NOPIA
NOCTURIA & POLYURIA
INTERNATIONAL NOCTURNAL POLYURIA RESEARCH GROUP (INPRG)

Liaison en nycturie

25 min

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http://nopia-inprg.org/

UZ GENT
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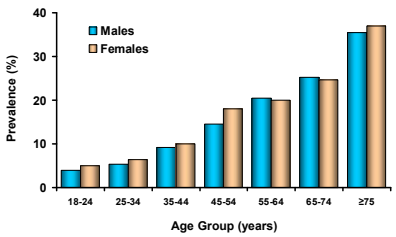
Reference: International Continence Society consensus on the diagnosis and treatment of nocturia. Karel Everaert, Francois Hervé, Ruud Bosch, Roger Dmochowski, Marcus Drake, Hashim Hashim, Christopher Chapple, Philip Van Kerrebroeck, Sherif Mourad, Paul Abrams, Alan Wein Neurourol Urodyn. 2019 Feb;38(2):478-498.

Disclosures:

- Grants, honoraria to institution from Ferring, Medtronic, Astellas
- Promotor Frederik Paulsen chair
- Promotor Medtronic OptiLuts chair
- Minority shareholder P2solutions (smart textiles) without salary

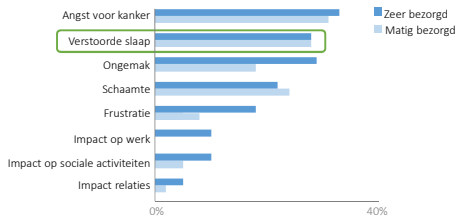
Prevalence of Nocturia in a US Community-Based Population



Coyne KS, et al. BJU Int. 2003;42:948-54.

Impact LUTS op levenskwaliteit

Bezorgdheden bij 502 patiënten met BPH symptomen

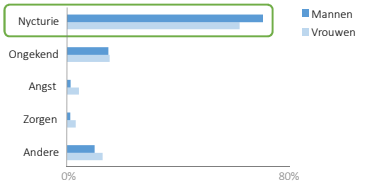


BPH = Benigne prostaathypertrofie, LUTS = Lower Urinary Tract Symptom

Imberton M et al. Int J Clin Pract 2008;62:28-36

Meest frequente oorzaak slaapfragmentatie

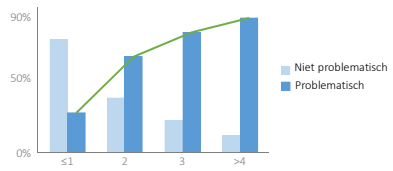
Meest frequente oorzaak slaapfragmentatie bij 1485 volwassenen >50 jaar



Middelkoop et al. J Geriatrist & Biol Sci Med Sci 1996;51:M28–M35

Eén van de meest storende LUTS

Hinder neemt toe met aantal nycturie episodes



Aantal nycturie episodes bij 1214 vrouwen

LUTS = Lower Urinary Tract Symptom

Fiske J et al. Neurourol Urodyn 23:138–143 , 2004

Gevolgen slaapfragmentatie

Levenskwaliteit	Stemmingswisselingen Cognitie en geheugen Energie Prestaties op het werk
Morbiditeit	Verkeersongevallen Valaccidenten en fracturen Cardiovasculaire aandoeningen Depressie Immunologische respons
Mortaliteit	Tengevolge van slaapstoornis

ACTA CLINICA BELGICA
2021, VOL. 76, NO. 2, 85-96
https://doi.org/10.1080/17843286.2019.1660022

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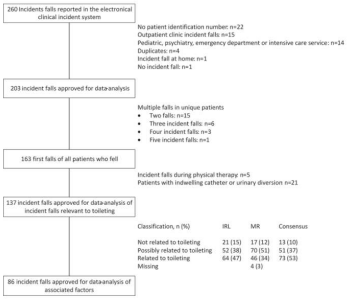
Prevalence and characteristics of incident falls related to nocturnal toileting in hospitalized patients

Veerle Decalf [a], Wendy Bower [a,b,c], Georgie Rose [b], Mirko Petrovic [d], Ronny Pieters [e], Kristof Eeckloo [f], and Karel Everaert [a,e]

An observational study was conducted in an academic, tertiary-care hospital in Belgium over a six months period (January–June 2016). We performed a retrospective review of the electronic incident reporting and learning system (IRL) and medical records (MR) for adult patients who experienced an incident fall during hospitalization in the hospital's medical, surgical and rehabilitation wards (305, 300 and 87 beds, respectively).

The prevalence of toileting-related incident falls is high, 53% of all incident falls in the hospital, with almost half of the episodes occurring during night-time. If nocturia is the leading cause of these nocturnal incident falls related to toileting, intravenous fluid therapy could be an important source of increased fluid intake in inpatients and may lead to iatrogenic nocturia.



ORIGINAL PAPER
Geriatrics

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

The Bladder at Night during Hospitalisation: Towards optimal care for elderly patients with nocturia

Wouter Van Besien[1] | Samia Shire[2] | Veerle Decalf[3] | Claire E. Ervin[4] | Sharyn King[4] | Christine Baldrey[4] | Alisha Da Silva[5] | Adrian Wagg[2] | Karel E. Everaert[3] | Wendy F. Bower[1,4,5,6]

Methods
A multisite mixed methods cross-sectional study of older hospitalized adults who were admitted for ≥2 days was conducted using a standardized researcher-administered questionnaire.

Nocturia – what are the causes?

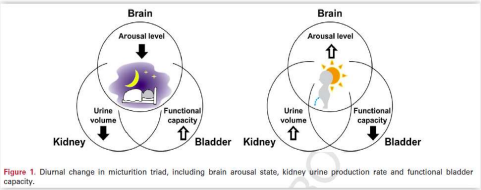


Figure 1. Diurnal change in micturition triad, including brain arousal state, kidney urine production rate and functional bladder capacity.

Is more an explanation than a causality or a diagnosis
Is helping us to phenotype

Negoro H et al 2013

Causalities of nocturia

NOCTURIA
Causative factors

OAB, BOO, neurogenic bladder, interstitial cystitis… having a reduced functional bladder capacity

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Which LUTS are most bothersome in a BPH population?

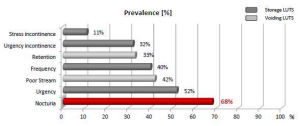
- follow-up investigation of the original study population in Herne 2 years after the initial assessment
- *have you visited a doctor for LUTS during the last 2 years?*
- multivariate regression analysis using patient-reported bother from each symptom of the IPSS questionniare (AUA-SPI)
- only nocturia was significantly asssociated with medical consultations

Variable	Odds ratio	Lower limit	Upper limit	p value
Bother from IPSS 1: incomplete emptying	1.2	0.576	2.354	0.633
Bother from IPSS 2: frequent voiding	1.5	0.746	2.910	0.265
Bother from IPSS 3: intermittent voiding	1.5	0.746	3.008	0.255
Bother from IPSS 4: urgency	1.5	0.866	2.617	0.147
Bother from IPSS 5: poor urinary stream	1.7	0.926	3.236	0.085
Bother from IPSS 6: straining	1.1	0.542	2.271	0.776
Bother from IPSS 7: nocturia	2.6	1.635	4.163	<0.001

Oelke M et al. *World J Urol.* 2014; 32: 1155 – 1162.

Which LUTS persist after prostatic surgery

- limited data on the type of LUTS which persist after prostatic surgery
- in retrospective case series, residual/recurrent LUTS after TURP were found in approx. 20 (30) % of patients (mean time from TURP 3.5 years), of those:



n = 129 men
(consecutive series, age 46-90 y, mean 72 y)

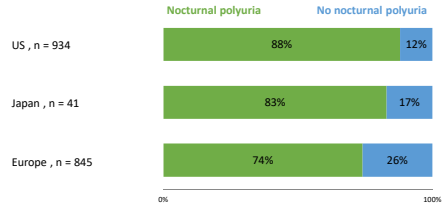
Seaman EK et al. *J Urol.* 1994; 152: 935 – 937.

Causalities of nocturia

Renal failure, nephrogenic diabetes insipidus, … ageing, abno/loss circadian rhythm of kidney, …

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

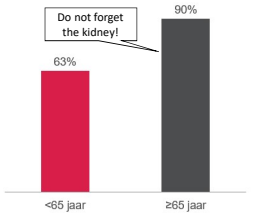
Nocturnal polyuria in patients with nocturia



Weiss JP 2011;Chang 2006;. Abrams P 2004

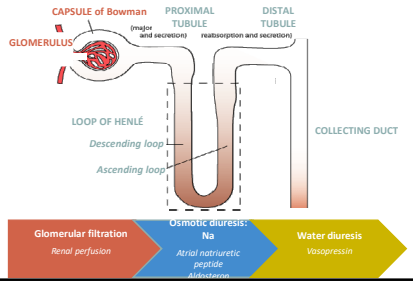
Causes – nocturnal polyuria

Nocturnal polyuria in patients with nocturia ≥2 increases with age (n=845) [43]



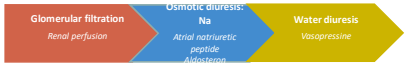
43. Abrams P et al. Neurourol Urodyn 2004;23:466

DYNAMICS OF URINEPRODUCTION



Diagnosing nocturnal polyuria: the renal function profile

Start	8 urinesamples: 1 / 3h							
Voids	U1	U2	U3	U4	U5	U6	U7	U8
	8-10h	11-13h	14-16h	17-19h	20-22h	23-01h	2-4h	5-7h



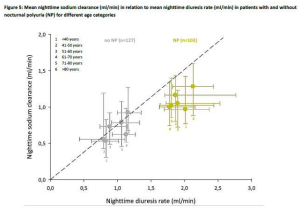
Creatinine
Creatinine clearance

Sodium, urea
Sodium clearance

Osmolarity
Free water clearance

Goessaert et al Eur Urol 2015

Circadian rhythm of water/salt clearance through adulthood



in subjects with NP, an increase in nighttime diuresis rate is more important than the increase in sodium diuresis, which strongly suggests that the increase in diuresis is not only solute driven, but should be considered as an important increase in overnight water diuresis, most likely related to decreased vasopressin levels.

Monaghan et al 2020
Asplund R 2002

Causalities of nocturia

(sex hormones, diabetes insipidus/mellitus…)

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Causalities of nocturia

Sleep disruption and shortage, OSAS, RLS, low dopamine diseases …

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Causalities of nocturia

leg edema, heart failure, hypertension, metabolic syndrome, lack of physical activity…

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Causalities of nocturia

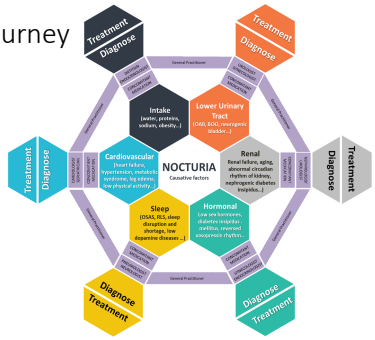
Excess water, proteins, sodium, calories (obesity as such without metabolic syndrome), …

EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

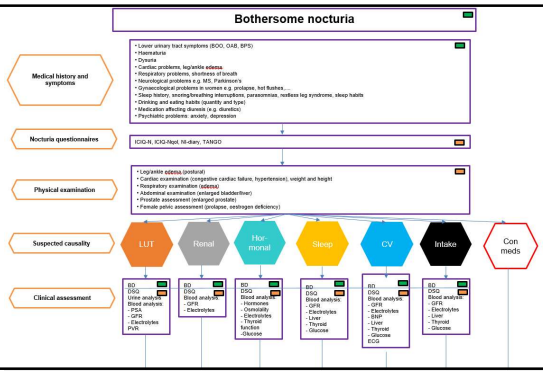
Causalities of nocturia: summary

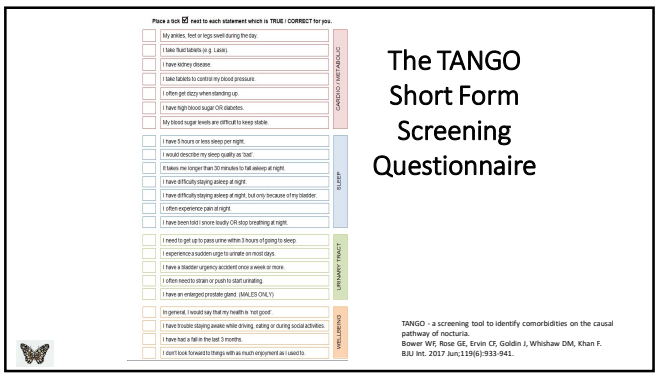
EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Nocturia Patient Journey



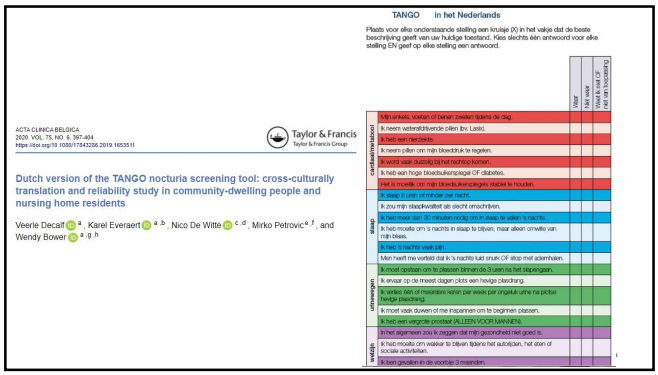
EAU-guidelines 2017;
ICI-RS 2017, NUU 2018
round 1a-b





The TANGO Short Form Screening Questionnaire

TANGO - a screening tool to identify comorbidities on the causal pathway of nocturia.
Bower WF, Rose GE, Ervin CF, Goldin J, Whishaw DM, Khan F.
BJU Int. 2017 Jun;119(6):933-941.



ACTA CLINICA BELGICA
2020, VOL. 75, NO. 6, 397–404
https://doi.org/10.1080/17843286.2019.1653511

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Dutch version of the TANGO nocturia screening tool: cross-culturally translation and reliability study in community-dwelling people and nursing home residents

Veerle Decalf [a], Karel Everaert [a,b], Nico De Witte [c,d], Mirko Petrovic [e,f], and Wendy Bower [a,g,h]

Volume 47, Issue 7, July 2018

Questions to ask a patient with nocturia

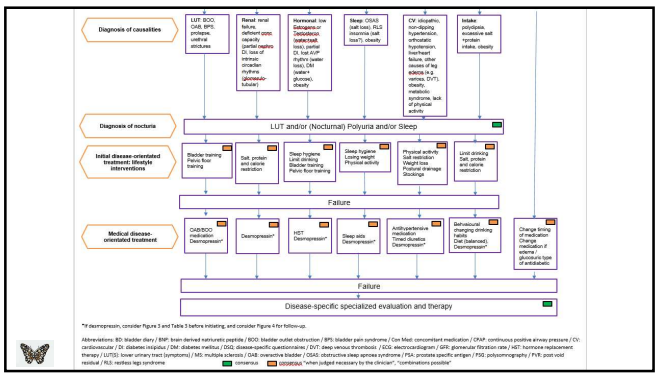
Wendy F Bower Karel Everaert Tee J Ong Claire F Ervin Jens P Norgaard Michael Whishaw

AJGP Australian Journal of General Practice
Formerly Australian Family Physician (AFP)

Question 1: How many times do you wake up at night to pass urine?
Question 2: How much does nocturia bother you?
Question 3: What medications are you taking?
Question 4: How much is your bladder actually storing day and night?
Question 5: How much urine do you make over night?
Question 6: Do you have hypertension or cardiac failure, with or without leg oedema?
Question 7: Are you a good sleeper?
Question 8: Have we checked your hormone levels recently?

Table 1. Impact of medications on nocturia mechanisms

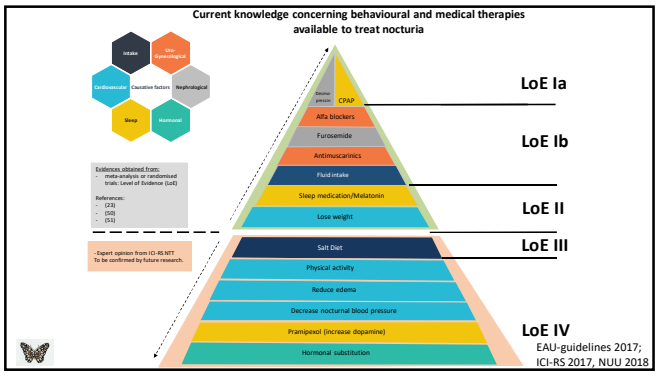
Mechanism	Drugs
Increase free water clearance (diuresis)	Diuretics, progesterone, melatonin
Increase osmotic clearance (diuresis)	All diuretics, ACE inhibitors, lithium, progesterone, SGLT2 inhibitors
Decrease free water clearance (antidiuresis)	dDAVP, oestrogens, testosterone, antipsychotics, chemotherapeutics, antidepressants, antiepileptics, older glucose-lowering medications, opiates
Decrease osmotic clearance (antidiuresis)	Calcium channel blockers, beta adrenoceptor antagonists, NSAIDs, lithium, oestrogen, testosterone, mineralocorticosteroids, corticosteroids, thiazolidinediones
Induce postural hypotension	Hypotensive drugs, anti-Parkinson's medication, older psychotropic agents, thiazides
Induce oedema	Calcium channel blockers, steroids, NSAIDs
Sleep disruption	Antiepileptics, decongestants, SSRIs, SNRIs, caffeine
Bladder stimulation	Caffeine, alcohol, anticholinesterase inhibitors, cyclophosphamide, ketamine



Lifestyle interventions in nocturia

PA = physical activity

Based on guidelines and Delphi



EAU-guidelines 2017;
ICI-RS 2017, NUU 2018

Desmopressin and nocturia: Why is this important?

- Desmopressin is a drug initially used for diabetes insipidus and later for bedwetting in healthy children and is now used for nocturia in older people with lots of comorbidities and concomitant medication:
  Bedwetting = keep them dry all night, low risk hyponatremia, high dose
  Nocturia = increase FUSP (first un-interrupted period of sleep), be safe, low dose
- Desmopressin = nocturnal water retention, add nocturnal salt loss = potentially more hyponatremia.
- How to improve efficacy and safety through better patient selection and adding concomitant therapies: avoid nocturnal salt loss, combine, ie improve bladder capacity and sleep so that we need less desmopressin to increase the FUSP.

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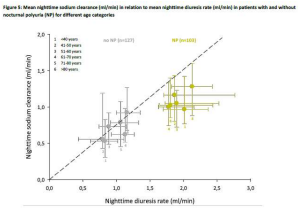
Circadian rhythm of water/salt clearance through adulthood



in subjects with NP, an increase in nighttime diuresis rate is more important than the increase in sodium diuresis, which strongly suggests that the increase in diuresis is not only solute driven, but should be considered as an important increase in overnight water diuresis, most likely related to decreased vasopressin levels.

Monaghan et al 2020
Asplund R 2002

Consensus summary of risk management for hyponatremia when considering desmopressin.

Risk management	Standard vigilance to hyponatremia symptoms	Standard vigilance to hyponatremia symptoms + SSC	Contraindication
	< 65 years	65 years or older	Frail older people
	Baseline sodium > 135	Baseline sodium 130-135	Baseline sodium below 130
	eGFR > 50-60	eGFR 50-60	eGFR < 50
	No concomitant medication that can cause hyponatremia	Concomitant medication weakly or moderately related to hyponatremia	Concomitant medication strongly related to hyponatremia
	No leg edema	Low to moderate leg edema	Important leg oedema
	No heart failure	Heart failure (NYHA class I)	Heart failure (NYHA class II or higher)
	No diabetes mellitus or hypertension	Controlled diabetes mellitus or hypertension	Uncontrolled diabetes mellitus or hypertension
		Need for higher dose, up-titration	Psychogenic polydipsia (>3L/day)
		Higher risk in women	Higher risk in women
Formulation	Any desmopressin formulation	Low dose desmopressin	Treat condition if possible and wait with desmopressin
SSC	No consensus on SSC	Consensus on SSC	-

SSC: serum sodium checks

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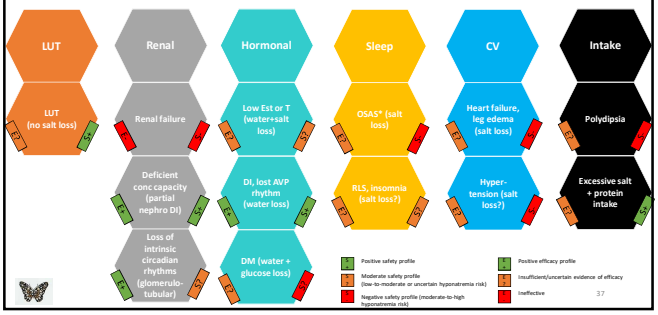
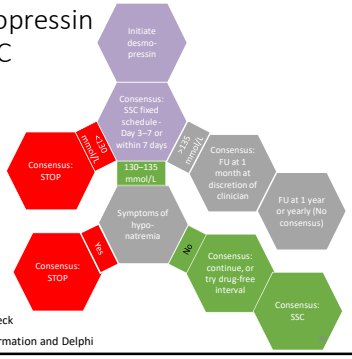
Phenotyping nocturia when prescribing desmopressin, based on guidelines, prescription information or Delphi panel



Follow-up after desmopressin Prescription, when SSC wanted or needed



Symptoms of hyponatremia include: nausea and vomiting, headache, confusion, loss of energy, drowsiness and fatigue, restlessness and irritability, muscle weakness, spasms or cramps, seizures and coma

Timing/empty stomach or not is of no importance for SSC, consensus

FU, follow up; SSC, serum sodium check

Based on guidelines, Prescribing information and Delphi

Conclusion (1)

A summary of the nocturia patient pathway across different medical specialisms is useful in the visualisation and phenotyping of patients for diagnosis and therapy.

It also highlights that nocturia is in general “not” or “not only” a urological symptom, but predominantly a symptom of a wide variety of causalities, many of which are easy to screen for with history taking, DS-questionnaires and physical examination. Need for liaison teams in hospitals.

Bladder and prostate are not the only cause of nocturnal LUTS in the majority of the cases, stop treating nocturia with OAB and BPH therapies unless the bladder/prostate is the major cause

We provided some basic knowledge of desmopressin, its contraindications, safety concerns and follow-up, easing its initiation and hopefully shorten the patient journey of nocturia.

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Conclusion (2)

As an abnormal circadian rhythm of vasopressin is the most prevalent cause of nocturnal LUTS it is the primary target for therapy. Desmopressin has a Loe 1a and a grade A recommendation in the treatment of Nocturia.

As nocturnal salt diuresis increases at higher age and is a significant extra cause of nocturnal LUTS, nocturnal sodium loss has to be decreased through life style interventions, improving general health and perhaps medication.

Combining therapies where relevant

Using "Low dose formulation" desmopressin is efficacious in prolonging the FUSP and the Quality of Life with a low risk of hyponatremia in nocturia patients

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