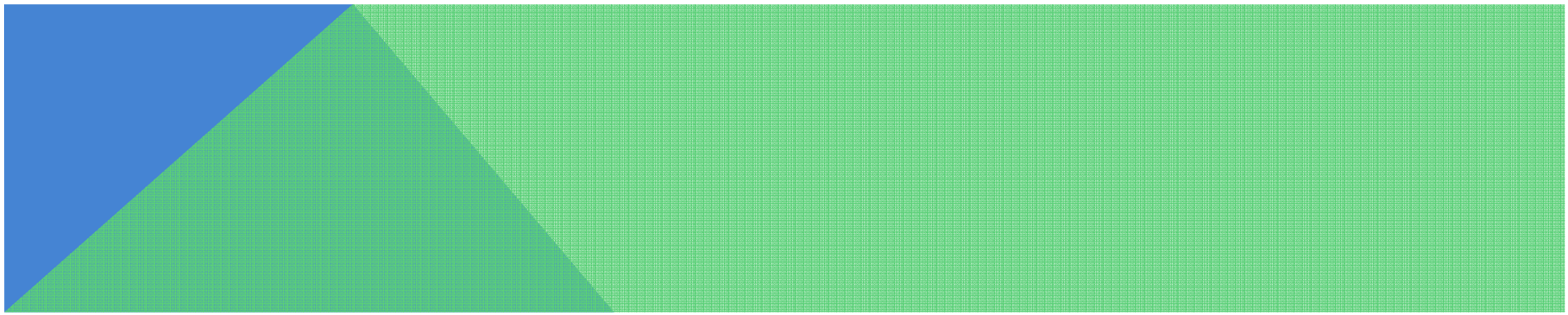
WHAT IS THE BEST APPROACH TO OBTAINING A CORRECT DIAGNOSIS?

Evaluation of the status of extracellular fluid volume (ECFV) is critical

- ✓ hypervolemic,
- ✓ Hypovolemic,
- ✓ euvolemic hyponatremia,

thus determining the treatment strategy

Risk of hyponatremia is higher in older adults in whom evaluation of volemic status is difficult.



FIRST STEP IS DETERMINATION OF URINARY SODIUM (SPOT URINE)

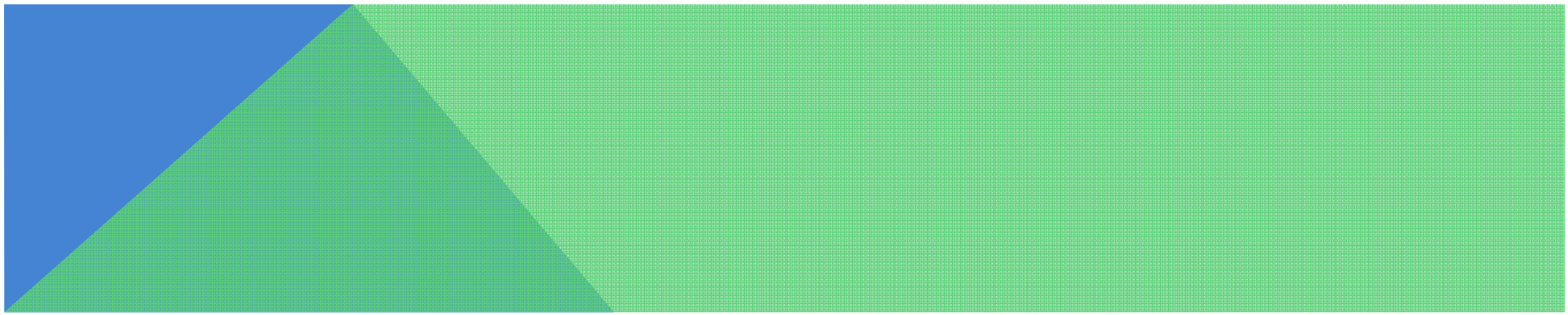
HYPOVOLEMIC OR HYPERVOLEMIC DISORDERS

U-Na<30 mmol/L

SYNDROME OF INAPPROPRIATE ANTIDIURESIS (SIAD)

U-Na>30 mmol/L

U-Na is of limited diagnostic utility in subjects on diuretic therapy due to inhibition of tubular Na reabsorption. In patients using diuretics a fractional excretion of uric acid<12% may be useful.



Contraction of ECFV decreases FEUa

Expansion of ECFV enhances FEUa

Case: U-Na 65 mmol/l

FE_{UA} 9 %

$$FEx = \frac{Ux * SCr}{UCr * Sx} * 100$$

WHAT IS THE BEST APPROACH TO RAISE SERUM NA?

Drugs known to be associated with syndrome of inappropriate antidiuresis (SIAD)

Table 1. Mechanisms of Drug-Induced Hyponatremia

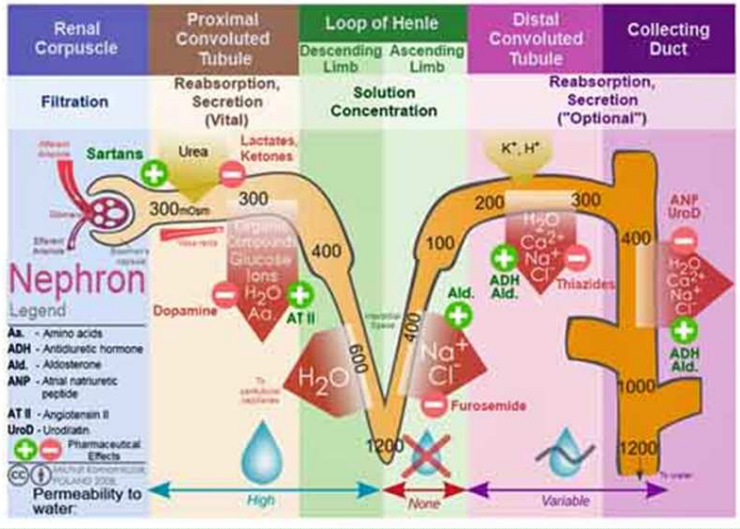
Class	Drug	Mechanism
Diuretics	*Thiazide:* indapamide, chlorthalidone, amiloride/hydrochlorothiazide *Loop:* furosemide	Hypovolemic/euvolemic (decreases total body sodium)
Antidepressants (SSRIs)	Sertraline, fluoxetine, paroxetine, citalopram, venlafaxine	SIADH
Antipsychotics	Amisulpride, aripiprazole, chlorpromazine, clozapine, fluphenazine, haloperidol, pimozide, risperidone, thioridazine, thiothixene, trifluoperazine	SIADH
Anticonvulsants	Carbamazepine, oxcarbazepine	SIADH
COX-2 inhibitor	Celecoxib	SIADH
Chemotherapeutic agents	Vincristine, vinblastine, carboplatin, cisplatin, cyclophosphamide	SIADH

COX-2: cyclooxygenase-2; SIADH: syndrome of inappropriate antidiuretic hormone secretion; SSRI: selective serotonin reuptake inhibitor.
Source: References 14-17.

WHAT IS THE BEST APPROACH TO RAISE SERUM NA?

Aging decreases the excretion of water due to reduced expression of Na-K-Cl cotransporter in the ascending limb of the loop of Henle and the Na-Cl cotransporter in the distal tubule (free water clearance is limited)

$$C_{H_2O} = V - V * \frac{Uosm}{Posm}$$



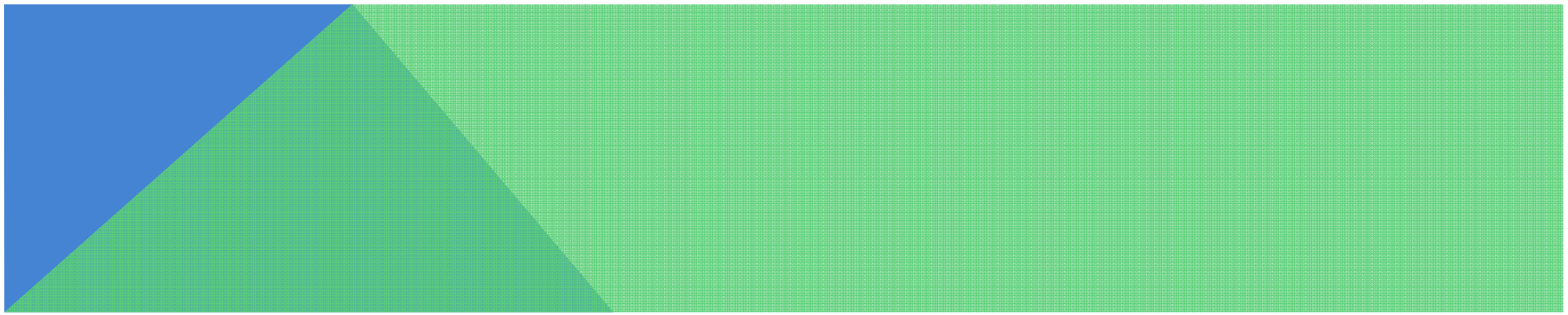
WHAT ARE THE RISK FACTORS, SYMPTOMS AND PATHOPHYSIOLOGY OF THIAZIDE INDUCED HYPONATREMIA?

The relative risk of hyponatremia is approximately 60% higher in patients exposed to thiazide diuretics compared to alternative therapy, especially if they are treated with selective serotonin reuptake inhibitors.

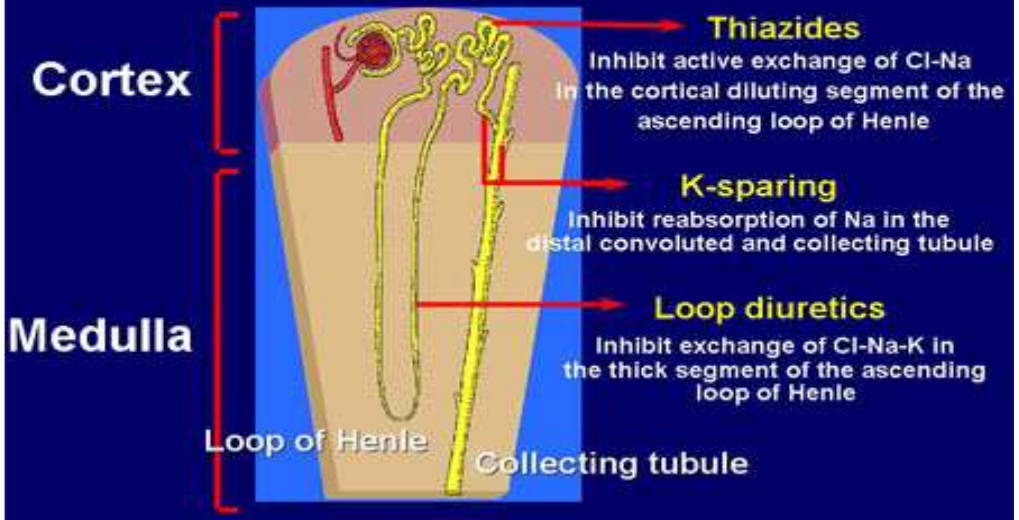
Thiazide diuretics may induce both inappropriate ADH secretion and ADH-independent water retention (Hix JK. Semin nephrol 2011; 31: 553-566).

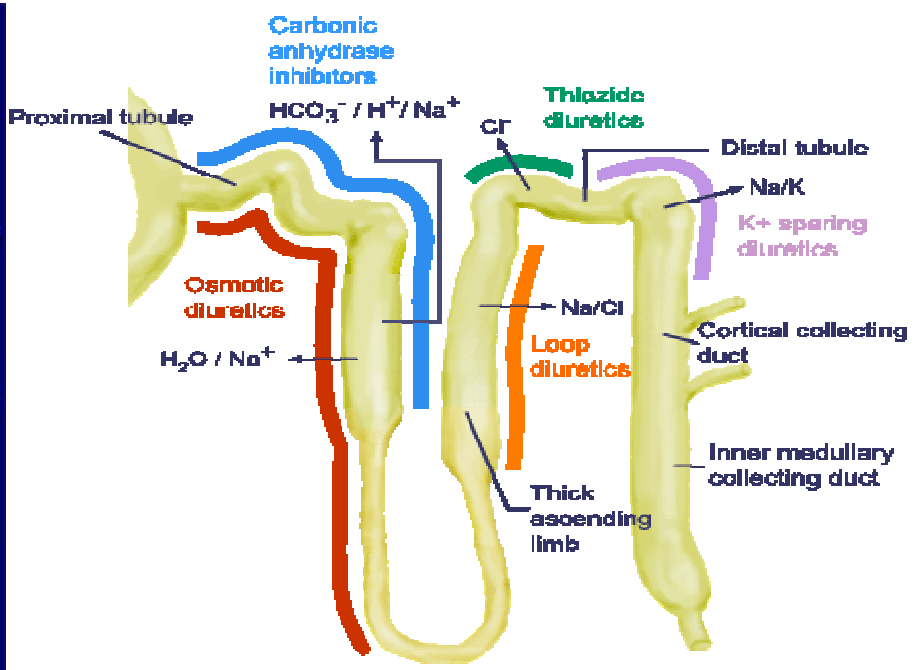
Thiazide diuretics block sodium chloride cotransport in the distal tubule.

Low distal delivery of filtrate and water reabsorption by residual water permeability



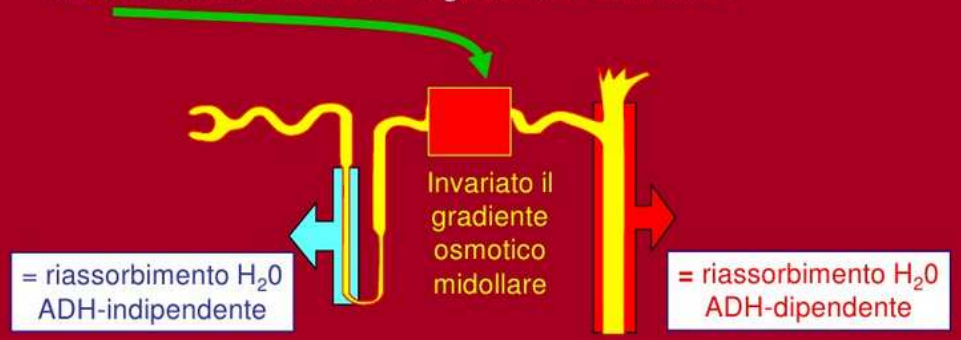
Diuretics: Mechanism of Action





IPONATRIEMIA E DIURETICI

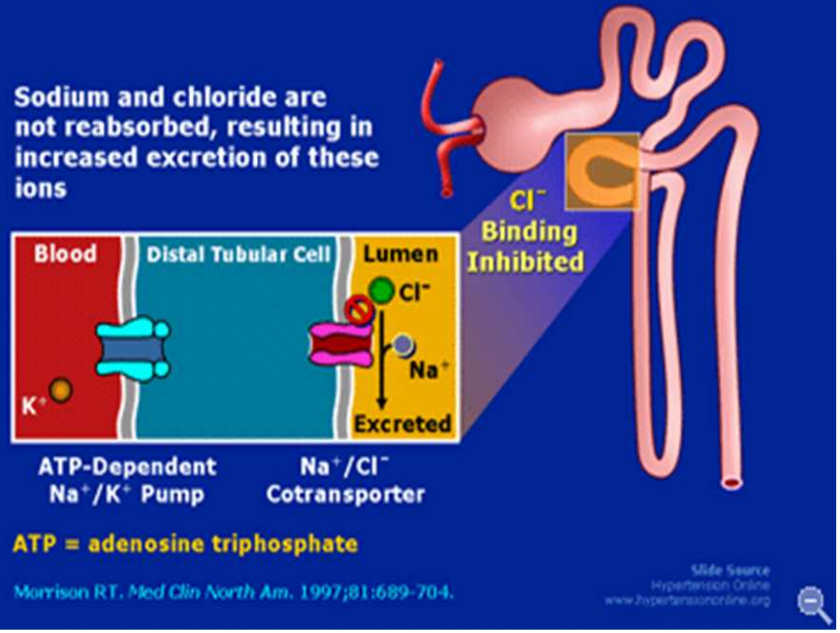
Tiazidici non influenzano il gradiente midollare.



Tiazidici possono → concentrazioni di Na^+ e K^+ superiori a quelle plasmatiche.

Se ADH è stimolato da ridotta volemia efficace → IPONATRIEMIA.

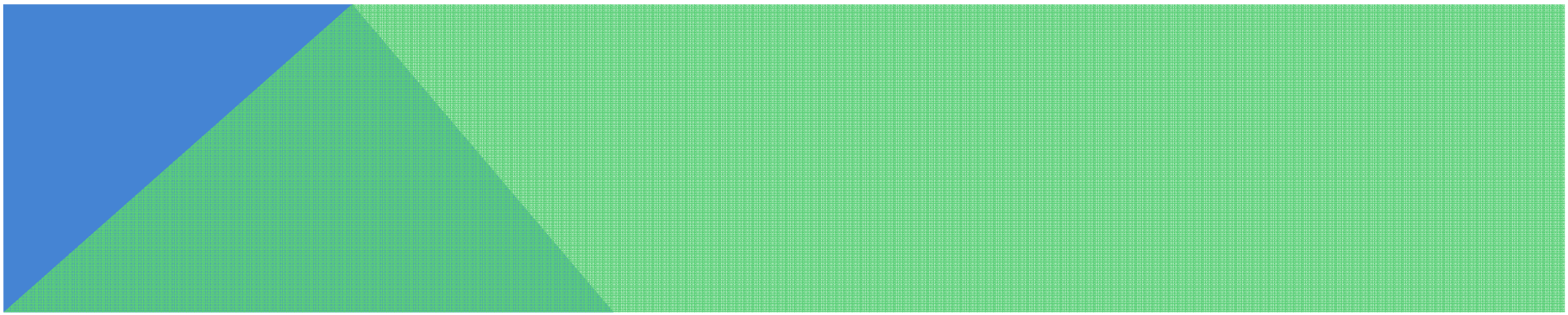
Thiazide Diuretics
Mechanism of Action



WHAT IS THE ROLE OF HYPOKALEMIA IN THE PATHOPHYSIOLOGY OF HYPONATREMIA?

Hypokalemia induced by thiazide diuretics is an independent predictive factor for the development of hyponatremia.

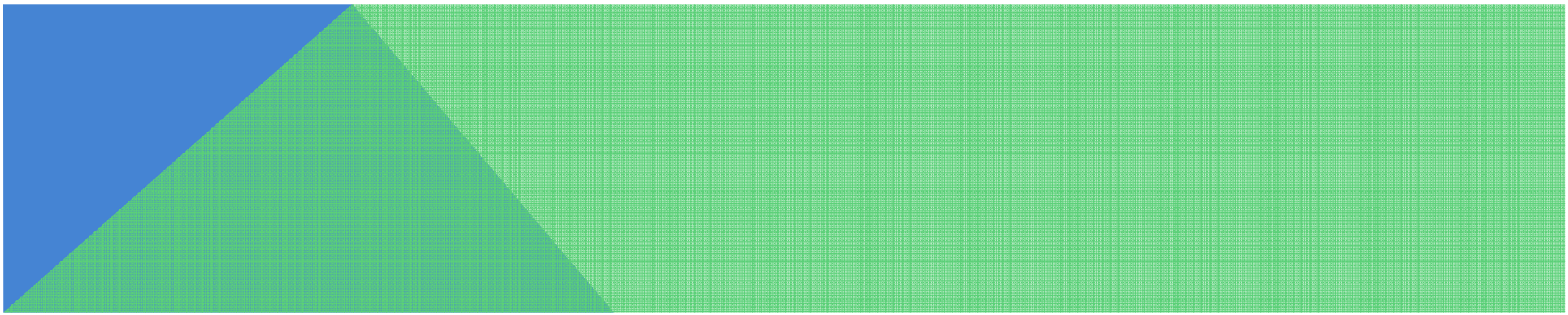
Potassium depletion results in a shift of sodium into the cells with a commensurate exit of potassium from the cell into extracellular fluid



WHAT ARE THE OPTIONS FOR THERAPY TO RAISE THE PLASMA SODIUM IN THIS PATIENT?

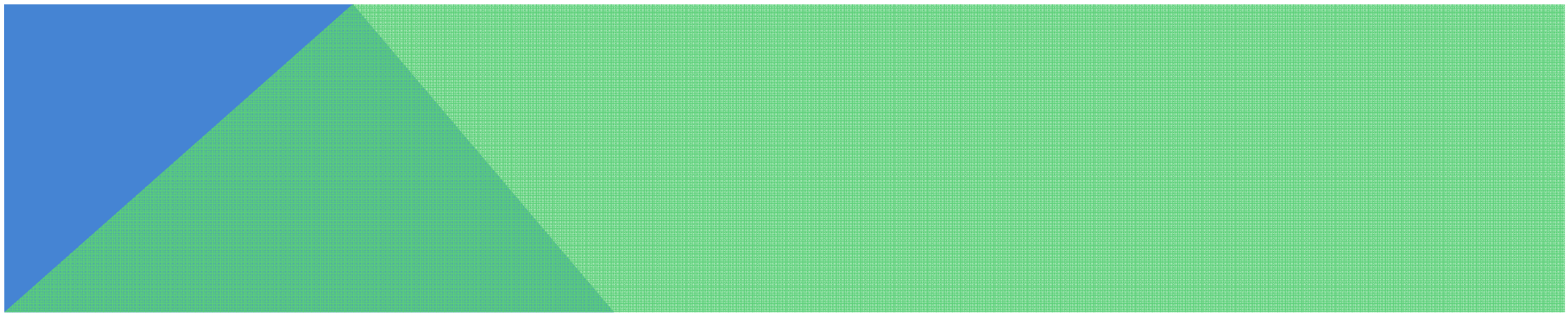
The main goal was to administer NaCl 0.9% + KCl aiming at raising plasma Na to an upper limit of ~8 mmol/L per 24 h due to the risk of osmotic demyelinization.

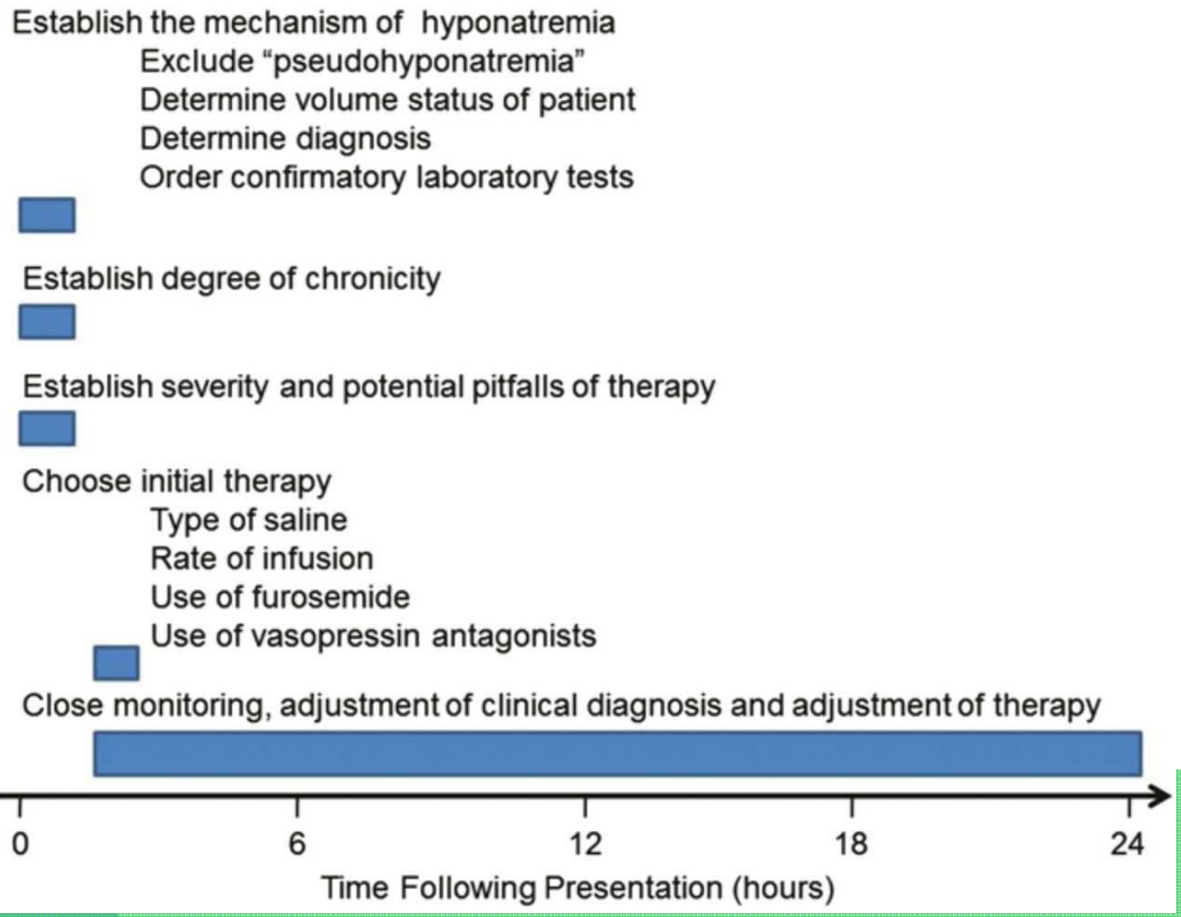
In the case like this one physicians should pay particular attention to plasma sodium correction at the time of diuresis onset, it could be that water diuresis, leading to a rapid rise in plasma Na, may increase the risk of osmotic demyelinization syndrome



HOW SHOULD CONCOMITANT HYPOKALEMIA BE TREATED, AND IS IT AN ADDITIONAL DANGER IN THE TREATMENT OF HYPONATREMIA?

- Many patients with hyponatremia resulting from thiazide diuretics therapy appear euvolemic and SIAD has been implicated in the pathogensis.
- Potassium depletion could increase the sensitivity for ADH release, however this mechanism has not been demonstrated yet.




Establish the mechanism of hyponatremia
Exclude "pseudohyponatremia"
Determine volume status of patient
Determine diagnosis
Order confirmatory laboratory tests
Establish degree of chronicity
Establish severity and potential pitfalls of therapy
Choose initial therapy
Type of saline
Rate of infusion
Use of furosemide
Use of vasopressin antagonists
Close monitoring, adjustment of clinical diagnosis and adjustment of therapy
0
6
12
18
24
Time Following Presentation (hours)

TIAZIDICI e TIAZIDO-SIMILI

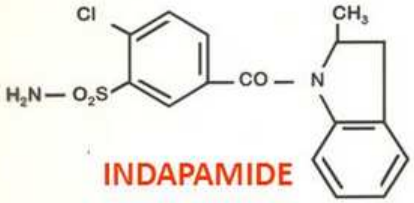
La clorotiazide è il capostipite di una serie di molecole a struttura benzotiadiazinica contenente il gruppo sulfamidico in posizione 7 e quasi sempre un alogeno in posizione 6.

Altre molecole a struttura non benzotiadiazinica ma contenenti sempre il gruppo sulfonamidico non sostituito sono denominate tiazido-simili.

IDROCLOROTIAZIDE

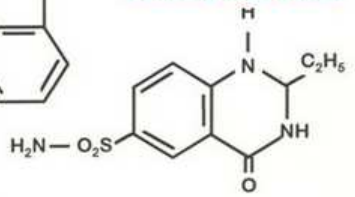
CLORTALIDONE

METOLAZONE

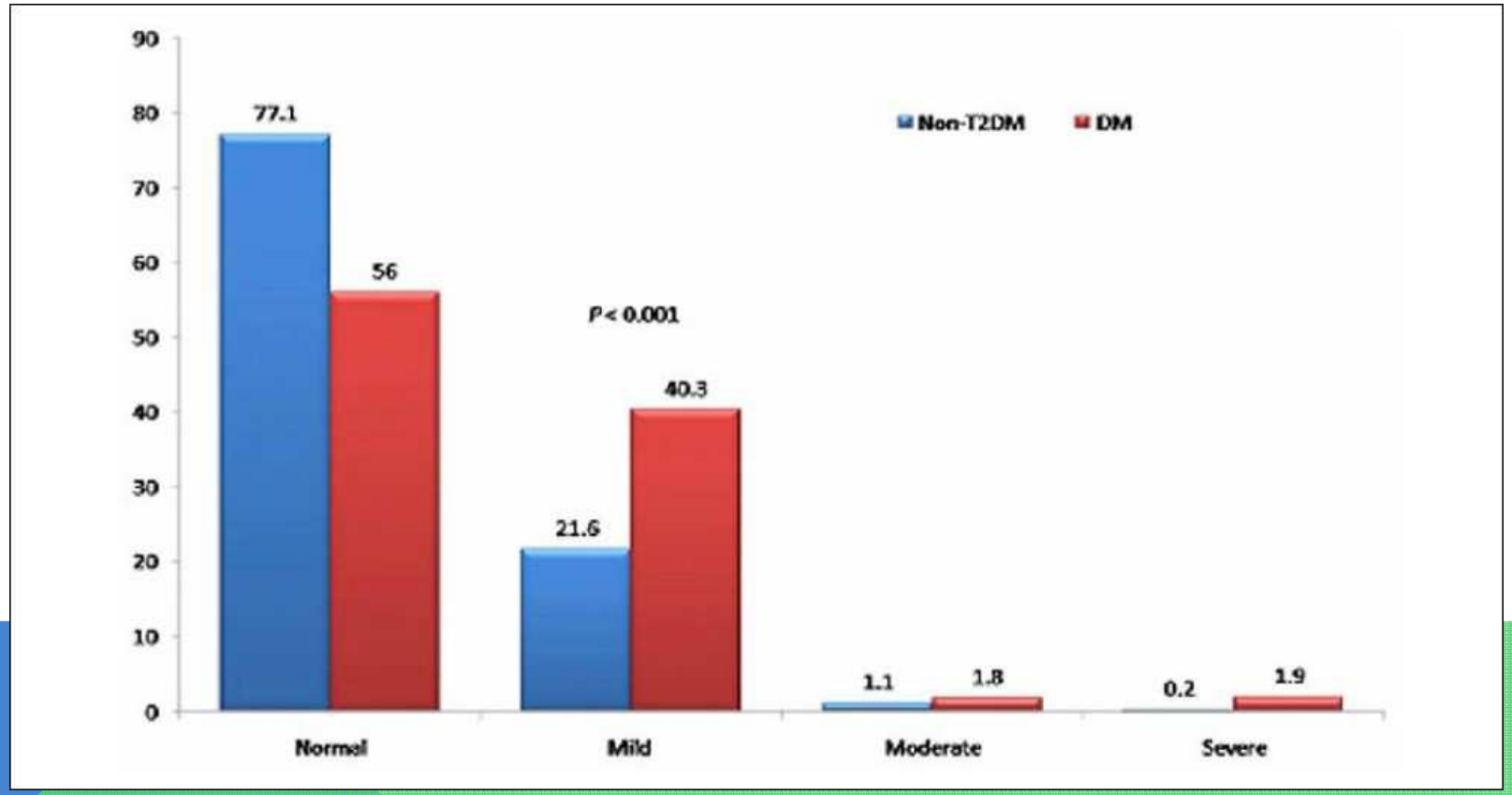


INDAPAMIDE

CHINETAZONE

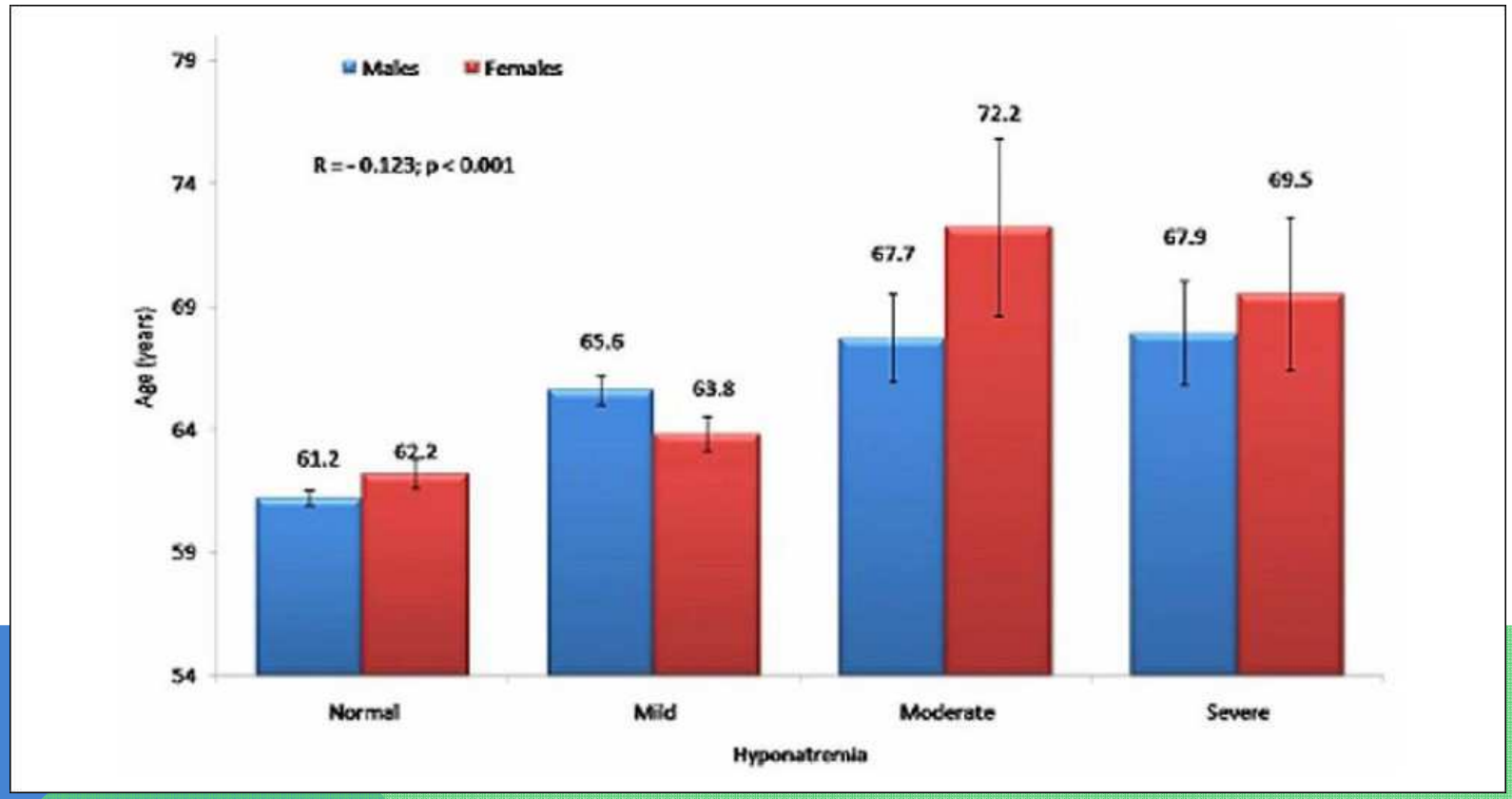


INCREASED PREVALENCE OF MILD HYPONATREMIA SEEN AMONG PATIENTS WITH TYPE-2 DIABETES MELLITUS AS COMPARED WITH THOSE WITHOUT DIABETES (AL QAHTANI M ET AL 2013)



SAUDI JOURNAL OF KIDNEY DISEASES AND TRANSPLANTATION

MEAN AGE OF THE PATIENTS WITH NORMAL SODIUM AND MILD, MODERATE AND SEVERE HYPONATREMIA, SHOWING THE SIGNIFICANT INVERSE ASSOCIATION BETWEEN SERUM SODIUM AND AGE (AL QAHTANI M ET AL 2013)



SAUDI JOURNAL OF KIDNEY DISEASES AND TRANSPLANTATION

HUANG CC ET AL. CLINICAL AND GENETIC FACTORS ASSOCIATED WITH THIAZIDE-INDUCED HYPONATREMIA. MEDICINE (BALTIMORE) 2015;94:E1422

Possible predictors of thiazide-induced hyponatremia.

A total of 48 patients admitted to the ward or to the emergency department due to severe thiazide-induced hyponatremia (Na < 125 mmol/L) were evaluated

Twelve tag single nucleotide polymorphism markers were selected from the Potassium Channel,

Multivariate logistic regression revealed that

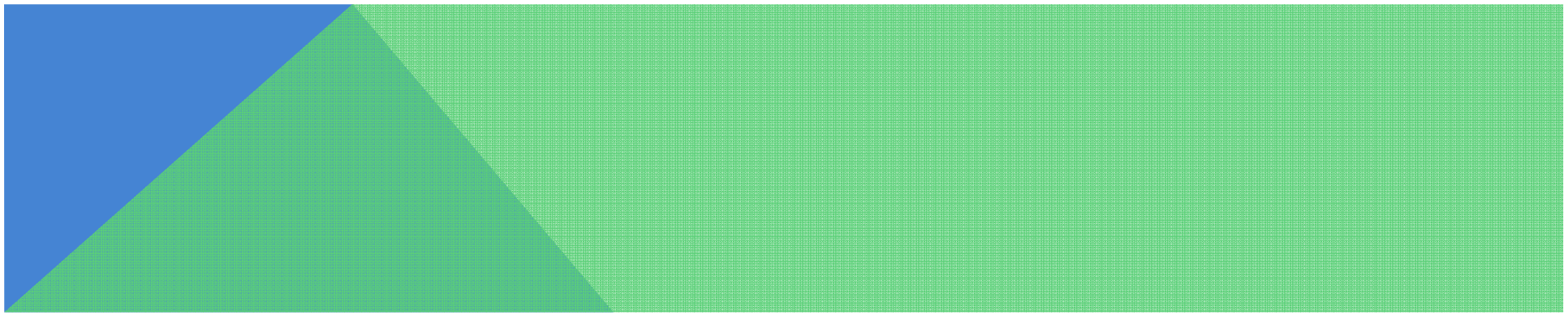
age (odds ratio [OR], 1.13; 95% confidence interval [CI], 1.08-1.19, P < 0.001),

female gender (OR, 4.49; 95% CI, 1.54-13.11, P = 0.006),

BMI (OR, 0.80; 95% CI, 0.69-0.93, P = 0.003),

and KCNJ1 rs2509585 C/T or T/T polymorphisms (OR, 5.75; 95% CI, 1.25-26.45, P = 0.03)

were independent predictors for thiazide-induced



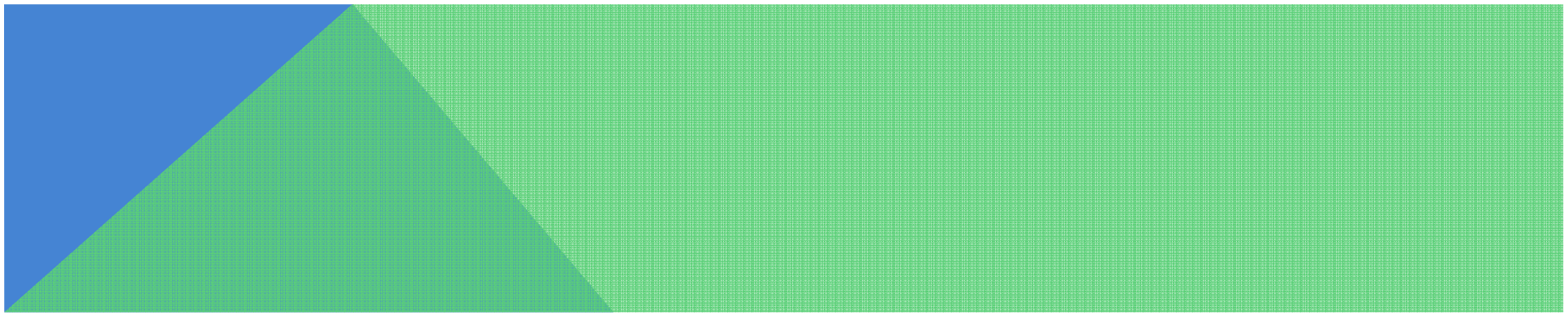
MAKAM AN, BOSCARDIN WJ, MIAO Y, STEINMAN MA. RISK OF THIAZIDE-INDUCED METABOLIC ADVERSE EVENTS IN OLDER ADULTS. J AM GERIATR SOC 2014;62:1039-45.

Over 9 months of follow-up, 14.3% of new thiazide users developed an adverse event AE (number needed to harm (NNH) 12))

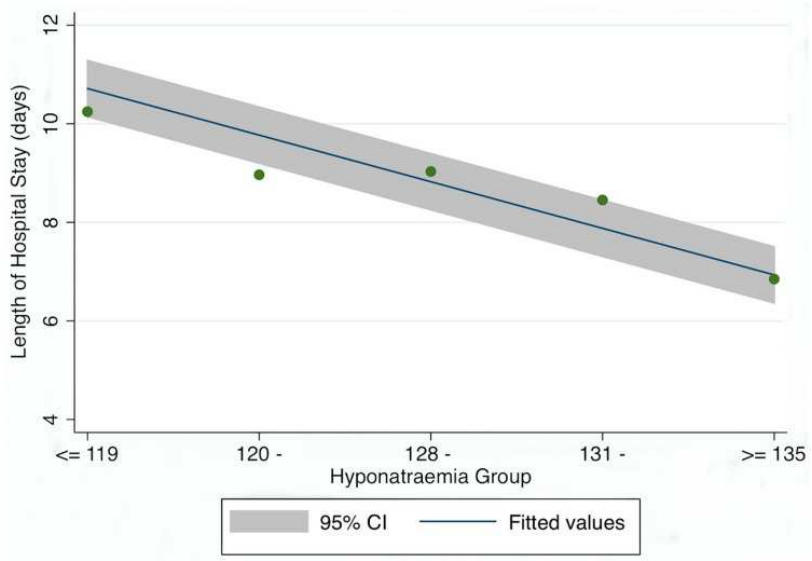
1.8% of new users developed a severe AE (NNH = 82)

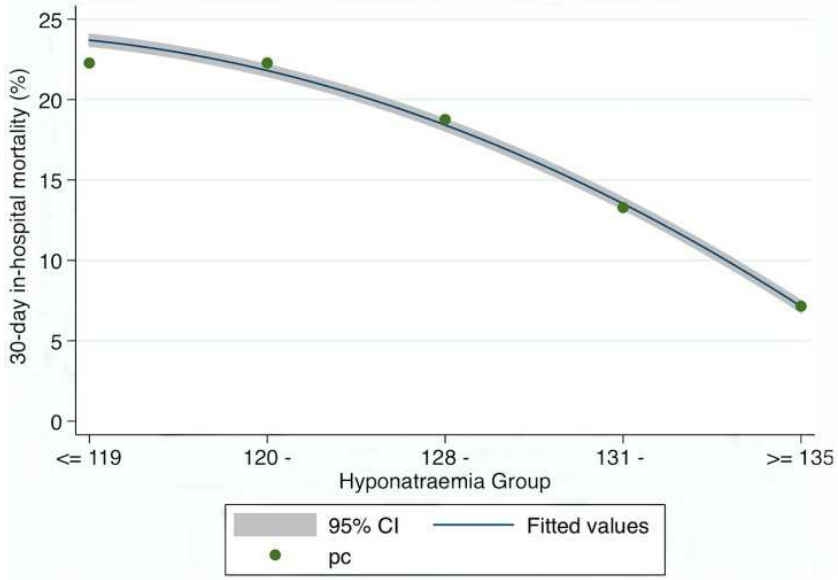
3.8% of new users had an emergency department visit or hospitalization with an AE (NNH = 56)

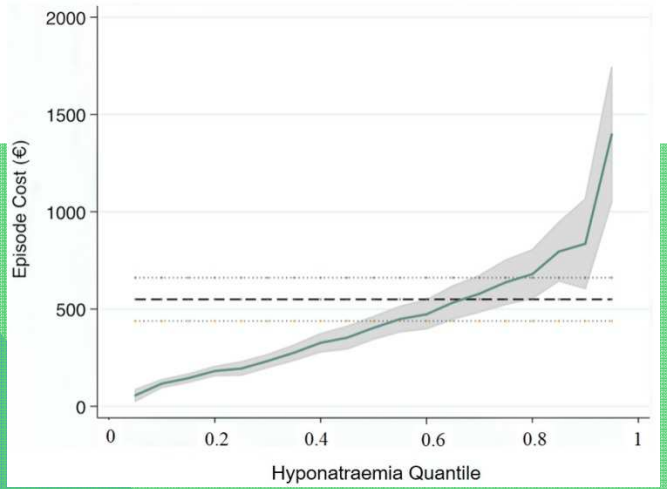
having five or more comorbidities was associated with 3.0 times the odds of developing an AE as having one comorbidity



AUTHORS EXPLORED THE IMPACT OF HYPONATRAEMIA ON OUTCOMES: 30 DAYS IN-HOSPITAL MORTALITY, LENGTH OF STAY AND COSTS (CONWAY R J CLIN MED 2014;3:1220-33)







HYPONATREMIA

ICD9-CM CODE 276.1

BMC Med. 2014; 12: 1.
Published online 2014 Dec 11. doi: 10.1186/s12916-014-0231-1
PMCID: PMC4276109

Diagnosis and treatment of hyponatremia: a systematic review of clinical practice guidelines and consensus statements

Evi V Nagler,[✉] Jill Vanmassenhove, Sabine N van der Veer, Ionut Nistor, Wim Van Biesen, Angela C Webster, and Raymond Vanholder

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Abstract

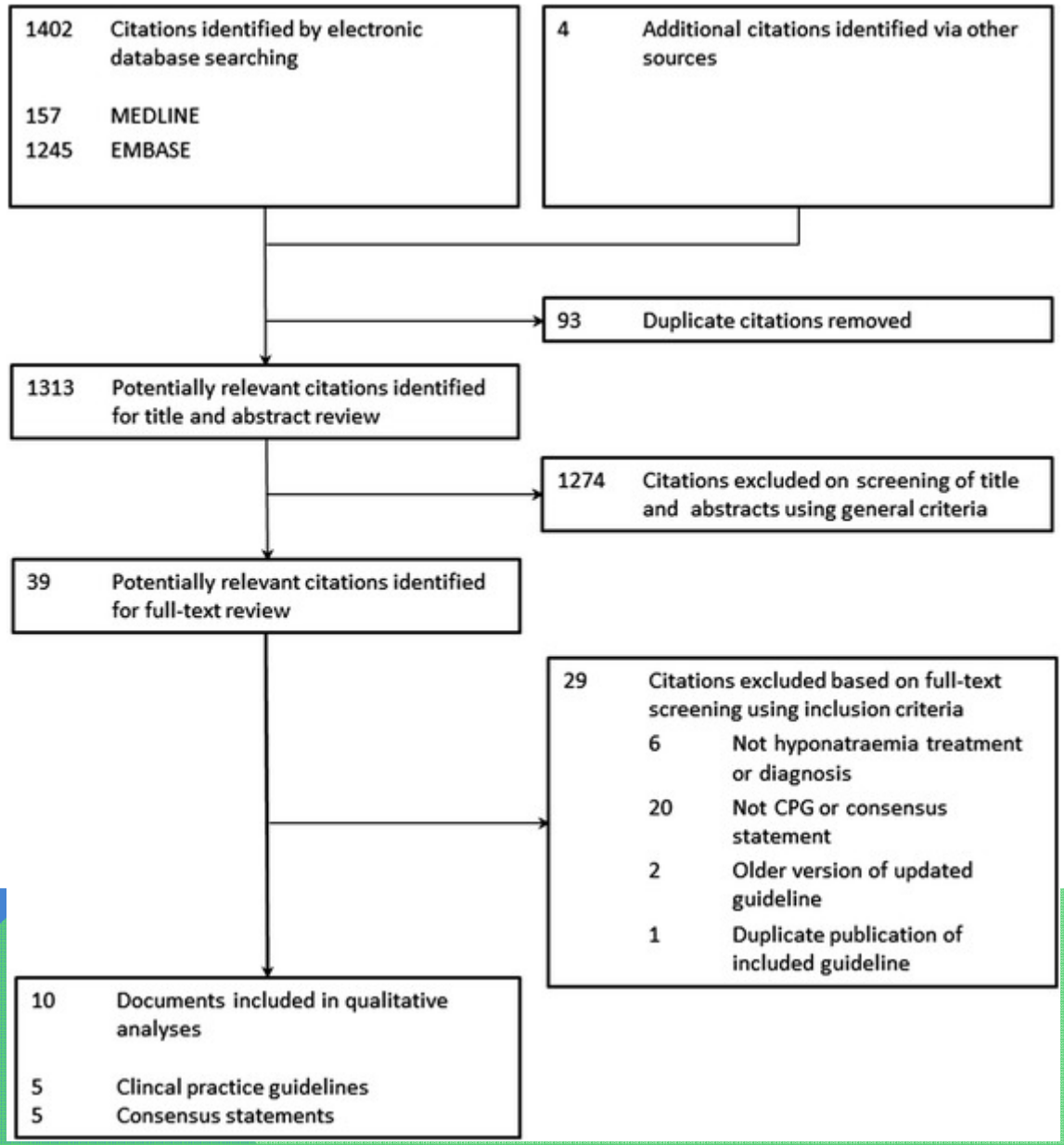
Go to:

Background

Hyponatremia is a common electrolyte disorder. Multiple organizations have published guidance documents to assist clinicians in managing hyponatremia. We aimed to explore the scope, content, and consistency of these documents.

Methods

We searched MEDLINE, EMBASE, and websites of guideline organizations and professional societies to September 2014 without language restriction for Clinical Practice Guidelines (defined as any document providing guidance informed by systematic literature review) and Consensus Statements (any other guidance document) developed specifically to guide differential diagnosis or treatment of hyponatremia. Four reviewers appraised guideline quality using the 23-item AGREE II instrument, which rates reporting of the guidance development process across six domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. Total scores were calculated as standardized averages by domain.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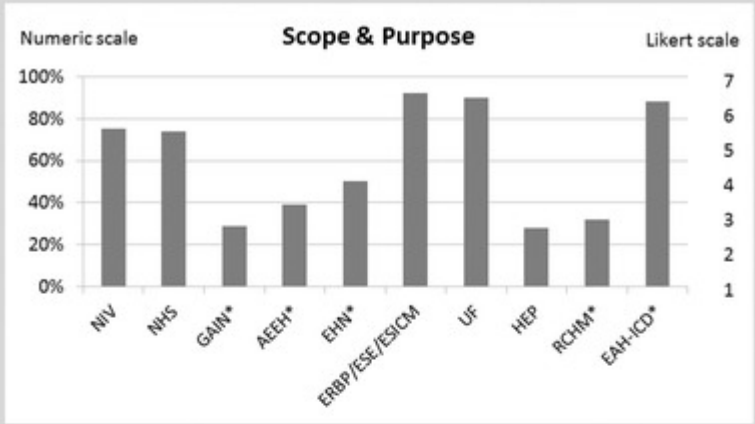
157 MEDLINE
1245 EMBASE
4 Additional citations identified via other sources
93 Duplicate citations removed
1313 Potentially relevant citations identified for title and abstract review
1274 Citations excluded on screening of title and abstracts using general criteria
39 Potentially relevant citations identified for full-text review
29 Citations excluded based on full-text screening using inclusion criteria
6 Not hyponatraemia treatment or diagnosis
20 Not CPG or consensus statement
2 Older version of updated guideline
1 Duplicate publication of included guideline
10 Documents included in qualitative analyses
5 Clincal practice guidelines
5 Consensus statements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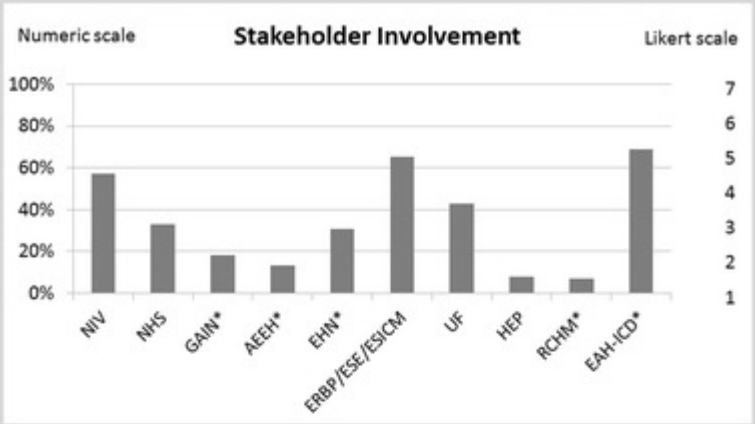
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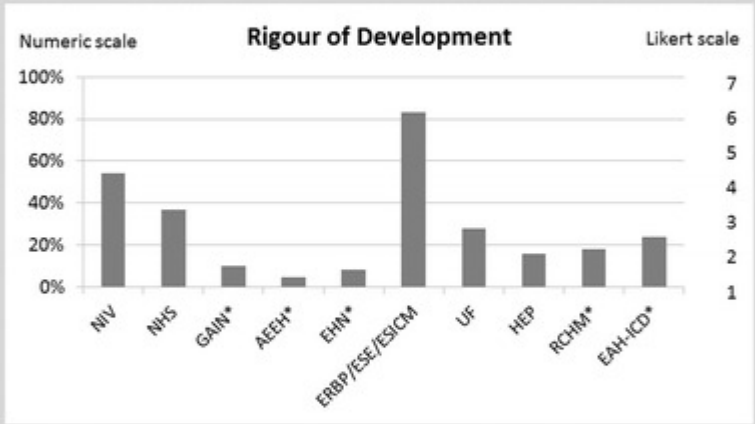
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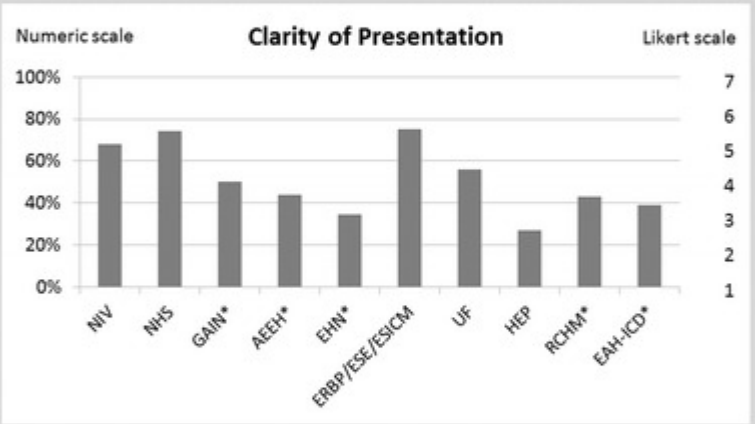
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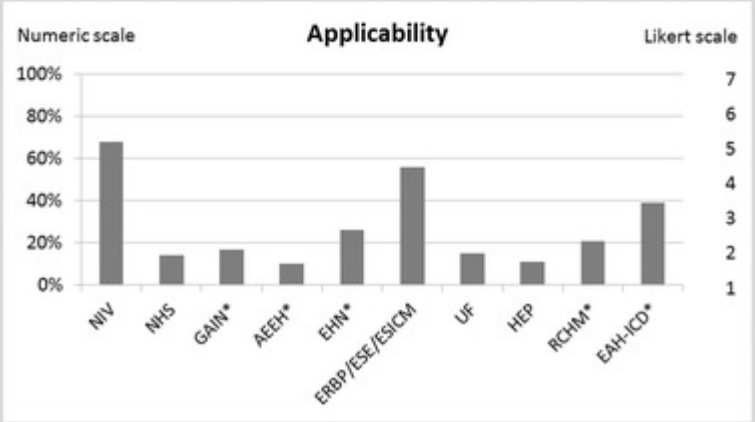
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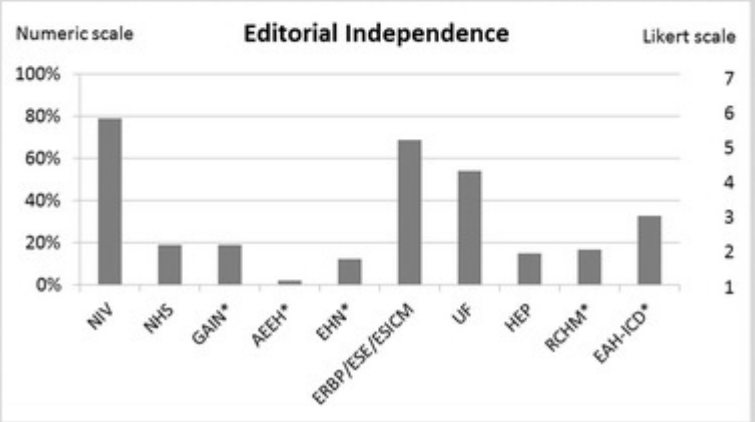
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Maxwell *BMC Medicine* (2015) 13:31
DOI 10.1186/s12916-015-0277-8

BMC Medicine

COMMENTARY Open Access

Diagnosis and management of hyponatraemia: AGREEing the guidelines

Alexander P Maxwell

Abstract

Hyponatraemia is a common electrolyte disorder associated with significant complications and controversies regarding its optimal management. Clinical practice guidelines and consensus statements have attempted to provide clinicians with evidence-based diagnostic and treatment strategies for hyponatraemia. Recently published guidance documents differ in their methods employed to review the quality of available evidence. Nagler et al. used the Appraisal of Guideline for Research and Evaluation (AGREE II) instrument in a systematic review of guidelines and consensus statements for the diagnosis and management of hyponatraemia. Nagler and colleagues highlighted the variability in methodological rigour applied to guideline development and inconsistencies between publications in relation to management of hyponatraemia (including the recommended rate of correction of a low serum sodium concentration). These differences could cause confusion for practising physicians managing patients with hyponatraemia.

Please see related article: http://www.biomedcentral.com/1741-7015/12/231.

Keywords: Hyponatraemia, Guidelines, Systematic review

In the "real world", the non-expert doctor who initially recognises and responds to severe hyponatraemia (serum sodium concentration <120 mmol/L) in a critically ill patient will often be a junior trainee working "out of routine office hours". In this emergency setting, the doctor may have limited immediate access to important additional diagnostic tests, e.g., serum and urine osmolality and urine electrolytes. Urgent treatment decisions may need to be taken to manage symptoms such as confusion and seizures, with incomplete patient history and diagnostic information. There is a general consensus that hypertonic saline is effective in the immediate management of acute symptomatic hyponatraemia but available guidelines differ on the volumes and rates of saline infusion. Ultimately, it is clinical judgement rather than adherence to a particular guideline that will determine an individual patient's treatment. Intuitive clinical algorithms, with proven efficacy, would help to encourage "best practice" in the diagnosis and management of hyponatraemia.